PROPIEDADES DE LAS NANOBURBUJAS DE OZONO Y SU POTENCIAL APLICACIÓN COMO AGENTE ANTIMICROBIANO EN ODONTOLOGÍA

Revisión Temática

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GUÍA DE CONTENIDO

RESUMEN

PROPIEDADES DE LAS NANOBURBUJAS DE OZONO Y SU POTENCIAL APLICACIÓN COMO AGENTE ANTIMICROBIANO EN ODONTOLOGÍA

Introducción: la cavidad oral alberga a más de 700 especies bacterianas distintas, es uno de los microbiomas más complejos del cuerpo humano convirtiéndolo en un reservorio ideal para el desequilibrio entre la flora bacteriana (Biofilm) y el huésped, siendo susceptible al desarrollo de enfermedades orales de origen bacteriano como lo es la periodontitis la cual genera cambios en la composición y organización de los microrganismos a nivel subgingival afectando los tejidos de soporte del diente. El uso de enjuagues y antibióticos como terapia terapia coadyuvante en el tratamiento de la periodontitis tiene varias desventajas la generación de resistencia bacteriana, efectos adversos y citotóxicos. Todo lo anterior ha motivado la búsqueda de alternativas antimicrobianas siendo las nanoburbujas de ozono una propuesta con potencial en el manejo de biofims bacterianos multiespecie como el subgingival entre otros. **Objetivo:** Revisar y analizar críticamente la literatura disponible en relación con las propiedades de las nanoburbujas y su potencial aplicación en odontología como agente antimicrobiano para el control de placa bacteriana con énfasis en biofilm subgingival. **Metodología:** Se realizó una revisión temática de la literatura en las bases de datos Pubmed y Google Scholar teniendo en cuenta el uso de términos Mesh, seleccionando los artículos en texto completo en español e inglés por parte de expertos y realizando una extracción de datos de la literatura para la caracterización de la información. **Resultados:** Se pre-seleccionaron 41 artículos para la extracción de la información según las temáticas propuestas de los cuales 22 artículos fueron incluidos en la revisión y caracterización de la información. **Conclusión:** El uso de nanoburbujas de ozono es una potencial alternativa para el control antimicrobiano de enfermedades orales como la periodontitis., sin embargo, se requiere mayor investigación regulatoria en términos de eficacia y seguridad.

Palabras claves: Placa dental, Periodontitis, Caries, Nanoburbujas, Ozono, Agente antibacteriano

ABSTRACT

ANTIMICROBIAL PROPERTIES OF OZONE NANOBUBBLES AND THEIR POTENTIAL APPLICATION IN DENTISTRY

Introduction: The oral cavity is home to over 700 different bacterial variants, making it one of the most complex microbiomes in the human body. As a result, it is an ideal reservoir for the imbalance between the bacterial flora (Biofilm) and the host, making it susceptible to the development of bacterial oral diseases like periodontitis, which causes changes in the composition and organization of microorganisms at the subgingival level affecting the supporting tissues of the tooth. The use of mouthwashes and antibiotics as supplementary therapy for periodontitis has various drawbacks, including the development of bacterial resistance, as well as unpleasant and cytotoxic effects. All of this has prompted researchers to look for antimicrobial alternatives, with ozone nanobubbles emerging as a promising candidate for the treatment of multispecies bacterial biofilms like subgingival, among others. **Objective:** Review and critically evaluate the literature on the properties of nanobubbles and their prospective application in dentistry as an antibacterial agent for bacterial plaque control, with a focus on subgingival biofilm. **Methodology:** Using Mesh keywords, a thematic review of the literature was conducted in the Pubmed and Google Scholar databases, with specialists picking full-text publications in Spanish and English and extracting data from the literature to characterize the material. **Outcomes:** The information was extracted from 41 documents that were pre-selected based on the suggested subjects, with 22 articles being included in the review and classification of the data. **Conclusion:** The use of ozone nanobubbles as an antibacterial control for oral disorders like periodontitis could be a viable option. In terms of efficacy and safety, however, more regulatory study is required.

Key words: Dental plaque, Periodontitis, Caries, Nanobubbles, Ozone, Antibacterial agent

1. INTRODUCCIÓN

La cavidad oral humana alberga un microbioma con más de 700 especies bacterianas distintas. La diversidad del ecosistema oral es un reservorio ideal para el desequilibrio entre la placa bacteriana o (biofilm) y el sustrato dental u oral circundante, el cual es capaz de desarrollar enfermedades orales de origen bacteriano, las cuales son cada vez más prevalentes en la población como la caries y la enfermedad periodontal (Aas et al., 2005). No obstante, la periodontitis ha sido de gran interés en la salud publica en las últimas décadas, debido también a su asociación con enfermedades sistémicas (Almeida et al., 2020).

La patogenia de la periodontitis es consecuencia del desequilibrio entre flora bacteriana y huésped, generando cambios en composición y organización de los microorganismos que integran el biofilm subgingival (*T. denticola, P. gingivalis* y *T. forsythia*), afectando de manera irreversible los tejidos de soporte como ligamento periodontal y hueso alveolar (Hajishengallis, 2015).

Se han desarrollado distintas terapias adjuntas a los procedimientos mecánicos de raspaje y alisado radicular, siendo los antibióticos y enjuague bucales como clorhexidina los principalmente utilizados como terapia coadyuvante (Leszczyńska et al., 2011). Sin embargo, las limitaciones en el uso de antibióticos como consecuencia de la resistencia bacteriana y los problemas de citotoxicidad de la clorhexidina han incentivado la búsqueda de alternativas farmacéuticas para el desarrollo de nuevos agentes antimicrobianos (Müller et al., 2017).

Las nanoburbujas son una tecnología emergente fundamentada en el desarrollo de burbujas ultrafinas menores a 1µm, que debido a sus actuales aplicaciones en distintos campos de la industria hídrica, energética y del medioambiente, se ha incrementado su estudio en otras áreas como la salud y desarrollo de fármacos (Meegoda et al., 2018). Recientes reportes sugieren que las nanoburbujas de ozono pueden ser una alternativa antimicrobiana en pacientes con periodontitis (Mukumoto et al., 2012). No obstante, este es un campo nuevo, especialmente en disciplinas como la odontología, donde recién se están abriendo nuevas líneas de investigación en relación al uso de nano burbujas.

Nuestro objetivo es realizar una exhaustiva revisión de la literatura que nos permita comprender mejor los principios básicos de esta tecnología llamada nanoburbujas, sus características físicas, químicas, eléctricas; así como su efecto sobre el biofilm oral, sus posibles mecanismos y futuras aplicaciones en odontología y en el sector salud.

2. PLANTEAMIENTO DEL PROBLEMA

La patogenia de la periodontitis, una de las enfermedades más prevalentes en la población mundial; se caracteriza por la disbiosis de la placa subgingival, un proceso que favorece el microambiente proinflamatorio y crónico a nivel del periodonto. Los cambios que experimenta el biofilm subgingival enfermo, se han asociado a la participación de cientos de microorganismos destacando aquellos agrupados como los patobiontes y los patógenos "keystone" como *T. denticola, P. gingivalis* y *T. forsythia* (Hajishengallis, 2015).

Sumado a la compleja diversidad del microbioma oral y subgingival, las infecciones polimicrobianas como la periodontitis son de difícil manejo microbiológico y clínico (Mosaddad et al., 2019). Gran parte de los desafíos que enfrentan los periodoncistas están dados por el biofilm, entiendo a este como una compleja barrera fisicoquímica que le confiere protección y evasión tanto de la respuesta inmune como de agentes antimicrobianos, enjuagues y antibióticos, estos últimos usados como coadyuvantes en periodontitis crónica y periodontitis agresiva (Kanwar et al., 2017).

Actualmente la prescripción sistémica de antibióticos es reconocida como una estrategia que podría beneficiar al paciente con periodontitis. Sin embargo, varios aspectos relacionados con la selección y prescripción empírica (sin previo análisis microbiológico), han hecho que la resistencia antimicrobiana a antibióticos y sus efectos adversos sean una problemática global en salud pública. Esto sumado a las preocupaciones manifestadas por distintas organizaciones como la Organización Mundial de la Salud (OMS) y la academia americana de periodoncia (Haque et al., 2019; Rams et al., 2014).

Por todo lo anteriormente mencionado, la investigación y desarrollo de estrategias antimicrobianas son de gran importancia para el manejo efectivo de infecciones relacionadas con biofilm (Ammons, 2009). Además, existe la necesidad constante de desarrollar nuevas nanotecnologías, particularmente para la eliminación y prevención de biofims polimicrobianos como el de la periodontitis y mitigar la dependencia al uso de antibióticos.

3. JUSTIFICACION

Las enfermedades orales de origen bacteriano como la enfermedad periodontal es una de las infecciones de mayor prevalencia a nivel global, apenas superada por el resfriado común (Ministerio de Salud y Protección Social, 2014). Algunas de las razones que explican su alta frecuencia es la baja tasa de efectividad de los antibióticos tradicionales y el desarrollo de resistencia bacteriana (Kanwar et al., 2017).

La formación del biofilm subgingival sumado a la disbiosis de la placa bacteriana, son aspectos indeseables en el manejo clínico de infecciones como la periodontitis, ya que incrementan la resistencia de microorganismos y evitan una resolución definitiva de la enfermedad. Sumado a lo anterior, la prescripción arbitraria de antibióticos es una preocupación global manifestada por distintas organizaciones como la OMS y la academia americana de periodoncia; generando efectos adversos en los pacientes y sobrecostos del tratamiento en salud pública (Haque et al., 2019; Rams et al., 2014).

Este trabajo busca atender la necesidad de profundizar en alternativas bactericidas, ya que la investigación y desarrollo de estrategias antimicrobianas son de gran importancia para el manejo efectivo de infecciones relacionadas con biopelículas polimicrobianas (Ammons, 2009). Además, existe la necesidad constante de desarrollar nuevas nanotecnologías, particularmente para la eliminación y prevención de biofims polimicrobianos como el de la periodontitis.

A corto plazo este trabajo es fundamental para establecer una exhaustiva revisión crítica de la literatura de las distintas tecnologías que actualmente son consideradas alternativas en el manejo de biofilm polimicrobianos. Adicionalmente, esta revisión puede ser la apertura a nuevas perspectivas con gran potencial y desarrollo en odontología como la nanotecnología basada en nanoburbujas, un campo nuevo en la disciplina y que requiere mayor investigación para futuros desarrollos.

En síntesis, la aplicación de nanoburbujas de ozono en odontología podría ser una solución a problemáticas como la resistencia antimicrobiana, además de ser potencialmente segura para la aplicación en células eucariotas, es factible de desarrollar, fácil de implementar y conveniente de usar para los protocolos de higiene oral de los pacientes. No obstante, se requiere de una revisión científica profunda en el área capaz de establecer los principios básicos de esta tecnología, comprender sus propiedades físicas, químicas y eléctricas, métodos de producción, síntesis, y micro/nano ingeniería, para así fomentar futuros procesos investigativos originales, innovadores y de impacto a la comunidad, así como su implementación en odontología y en distintos campos de la medicina.

4. MARCO TEORICO

1 Biofilm polimicrobianos orales y la necesidad de proponer alternativas antimicrobianas en odontología

La cavidad oral es huésped de uno de los microbiomas más diversos en el cuerpo humano, el cual está compuesto por un complejo ecosistema integrado por más de 700 especies bacterianas (Huang et al., 2011). Estos organismos ayudan a mantener la homeostasis oral previniendo la adhesión de flora patógena en la superficie de las mucosas y tejidos dentales (Aas et al., 2005).

En la cavidad oral se han descrito distintos hábitats y reservorios naturales para la microbiota que allí reside. La variedad de superficies mucosas (labios, carrillos, paladar y la lengua y encía) se compone en su mayoría microrganismos aerobios facultativos. Por otro lado, las superficies no mucosas como los dientes y/o materiales dentales descritos como biopelícula o placa dental, que a su vez puede ser supra gingival y/o subgingival (Zaura et al., 2009).

1.1 *Definición, estructura general del biófilm bacteriano*

Todo biofilm oral se define como un complejo y dinámico ecosistemas de comunidades polimicrobianas y multiespecies embebidas en una matriz de exopolimeros (proteínas, carbohidratos y ácidos nucleicos) y bañadas en fluidos circundantes como la saliva y el líquido crevicular que le confieren un constante aporte de nutrientes y transporte (Mosaddad et al., 2019). Por todos estos factores, la cavidad oral es un hábitat ideal para nichos bacterianos de una gran diversidad multiespecie. Por lo que el desequilibrio en su composición y su interacción con el huésped se ve reflejado en desarrollar enfermedades que hoy por hoy siguen representando un problema en salud pública, como es el caso de la disbiosis subgingival y el desarrollo de enfermedad periodontal como la periodontitis (Kilian et al., 2016).

2. El papel del biofilm subgingival en la periodontitis

La periodontitis es una enfermedad inflamatoria provocada por una infección en los tejidos de soporte de los dientes, influida por la genética y los factores ambientales y de comportamiento que están involucrados en el desarrollo de la enfermedad, la cual es producida por un desbalance de los organismos que componen el microbioma subgingival (Könönen et al., 2019).

La transición de un periodonto sano hacia un periodonto enfermo está asociada a cambios en la composición del biofilm simbiótico, promoviendo el desbalance de la sinergia polimicrobiana hacia interacciones oportunistas y de disbiosis subgingival (Hajishengallis, 2015).

La periodontitis es inducida en huéspedes susceptibles por una comunidad polimicrobiana, que convergen sinérgicamente para desencadenar una inflamación destructiva. Dicha inflamación es principalmente promovida por patógenos protagonistas (*P. gingivalis, T. denticola y T. forsythia*), mientras que la colonización de estos patógenos clave es facilitada por patógenos accesorios (patobiontes) -los cuales subvierten inicialmente la respuesta del huésped hacia procesos de disbiosis subgingival y de inflamación (Hajishengallis, 2015).

3 **El papel del biofilm subgingival en la resistencia antimicrobiana**

La resistencia antimicrobiana representa la característica de aquellos microorganismos capaces de sobrevivir en presencia de elevados niveles de agentes antimicrobianos. Actualmente se sabe que el biofilm es un componente fundamental para el desarrollo de tolerancia a los antimicrobianos, sobre todo en biofilms polimicrobianos o multiespecies (Kanwar et al., 2017). Este incremento se asocia a varios factores como la presencia de una barrera física (matriz extracelular), la alta densidad microbiana, la baja tasa de crecimiento bacteriano, la expresión génica diferencial así como las alteraciones del microambiente (acidificación del pH, disminución en las tensiones de oxígeno, desbalance del potencial oxido-redox, etc)(Brinkac et al., 2017).

3.1 La matriz extracelular como barrera física y química:

En primera instancia las características fisicoquímicas de la matriz extracelular que rodea a las células microbianas tienen la habilidad de repeler o retardar la penetración de los agentes antibióticos por las diferencias de cargas entre los antimicrobianos algunos con carga positiva y la matriz extracelular con carga negativa respectivamente (Flemming & Wingender, 2010). La matriz y sus sustancias poliméricas extracelulares (EPS) también le proveen protección ante radiación UV y deshidratación (Tan et al., 2018).

Otros factores físicos que disminuyen la efectividad de la antibioticoterapia, son la disminución en la tensión de oxígeno, sobre todo en biopelículas subgingivales, por lo que se genera una atmósfera anaerobia y de bajo pH adecuada para estos microorganismos, pero que le restan propiedades antimicrobianas a algunos antibióticos (Almeida et al., 2020).

3.2 Baja tasa de crecimiento bacteriano:

En consecuencia a la alta densidad microbiana, sumado a factores medioambientales, se ha observado que el metabolismo bacteriano disminuye, al igual que los tiempos de replicación, de esta manera antibióticos con un mecanismo de acción dirigido al bloqueo del metabolismo bacteriano no podrán ejercer su efecto (Lebeaux et al., 2014).

3.3 La expresión de genes asociados a resistencia:

Sumado a los factores anteriormente mencionados, uno de los mecanismos más eficientes en proveer resistencia antimicrobiana es la expresión de genes específicos que les permiten activar rutas de señalización como mecanismos de resistencia (Flemming & Wingender, 2010).

Este tipo de mecanismos se da principalmente por la formación de subgrupos de microorganismos con características de células persistentes, presentando un estado metabólico disminuido o latente. Además, frecuentemente asociado con cambios fenotípicos y transferencia horizontal de plásmidos. Actualmente se sabe que este tipo de bacterias ahora resistentes migran a nuevos hábitats, desarrollan biofilms resistentes generalmente por la expresión de distintos mecanismos (bombas de eflujo, enzimas degradadoras)(Ortega-Peña & Hernández-Zamora, 2018).

Entre los genes que codifican las bacterias periodonto patógenas en el biofilm oral para la resistencia a antibióticos se encuentran genes de la familia de proteínas *tet*, los cuales son encontrados en mayor proporción en pacientes que presentan periodontitis crónica y periodontitis agresiva (Collins et al., 2016). Análisis de muestras subgingivales en pacientes con periodontitis demuestran que *tet(Q)*, *tet(32)* y *tet(W)* son las principales proteínas asociadas con resistencia a tetraciclinas, disminuyendo significativamente su efecto (Collins et al., 2016).

La comprensión de la enfermedad periodontal como una enfermedad crónica de origen polimicrobiano es de gran importancia para comprender, el desafío que implica su manejo clínico y microbiológico. Adicionalmente, existe la necesidad de desarrollar alternativas terapéuticas que sustituyan los antibióticos o su indicación indiscriminada durante el tratamiento de enfermedades como la periodontitis.

4. Las nanoburbujas y sus principios básicos para futuros desarrollos en salud.

Entre los distintos campos con potencial aplicación de las nanoburbujas se encuentra el de la salud donde juegan un papel fundamental para el desarrollo de nuevas terapias y estrategias que permitan la optimización y evolución en la solución de problemas médicos y odontológicos. Entre las aplicaciones encontramos preservación de tejidos, injuria isquémica, medicina regenerativa, agente de contraste en imágenes diagnósticas y teragnosis, además de poseer un efecto bactericida, entre otros (Michailidi et al., 2019). No obstante, es indispensable establecer los pilares fundamentales de sus características y propiedades que definen actualmente a esta emergente tecnología, así como los hitos más importantes de su historia reciente y sus principales métodos de producción.

4.1 Definición y generalidades de las nanoburbujas

La organización Internacional para la estandarización (ISO) ha realizado distintas definiciones referentes a las burbujas, determinando que una burbuja es un gas contenido en un medio encerrado por una interfaz (ISO 20480-1:2017). Según su tamaño pueden ser caracterizadas, así bien burbujas con un diámetro menor a 100 µm serán definidas como burbujas finas, mientras burbujas mayores a 1 µm son conocidas como micro burbujas y por ultimo las nano burbujas o burbujas ultrafinas serán menores a 1 µm generalmente entre rangos de 100nm a 200nm. Este tipo de burbuja también se ha definido como nanoburbujas tipo bulk o a granel y hace referencia a geometrías esféricas de nanoburbujas las cuales se mantienen en suspensión dentro de soluciones liquidas o de interfaz liquida (Alheshibri et al., 2016).

Se pueden generar nano burbujas en distintos medios líquidos y pueden contener aire u otro tipo de gas en su interior, las burbujas pueden mantenerse en un medio mediante su tensión superficial o al rodearse con un revestimiento en su interfaz, está ya sea hidrofílica (lípidos, proteínas) o anfipática brindada por biomateriales (poliméricos) que le conferirán distintas propiedades llamativas en aplicaciones médicas como la distribución de gases, fármacos, y en terapias génicas (Khan, Hwang, Lee, et al., 2018).

Las nanoburbujas presentan características únicas que atraen a la comunidad científica, las cuales son asociadas principalmente a su tamaño nanométrico y estabilidad a largo plazo (semanas e incluso durante meses en un medio líquido), además de sus propiedades como la transferencia de masa/gases, generación de radicales libres, aplicaciones en imagenología y teragnosis (Leewananthawet et al., 2019; Temesgen et al., 2017; Uchida et al., 2011; X. H. Zhang et al., 2006).

4.2 Breve reseña histórica en Nanoburbujas

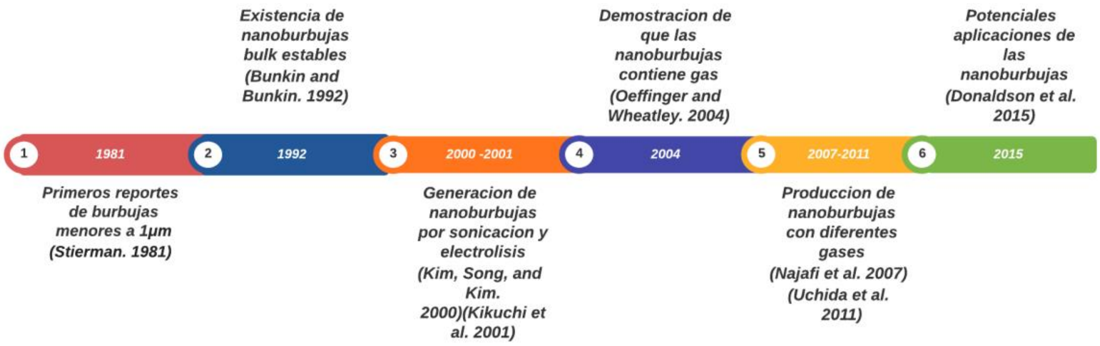


Figura 1 Hallazgos destacados en la historia de las nanoburbujas tipo bulk

Los primeros reportes que describen presuntivamente nanoburbujas bulk con diámetros menores a 1 μm; se realizaron al observar burbujas producidas en el movimiento de las olas del mar (Stierman, 1981). Años más tarde se evidencio la dinámica en la variación del tamaño de la nanoburbuja, ya que al aplicar diferentes presiones del gas en solución; este conlleva a la expansión o disminución de tamaño en la burbuja (Craig et al., 1993).

Fue hasta 1990 que se reporta la existencia de microburbujas bulk estables a partir de interacciones repulsivas entre iones en soluciones diluidas con electrolitos (Bunkin & Bunkin, 1992). Fue a comienzos de los años 2000 que se visualizó por primera vez una nanoburbuja (Oeffinger & Wheatley, 2004; Uchida et al., 2011), seguido a que surgen los primeros reportes de la producción de nanoburbujas mediante sonicación y electrolisis (Kikuchi et al., 2001; Kim et al., 2000). (Ver figura 1)

La creciente investigación en nanoburbujas y sus propiedades como la transferencia de gases ha incentivado en la última década su desarrollo en múltiples campos crecimiento de plantas, peces y ratones, en el tratamiento de aguas residuales, y aplicaciones biomédicas (Agarwal et al., 2011; Donaldson et al., 2015; Ebina et al., 2013; Li et al., 2015; Wheatley et al., 2006). Los primeros desarrollos biomédicos en la historia de las nanoburbujas han sido entorno a su potencial aplicación como agentes de contraste por ultrasonido (Oeffinger & Wheatley, 2004). No obstante tras casi dos décadas de investigación en el sector salud son múltiples las potenciales aplicaciones que se le ha asociados como la distribución de medicamentos, terapia génica, teragnosis, terapia anticáncer, oxigenación, preservación de tejidos (Batchelor et al., 2020; Endo-Takahashi & Negishi, 2020; Khan et al., 2019; Oeffinger & Wheatley, 2004; Owen et al., 2016).

4.3 Métodos de síntesis o generación de nanoburbujas tipo Bulk:

La formación de nanoburbujas se logra cuando la fase de un líquido homogéneo sufre un cambio de fase causado por la reducción repentina de la presión por debajo de un valor crítico, formando una cavitación (Michailidi et al., 2020).

A través del paso del tiempo y con la ayuda de nuevas tecnologías, se han desarrollado distintas técnicas para la generación de nanoburbujas con diferentes contenidos y propiedades, entre los métodos más reportados se encuentran la cavitación hidrodinámica, por sonicación y/o por agitación vigorosa, además de aquellas alternativas que incorporan dispositivos de microfluídica, emulsión y ablación laser (Agrahari & Mitra, 2016; Huynh et al., 2014; Lee et al., 2015; Stride & Edirisinghe, 2008; Xu, 2011). (Ver figura 2)

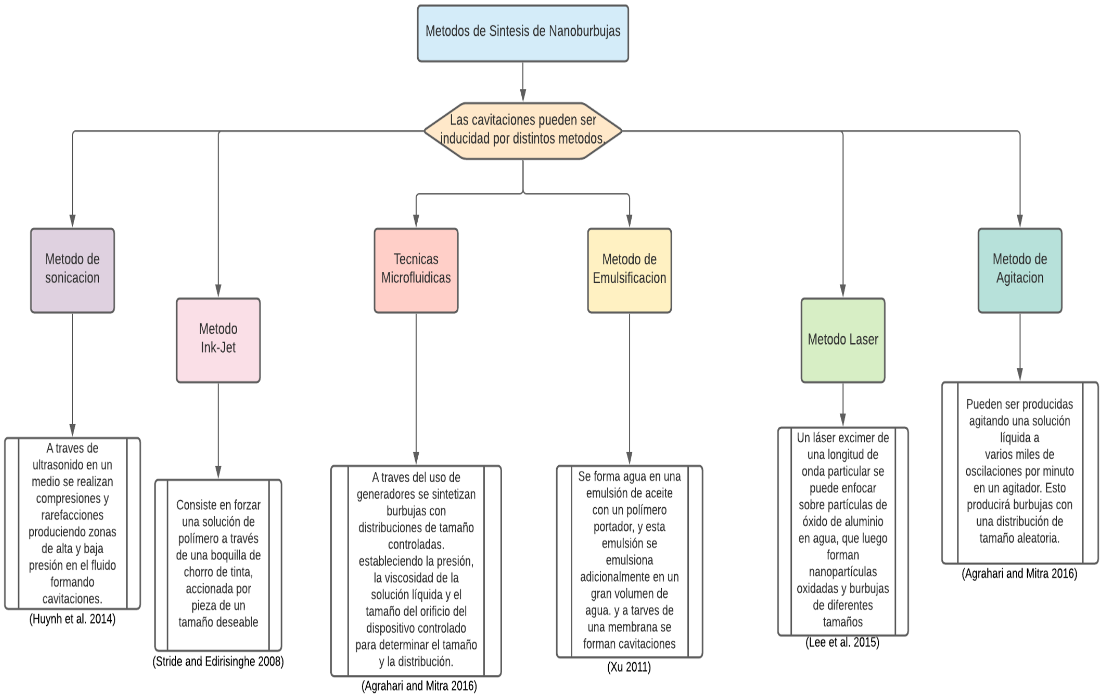


Figura 2 Métodos de Síntesis de Nanoburbujas

4.4 Características físicas, químicas y eléctricas de las nanoburbujas

El tamaño de una burbuja es la primer característica determinante para comprender sus propiedades, ya que una distribución de tamaño en escala nanométrica se asocia con mejor estabilidad, transferencia de masa, influyendo significativamente en su comportamiento y demás características fisicoquímicas y eléctricas dentro de un líquido (X. yu Zhang et al., 2020).

Las burbujas son distribuidas en una solución mediante fuerzas de flotabilidad y por el movimiento al azar entre las moléculas que se encuentran suspendidas en un líquido (movimiento browniano). Las burbujas de mayor tamaño tienden a emerger mostrando una mayor fuerza de flotación y mientras que las burbujas más pequeñas permanecerán en el medio liquido con mayor facilidad y duración debido con un patrón de movimiento aleatorio o movimiento browniano (Azevedo et al., 2016).

Otra de las características físicas que hacen únicas a las nanoburbujas es la velocidad de ascenso, la cual va ligada a su estabilidad y vida media en suspensión. El diámetro de la burbuja y la viscosidad del líquido condicionan la velocidad de ascenso, siendo mayor para las macroburbujas (> 100µm) y menor para microburbujas (< 100 µm) y casi despreciable para las nanoburbujas (< 1 µm) (Azgomi et al., 2007).

Las nanoburbujas a diferencia de otras burbujas de mayor tamaño, también poseen características únicas como su carga de superficie que les confiere una vida media de hasta 6 meses en condiciones *in vitro* (Nirmalkar et al., 2018). Las nanoburbujas son consideradas partículas electrostáticas que se distribuyen a partir de iones de hidróxido (anión) sobre iones de hidrogeno (catión), formando puentes hidrógenos estables entre su interfaz, evitando la dispersión del gas que contiene y manteniendo un equilibro cinético frente a las altas presiones, lo que les ayuda a tener una vida media más prolongada (Allaker & Douglas, 2009).

Entre las propiedades que tienen las burbujas se encuentra su capacidad de retener gases versus la ocupación del gas disuelto en solución (Tao et al., 2019). Esto se explica por la mayor superficie que confieren las nanoburbujas por unidad de área, lo que las hace hasta 200 veces más eficientes que una burbuja normal (Bouaifi et al., 2001). (Ver figura 3)

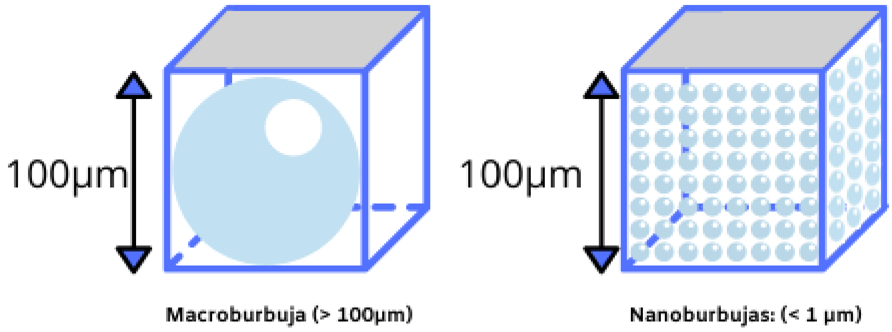


Figura 3 Esquema representativo de la relación entre superficie por unidad de área en nanoburbujas

Dentro de las características químicas de las nanoburbujas, se sabe que estas también son afectadas por el pH del medio en el que se encuentren. Diferentes reportes observaron que cambios en el pH no provocan cambios significativos en su tamaño y distribución, pero si influyen en su estabilidad. A pH alcalino, las nanoburbujas incrementaran su estabilidad gracias a su carga superficial volviéndose más negativas y por lo tanto más estable, mientras en una solución a pH acido, desciende su estabilidad al verse vulnerada la fuerza iónica de la solución en la que se encuentran (Hamamoto et al., 2018).

4.4.1 El rol del potencial zeta en la estabilidad de las nanoburbujas

Para un efectivo uso de las nanoburbujas es importante conocer la razón por la cual presentan una estabilidad a largo plazo, comprendiendo la importancia de su potencial zeta y la relevancia del tamaño en su estabilidad al ser una partícula electrostáticamente estable.

El potencial zeta se debe entender como el potencial que tiene una partícula en un plano de corte en la doble capa eléctrica de una solución, esta se representa como una medida de magnitud como parámetro electrostático de las partículas en un estado se suspensión, evaluando la estabilidad de la dispersión en un medio líquido, esta se puede medir por diferentes formas como técnicas de electroforesis y electroacústicas (Bibiana et al., 2012).

Las nanoburbujas tipo bulk al estar suspendidas en un medio acuoso pueden ser medido su potencial zeta y así mismo identificar su vida media, confirmando así su estabilidad, la cual está directamente relacionada con su tamaño (Bui et al., 2019).

4.5 Clasificación de las Nanoburbujas según tipo de gases

Las nanoburbujas pueden contener diferentes gases en su interior, y según el gas que se utilice al momento de su generación, estos tienen la capacidad de influir en su estabilidad y conferirles propiedades diferentes. Entre los distintos tipos de gases que se reportan se encuentran el uso de ozono, oxígeno, aire y nitrógeno, a su vez dependiendo del gas que contengan y de sus propiedades especiales serán utilizados para diferentes fines, como el oxígeno el cual es ampliamente utilizado en procesos de distribución de oxígeno (Khan, Hwang, Seo, et al., 2018; Meegoda et al., 2018).

El potencial zeta de las nanoburbujas cambiara según el gas que contengan, siendo más alto para gases que presenten una mayor solubilidad como es el caso del ozono y el oxígeno debido a que generan radicales libres de grupos hidroxilo, aumentando así los valores de cargas negativas en la solución; y a su vez gases con menor solubilidad (Nitrógeno y aire) se encontraran menos estables en una solución (Ushikubo et al., 2010).

El mínimo absoluto de potencial zeta para considerar una partícula como estable debe ser un valor cercano -30 mV (milivoltios), y los valores de referencia que se han encontrado en nanoburbujas con diferentes contenidos de gas generadas en agua, tienden a ser valores negativos más altos, como lo son de 34-45 mV para nanoburbujas de oxígeno, 29-35 mV para nanoburbujas de nitrógeno y de 20-27 mV para nanoburbujas de ozono (Ushikubo et al., 2010).

5. El ozono y las nanoburbujas como potencial agente antimicrobiano

5.1 Efecto antimicrobiano del ozono y sus beneficios

El ozono es un gas incoloro compuesto por 3 moléculas de oxígeno presente como una forma alotrópica del oxígeno y que se encuentra naturalmente en la atmosfera y especialmente a nivel de la estratosfera ayudando a la filtración de los rayos UV (Azarpazhooh & Limeback, 2008; Bansal & Lecturer, 2012). (Ver figura 4).

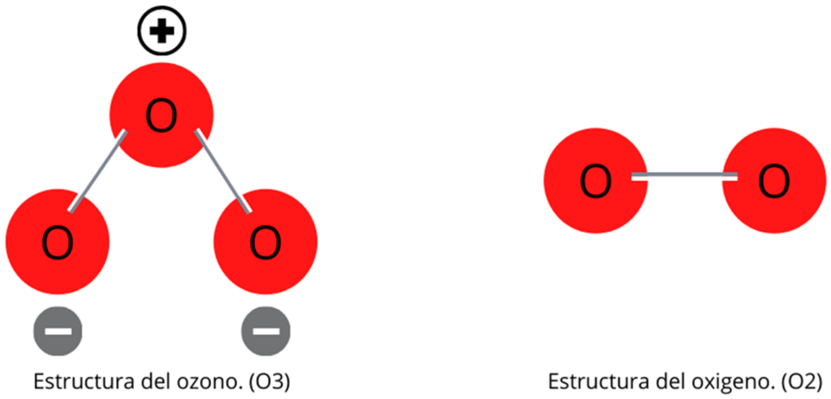


Figura 4 Estructura Molecular del Ozono y el Oxigeno

Las distintas terapias de ozono han demostrado beneficios como la estimulación de células inmunocompetentes y la síntesis de inmunoglobulinas, interleucinas y prostaglandinas que beneficiaran los procesos de inflamación y cicatrización, así mismo estimula la circulación y transporte de oxígeno promoviendo la secreción de vasodilatadores y aportando a la síntesis de proteínas (Seidler et al., 2008). Adicionalmente, se destacan los efectos antimicrobianos de las terapias de ozono actualmente descritas, un aspecto fundamental que ha significado el desarrollo de agentes antimicrobianos cargados con ozono.

5.2 Mecanismos antimicrobianos del Ozono

Los principales mecanismos antimicrobianos del ozono son explicados como resultado del daño a nivel de la membrana citoplasmática de los microorganismos, así como la oxidación de sus proteínas y en consecuencia perdida de función celular, El espectro de acción no es especifico, ni selectivo, no obstante es muy llamativo como no daña las células eucariotas debido a que cuentan con diferentes estrategias antioxidantes que les permite mantener el balance redox sin comprometer su función en células como neuronas y células epiteliales (Himuro, 2017; P. et al., 2013).

5.3 Sistemas para la generación de gas ozono y su aplicación en Odontología

El ozono es producido comercialmente mediante generadores capaces de enviar cargas eléctricas través de un condensador que contiene oxígeno permitiendo que sus átomos se reordenen en estructura de ozono (Bansal & Lecturer, 2012).

Existen diferentes sistemas de distribución en el mercado para la utilización de terapias de ozono durante la práctica clínica odontológica, entre ellos se encuentran diferentes generadores como lo son el Healozone(KaVO), Ozonitron(MyMedGmbH), Prozone(W&H) y Ozotop (OZO) que se pueden utilizar de manera portátil en la atención a pacientes en la eliminación bacteriana de los distintos tejidos dentales (Ari et al., 2020).

En odontología se han buscado diferentes formas para la administración de ozono como tratamiento, ya sean en forma de gas o en soluciones acuosas, dentro de las formas de administración encontramos el agua ozonizada, ozono gaseoso propiamente dicho, aceite ozonizado y las nanoburbujas de ozono (Ari et al., 2020; P. et al., 2013). (Ver figura 5).

Formas de Administracion de Terapias de Ozono en Odontologia			
Ozono Gaseoso	Agua Ozonizada	Nanoburbujas de Ozono	Aceite Ozonizado
El ozono en su forma gaseosa debe ser administrada mediante un sistema abierto o con succion para evitar su inhalacion y sus efectos adversos pero puede ser una terapia no invasiva a tener en cuenta (Azarpazhooh and Limeback 2008)	Los procesos de irrigacion subgingival con agua ozonizada provoca una rápida inactivación de microorganismos por ruptura de la membrana de la pared celular de los organismos asociados con la lesión. (Srikanth, Sathish, and Harsha 2013)	Estas provocan perfusiones más profundas, debido a su minúsculo tamaño, y su efecto de cavitación liberan ozono y energía cinética, al mismo tiempo que perturba las biopelículas y destruye los microorganismos. (Ari et al. 2020)	En adicion a las terapias de ozono convencionales, se ha utilizado el aceite ozonizado de girasol como agente antimicrobiano competitivo y eficaz contra Staphylococcos, Streptococcos, Enterococcos, Pseudomonas, Escherichia coli y especialmente Mycobacterias. (Bansal and Lecturer 2012)

Figura 5 Formas de administración de terapias de ozono en odontología.

Las terapias de ozono se han intentado utilizar en el manejo de la periodontitis como un posible sustituto de agente antiséptico e irrigante en la eliminación de patógenos orales (*Porphyromonas gingivalis, Porphyromonas endodontalis, Aggregatibacter actinomycetemcomitans*). De este modo se ha utilizado en conjunto a los procedimientos mecánicos, logrando buenos resultados en la reducción del número de microorganismos asociados a enfermedades periodontales. Sin embargo, cabe destacar que debido a la corta estabilidad del ozono en fases liquidas, las nanoburbujas parecen ser una buena alternativa para mejorar su transferencia al medio por más tiempo (Ari et al., 2020; Srikanth et al., 2013).

5.3 Nanoburbujas de ozono y su potencial aplicación bactericida en odontología.

La acción antimicrobiana de las nanoburbujas de ozono es ejercida a partir de los radicales libres que se generan al momento de la cavitación de las nanoburbujas, así mismo el pH de las soluciones donde se encuentren afectan significativamente a la cantidad de radicales libres que se generan, donde un pH más bajo incrementara el número de radicales libres de grupos hidroxilo (Huth et al., 2011).

En odontología se ha evaluado la actividad bactericida de las nanoburbujas de ozono contra bacterias periodonto patógenas y su citotoxicidad contra células propias de cavidad oral; el efecto bactericida fue evaluado contra *Porphyromonas gingivalis* y *Aggregatibacter actinomycetemcomitans* en un estudio de experimental en modelos *in vitro*, identificando el número de unidades formadoras de colonias al exponerlas con agua modificada con nanoburbujas de ozono durante un determinado periodo de tiempo, demostrando una alta efectividad en su capacidad bactericida contra estas bacterias representativas de las enfermedades periodontales y nula citotoxicidad a las células propias de los tejidos de la cavidad oral (Hayakumo et al., 2014).

Igualmente otro estudio analítico experimental modelo *in vivo* ha utilizado como complemento a la terapia mecánica periodontal al utilizarlas durante el procedimiento en 10 pacientes adultos de un total de 22 de forma aleatorizada, intercambiando el uso de agua convencional por agua con nanoburbujas de ozono, realizando un examen microbiológico para determinar su efectividad, demostrando cambios significativos después de 4 semanas en la reducción de las bolsas y mejorando su inserción en comparación al grupo que utilizo agua convencional, reduciendo significativamente el número de colonias de *P. gingivalis* y *T. forsythia* en la placa subgingival (Hayakumo et al., 2013).

En áreas odontológicas distintas a la periodontitis, en un estudio experimental *in vitro* donde se utilizaron muestras de 6 premolares superiores de pacientes que presentaban aparatología ortodóntica, se evaluaron los efectos del agua con nanoburbujas de ozono en la eliminación de biopelículas previamente formadas con *Streptococcus mutans* o *Candida albicans* en aparatos de ortodoncia, mostrando un efecto significativo en la eliminación de la biopelícula. Sugiriendo que la aplicación de agua con nanoburbujas tiene el potencial de eliminar las biopelículas en la boca de los pacientes con aparatología ortodóntica (Mukumoto et al., 2012). Datos clínicos también han sido reportados en 12 pacientes con aparatología ortodóntica, demostrando que las altas concentraciones de nanoburbujas fueron más efectivas en la limpieza en comparación al agua destilada concluyendo que el agua con nanoburbujas puede reducir la incidencia de caries dental durante los tratamientos de ortodoncia (SUEISHI et al., 2020).

El desarrollo de dispositivos orales para la producción de nanoburbujas directamente en boca también ha sido estudiada. La modificación de equipos comercialmente disponibles como el MD20, permiten la producción de nanoburbujas mediante la incorporación de un “nozzle-multicapa”, lo cual ha resultado en otra alternativa para el uso de nanoburbujas como carriers capaces de remover placa bacteriana oral (Lin, 2020). Aunque este dispositivo solo ha sido probado en prótesis removibles orales que previamente fueron suspendidas en soluciones bacterianas, la eliminación del 95% de los microorganismos sugiere un alto efecto higiénico, el cual está directamente asociado a la entrega de nanoburbujas en cavidad oral(Lin, 2020).

En síntesis, la aplicación de nanoburbujas de ozono en odontología puede ser una solución a la resistencia antimicrobiana, seguro para células eucariotas, factible de desarrollar, fácil de implementar y conveniente de usar para la higiene oral de los pacientes. Así bien, según lo propuesto anteriormente el ozono es un gas con posible potencial antimicrobiano para su uso en la cavidad oral, gracias a sus cualidades en la eliminación altamente efectiva de bacterias patógenas, selectivo y seguro permitiendo su utilización sin riesgos de efectos adversos por estrés oxidativo durante el control bacteriano.

5. OBJETIVOS

Objetivo general:

- Revisar y analizar críticamente la literatura disponible en relación a las propiedades de las nanoburbujas y su potencial aplicación en odontología como agente antimicrobiano para el control de placa bacteriana.

Objetivos específicos:

- Comprender los principios básicos que definen y caracterizan a las nanoburbujas, así como su clasificación.
- Describir la historia de las nanoburbujas y sus actuales métodos de producción en el sector salud.
- Revisar las propiedades antimicrobianas de las nanoburbujas de ozono, sus actuales investigaciones en periodontitis y futuros desarrollos en el área.

6. Metodología para el desarrollo de la revisión

a. Tipo de estudio:

Revisión Temática

b. Métodos:

El diseño de esta revisión temática fue basado en una búsqueda sistemática de información, para evaluar los datos que se desean conocer de forma exhaustiva a partir de literatura especializada sobre las temáticas propuestas.

Esta revisión sistemática se centró a partir de 4 preguntas orientadoras de investigación, ante las cuales, se generó una búsqueda de información fundamentada en las bases de datos Pubmed y una búsqueda manual por Google Scholar. Los artículos fueron seleccionados a partir de criterios de inclusión tales como: el artículo debía contener información sobre su definición, clasificación, propiedades, contenido y contexto histórico de las nanoburbujas; además también de la implementación de nanoburbujas de contenido ozono en diferentes áreas, más específicamente en odontología; y sus mecanismos de efecto antimicrobiano para caries y enfermedad periodontal. En general se utilizaron artículos que contenían información de nanoburbujas y/o que estuvieran relacionados con el campo de la salud. Fueron tomados en cuenta artículos sin restricción de tiempo o periodo de publicación, artículos disponibles de texto completo, en idioma de inglés y español, así como diferentes tipos de estudios tales ensayos clínicos, reportes de caso, revisiones de literatura, estudios de seguimiento, estudios retrospectivos y observacionales. sin criterios de exclusión definidos.

Luego de la selección de artículos se realizó una extracción de la información en tablas de Excel, dicha extracción definir las características que se puedan encontrar, tales como: si presentaban la definición de nanoburbuja y su contexto histórico, su clasificación o tipo, sus característica físicas o químicas, la capacidad de su efecto antimicrobiano, la zona anatómica en la cual se utilizó, la evaluación del efecto causante y variables como el año de publicación, revista, tipo de artículo, país, idioma y base de datos de la que fue tomado. Se realizó un análisis de la información extraída de los artículos en relación al tema generando y posteriormente se realizó una síntesis narrativa de la información.

Adicionalmente se realizó un análisis de las tendencias actuales de las nanoburbujas identificando en que áreas del conocimiento se está investigando actualmente por medio de una estrategia de visualización de datos, en la cual se utilizó el termino nanoburbuja en las bases de datos Web of Science (WoS) y Scopus identificando las métricas según el número de artículos asociados a su utilización según el área del conocimiento y posteriormente reportando de manera gráfica la distribución general del número de artículos según el área del conocimiento donde son aplicadas y de manera específica para las investigaciones en aplicaciones a nivel clínico médico y odontológico mediante el software Tableau V21 y Diagrama Treemap de Excel.

1. Preguntas orientadoras de investigación.

Pregunta de revisión #1

¿Por qué se necesitan alternativas antimicrobianas en odontología?

Pregunta de revisión #2

¿Cuáles son las generalidades y antecedentes acerca de las nanoburbujas?

Pregunta de revisión #3

¿Cómo actúa el efecto de las nanoburbujas de ozono en el área odontológica?

Pregunta de revisión #4

¿Cómo se percibe el futuro de las nanoburbujas en el área odontológica?

2. Estructura de la revisión

- Introducción/objetivos
- Antecedentes
- Metodología de búsqueda de la información
- Temáticas
- Necesidad de buscar alternativas antimicrobianas en odontología.
- Generalidades de las nanoburbujas
- Nanoburbujas de ozono y su efecto bactericida en odontología
- Perspectivas a futuro de las nanoburbujas en odontología

- Conclusiones
- Referencias

3. **Búsqueda de información:**

Para la realización de esta revisión temática y encontrar la literatura pertinente sobre nanoburbujas y la información proporcionada por diferentes estudios; se ejecutaron búsquedas computarizadas fundamentadas en estrategias PICO (Santos et al., 2007). Se inició a partir de preguntas de investigación orientadas por temáticas de las cuales se seleccionaron una serie de palabras claves y lenguaje controlado que fueron utilizadas como variables para la definición específica de términos MESH, con ayuda de un tesauro de ciencias de la salud (Decs) así, en conjunto con operadores booleanos se definieron las estrategias de búsqueda para la base de datos Pubmed en adición también se utilizó una búsqueda manual de artículos en Google Scholar debido a la limitada cantidad de información. La selección de artículos se hizo en duplicado y de manera independiente a partir de título y abstract los cuales fueron aprobados por expertos; para posteriormente realizar la extracción de datos de cada uno de ellos.

a. Selección de palabras claves por temática

Se establecen las variables para cada temática de la revisión a partir de las de las cuales se establecen palabras claves para poder elaborar estrategias de búsqueda avanzada de cada una de las temáticas propuestas: definición de los términos Mesh, Decs y Sinónimos o términos relacionados (Tabla 1).

Tabla 1.- SELECCIÓN DE PALABRAS CLAVES POR TEMÁTICA DE REVISIÓN		
Temática	La necesidad de buscar alternativas antimicrobianas en odontología.	
Variable	**Palabras claves**	
Terapias complementarias	Palabra clave	**Complementary Therapies**
	Términos [MeSH] inglés	Complementary Therapies Therapies, Complementary Therapy, Complementary Complementary Medicine Medicine, Complementary

		Alternative Medicine Medicine, Alternative Alternative Therapies Therapies, Alternative Therapy, Alternative
	Términos [DeSC] español/ inglés/ portugués	Complementary Therapies/Terapias Complementarias/Terapias Complementares
Bactericida	Palabra clave	**Anti-Bacterial Agents**
	Términos [MeSH] inglés	Anti-Bacterial Agents Agents, Anti-Bacterial Anti Bacterial Agents Antibacterial Agents Agents, Antibacterial Anti-Bacterial Compounds AntiBacterial Compounds Compounds, Anti-Bacterial Bacteriocidal Agents Agents, Bacteriocidal Bacteriocides Anti-Mycobacterial Agents Agents, Anti-Mycobacterial Anti Mycobacterial Agents Antimycobacterial Agents Agents, Antimycobacterial Antibiotics Antibiotic
	Términos [DeSC] español/ inglés/ portugués	Anti-Bacterial Agents / Antibacterianos/Antibacterianos
Odontología	Palabra clave	**Dentistry**
	Términos [MeSH] inglés	Dentistry Dental Equipment Dental Instruments Economics, Dental Education, Dental History of Dentistry Legislation, Dental Oral Medicine Evidence-Based Dentistry Dentistries, Evidence-Based Evidence Based Dentistry Evidence-Based Dentistries Dentistry, Evidence-Based Dentistry, Evidence Based
	Términos [DeSC] español/ inglés/ portugués	Dentistry/Odontología/Odontología
Nanoburbujas	Palabra clave	**RNS60**
	Términos [MeSH] inglés	RNS60 Nanobubbles Nbw3

		Ultrafine bubbles Taylor-Couette-Poiseuille Charge-stabilized nanobubbles Microbubbles
	Términos [DeSC] español/ inglés/ portugués	

Tabla 1.- SELECCIÓN DE PALABRAS CLAVES POR TEMÁTICA DE REVISIÓN		
Temática	Generalidades de las nanoburbujas	
Variable	**Palabras claves**	
Nanoburbujas	Palabra clave	**RNS60**
	Términos [MeSH] inglés	RNS60 Nanobubbles Nbw3 Ultrafine bubbles Taylor-Couette-Poiseuille Charge-stabilized nanobubbles Microbubbles
	Términos [DeSC] español/ inglés/ portugués	
Propiedades	Palabra clave	**Physical and Chemical Properties**
	Términos [MeSH] inglés	Physical and Chemical Properties Physical Phenomena Phenomena, Physical Physical Phenomenon Phenomenon, Physical Physical Concepts Concept, Physical Concepts, Physical Physical Concept Physical Processes Processes, Physical Physical Process Process, Physical Electromagnetic Phenomena Electromagnetic Phenomenas Phenomena, Electromagnetic Electromagnetic Phenomenon Phenomenon, Electromagnetic Electromagnetic Concepts Concept, Electromagnetic Concepts, Electromagnetic Electromagnetic Concept Electrical Phenomena Phenomena, Electrical Electrical Phenomenon Phenomenon, Electrical

		Electrical Concepts Concept, Electrical Concepts, Electrical Electrical Concept Electromagnetics
	Términos [DeSC] español/ inglés/ portugués	Physical and chemical properties/propiedades fisicas y quimicas/ propiedades fisicas y quimicas
Historia	Palabra clave	**History**
	Términos [MeSH] inglés	History Histories Historical Aspects Aspects, Historical Aspect, Historical Historical Aspect
	Términos [DeSC] español/ inglés/ portugués	History / Historia /História
Clasificación	Palabra clave	**Classification**
	Términos [MeSH] inglés	Classification Classifications Systematics Taxonomy Taxonomies systematics hierarchies hierarchy
	Términos [DeSC] español/ inglés/ portugués	Classification/Clasificación/Classificaçã o
Potencial zeta	Palabra clave	**Zeta potential**
	Términos [MeSH] inglés	zeta potential
	Términos [DeSC] español/ inglés/ portugués	zeta Potential/Potencial zeta/Potencial zeta

Tabla 1.- SELECCIÓN DE PALABRAS CLAVES POR TEMÁTICA DE REVISIÓN		
Temática	Nanoburbujas de ozono y su efecto bactericida en odontología	
Variable	**Palabras claves**	
Ozono	Palabra clave	**Ozone**
	Términos [MeSH] inglés	Tropospheric Ozone Ozone, Tropospheric Low Level Ozone Level Ozone, Low Ozone, Low Level Ground Level Ozone

		Level Ozone, Ground Ozone, Ground Level
	Términos [DeSC] español/ inglés/ portugués	
Nanoburbujas	Palabra clave	**RNS60**
	Términos [MeSH] inglés	RNS60 Nanobubbles Nbw3 Ultrafine bubbles Taylor-Couette-Poiseuille Charge-stabilized nanobubbles Microbubbles
	Términos [DeSC] español/ inglés/ portugués	No se encontraron términos relacionados
Bactericida	Palabra clave	**Anti-Bacterial Agents**
	Términos [MeSH] inglés	Anti-Bacterial Agents Agents, Anti-Bacterial Anti Bacterial Agents Antibacterial Agents Agents, Antibacterial Anti-Bacterial Compounds AntiBacterial Compounds Compounds, Anti-Bacterial Bacteriocidal Agents Agents, Bacteriocidal Bacteriocides Anti-Mycobacterial Agents Agents, Anti-Mycobacterial Anti Mycobacterial Agents Antimycobacterial Agents Agents, Antimycobacterial Antibiotics Antibiotic
	Términos [DeSC] español/ inglés/ portugués	Anti-Bacterial Agents / Antibacterianos/Antibacterianos
Odontología	Palabra clave	**Dentistry**
	Términos [MeSH] inglés	Dentistry Dental Equipment Dental Instruments Economics, Dental Education,Dental History of Dentistry Legislation, Dental Oral Medicine Evidence-Based Dentistry Dentistries, Evidence-Based Evidence Based Dentistry Evidence-Based Dentistries Dentistry, Evidence-Based Dentistry, Evidence Based

	Términos [DeSC] español/ inglés/ portugués	Dentistry/Odontología/Odontología

Tabla 1.- SELECCIÓN DE PALABRAS CLAVES POR TEMÁTICA DE REVISIÓN		
Temática	Perspectivas	
Variable	**Palabras claves**	
Apoyo a la investigación como asunto	Palabra clave	**Research Support as Topic**
	Términos [MeSH] inglés	Research Support as Topic Subsidies, Research Research Subsidies Research Subsidy Grants and Subsidies, Research
	Términos [DeSC] español/ inglés/ portugués	
Nanoburbujas	Palabra clave	**RNS60**
	Términos [MeSH] inglés	RNS60 Nanobubbles Nbw3 Ultrafine bubbles Taylor-Couette-Poiseuille Charge-stabilized nanobubbles Microbubbles
	Términos [DeSC] español/ inglés/ portugués	
Caries dental	Palabra clave	**Dental caries**
	Términos [MeSH] inglés	Dental caries Dental Decay Decay, Dental Carious Lesions Carious Lesion Lesion, Carious Lesions, Carious Caries, Dental Carious Dentin Carious Dentins Dentin, Carious Dentins, Carious Dental White Spot Spot, Dental White Spots, Dental White White Spot, Dental White Spots, Dental Dental White Spots

	Términos [DeSC] español/ inglés/ portugués	Dental Caries/Caries Dental/Cárie Dentária
Enfermedad periodontal	Palabra clave	**Periodontal Diseases**
	Términos [MeSH] inglés	Periodontal Diseases Disease, Periodontal Disease, Periodonta Diseases, Periodontal Periodontal Disease Parodontosis Parodontoses Pyorrhea Alveolaris
	Términos [DeSC] español/ inglés/ portugués	Enfermedades Periodontales/Periodontal Diseases/Doenças Periodontais

b. Estructuración de estrategia de búsqueda por temática

A partir de la tabla 2 se seleccionan las palabras claves más pertinentes para estructurar los algoritmos de las estrategias de búsqueda por temática y se diligencia en la tabla 2

Tabla 2. ESTRATEGIA DE BÚSQUEDA	
Temática	La necesidad de buscar alternativas antimicrobianas en odontología.
#1	((((((((((Complementary Therapies) OR (Therapies, Complementary)) OR (Therapy, Complementary)) OR (Complementary Medicine)) OR (Medicine, Complementary)) OR (Alternative Medicine)) OR (Medicine, Alternative)) OR (Alternative Therapies)) OR (Therapies, Alternative)) OR (Therapy, Alternative))
#2	(((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic)))
#3	((((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral

	Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))
#4	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND (((((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic))) AND ((((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))
#5(final)	((((((((((Complementary Therapies) OR (Therapies, Complementary)) OR (Therapy, Complementary)) OR (Complementary Medicine)) OR (Medicine, Complementary)) OR (Alternative Medicine)) OR (Medicine, Alternative)) OR (Alternative Therapies)) OR (Therapies, Alternative)) OR (Therapy, Alternative)) AND (((((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic))) AND ((((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))

Tabla 2. ESTRATEGIA DE BÚSQUEDA	
Temática	Generalidades de las nanoburbujas
#1	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND (zeta potential)
#2	((((((History) OR (Histories)) OR (Historical Aspects)) OR (Aspects, Historical)) OR (Aspect, Historical)) OR (Historical Aspect)) AND ((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))
#3	(((((((((Classification) OR (Classifications)) OR (Systematics)) OR (Taxonomy)) OR (Taxonomies)) OR (systematics)) OR (hierarchies)) OR (hierarchy))) AND ((((((((rns60) OR

	(nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))
#4(final)	(((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))) AND (((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Concepts, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR (Electromagnetic Phenomenon)) OR (Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics))

Tabla 2. ESTRATEGIA DE BÚSQUEDA	
Temática	Nanoburbujas de ozono y su efecto bactericida en odontología
#1	((((((((((Ozone) OR (Tropospheric Ozone)) OR (Ozone, Tropospheric)) OR (Low Level Ozone)) OR (Level Ozone, Low)) OR (Ozone, Low Level)) OR (Ground Level Ozone)) OR (Level Ozone, Ground)) OR (Ozone, Ground Level))
#2	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))))
#3	((((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR (Electromagnetic Phenomenon)) OR (Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics))
#4	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))))
#5	(((((((((((Ozone) OR (Tropospheric Ozone)) OR (Ozone, Tropospheric)) OR (Low Level Ozone)) OR (Level Ozone, Low)) OR (Ozone, Low Level)) OR (Ground Level Ozone)) OR (Level Ozone, Ground)) OR (Ozone, Ground Level)) AND ((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))) AND ((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR

	(Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic))) AND (((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))
#6(final)	(((((((((Ozone) OR (Tropospheric Ozone)) OR (Ozone, Tropospheric)) OR (Low Level Ozone)) OR (Level Ozone, Low)) OR (Ozone, Low Level)) OR (Ground Level Ozone)) OR (Level Ozone, Ground)) OR (Ozone, Ground Level)) AND (((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))) AND ((((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR (Electromagnetic Phenomenon)) OR (Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics)) AND (((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))))

Tabla 2. ESTRATEGIA DE BÚSQUEDA	
Temática	Perspectivas
#1	(((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))
#2	(((((((Periodontal Diseases) OR (Disease, Periodontal)) OR (Disease, Periodonta)) OR (Diseases, Periodontal)) OR (Periodontal Disease)) OR (Parodontosis)) OR (Parodontoses)) OR (Pyorrhea Alveolaris))
#3	(((((research support as topic) OR (subsides, research)) OR (research subsides)) OR (research subsidy)) OR (grants and subsides, research)) AND (((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))
#4	(((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND ((((((((((((((((dental caries) OR (Dental Decay)) OR (Decay, Dental)) OR (Carious Lesions)) OR (Carious Lesion)) OR (Lesion, Carious)) OR (Lesions, Carious)) OR (Caries, Dental)) OR (Carious Dentin)) OR (Carious Dentins)) OR (Dentin, Carious)) OR (Dentins, Carious)) OR (Dental White Spot)) OR (Spot, Dental White)) OR (Spots, Dental White)) OR (White Spot, Dental)) OR (White Spots, Dental)) OR (Dental White Spots))
#5(Final)	(((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND ((((((((Periodontal

	Diseases) OR (Disease, Periodontal)) OR (Disease, Periodonta)) OR (Diseases, Periodontal)) OR (Periodontal Disease)) OR (Parodontosis)) OR (Parodontoses)) OR (Pyorrhea Alveolaris))

c. Resultados de aplicación de estrategia de búsqueda por temática en bases de datos (Pubmed)

Se aplica la estrategia de búsqueda en las diferentes bases de datos y se registran los resultados en la tabla 3.

Tabla 3. Resultados aplicación de Estrategia de búsqueda por Temática PubMed. Sort by: BEST MATCH Fecha: Abr /2021			
Temática	La necesidad de buscar alternativas antimicrobianas en odontología.		
Búsqueda	**Algoritmos**	**Cantidad de artículos encontrados**	**Cantidad seleccionada por Título/ abstract**
#1	((((((((((Complementary Therapies) OR (Therapies, Complementary)) OR (Therapy, Complementary)) OR (Complementary Medicine)) OR (Medicine, Complementary)) OR (Alternative Medicine)) OR (Medicine, Alternative)) OR (Alternative Therapies)) OR (Therapies, Alternative)) OR (Therapy, Alternative))	504,701	
#2	((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic)))	972,866	

#3	((((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))	832,529	
#4	(((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND ((((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic))) AND ((((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))	4	

#5(Final)	((((((((((Complementary Therapies) OR (Therapies, Complementary)) OR (Therapy, Complementary)) OR (Complementary Medicine)) OR (Medicine, Complementary)) OR (Alternative Medicine)) OR (Medicine, Alternative)) OR (Alternative Therapies)) OR (Therapies, Alternative)) OR (Therapy, Alternative)) AND (((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic))) AND ((((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based)	11,471	**17**

Tabla 3. Resultados aplicación de Estrategia de búsqueda por Temática PubMed. Sort by: BEST MATCH Fecha: Abr /2021			
Temática	Generalidades de las nanoburbujas		
Búsqueda	**Algoritmos**	**Cantidad de artículos encontrados**	**Cantidad seleccionada por Título/ abstract**

#1	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND (zeta potential)	113	
#2	(((((History) OR (Histories)) OR (Historical Aspects)) OR (Aspects, Historical)) OR (Aspect, Historical)) OR (Historical Aspect)) AND ((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))	82	
#3	((((((((Classification) OR (Classifications)) OR (Systematics)) OR (Taxonomy)) OR (Taxonomies)) OR (systematics)) OR (hierarchies)) OR (hierarchy))) AND ((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))	254	
#4(Final)	((((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))) AND ((((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Concepts, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR (Electromagnetic Phenomenon)) OR	2244	**16**

	(Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics))		

Tabla 3. Resultados aplicación de Estrategia de búsqueda por Temática PubMed. **<u>Sort by:</u> BEST MATCH Fecha: Abr /2021**			
Temática	Nanoburbujas de ozono y su efecto bactericida en odontología		
Búsqueda	**Algoritmos**	**Cantidad de artículos encontrados**	**Cantidad seleccionada por Título/ abstract**
#1	(((((((((Ozone) OR (Tropospheric Ozone)) OR (Ozone, Tropospheric)) OR (Low Level Ozone)) OR (Level Ozone, Low)) OR (Ozone, Low Level)) OR (Ground Level Ozone)) OR (Level Ozone, Ground)) OR (Ozone, Ground Level))	26,260	
#2	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))))	9,346	
#3	((((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR	4,004,666	

	(Electromagnetic Phenomenon)) OR (Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics))		
#4	(((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))))	9,346	
#5	((((((((((Ozone) OR (Tropospheric Ozone)) OR (Ozone, Tropospheric)) OR (Low Level Ozone)) OR (Level Ozone, Low)) OR (Ozone, Low Level)) OR (Ground Level Ozone)) OR (Level Ozone, Ground)) OR (Ozone, Ground Level)) AND (((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))) AND ((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic))) AND ((((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education,	1	

	Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))		
#6 (Final)	((((((((((Ozone) OR (Tropospheric Ozone)) OR (Ozone, Tropospheric)) OR (Low Level Ozone)) OR (Level Ozone, Low)) OR (Ozone, Low Level)) OR (Ground Level Ozone)) OR (Level Ozone, Ground)) OR (Ozone, Ground Level)) AND ((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))) AND (((((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR (Electromagnetic Phenomenon)) OR (Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics)) AND ((((((((rns60) OR (nanobubbles)) OR	20	**11**

	(nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))))		

Tabla 3. Resultados aplicación de Estrategia de búsqueda por Temática PubMed. <u>Sort by:</u> BEST MATCH Fecha: Abr /2021			
Temática	Perspectiva		
Búsqueda	**Algoritmos**	**Cantidad de artículos encontrados**	**Cantidad seleccionada por Título/ abstract**
#1	(((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))	9,346	
#2	((((((((Periodontal Diseases) OR (Disease, Periodontal)) OR (Disease, Periodonta)) OR (Diseases, Periodontal)) OR (Periodontal Disease)) OR (Parodontosis)) OR (Parodontoses)) OR (Pyorrhea Alveolaris))	100,700	
#3	(((((research support as topic) OR (subsides, research)) OR (research subsides)) OR (research subsidy)) OR (grants and subsides, research)) AND (((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))	50	
#4	(((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND ((((((((((((((((dental caries) OR (Dental Decay)) OR (Decay, Dental)) OR (Carious Lesions)) OR (Carious Lesion)) OR (Lesion, Carious)) OR (Lesions, Carious)) OR (Caries, Dental)) OR (Carious Dentin)) OR (Carious Dentins)) OR (Dentin, Carious)) OR (Dentins, Carious)) OR (Dental White Spot)) OR (Spot,	3	

	Dental White)) OR (Spots, Dental White)) OR (White Spot, Dental)) OR (White Spots, Dental)) OR (Dental White Spots))		
#5(Final)	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND ((((((((Periodontal Diseases) OR (Disease, Periodontal)) OR (Disease, Periodonta)) OR (Diseases, Periodontal)) OR (Periodontal Disease)) OR (Parodontosis)) OR (Parodontoses)) OR (Pyorrhea Alveolaris))	12	**9**

d. **Resultados aplicación de Estrategia de búsqueda por Temática Google Scholar.**

Tabla Temática: La necesidad de buscar alternativas antimicrobianas en odontología.

Fecha de Búsqueda	**Estrategia**	**# Referencias Evaluadas**	**# Referencias Incluidas**
25 de abril del 2021	(Complementary therapies) OR (Therapies, complementary) OR (Complementary Medicine) AND (Dentistry) OR (Oral medicine) OR (Dental Equipment) AND (Anti-bacterial agents) OR (Antibiotics) OR (Bacteriocides)	100	6
25 de abril del 2021	(Complementary therapies) OR (Therapies, complementary) OR (Alternative therapies) AND (Dentistry) OR (Oral medicine) OR (Dental instruments) AND (Anti-bacterial agents) OR (Antibiotics) OR (Bacteriocidal agents)	100	5
25 de abril del 2021	(Complementary medicine) OR (Medicine, Alternative) OR (Complementary Medicine) AND (Dentistry) OR (Oral medicine) OR (Evidence Based Dentistry) AND (Anti-bacterial agents) OR (Antibiotics) OR (Bacteriocides)	100	3
25 de abril del 2021	(Alternative Medicine) OR (Medicine, Alternative) OR (Complementary Medicine) AND (Dentistry) OR (Oral medicine) OR (Evidence Based Dentistry) AND (Anti-bacterial agents) OR (Antibiotics) OR (Bacteriocidal Agents)	100	1
25 de abril del 2021	(Complementary therapies) OR (Therapies, complementary) OR (Complementary Medicine) AND (Dentistry) OR (Oral medicine) OR (Dental Equipment) AND (Anti-bacterial agents) OR (Antibiotics) OR (Antibiotic) AND (rns60) OR (nanobubbles) OR (ultrafine bubbles)	11	0

Tabla Temática: Generalidades de las nanoburbujas

Fecha de Búsqueda	Estrategia	# Referencias Evaluadas	# Referencias Incluidas
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Physical and chemical properties) OR (Physical concepts) OR (Physical Phenomena) (Physical Process)	100	11
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (History) OR (Histories) OR (Historical Aspects) OR (Historical Aspect)	100	3
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Classification) OR (Classifications) OR (Taxonomy) OR (hierarchies)	100	4
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (zeta potential)	100	11

Tabla Temática: Nanoburbujas de ozono y su efecto bactericida en odontología

Fecha de Búsqueda	Estrategia	# Referencias Evaluadas	# Referencias Incluidas
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Ozone) OR (Tropospheric Ozone) OR (Low Level Ozone)	100	4
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Anti-bacterial agents) OR (Antibacterial Agents) OR (Bacteriocidal Agents) OR (Anti-Mycobacterial Agents)	100	0
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Ozone) OR (Tropospheric Ozone) OR (Low Level Ozone) AND (Anti-bacterial agents) OR (Antibacterial Agents) OR (Bacteriocidal Agents)	75	1
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Ozone) OR (Tropospheric Ozone) OR (Low Level Ozone) AND (Dentistry) OR (Oral medicine) OR (Dental Equipment)	100	5
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Ozone) OR (Tropospheric Ozone) OR (Low Level Ozone) AND (Anti-bacterial agents) OR (Antibacterial Agents) OR (Bacteriocidal Agents) AND (Dentistry) OR (Oral medicine) OR (Dental Equipment)	25	0

Tabla Temática: Perspectivas

Fecha de Búsqueda	Estrategia	# Referencias Evaluadas	# Referencias Incluidas
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Research) OR (Research Support as Topic) OR (Research Subsidy)	100	2

25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Dental caries) OR (Dental Decay) OR (Carious Lesions) OR (Carious Dentin) OR (Caries, Dental)	110	3
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Periodontal Diseases) OR (Disease, Periodontal) OR (Periodontal Disease) OR (Parodontosis)	100	1
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Research) OR (Research Support as Topic) OR (Research Subsidy) AND (Dental caries) OR (Dental Decay) OR (Carious Lesions) OR (Carious Dentin) OR (Caries, Dental)	34	0
25 de abril del 2021	(rns60) OR (nanobubbles) OR (ultrafine bubbles) OR (Nbw3) AND (Research) OR (Research Support as Topic) OR (Research Subsidy) AND (Periodontal Diseases) OR (Disease, Periodontal) OR (Periodontal Disease) OR (Parodontosis)	96	3

e. Preselección de artículos por temática

Los artículos encontrados y preseleccionados por título o abstract se registran en la siguiente tabla. ***(Tabla 4)***

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	Necesidad de buscar alternativas antimicrobianas en odontología.
BASE DE DATOS	**PUBMED**
ALGORITMO FINAL	((((((((((Complementary Therapies) OR (Therapies, Complementary)) OR (Therapy, Complementary)) OR (Complementary Medicine)) OR (Medicine, Complementary)) OR (Alternative Medicine)) OR (Medicine, Alternative)) OR (Alternative Therapies)) OR (Therapies, Alternative)) OR (Therapy, Alternative)) AND ((((((((((((((((Anti-Bacterial Agents) OR (Agents, Anti-Bacterial)) OR (Anti Bacterial Agents)) OR (Antibacterial Agents)) OR (Agents, Antibacterial)) OR (Anti-Bacterial Compounds)) OR (Anti Bacterial Compounds)) OR (Compounds, Anti-Bacterial)) OR (Bacteriocidal Agents)) OR (Agents, Bacteriocidal)) OR (Bacteriocides)) OR (Anti-Mycobacterial Agents)) OR (Agents, Anti-Mycobacterial)) OR (Anti Mycobacterial Agents)) OR (Antimycobacterial Agents)) OR (Agents, Antimycobacterial)) OR (Antibiotics)) OR (Antibiotic))) AND (((((((((((((dentistry) OR (dental equipment)) OR (Dental Instruments)) OR (Economics, Dental)) OR (Education, Dental)) OR (History of Dentistry)) OR (Legislation, Dental)) OR (Oral Medicine)) OR (Evidence-Based Dentistry)) OR (Dentistries, Evidence-Based)) OR (Evidence Based Dentistry)) OR (Evidence-Based Dentistries)) OR (Dentistry, Evidence-Based)) OR (Dentistry, Evidence Based))
artículos preseleccionados Referencia -estilo Vancouver y abstract	
Allaker RP, Douglas CWI. Novel anti-microbial therapies for dental plaque-related diseases. Int J Antimicrob Agents. 2009;33(1):8–13.	

Abstract

Control of dental plaque-related diseases has traditionally relied on non-specific removal of plaque by mechanical means. As our knowledge of oral disease mechanisms increases, future treatment is likely to be more targeted, for example at small groups of organisms, single species or at key virulence factors they produce. The aim of this review is to consider the current status as regards novel treatment approaches. Maintenance of oral hygiene often includes use of chemical agents; however, increasing problems of resistance to synthetic antimicrobials have encouraged the search for alternative natural products. Plants are the source of more than 25% of prescription and over-the-counter preparations, and the potential of natural agents for oral prophylaxis will therefore be considered. Targeted approaches may be directed at the black-pigmented anaerobes associated with periodontitis. Such pigments provide an opportunity for targeted phototherapy with high-intensity monochromatic light. Studies to date have demonstrated selective killing of Porphyromonas gingivalis and Prevotella intermedia in biofilms. Functional inhibition approaches, including the use of protease inhibitors, are also being explored to control periodontitis. Replacement therapy by which a resident pathogen is replaced with a non-pathogenic bacteriocin-producing variant is currently under development with respect to Streptococcus mutans and dental caries.

Connors WJ, Rabie HH, Figueiredo RL, Holton DL, Parkins MD. Acute dental infections managed in an outpatient parenteral antibiotic program setting: Prospective analysis and public health implications. BMC Infect Dis. 2017;17(1):1–8.

Abstract

Background: The number of Acute Dental Infections (ADI) presenting for emergency department (ED) care are steadily increasing. Outpatient Parenteral Antibiotic Therapy (OPAT) programs are increasingly utilized as an alternative cost-effective approach to the management of serious infectious diseases but their role in the management of severe ADI is not established. This study aims to address this knowledge gap through evaluation of ADI referrals to a regional OPAT program in a large Canadian center.

Methods: All adult ED and OPAT program ADI referrals from four acute care adult hospitals in Calgary, Alberta, were quantified using ICD diagnosis codes in a regional reporting system. Citywide OPAT program referrals were prospectively enrolled over a five-month period from February to June 2014. Participants completed a questionnaire and OPAT medical records were reviewed upon completion of care.

Results: Of 704 adults presenting to acute care facilities with dental infections during the study period 343 (49%) were referred to OPAT for ADI treatment and 110 were included in the study. Participant mean age was 44 years, 55% were women, and a majority of participants had dental insurance (65%), had seen a dentist in the past six months (65%) and reported prior dental infections (77%), 36% reporting the current ADI as a recurrence. Median length of parenteral antibiotic therapy was 3 days, average total course of antibiotics was 15-days, with a cumulative 1326 antibiotic days over the study period. There was no difference in total duration of antibiotics between broad and narrow spectrum regimes. Conservative cost estimate of OPAT care was $120,096, a cost savings of $597,434 (83%) compared with hospitalization.

Conclusions: ADI represent a common preventable cause of recurrent morbidity. Although OPAT programs may offer short-term cost savings compared with hospitalization, risks associated with extended antibiotic exposures and delayed definitive dental management must also be gauged.

Keywords: Antibiotics; Healthcare costs; Odontogenic infection; Parenteral infusions; Periapical abscess; Public health dentistry**.**

Drisko CH. Nonsurgical periodontal therapy. Periodontol 2000. 2001;25(1):77–88.

Abstract

Regular home care by the patient in addition to professional removal of subgingival plaque is generally very effective in controlling most inflammatory periodontal diseases. When disease does recur, despite frequent recall, it can usually be attributed to lack of sufficient supragingival and subgingival plaque control or to other risk factors that influence host response, such as diabetes or smoking. Causative factors contributing to recurrent disease include deep inaccessible pockets, overhangs, poor crown margins and plaque-retentive calculus. In most cases, simply performing a thorough periodontal debridement under local anesthesia will stop disease progression and result in improvement in the clinical signs and symptoms of active disease. If however, clinical signs of disease activity persist following thorough mechanical therapy, such as increased pocket depths, loss of attachment and bleeding on probing, other pharmacotherapeutic therapies should be considered. Augmenting scaling and root planing or maintenance visits with adjunctive chemotherapeutic agents for controlling plaque and gingivitis could be as simple as placing the patient on an antimicrobial mouthrinse and/or toothpaste with agents such as fluorides, chlorhexidine or triclosan, to name a few. Since supragingival plaque reappears within hours or days after its removal, it is important that patients have access to effective alternative chemotherapeutic products that could help them achieve adequate supragingival plaque control. Recent studies, for example, have documented the positive effect of triclosan toothpaste on the long-term maintenance of both gingivitis and periodontitis patients. Daily irrigation with a powered irrigation device, with or without an antimicrobial agent, is also useful for decreasing the inflammation associated with gingivitis and periodontitis. Clinically significant changes in probing depths and attachment levels are not usually expected with irrigation alone. Recent reports, however, would indicate that, when daily irrigation with water was added to a regular oral hygiene home regimen, a significant reduction in probing depth, bleeding on probing and Gingival Index was observed. A significant reduction in cytokine levels (interleukin-1beta and prostaglandin E2, which are associated with destructive changes in inflamed tissues and bone resorption also occurs. If patient-applied antimicrobial therapy is insufficient in preventing, arresting, or reversing the disease progression, then professionally applied antimicrobial agents should be considered including sustained local drug delivery products. Other, more broadly based pharmacotherapeutic agents may be indicated for multiple failing sites. Such agents would include systemic antibiotics or host modulating drugs used in conjunction with periodontal debridement. More aggressive types of juvenile periodontitis or severe rapidly advancing adult periodontitis usually require a combination of surgical intervention in conjunction with systemic antibiotics and generally are not controlled with nonsurgical anti-infective therapy alone. It should be noted, however, that, to date, no home care products or devices currently available can completely control or eliminate the pathogenic plaques associated with periodontal diseases for extended periods of time. Daily home care and frequent recall are still paramount for long-term success. Nonsurgical therapy remains the cornerstone of periodontal treatment. Attention to detail, patient compliance and proper selection of adjunctive antimicrobial agents for sustained plaque control are important elements in achieving successful long-term results. Frequent re-evaluation and careful monitoring allows the practitioner the opportunity to intervene early in the disease state, to reverse or arrest the progression of periodontal disease with meticulous nonsurgical anti-infective therapy

Goudouri OM, Kontonasaki E, Lohbauer U, Boccaccini AR. Antibacterial properties of metal and metalloid ions in chronic periodontitis and peri-implantitis therapy. Acta Biomater [Internet]. 2014;10(8):3795–810. Available from: http://dx.doi.org/10.1016/j.actbio.2014.03.028

Abstract

Periodontal diseases like periodontitis and peri-implantitis have been linked with Gram-negative anaerobes. The incorporation of various chemotherapeutic agents, including metal ions, into several materials and devices has been extensively studied against periodontal bacteria, and materials doped with metal ions have been proposed for the treatment of periodontal and peri-implant diseases. The aim of this review is to discuss the effectiveness of materials doped with metal and metalloid ions already used in the treatment of periodontal diseases, as well as the potential use of alternative materials that are currently available for other applications but have been proved to be cytotoxic to the specific periodontal pathogens. The sources of this review included English articles using Google Scholar™, ScienceDirect, Scopus and PubMed. Search terms included the combinations of the descriptors "disease", "ionic species" and "bacterium". Articles that discuss the biocidal properties of materials doped with metal and metalloid ions against the specific periodontal bacteria were included. The articles were independently extracted by two authors using predefined data fields. The evaluation of resources was based on the quality of the content and the relevance to the topic, which was evaluated by the ionic species and the bacteria used in the study, while the final application was not considered as relevant. The present review summarizes the extensive previous and current research efforts concerning the use of metal ions in periodontal diseases therapy, while it points out the challenges and opportunities lying ahead.

Grzech-Leśniak K, Matys J, Dominiak M. Comparison of the clinical and microbiological effects of antibiotic therapy in periodontal pockets following laser treatment: An in vivo study. Adv Clin Exp Med. 2018;27(9):1263–70.

Abstract

Background: Laser technology in periodontal therapy could help in reducing total bacterial count.

Objectives: The aim of this study was to evaluate the effects of pocket debridement using an erbium-doped yttrium aluminium garnet laser (Er:YAG laser - ERL), scaling and root planing (SRP) with photodynamic therapy (PDT), or SRP alone. Teeth vitality and soft tissue carbonization were also assessed.

Material and methods: This study included 1,169 single-rooted teeth from 84 patients divided into 3 groups (n = 28). The G1 group had ERL with 40 mJ of energy, a frequency of 40 Hz and a fluence of 63.66 J/cm2. The G2 group had SRP + PDT (635 nm diode laser, 12 J of energy and irradiation time of 30 s) and a Toluidine Blue photosensitizer (PS) (application time of 60 s). The G3 group was administered SRP alone. In the 42 subjects (G1: n = 11, G2: n = 14 and G3: n = 17) with high amounts of Aggregatibacter actinomycetemcomitans (Aa), Porphyromonas gingivalis (Pg), Treponema denticola (Td) and Tannerella forsythia (Tf), additional 1-week antibiotic treatments with clindamycin or amoxicillin + clavulanic acid - in doses of 600 mg/day or 1000 mg/day, respectively - were prescribed 3 months after the therapy. Microbiological and clinical analyses of the probing depth (PD), recession (RC), plaque index (PI), bleeding on probing (BOP), and attachment loss (AT) were performed at baseline and at the follow-up of 3 months, 3 months and 1 week, and 6 months.

Results: Plaque index decreased in G1 after 3 months, 3 months and 1 week, and 6 months ($p < 0.05$) and was lower in G1 vs G2 after 3 months ($p < 0.05$). The reduction in BOP in G1 after 3 months and 1 week was higher in comparison with G2 or G3 ($p < 0.02$). Probing depth decreased in all groups ($p < 0.05$). We found a reduction in the percentage of sites with some bacteria after 3 months - Prevotella intermedia (Pi) (G1 and G2), Capnocytophaga gingivalis (Cg) and Eubacterium nucleatum (En) (G3), and after 3 months and 1 week with En, Td, Tf (G1, G2 and G3), Pi (G1 and G2), Aa, Peptostreptococcus micros (Pm), and Cg (G3), and with Pi (G1 and G2), Tf (G2), Pg, En (G2 and G3), and Pm (G3) after 6 months ($p < 0.05$). We observed no signs of carbonization or teeth injury.

Conclusions: Scaling and root planing + PDT and ERL may be an alternative therapy for chronic periodontitis.

Keywords: Er:YAG laser; antibacterial therapy; chronic periodontitis; photodynamic therapy; scaling and root planning.

Holmes CJ, Pellecchia R. Antimicrobial Therapy in Management of Odontogenic Infections in General Dentistry. Dent Clin North Am [Internet]. 2016;60(2):497–507. Available from: http://dx.doi.org/10.1016/j.cden.2015.11.013

Abstract

This article focuses on the diagnosis and management of odontogenic infections. Current antibiotic regimens are reviewed and discussed including use of alternative antibiotics with patients known to have a penicillin allergy. Emphasis is made on proper examination of the patient with use of diagnostic aids to provide the correct treatment of choice.

Keywords: Allergy; Antibiotic therapy; Antibiotics; Antimicrobial therapy; Dental abscess; Diagnosis and treatment plan; Odontogenic infections.

Jentsch HFR, Buchmann A, Friedrich A, Eick S. Nonsurgical therapy of chronic periodontitis with adjunctive systemic azithromycin or amoxicillin/metronidazole. Clin Oral Investig. 2016;20(7):1765–73.

Abstract

Objectives: The objective of the present study is to compare the effect of systemic adjunctive use of azithromycin with amoxicillin/metronidazole to scaling and root planing (SRP) in a clinical study.

Materials and methods: Data from 60 individuals with chronic periodontitis were evaluated after full-mouth SRP. Antibiotics were given from the first day of SRP, in the test group ($n = 29$), azithromycin for 3 days and, in the control group ($n = 31$), amoxicillin/metronidazole for7 days. Probing depth (PD), attachment level (AL), and bleeding on probing (BOP) were recorded at baseline and after 3 and 12 months. Gingival crevicular fluid was analyzed for matrix metalloprotease (MMP)-8 and interleukin (IL)-1beta levels. Subgingival plaque was taken for assessment of the major bacteria associated with periodontitis.

Results: In both groups, PD, AL, and BOP were significantly reduced ($p < 0.001$). A few significant differences between the groups were found; AL and BOP were significantly better in the test than in the control group at the end of the study ($p = 0.020$ and 0.009). Periodontopathogens were reduced most in the test group.

Conclusions: A noninferiority of the treatment with azithromycin in comparison with amoxicillin/metronidazole can be stated. The administration of azithromycin could be an alternative to the use of amoxicillin/metronidazole adjunctive to SRP in patients with moderate or severe chronic periodontitis; however, a randomized placebo-controlled multicenter study is needed.

Clinical relevance: Application of azithromycin as a single antibiotic for 3 days might be considered as an additional adjunctive antibiotic to SRP in selected patients.

Keywords: Antibiotics; Chronic periodontitis; Cytokines; Periodontopathogens; Scaling and root planing.

Junior SS, Ribeiro FV, Villalpando KT, Cirano FR, Pimentel SP. Maintenance periodontal therapy after systemic antibiotic and regenerative therapy of generalized Aggressive periodontitis. A case report with 10-year follow-up. Dent Update. 2015;42(4):385–93.

Abstract

Aggressive periodontitis (AgP) is an inflammatory disease characterized by rapid attachment loss and bone destruction. This case report presents the 10-year results in a subject with generalized AgP treated by a regenerative periodontal therapeutic approach and the adjunctive use of antibiotics, following a systematic maintenance periodontal therapy. The use of enamel matrix derivatives (EMD) and adjunctive antibiotic therapy to treat AgP yielded improvements in clinical parameters and radiographic bony fill. This combined therapeutic approach following a systematic supportive periodontal therapy supports the long-term maintenance of teeth with previous advanced periodontal defects, demonstrating successful stability after 10-years follow-up. Clinical Relevance: The combined treatment protocol using EMD plus adjunctive antibiotic therapy, associated with a systematic supportive periodontal therapy, benefits the long-term maintenance of teeth with previous advanced periodontal defects in subjects presenting AgP, supporting this approach as an alternative in the treatment of AgP.

Leszczyńska A, Buczko P, Buczko W, Pietruska M. Periodontal pharmacotherapy-an updated review. Adv Med Sci. 2011;56(2):123–31.

ABSTRACT

Periodontal disease is mainly associated with the activity of bacteria which adhere to the tooth surface and form specific structure of bacterial biofilm. Periodontal bacteria cause inflammation of the gums and aggressive immune response, affecting the periodontium. The first phase of initial therapy - mechanical removal of dental plaque and calculus - is necessary. If this non-surgical therapy has proved to be unsuccessful, an alternative treatment with antimicrobial agents is then considered. Pharmacotherapy is based on systemic or local antibiotics and/or antiseptics, which are applied according to the severity of the disease. A number of recent periodontal studies present some of the pharmacological agents, that are directed against bacteria or a host immune response, are often chosen as an adjunct treatment option, but none of these antimicrobials were established as 'a gold standard' in the periodontal treatment. This review provides some present recommendation of pharmacological strategies, with particular emphasis on systemic and local antimicrobial therapy of periodontal disease

Lin PJ, Chuang MC, Chang SC. Efficacy of using oxygen microbubble device for facultative anaerobe removal. IET Nanobiotechnology. 2018;12(7):973–80.

Abstract

Patients with serious gingivitis or periodontal diseases suffer from receding gums. Brushing teeth with a toothbrush may result in bleeding gums and new wounds, which increases the difficulty of removing facultative anaerobes from gum pockets, to decrease the damage inflicted on gums, this study proposed a cleaning device that can generate and emit oxygen microbubbles for eliminating facultative anaerobes in the mouth cavity. In this study, the authors conducted simulations with a denture to investigate the efficacy of using this method to remove facultative anaerobes. In this research for the optimal device design, several variables were manipulated including rotation speeds of the bubble generator, different nozzle diameters, and different numbers of nozzle holes. The results revealed that the device is effective in removing facultative anaerobes; moreover, of all design variables, the number of nozzle holes was the factor having the largest effect on anaerobe removal, as it influenced the flow volume and oxygen content of the discharge: the greater the number of nozzles, the greater the flow volume, oxygen content, and efficacy of anaerobe removal.

Manresa C, Sanz-miralles EC, Twigg J, Bravo M. Supportif Periodontal Therapy in adults treated for periodontitis. Cochrane Database Syst Rev. 2018;(1):1-.

Abstract

Background: Periodontitis is a bacterially-induced, chronic inflammatory disease that destroys the connective tissues and bone that support teeth. Active periodontal treatment aims to reduce the inflammatory response, primarily through eradication of bacterial deposits. Following completion of treatment and arrest of inflammation, supportive periodontal therapy (SPT) is employed to reduce the probability of re-infection and progression of the disease; to maintain teeth without pain, excessive mobility or persistent infection in the long term, and to prevent related oral diseases.According to the American Academy of Periodontology, SPT should include all components of a typical dental recall examination, and importantly should also include periodontal re-evaluation and risk assessment, supragingival and subgingival removal of bacterial plaque and calculus, and re-treatment of any sites showing recurrent or persistent disease. While the first four points might be expected to form part of the routine examination appointment for periodontally healthy patients, the inclusion of thorough periodontal evaluation, risk assessment and subsequent treatment - normally including mechanical debridement of any plaque or calculus deposits - differentiates SPT from routine care.Success of SPT has been reported in a number of long-term, retrospective studies. This review aimed to assess the evidence available from randomised controlled trials (RCTs).

Objectives: To determine the effects of supportive periodontal therapy (SPT) in the maintenance of the dentition of adults treated for periodontitis.

Search methods: Cochrane Oral Health's Information Specialist searched the following databases: Cochrane Oral Health's Trials Register (to 8 May 2017), the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library, 2017, Issue 5), MEDLINE Ovid (1946 to 8 May 2017), and Embase Ovid (1980 to 8 May 2017). The US National Institutes of Health Trials Registry (ClinicalTrials.gov) and the World Health Organization International Clinical Trials Registry Platform were searched for ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases.

Selection criteria: Randomised controlled trials (RCTs) evaluating SPT versus monitoring only or alternative approaches to mechanical debridement; SPT alone versus SPT with adjunctive interventions; different approaches to or providers of SPT; and different time intervals for SPT delivery.We excluded split-mouth studies where we considered there could be a risk of contamination.Participants must have completed active periodontal therapy at least six months prior to randomisation and be enrolled in an SPT programme. Trials must have had a minimum follow-up period of 12 months.

Data collection and analysis: Two review authors independently screened search results to identify studies for inclusion, assessed the risk of bias in included studies and extracted study data. When possible, we calculated mean differences (MDs) and 95% confidence intervals (CIs) for continuous variables. Two review authors assessed the quality of evidence for each comparison and outcome using GRADE criteria.

Main results: We included four trials involving 307 participants aged 31 to 85 years, who had been previously treated for moderate to severe chronic periodontitis. Three studies compared adjuncts to mechanical debridement in SPT versus debridement only. The adjuncts were local antibiotics in two studies (one at high risk of bias and one at low risk) and photodynamic therapy in one study (at unclear risk of bias). One study at high risk of bias compared provision of SPT by a specialist versus general practitioner. We did not identify any RCTs evaluating the effects of SPT versus monitoring only, or of providing SPT at different time intervals, or that compared the effects of mechanical debridement using different approaches or technologies.No included trials measured our primary outcome 'tooth loss'; however, studies evaluated signs of inflammation and potential periodontal disease progression, including bleeding on probing (BoP), clinical attachment level (CAL) and probing pocket depth (PPD).There was no evidence of a difference between SPT delivered by a specialist versus a general practitioner for BoP or PPD at 12 months (very low-quality evidence). This study did not measure CAL or adverse events.Due to heterogeneous outcome reporting, it was not possible to combine data from the two studies comparing mechanical debridement with or without the use of adjunctive local antibiotics. Both studies found no evidence of a difference between groups at 12 months (low to very low-quality evidence). There were no adverse events in either study.The use of adjunctive photodynamic therapy did not demonstrate evidence of benefit compared to mechanical debridement only (very low-quality evidence). Adverse events were not measured.The quality of the evidence is low to very low for these comparisons. Future research is likely to change the findings, therefore the results should be interpreted with caution.

Authors' conclusions: Overall, there is insufficient evidence to determine the superiority of different protocols or adjunctive strategies to improve tooth maintenance during SPT. No trials evaluated SPT versus monitoring only. The evidence available for the comparisons evaluated is of low to very low quality, and hampered by dissimilarities in outcome reporting. More trials using uniform definitions and outcomes are required to address the objectives of this review.

Martíınez CC, Gómez MD, Oh MS. Use of traditional herbal medicine as an alternative in dental treatment in mexican dentistry: A review. Pharm Biol [Internet]. 2017;55(1):1992–8. Available from: https://doi.org/10.1080/13880209.2017.1347188

Abstract

Context: Herbal therapies are used worldwide to treat health conditions. In Mexico, generations have used them to treat gingivitis, periodontitis, mouth infections, and discoloured teeth. However, few studies have collected scientific evidence on their effects.

Objective: This study aimed at searching and compiling scientific evidence of alternative oral and dental treatments using medicinal herbs from Mexico.

Methods: We collected various Mexican medicinal plants used in the dental treatment from the database of the Institute of Biology at the National Autonomous University of Mexico. To correlate with existing scientific evidence, we used the PubMed database with the key term '(scientific name) and (oral or dental)'.

Results: Mexico has various medical herbs with antibacterial and antimicrobial properties, according to ancestral medicinal books and healers. Despite a paucity of experimental research demonstrating the antibacterial, antimicrobial, and antiplaque effects of these Mexican plants, they could still be useful as an alternative treatment of several periodontal diseases or as anticariogenic agents. However, the number of studies supporting their uses and effects remains insufficient.

Discussion and conclusion: It is important for the health of consumers to scientifically demonstrate the real effects of natural medicine, as well as clarify and establish their possible therapeutic applications. Through this bibliographical revision, we found papers that testify or refute their ancestral uses, and conclude that the use of plants to treat oral conditions or to add to the dental pharmacological arsenal should be based on experimental studies verifying their suitability for dental treatments.

Mombelli A. Microbiological monitoring. J Clin Periodontol. 1996;23(3 PART II):251–7.

Ahstiacl. If periodontal disease is due to a limited number of bacteria! species, then continuous maximal plaque suppression is not the only possibility for prevention and therapy. Specific elimination or reduction of pathogenic bacteria from plaque becomes a valid alternative. Recent studies indicate that the elimination of certain putative pathogens is particularly difficult. New diagnostic methods should allow the choice of better suited procedures, make chosen procedures more effective (through better timing, dosage, selection of devices or drugs, increase of specificity, etc.) or lead to the elimination of unnecessary work (e.g.. the treatment of non-susceptible sites or patients). The benefit of newly proposed tests depends on the possible impact of the obtained information on clinical decisions and on the consequences these decisions have for treatment. Thus, diagnostic methods and therapeutical options have to be evaluated together

Shrestha A, Fong SW, Khoo BC, Kishen A. Delivery of Antibacterial Nanoparticles into Dentinal Tubules Using High-intensity Focused Ultrasound. J Endod [Internet]. 2009;35(7):1028–33. Available from: http://dx.doi.org/10.1016/j.joen.2009.04.015

Abstract

Introduction: High-intensity focused ultrasound (HIFU) produces collapsing cavitation bubbles. This study aims to investigate the efficacy of collapsing cavitation bubbles to deliver antibacterial nanoparticles into dentinal tubules to improve root canal disinfection.

Methods: In stage 1, experiments were performed to characterize the efficacy of collapsing cavitation bubbles to deliver the miniature plaster beads into a tubular channel model. In stage 2, experiments were conducted on root-dentin blocks to test the efficacy of HIFU applied at 27 kHz for 2 minutes to deliver antibacterial nanoparticles into dentinal tubules. After the stage 2 experiment, the samples were sectioned and analyzed using field-emission scanning electron microscopy and energy dispersive X-ray analysis.

Results: The stage 1 experiment showed that collapsing cavitation bubbles using HIFU delivered plaster beads along the entire length of the tubular channel. It was observed from the stage 2 experiments that the diffusion of fluids alone was not able to deliver antibacterial nanoparticles into dentinal tubules. The collapsing cavitation bubbles treatment using HIFU resulted in significant penetration up to 1,000 microm of antibacterial nanoparticles into the dentinal tubules. The statistical analysis showed a highly significant difference in the depth of penetration of antibacterial nanoparticles between the two groups (<0.005).

Conclusion: The cavitation bubbles produced using HIFU can be used as a potential method to deliver antibacterial nanoparticles into the dentinal tubules to enhance root canal disinfection.

Teughels W, Dhondt R, Dekeyser C, Quirynen M. Treatment of aggressive periodontitis. Periodontol 2000. 2014;65(1):107–33.

Abstract

Despite etiological differences between aggressive and chronic periodontitis, the treatment concept for aggressive periodontitis is largely similar to that for chronic periodontitis. The goal of treatment is to create a clinical condition that is conducive to retaining as many teeth as possible for as long as possible. When a diagnosis has been made and risk factors have been identified, active treatment is commenced. The initial phase of active treatment consists of mechanical debridement, either alone or supplemented with antimicrobial drugs. Scaling and root planing has been shown to be effective in improving clinical indices, but does not always guarantee long-term stability. Antimicrobials can play a significant role in controlling aggressive periodontitis. Few studies have been published on this subject for localized aggressive periodontitis, but generalized aggressive periodontitis has been subject to more scrutiny. Studies have demonstrated that systemic antibiotics as an adjuvant to scaling and root planing are more effective in controlling disease compared with scaling and root planing alone or with supplemental application of local antibiotics or antiseptics. It has also become apparent that antibiotics ought to be administered with, or just after, mechanical debridement. Several studies have shown that regimens of amoxicillin combined with metronidazole or regimens of clindamycin are the most effective and are preferable to regimens containing doxycycline. Azithromycin has been shown to be a valid alternative to the regimen of amoxicillin plus metronidazole. A limited number of studies have been published on surgical treatment in patients with aggressive periodontitis, but the studies available show that the effect can be comparable with the effect on patients with chronic periodontitis, provided that proper oral hygiene is maintained, a strict maintenance program is followed and modifiable risk factors are controlled. Both access surgery and regenerative techniques have shown good results in patients with aggressive periodontitis. Once good periodontal health has been obtained, patients must be enrolled in a strict maintenance program that is directed toward controlling risk factors for disease recurrence and tooth loss. The most significant risk factors are noncompliance with regular maintenance care, smoking, high gingival bleeding index and poor plaque control. There is no evidence to suggest that daily use of antiseptic agents should be part of the supportive periodontal therapy for aggressive periodontitis.

Thornhill MH, Dayer MJ, Durkin MJ, Lockhart PB, Baddour LM. Oral antibiotic prescribing by NHS dentists in England 2010-2017. Br Dent J. 2019;227(12):1044–50.

Abstract

Introduction Dentists prescribe a significant proportion of all antibiotics, while antimicrobial stewardship aims to minimise antibiotic-prescribing to reduce the risk of developing antibiotic-resistance and adverse drug reactions.Aims To evaluate NHS antibiotic-prescribing practices of dentists in England between 2010-2017.Methods NHS Digital 2010-2017 data for England were analysed to quantify dental and general primary-care oral antibiotic prescribing.Results Dental prescribing accounted for 10.8% of all oral antibiotic prescribing, 18.4% of amoxicillin and 57.0% of metronidazole prescribing in primary care. Amoxicillin accounted for 64.8% of all oral antibiotic prescribing by dentists, followed by metronidazole (28.0%), erythromycin (4.4%), phenoxymethylpenicillin (0.9%), clindamycin (0.6%), co-amoxiclav (0.5%), cephalosporins (0.4%) and tetracyclines (0.3%). Prescriptions by dentists declined during the study period for all antibiotics except for co-amoxiclav. This increase is of concern given the need to restrict co-amoxiclav use to infections where there is no alternative. Dental prescribing of clindamycin, which accounted for 43.9% of primary care prescribing in 2010, accounted for only 14.6% in 2017. Overall oral antibiotic prescribing by dentists fell 24.4% as compared to 14.8% in all of primary care.Conclusions These data suggest dentists have reduced antibiotic prescribing, possibly more than in other areas of primary-care. Nonetheless, opportunities remain for further reduction.

Trombelli L, Farina R, Pollard A, Claydon N, Franceschetti G, Khan I, et al. Efficacy of alternative or additional methods to professional mechanical plaque removal during supportive periodontal therapy: A systematic review and meta-analysis. J Clin Periodontol. 2020;47(S22):144–54.

Abstract

Aims: To systematically review the literature addressing the following focused questions: "What is the efficacy of either (#1) alternative or (#2) additional methods to professional mechanical plaque removal (PMPR) on progression of attachment loss during supportive periodontal therapy (SPT) in periodontitis patients?".

Methods: A systematic search for randomized clinical trials was performed. Change in clinical attachment level (CAL) from baseline was the primary outcome.

Results: Routine PMPR performed with either a combination of ultrasonic/hand instruments or Er:Yag laser showed similarly effective in preventing CAL loss. Moreover, a routine SPT regimen based on PMPR led to stability of CAL irrespective of a daily sub-antimicrobial doxycycline dose (SDD). Finally, an adjunctive photodynamic therapy (PDT) did not enhance the magnitude of CAL gain when sites with probing depth ≥4 mm were repeatedly treated. After pooling all data, the results of the meta-analysis showed no statistical differences in CAL change from baseline: mean overall CAL change was -0.233 mm (95% confidence interval: -1.065, 0.598; p = .351).

Conclusions: Weak evidence indicate that in treated periodontitis patients enrolled in a 3-4 month SPT based on PMPR, Er:Yag laser (as alternative), SDD and PDT (as additional) do not produce a greater clinical effect on periodontal conditions compared to PMPR.

Keywords: disease progression; periodontal diseases; periodontitis; secondary prevention.

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	Generalidades de las nanoburbujas
BASE DE DATOS	**PUBMED**
ALGORITMO FINAL	((((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR

	(microbubbles)))) AND (((((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Concepts, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR (Electromagnetic Phenomenon)) OR (Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics))

artículos preseleccionados

Referencia -estilo Vancouver y abstract

Alheshibri M, Qian J, Jehannin M, Craig VSJ. A History of Nanobubbles. Langmuir. 2016;32(43):11086–100.

Abstract

We follow the history of nanobubbles from the earliest experiments pointing to their existence to recent years. We cover the effect of Laplace pressure on the thermodynamic stability of nanobubbles and why this implies that nanobubbles are thermodynamically never stable. Therefore, understanding bubble stability becomes a consideration of the rate of bubble dissolution, so the dominant approach to understanding this is discussed. Bulk nanobubbles (or fine bubbles) are treated separately from surface nanobubbles as this reflects their separate histories. For each class of nanobubbles, we look at the early evidence for their existence, methods for the production and characterization of nanobubbles, evidence that they are indeed gaseous, or otherwise, and theories for their stability. We also look at applications of both surface and bulk nanobubbles.

Demangeat JL. Gas nanobubbles and aqueous nanostructures: The crucial role of dynamization. Homeopathy [Internet]. 2015;104(2):101–15. Available from: http://dx.doi.org/10.1016/j.homp.2015.02.001

Abstract

Nanobubbles (NBs) have been a subject of intensive research over the past decade. Their peculiar characteristics, including extremely low buoyancy, longevity, enhanced solubility of oxygen in water, zeta potentials and burst during collapse, have led to many applications in the industrial, biological and medical fields. NBs may form spontaneously from dissolved gas but the process is greatly enhanced by gas supersaturation and mechanical actions such as dynamization. Therefore, the formation of NBs during the preparation of homeopathic dilutions under atmospheric pressure cannot be ignored. I suggested in 2009 the involvement of NBs in nanometric superstructures revealed in high dilutions using NMR relaxation. These superstructures seemed to increase in size with dilution, well into the ultramolecular range (>12c). I report here new experiments that confirm the involvement of NBs and prove the crucial role of dynamization to create superstructures specific to the solute. A second dynamization was shown to enhance or regenerate these superstructures. I postulate that superstructures result from a nucleation process of NBs around the solute, with shells of highly organized water (with ions and silicates if any) which protect the solute against out-diffusion and behave as nucleation centres for further dilution steps. The sampling tip may play an active role by catching the superstructures and thus carry the encaged solute across the dilution range, possibly up to the ultramolecular range. The superstructures were not observed at low dilution, probably because of a destructuring of the solvent by the solute and/or of an inadequate gas/solute ratio.

Han MY, Kim MK, Ahn HJ. Effects of surface charge, micro-bubble size and particle size on removal efficiency of electro-flotation. Water Sci Technol. 2006;53(7):127–32.

Abstract

Flotation is a water treatment alternative to sedimentation, and uses small bubbles to remove low-density particles from potable water and wastewater. The effect of zeta potential, bubble size and particle size on removal efficiency of the electro-flotation process was investigated because previous model-simulations indicated that these attributes are critical for high collision efficiency between micro-bubbles and particles. Solutions containing Al3+ as the metal ion were subjected to various conditions. The zeta potentials of bubbles and particles were similar under identical conditions, and their charges were influenced by metal ion concentration and pH. Maximum removal efficiency was 98 and 12% in the presence and absence of flocculation, respectively. Removal efficiency was higher when particle size was similar to bubble size. These results agree with modelling simulations and indicate that collision efficiency is greater when the zeta potential of one is negative and that of the other is positive and when their sizes are similar.

Jin J, Feng Z, Yang F, Gu N. Bulk Nanobubbles Fabricated by Repeated Compression of Microbubbles. Langmuir. 2019;35(12):4238–45.

Abstract

Nanobubbles (NBs), given its extraordinary properties, have drawn keen attention in the field of nanotechnology worldwide. However, compared to that of surface NBs, generation of stable bulk NBs remains an arduous task with the prevailing method. In this study, we developed a pressure-driven method to prepare bulk NBs by repeatedly compressing sulfur hexafluoride (SF6) gas into water. The results show that NBs with a mean diameter of 240 ± 9 nm and a polydispersity index of 0.25 were successfully prepared. The generated NBs had a high negative zeta potential (-40 ± 2 mV) with stability of more than 48 h. Under the condition of 600 times repeated compression, the NB concentration could reach about 1.92 × 1010 bubbles/mL. Furthermore, we examine the possible formation mechanism involved in NB generation by virtue of optical microscopy and attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy. The microscopic results showed that microbubbles about 10-50 μm formed first and then decreased to be nanoscale-sized. A stronger hydrogen bond was detected by ATR-FTIR spectroscopy during the shrinking of microbubbles into NBs. It is speculated that the disappearance of microbubbles contributes to the formation of NBs, and the strong hydrogen bond at the gas-water interface prompts the stability of NBs. Therefore, repeated compression of the gas in aqueous solution could be a new method to prepare stable nanosized bubbles for wide applications in the future.

Li C, Li X, Xu M, Zhang H. Effect of ultrasonication on the flotation of fine graphite particles: Nanobubbles or not? Ultrason Sonochem. 2020;69(April).

Abstract

It has been reported that nanobubbles can be produced by ultrasonication. However, it remains unclear whether part of the contribution of ultrasonication on flotation performance can be attributed to the generation of nanobubbles. In this work, we systematically studied this point of ultrasonication by combining a series of techniques including flotation testing, AFM (atomic force microscope) measurement, and settling testing. AFM imaging showed that no surface nanobubbles were found at the HOPG-water interface before and after subjection to ultrasonication. Further, surface nanobubbles were generated with solution exchange before ultrasonciation and then they were subjected to ultrasonication. It was found that ultrasonication did not destroy the pre-existing surface nanobubbles at the HOPG (highly oriented pyrolytic graphite) -water interface. Settling tests and flotation tests indicate that ultrasonication has a negligible influence on the interaction between graphite particles and thus flotation performance. Nanobubbles were not one of the outcomes for ultrasonication.

Li M, Ma X, Eisener J, Pfeiffer P, Ohl CD, Sun C. How bulk nanobubbles are stable over a wide range of temperatures. J Colloid Interface Sci [Internet]. 2021;596:184–98. Available from: https://doi.org/10.1016/j.jcis.2021.03.064

Abstract

Hypothesis: Bulk nanobubbles are nanoscopic gaseous domains in an aqueous solution. Their surprising long-term stability remains controversial due to the widespread assumption that spherical bubbles cannot achieve stable equilibrium. To uncover the intrinsic mechanisms underlying stabilization, the thermodynamic behavior of nanobubbles in water over a wide range of temperatures is explored.

Experiments: Bulk nanobubbles with a typical radius of 50 - 200 nm are generated using acoustic cavitation. Increasing temperature significantly narrows the bubble-size distribution and their mean radius shrinks to a minimum of approx. 50 nm at 45 °C. For higher temperatures a slight increase is observed. The thermal induced shrinkage is reversible: upon cooling they return to the original state.

Findings: The observation can be explained with a charge-stabilization mechanism. The intricate balance of competing interactions between water self-ionization and mobility of ions on the surface gives rise to this non-monotonic dependency. Nanobubbles consequently undergo charge loss at lower temperatures and charge conservation at higher temperatures, corresponding to their shrinkage and slight expansion. With theoretical calculations, we further quantity the equilibrium properties of nanobubbles and their zeta potential under various initial conditions. The temperature-sensitive nature of bulk nanobubbles offers a vital step forward exploring and industrializing their stability.

Michailidi ED, Bomis G, Varoutoglou A, Kyzas GZ, Mitrikas G, Mitropoulos AC, et al. Bulk nanobubbles: Production and investigation of their formation/stability mechanism. J Colloid Interface Sci [Internet]. 2020;564:371–80. Available from: https://doi.org/10.1016/j.jcis.2019.12.093

Abstract

Nanobubbles (NBs) have attracted concentrated scientific attention due to their unique physicochemical properties and large number of potential applications. In this study, a novel nanobubble generator with low energy demand, operating continuously, is presented. Air and oxygen bulk nanobubbles (NBs@air and NBs@O2) with narrow size distribution and outstanding stability were prepared in water solution. The bulk NBs' behavior was evaluated taking into consideration the hydrodynamic diameter and ζ-potential as a function of processing time, gas type, pH value and NaCl concentration. According to the results the optimum processing time was 30 min, whereas the effect of water salinity was stronger in NBs@O2 than NBs@air. In order to investigate further the NBs properties, Electron Paramagnetic Resonance (EPR) spectroscopy was applied for quantitative analysis of free radicals following the spin trapping methodology. The mechanism of bulk NBs' generation and their extremely long-time stability can be attributed mainly to the hydrogen bonding interactions. The formation of a diffusion layer, by absorption of OH- due to electrostatic interaction, contributing to negative surface charge, whereas the interaction of ions with the surface hydroxylic groups provide the equilibrium between the protonation and deprotonation of water and finally the formation of a stable interface layer. A remarkable highlight of this work is the long-time stability of generated bulk NBs which is up to three months.

Nirmalkar N, Pacek AW, Barigou M. On the Existence and Stability of Bulk Nanobubbles. Langmuir. 2018;34(37):10964–73.

Abstract

Bulk nanobubbles are a novel type of nanoscale bubble system. Because of their extraordinary behavior, however, their existence is not widely accepted. In this paper, we shed light on the hypothesis that bulk nanobubbles do exist, they are filled with gas, and they survive for long periods of time, challenging present theories. An acoustic cavitation technique has been used to produce bulk nanobubbles in pure water in relatively large numbers approaching 109 bubble·mL-1 with a typical diameter of 100-120 nm. We provide multiple evidence that the nanoentities observed in suspension are nanobubbles given that they disappear after freezing and thawing of the suspensions, their nucleation rate depends strongly on the amount of air dissolved in water, and they gradually disappear over time. The bulk nanobubble suspensions were stable over periods of many months during which time the mean diameter remained unchanged, suggesting the absence of significant bubble coalescence, bubble breakage, or Ostwald ripening effects. Measurements suggest that these nanobubbles are negatively charged and their zeta potential does not vary over time. The presence of such a constant charge on the nanobubble surfaces is probably responsible for their stability. The effects of pH, salt, and surfactant addition on their colloidal stability are similar to those reported in the literature for solid nanoparticle suspensions, that is, nanobubbles are more stable in an alkaline medium than in an acidic one; the addition of salt to a nanobubble suspension drives the negative zeta potential toward zero, thus reducing the repulsive electrostatic forces between nanobubbles; and the addition of an anionic surfactant increases the magnitude of the negative zeta potential, thus improving nanobubble electrostatic stabilization.

Oh SH, Kim JM. Generation and Stability of Bulk Nanobubbles. Langmuir. 2017;33(15):3818–23.

Abstract

Recently, extremely small bubbles, referred to as nanobubbles, have drawn increased attention due to their novel properties and great potential for various applications. In this study, a novel method for the generation of bulk nanobubbles (BNBs) was introduced, and stability of fabricated BNBs was investigated. BNBs were created from CO2 gas with a mixing method; the chemical identity and phase state of these bubbles can be determined via infrared spectroscopy. The presence of BNBs was observed with a nanoparticle tracking analysis (NTA). The ATR-FTIR spectra of BNBs indicate that the BNBs were filled with CO2 gas. Furthermore, the BNB concentration and its ζ-potential were about 2.94 × 108 particles/mL and -20 mV, respectively (24 h after BNB generation with a mixing time of 120 min). This indicates the continued existence and stability of BNBs in water for an extended period of time.

Seddon JRT, Kooij ES, Poelsema B, Zandvliet HJW, Lohse D. Surface bubble nucleation stability. Phys Rev Lett. 2011;106(5):19–22.

Abstract

Recent research has revealed several different techniques for nanoscopic gas nucleation on submerged surfaces, with findings seemingly in contradiction with each other. In response to this, we have systematically investigated the occurrence of surface nanobubbles on a hydrophobized silicon substrate for various different liquid temperatures and gas concentrations, which we controlled independently. We found that nanobubbles occupy a distinct region of this parameter space, occurring for gas concentrations of approximately 100%-110%. Below the nanobubble region we did not detect any gaseous formations on the substrate, whereas micropancakes (micron wide, nanometer high gaseous

domains) were found at higher temperatures and gas concentrations. We moreover find that supersaturation of dissolved gases is not a requirement for nucleation of bubbles.

Skyba DM, Kaul S. Advances in microbubble technology. Coron Artery Dis. 2000;11(3):211–9.

Tan BH, An H, Ohl CD. Stability, Dynamics, and Tolerance to Undersaturation of Surface Nanobubbles. Phys Rev Lett [Internet]. 2019;122(13):134502. Available from: https://doi.org/10.1103/PhysRevLett.122.134502

Abstract

The theoretical understanding of surface nanobubbles-nanoscale gaseous domains on immersed substrates-revolves around two contrasting perspectives. One perspective, which considers gas transport in the nanobubbles' vicinity, explains numerous stability-related properties but systematically underestimates the dynamical response timescale by orders of magnitude. The other perspective, which considers gas transport as the bulk liquid equilibrates with the external environment, recovers the experimentally observed dynamical timescale but incorrectly predicts that nanobubbles progressively shrink until dissolution. We propose a model that couples both perspectives, which is capable of explaining the stability, dynamics, and unexpected tolerance of surface nanobubbles to undersaturated environments.

Tan BH, An H, Ohl CD. How Bulk Nanobubbles Might Survive. Phys Rev Lett [Internet]. 2020;124(13):134503. Available from: https://doi.org/10.1103/PhysRevLett.124.134503

Abstract

The existence of bulk nanobubbles has long been regarded with scepticism, due to the limitations of experimental techniques and the widespread assumption that spherical bubbles cannot achieve stable equilibrium. We develop a model for the stability of bulk nanobubbles based on the experimental observation that the zeta potential of spherical bubbles abruptly diverges from the planar value below 10 μm. Our calculations recover three persistently reported-but disputed-properties of bulk nanobubbles: that they stabilize at a typical radius of ∼100 nm, that this radius is bounded below 1 μm, and that it increases with ionic concentration.

Uchida T, Liu S, Enari M, Oshita S, Yamazaki K, Gohara K. Effect of NaCl on the lifetime of micro- and nanobubbles. Nanomaterials. 2016;6(2):1–10.

Abstract

Micro- and nanobubbles (MNBs) are potentially useful for industrial applications such as the purification of wastewater and the promotion of physiological activities of living organisms. To develop such applications, we should understand their properties and behavior, such as their lifetime and their number density in solution. In the present study, we observed oxygen MNBs distributed in an electrolyte (NaCl) solution using a transmission electron microscope to analyze samples made with the freeze-fracture replica method. We found that MNBs in a 100 mM NaCl solution remain for at least 1 week, but at higher concentrations decay more quickly. To better understand their lifetimes, we compared measurements of the solution's dissolved oxygen concentration and the ζ-potential of the MNBs. Our detailed observations of transmission electron microscopy (TEM) images allows us to conclude that low concentrations of NaCl stabilize MNBs due to the ion shielding effect. However, higher concentrations accelerate their disappearance by reducing the repulsive force between MNBs.

Zhang C, Li Y, Ma X, He W, Liu C, Liu Z. Functional micro/nanobubbles for ultrasound

Abstract

Chemically functionalized gas-filled bubbles with a versatile micro/nano-sized scale have witnessed a long history of developments and emerging applications in disease diagnosis and treatments. In combination with ultrasound and image-guidance, micro/nanobubbles have been endowed with the capabilities of biomedical imaging, drug delivery, gene transfection and disease-oriented therapy. As an external stimulus, ultrasound (US)-mediated targeting treatments have been achieving unprecedented efficiency. Nowadays, US is playing a crucial role in visualizing biological/pathological changes in lives as a reliable imaging technique and a powerful therapeutic tool. This review retrospects the history of ultrasound, the chemistry of functionalized agents and summarizes recent advancements of functional micro/nanobubbles as US contrast agents in preclinical and trans-clinical research. Latest ultrasound-based treatment modalities in association with functional micro/nanobubbles have been highlighted as their great potentials for disease precision therapy. It is believed that these state-of-the-art

micro/nanobubbles will become a booster for ultrasound medicine and visualizable guidance to serve future human healthcare in a more comprehensive and practical manner.

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	Nanoburbujas de ozono y su efecto bactericida en odontología
BASE DE DATOS	**PUBMED**
ALGORITMO FINAL	(((((((((((Ozone) OR (Tropospheric Ozone)) OR (Ozone, Tropospheric)) OR (Low Level Ozone)) OR (Level Ozone, Low)) OR (Ozone, Low Level)) OR (Ground Level Ozone)) OR (Level Ozone, Ground)) OR (Ozone, Ground Level)) AND (((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles)))) AND ((((((((((((((((((((((((((((((Physical and Chemical Properties) OR (Physical Phenomena)) OR (Phenomena, Physical)) OR (Physical Phenomenon)) OR (Phenomenon, Physical)) OR (Physical Concepts)) OR (Concept, Physical)) OR (Physical Concept)) OR (Physical Processes)) OR (Processes, Physical)) OR (Physical Process)) OR (Process, Physical)) OR (Electromagnetic Phenomena)) OR (Electromagnetic Phenomenas)) OR (Phenomena, Electromagnetic)) OR (Electromagnetic Phenomenon)) OR (Phenomenon, Electromagnetic)) OR (Electromagnetic Concepts)) OR (Concept, Electromagnetic)) OR (Concepts, Electromagnetic)) OR (Electromagnetic Concept)) OR (Electrical Phenomena)) OR (Phenomena, Electrical)) OR (Electrical Phenomenon)) OR (Phenomenon, Electrical)) OR (Electrical Concepts)) OR (Concept, Electrical)) OR (Concepts, Electrical)) OR (Electrical Concept)) OR (Electromagnetics)) AND (((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))))
artículos preseleccionados Referencia -estilo Vancouver y abstract	

Hayakumo S, Arakawa S, Mano Y, Izumi Y. Clinical and microbiological effects of ozone nano-bubble water irrigation as an adjunct to mechanical subgingival debridement in periodontitis patients in a randomized controlled trial. Clin Oral Investig. 2013;17(2):379–88.

Abstract

Aim: Ozone nano-bubble water (NBW3) seems to be suitable as an adjunct to periodontal treatment owing to its potent antimicrobial effects, high level of safety, and long storage stability. The aim of the present study was to evaluate the clinical and microbiological effects of NBW3 irrigation as an adjunct to subgingival debridement for periodontal treatment.

Methods: Twenty-two subjects were randomly assigned to one of the two treatment groups: full-mouth mechanical debridement with tap water (WATER) or full-mouth mechanical debridement with NBW3 (NBW3). Clinical examination was performed at baseline and 4 and 8 weeks after treatment. Microbiological examination was carried out just before and after treatment and at 1 and 8 weeks posttreatment.

Results: There were significant improvements in all clinical parameters after 4 weeks in both groups. The reduction in the probing pocket depth and the clinical attachment gain after 4 and 8 weeks in the NBW3 group were significantly greater than those in the WATER group. Moreover, only the NBW3 group showed statistically significant reductions in the mean total number of bacteria in subgingival plaque over the study period.

Conclusions: The present study suggests that subgingival irrigation with NBW3 may be a valuable adjunct to periodontal treatment.

Clinical relevance: This study verified the potential of new antimicrobial agent, MNW3, as an adjunct to periodontal treatment.

Achar JC, Nam G, Jung J, Klammler H, Mohamed MM. Microbubble ozonation of the antioxidant butylated hydroxytoluene: Degradation kinetics and toxicity reduction. Environ Res [Internet]. 2020;186(March):109496. Available from: https://doi.org/10.1016/j.envres.2020.109496

Abstract

Butylated hydroxytoluene (BHT) is recognized as a crucial pollutant in aquatic environments, but efforts to achieve its complete removal are without success. The aim of this study was to investigate the degradation efficiency of BHT in water using ozone microbubbles (OMB), coupled with toxicity change assessment at sub-lethal BHT concentrations (0.34, 0.45 and 0.90 μM) based on oxidative stress biomarkers in Daphnia magna. The efficiency of OMB on ozone gas mass transfer was assessed and the contribution of hydroxyl radicals (·OH) in the degradation of BHT was determined using p-chlorobenzoic acid (pCBA) probe compound and a ·OH radical scavenger (sodium carbonate, Na2CO3). The ozone gas mass transfer coefficient (kLa = 1.02 × 10-2 s-1) was much larger than the ozone self-decomposition rate (kd = 8 × 10-4 s-1) implying little influence of self-decomposing ozone in the volumetric ozone transfer during OMB generation. Generally, OMB improved ozone gas mass transfer (1.3-19-fold) relative to conventional ozone techniques, while indirect reaction of BHT with ·OH was dominant (82%) over the direct reaction with molecular ozone. Addition of 15, 25 and 35 mM Na2CO3 reduced BHT degradation by 30, 50 and 65%, respectively, indicating the significance of ·OH in the degradation of BHT. Increase in initial BHT concentration correspondingly reduced its removal rate by OMB possibly due to increase in metabolites produced during ozonation. Post BHT treatment exposure tests recorded significant ($p < 0.05$) reductions in oxidative stress (according to enzyme activities changes) in D. magna compared to pretreatment tests, demonstrating the effectiveness of OMB in detoxification of BHT. Overall, the results of the study indicate that OMB is extremely efficient in complete degradation of BHT in water and, consequently, significantly ($p < 0.05$) reducing its toxicity.

Chu LB, Xing XH, Yu AF, Zhou YN, Sun XL, Jurcik B. Enhanced ozonation of simulated dyestuff wastewater by microbubbles. Chemosphere. 2007;68(10):1854–60.

Abstract

The ozonation of synthetic wastewater containing azo dye, CI Reactive Black 5, was investigated using a microbubble generator and a conventional bubble contactor. The microbubble generator produced a milky and high intensity microbubble solution in which the bubbles had a mean diameter of less than 58 microm and a numerical density of more than 2.9 x 10(4) counts ml(-1) at a gas flow rate of less than 0.5 l min(-1). Compared with the bubble contactor, the total mass transfer coefficient was 1.8 times higher and the pseudo-first order rate constant was 3.2-3.6 times higher at the same initial dye concentration of 100 mg l(-1), 230 mg l(-1) and 530 mg l(-1) in the proposed microbubble system. The amount of total organic carbon removed per g of ozone consumed was about 1.3 times higher in the microbubble system than in the bubble contactor. The test using terephthalic acid as the chemical probe implied that more hydroxyl radicals were produced in the microbubble system, which contributed to the degradation of the dye molecules. The results suggested that in addition to the enhancement of mass transfer, microbubbles, which had higher inner pressure, could accelerate the formation of hydroxyl radicals and hence improve the oxidation of dye molecules.

Gao Y, Duan Y, Fan W, Guo T, Huo M, Yang W, et al. Intensifying ozonation treatment of municipal secondary effluent using a combination of microbubbles and ultraviolet irradiation. Environ Sci Pollut Res. 2019;26(21):21915–24.

Abstract

Ozonation treatment of municipal secondary effluent is complicated by the low solubility of ozone and inefficient production of hydroxyl free radicals from ozone decomposition. To resolve these problems, this study investigated methods for intensifying ozonation treatment, using a combination of microbubbles and ultraviolet (UV) irradiation (UV/MBO). The high efficiency of the method was illustrated by treating river water containing refractory components derived from secondary effluent in a wastewater treatment plant. The results showed that the ozone mass transfer coefficient in a microbubble system was an order of magnitude compared with a conventional macrobubble system at the initial stage. The amount of ·OH generated during the treatment was quantified using a fluorescent probe analysis. The amount of ·OH in the UV/MBO system was almost 2-6 times more than the amount found with conventional ozonation using macrobubbles (CO), CO with UV irradiation (UV/CO), and microbubble ozonation (MBO) units. The UV/MBO system achieved chemical oxygen demand (COD), UV254, and UV400 removal performance rates of up to 37.50%, 81.15%, and 94.74% respectively. These levels were 2-36% higher than those in other systems. The coupling UV/MBO treatment significantly reduced all five categories of substances according to EEM spectra and fluorescence regional integration. The distribution of fractions with different molecular weights (MW) was altered and the UV254 of MW (< 500 Da) increased by 15.8%. The biodegradability of the water was significantly improved, as indicated by the TOC/UV254. This is ascribed to the enhanced degradation of refractory organics in the water. The combination of the UV/microbubble technique with ozonation could provide an efficient approach for advanced wastewater treatment. Graphical abstract.

Ikeura H, Hamasaki S, Tamaki M. Effects of ozone microbubble treatment on removal of residual pesticides and quality of persimmon leaves. Food Chem [Internet]. 2013;138(1):366–71. Available from: http://dx.doi.org/10.1016/j.foodchem.2012.09.139

Jabesa A, Ghosh P. Removal of diethyl phthalate from water by ozone microbubbles in a pilot plant. J Environ Manage [Internet]. 2016;180:476–84. Available from: http://dx.doi.org/10.1016/j.jenvman.2016.05.072

Abstract

This study investigated the effects of ozone microbubble (OMCB) treatment on the removal of residual fenitrothion (FT) and benomyl pesticides from red and green persimmon leaves, and also the treatment effect on the leaf colours, physical properties and flavour. The continuous bubbling OMCB treatment was more effective than the non-bubbling OMCB treatments at reducing the FT and benomyl agricultural pesticide residues from both the red and green persimmon leaves. Moreover, the bubbling OMCB treatment had no effect on the colour and pulling strength of the leaves. These results indicate that the treatment by bubbling OMCB is an extremely effective method for removing the residues of FT and benomyl in persimmon leaves and has relatively little effect on leaf quality characteristics.

Jabesa A, Ghosh P. Removal of dimethyl phthalate from water by ozone microbubbles. Environ Technol (United Kingdom) [Internet]. 2017;38(16):2093–103. Available from: http://dx.doi.org/10.1080/09593330.2016.1246610

Abstract

This work investigates the removal of dimethyl phthalate (DMP) from water using ozone microbubbles in a pilot plant of 20 dm3 capacity. Experiments were performed under various reaction conditions to examine the effects of the initial concentration of DMP, pH of the medium, ozone generation rate, and the role of H_2O_2 on the removal of DMP. The DMP present in water was effectively removed by the ozone microbubbles. The removal was effective in neutral and alkaline media. Increase in the initial concentration of the target pollutant negatively affected its removal efficiency. The removal efficiency dramatically increased from 1% to 99% when the ozone generation rate was increased from 0.28 to 1.94 mg s-1 at pH 7. The total organic carbon measurements revealed that a complete mineralization of DMP was achieved within 1.8 ks at the high ozone feed rate. The use of t-butyl alcohol as the hydroxyl radical scavenger confirmed that the reaction between the target organic compound and ·OH radical dominated over its direct reaction with ozone. The reaction between DMP and ozone followed an overall second-order kinetics. The volumetric mass transfer coefficient of ozone in the reacting system and the enhancement factor increased with increasing initial concentration of DMP. Very low values of Hatta number were obtained at all initial concentrations of DMP and pH, which show that the mass transfer resistance was small.

Lee BH, Song WC, Kim HY, Kim JH. Enhanced separation of water quality parameters in the DAF (Dissolved Air Flotation) system using ozone. Water Sci Technol. 2007;56(10):149–55.

Abstract

Dissolved Air Flotation (DAF) has been used in water and wastewater treatment because it has an excellent separation capability. It was found that the separation capability of the DAF system could be even more enhanced by ozone. Ozone was applied as a substitute for air in the DAF system, so that the system was named as the DOF (Dissolved Ozone Flotation) system. Ozone not only enhances coagulation as is well known, but also provides larger micro-bubble volume because the solubility of ozone in water is much higher than that of air. Ozone enhanced the separation rate of SS by 13.6%, and turbidity by 21% in the DOF system compared to the DAF system. T-P was also removed 7.7% more in the DOF system. 41.5% of color and 7.4% of COD(Cr) were enhanced in their removal rate. Coliform and heterotrophic bacteria were removed 54% and 57.3% more in the DOF system. Separation capability of the DOF system was greatly enhanced for most of the water quality parameters because ozone provides strong oxidation power with large volume of micro-bubbles.

Li C, Yuan S, Jiang F, Xie Y, Guo Y, Yu H, et al. Degradation of fluopyram in water under ozone enhanced microbubbles: Kinetics, degradation products, reaction mechanism, and toxicity evaluation. Chemosphere [Internet]. 2020;258:127216. Available from: https://doi.org/10.1016/j.chemosphere.2020.127216

Abstract

The degradation of fluopyram (FLP) was investigated under ozone-microbubble treatment (OMBT). Kinetic models were established to study the influence of three treatments: ozonated water, microbubbles (MCB), and OMBT. FLP degraded completely in OMBT, and a clearance rate of 89.8-100% was achievable. Three direct transformation products [product 1 (F1), product 2 (F2), and product 3(F3)] were isolated and identified using a hybrid ion trap-orbitrap mass spectrometer. Moreover, a transformation theory of FLP degradation was developed according to targeted fragmentation, accurate mass measurements, and degradation profiles. These analyses showed that the products originated from a series of chemical reactions involving dechlorination, hydroxyl substitution, cleavage and oxidation, and were further confirmed based on molecular electrostatic potential and molecular orbital theory. In addition, the stability and toxicity of FLP and its transformation products were tested using the Toxicity Estimation Software Tool (T.E.S.T.) and the Ecological Structure Activity Relationships (ECOSAR) program. Products F1, F2 and F3 were found to be toxic substances, but their toxicity to aquatic organisms was lower than that of FLP. However, they were more toxic to rats than FLP, and their physicochemical properties were more stable. Overall, OMBT is a highly effective method for FLP removal during wastewater treatment.

Qadafi M, Notodarmojo S, Zevi Y. Effects of microbubble pre-ozonation time and pH on trihalomethanes and haloacetic acids formation in pilot-scale tropical peat water treatments for drinking water purposes. Sci Total Environ. 2020;747.

Abstract

The high concentrations of dissolved organic matter (DOM), chloride, and bromide in tropical peat water have a significant impact on the formation of carcinogenic disinfection by-products (DBPs) such as trihalomethanes (THMs) and haloacetic acids (HAAs), especially during the chlorination process. Therefore, other pretreatment methods to effectively remove these harmful substances in the water during treatment are needed. The aim of this study was to determine the effects of microbubble pre-ozonation pH on the reduction of THM4 and HAA5 formed during the peat water treatment process and to determine the best conditions for microbubble pre-ozonation to reduce the formation of these two classes of DBPs. The microbubble pre-ozonation was conducted at a pH of 5.5, 7, and 8.5. Furthermore, the primary treatments applied after this pretreatment were coagulation and activated carbon adsorption before post-chlorine disinfection. The coagulation process using aluminum sulfate and activated carbon adsorption succeeded in reducing the formation of THM4 after chlorination, to a level below USEPA standards, but the concentration of HAA5 was still high. However, the use of microbubble pre-ozonation significantly reduced the formation of both classes of compounds during the chlorination process of the peat water. Also, the concentration of THM4 increased during the pre-ozonation process in all pH conditions, but HAA5 decreased except in alkaline state. Furthermore, the ideal conditions for microbubble pre-ozonation on peat water were at pH 7 (neutral) after 30 min, with the total THM4 concentration at 33.73 ± 0.40 μg/L, and that of HAA5 at 49.89 ± 0.09 μg/L, falling below the USEPA standard.

Tasaki T, Wada T, Fujimoto K, Kai S, Ohe K, Oshima T, et al. Degradation of methyl orange using short-wavelength UV irradiation with oxygen microbubbles. J Hazard Mater. 2009;162(2–3):1103–10.

Abstract

A novel wastewater treatment technique using 8 W low-pressure mercury lamps in the presence of uniform-sized microbubbles (diameter = 5.79 microm) was investigated for the decomposition of methyl orange as a model compound in aqueous solution. Photodegradation experiments were conducted with a BLB black light blue lamp (365 nm), a UV-C germicidal lamp (254 nm) and an ozone lamp (185 nm+254 nm) both with and without oxygen microbubbles. The results show that the oxygen microbubbles accelerated the decolorization rate of methyl orange under 185+254 nm irradiation. In contrast, the microbubbles under 365 and 254 nm irradiation were unaffected on the decolorization of methyl orange. It was found that the pseudo-zero order decolorization reaction constant in microbubble system is 2.1 times higher than that in conventional large bubble system. Total organic carbon (TOC) reduction rate of methyl orange was greatly enhanced by oxygen microbubble under 185+254 nm irradiation, however, TOC reduction rate by nitrogen microbubble was much slower than that with 185+254 nm irradiation only. Possible reaction mechanisms for the decolorization and mineralization of methyl orange both with oxygen and nitrogen microbubbles were proposed in this study.

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	**Perspectivas**
BASE DE DATOS	**PUBMED**
ALGORITMO FINAL	((((((((rns60) OR (nanobubbles)) OR (nbw3)) OR (ultrafine bubbles)) OR (Taylor-Couette-Poiseuille)) OR (Charge-stabilized nanobubbles)) OR (microbubbles))) AND ((((((((Periodontal Diseases) OR (Disease, Periodontal)) OR (Disease, Periodonta)) OR (Diseases, Periodontal)) OR (Periodontal Disease)) OR (Parodontosis)) OR (Parodontoses)) OR (Pyorrhea Alveolaris))
artículos preseleccionados Referencia -estilo Vancouver y abstract	

Chen R, Chiba M, Mori S, Fukumoto M, Kodama T. Periodontal gene transfer by ultrasound and nano/ microbubbles. J Dent Res. 2009;88(11):1008–13.

Abstract

A non-viral gene delivery approach with nano/microbubbles and ultrasound offers opportunities for targeting soft tissues for gene therapy. The periodontium is a complex structure comprised of hard (cementum, alveolar bone) and soft tissues (periodontal ligament, gingivae). We hypothesized that our established gene delivery method would allow the periodontal tissue to be targeted for transfection for gene therapy. Expression kinetics and sites of transfection sites with this approach were investigated in rat periodontal tissue. Bioluminescence imaging revealed that transient gene expression was induced at day 1 posttransfection, while confocal microscopy showed that gene expression was localized in the muscle cells of gingival tissues. These findings indicate that regular transfection with this approach results in high gene expression, facilitating gene therapy for periodontal disease involving alveolar bone resorption.

Hayakumo S, Arakawa S, Mano Y, Izumi Y. Clinical and microbiological effects of ozone nano-bubble water irrigation as an adjunct to mechanical subgingival debridement in periodontitis patients in a randomized controlled trial. Clin Oral Investig. 2013;17(2):379–88.

Abstract

Aim: Ozone nano-bubble water (NBW3) seems to be suitable as an adjunct to periodontal treatment owing to its potent antimicrobial effects, high level of safety, and long storage stability. The aim of the present study was to evaluate the clinical and microbiological effects of NBW3 irrigation as an adjunct to subgingival debridement for periodontal treatment.

Methods: Twenty-two subjects were randomly assigned to one of the two treatment groups: full-mouth mechanical debridement with tap water (WATER) or full-mouth mechanical debridement with NBW3 (NBW3). Clinical examination was performed at baseline and 4 and 8 weeks after treatment. Microbiological examination was carried out just before and after treatment and at 1 and 8 weeks posttreatment.

Results: There were significant improvements in all clinical parameters after 4 weeks in both groups. The reduction in the probing pocket depth and the clinical attachment gain after 4 and 8 weeks in the NBW3 group were significantly greater than those in the WATER group. Moreover, only the NBW3 group showed statistically significant reductions in the mean total number of bacteria in subgingival plaque over the study period.

Conclusions: The present study suggests that subgingival irrigation with NBW3 may be a valuable adjunct to periodontal treatment.

Clinical relevance: This study verified the potential of new antimicrobial agent, MNW3, as an adjunct to periodontal treatment.

Iwanaga K, Tominaga K, Yamamoto K, Habu M, Maeda H, Akifusa S, et al. Local delivery system of cytotoxic agents to tumors by focused sonoporation. Cancer Gene Ther. 2007;14(4):354–63.

Abstract

Recently, ultrasound-targeting microbubble destruction has been employed in molecular gene therapy, and a new potent nonviral gene transfer method known as 'sonoporation' has been developed. We investigated the efficiency of sonoporation toward growth inhibition of human gingival squamous carcinoma cell line, Ca9-22, in vitro and in vivo. The cytotoxicity of bleomycin (BLM) was investigated using flow-cytometric analysis and Hoechst's staining in vitro assay systems. We found that the delivery of BLM by sonoporation induced cytotoxic effect toward Ca9-22 cells in vitro. Our in vivo results showed that tumors nearly disappeared in Ca9-22 cell-implanted nude KSN/slc mice treated with a low dose of BLM followed by sonoporation during the 4-week experimental period. Histological analysis revealed that the cytotoxic effect was mainly apoptosis. We previously reported that the cytolethal distending toxin B (cdtB) from Actinobacillus actinomycetemcomitans, a periodontopathic bacterium, is responsible for cell cycle arrest and apoptosis in vitro. Thus, we used sonoporation to transfect a cdtB-expressing plasmid into Ca9-22 cells and examined cell viability in vitro and in vivo. We found that an administration of cdtB-expressing plasmid followed by sonoporation-induced marked growth inhibition of Ca9-22 cells and apoptotic cells were also observed in vitro and in vivo. These findings suggest that local administration of cytotoxic agents with sonoporation is a useful method for molecular cancer therapy.

Leewananthawet A, Arakawa S, Okano T, Daitoku Kinoshita R, Ashida H, Izumi Y, et al. Ozone ultrafine bubble water induces the cellular signaling involved in oxidative stress responses in human periodontal ligament fibroblasts. Sci Technol Adv Mater [Internet]. 2019;20(1):589–98. Available from: https://doi.org/10.1080/14686996.2019.1614980

Abstract

Periodontitis is a chronic inflammatory disease caused by oral microorganisms in the subgingival biofilm. Stable aqueous ozone ultrafine bubble water (OUFBW) has recently begun to be used as an antiseptic in the treatment of periodontitis. The effectiveness of OUFBW is thought to depend on the bactericidal actions of dissolved ozone exerted via its oxidizing effect. On the other hand, the effects of ozone on the periodontal tissues are largely unknown. In this paper we examined the cellular responses after OUFBW treatment. Human primary periodontal ligament fibroblasts (hPDLFs) or Ca9-22 human gingival epithelial cells were treated with OUFBW or UV-inactivated OUFBW. The production of reactive oxygen species (ROS), the activation of mitogen-activated protein kinase (MAPK) and the nuclear factor-kappa B (NF-κB) activation were analyzed. The transcript profiles of hPDLFs after OUFBW treatment were also analyzed by RNA sequencing (RNA-seq). Our results showed that OUFBW induces oxidative stress by generating ROS, which, in turn, activated the MAPK pathway. OUFBW triggered activation of c-Fos, a major component of the transcription factor activator protein 1 (AP-1), and also nuclear factor erythroid 2 (NF-E2)-related factor 2 (Nrf2), which possessed a high sensitivity to oxidative stress. The results of RNA-seq analysis revealed that the numerous genes involved in oxidative stress responses or MAPK signaling pathway were up-regulated after OUFBW treatment. Investigation of the signaling pathways activated by OUFBW highlights another aspect of the biological roles of OUFBW, in addition to its bactericidal activity, in the treatment of periodontitis.

Lin PJ. Study on oral hygiene by nanobubbles from high-density nozzle. J Appl Biomater Funct Mater. 2020;18(129).

Abstract

An experiment was performed on oral bacteria removal using the design variables, which included the three-segment rotor speed of the testing device and three types of stainless steel meshes (with different layers). The overall hygienic results showed an effect of up to 95% bacteria removal, and some combinations had 100% hygienic effect. The study proposed that the use of nanobubble generated by a high-density stainless-steel mesh-manufactured nozzle removes dental bacteria. In addition, the device could also be used for auxiliary oral hygiene to decrease the frequency of future medical visits due to periodontal diseases or to enable the device to assist patients with severe periodontal disease more conveniently for oral hygiene.

Lin PJ, Chuang MC, Chang SC. Efficacy of using oxygen microbubble device for facultative anaerobe removal. IET Nanobiotechnology. 2018;12(7):973–80.

Abstract

Patients with serious gingivitis or periodontal diseases suffer from receding gums. Brushing teeth with a toothbrush may result in bleeding gums and new wounds, which increases the difficulty of removing facultative anaerobes from gum pockets, to decrease the damage inflicted on gums, this study proposed a cleaning device that can generate and emit oxygen microbubbles for eliminating facultative anaerobes in the mouth cavity. In this study, the authors conducted simulations with a denture to investigate the efficacy of using this method to remove facultative anaerobes. In this research for the optimal device design, several variables were manipulated including rotation speeds of the bubble generator, different nozzle diameters, and different numbers of nozzle holes. The results revealed that the device is effective in removing facultative anaerobes; moreover, of all design variables, the number of nozzle holes was the factor having the largest effect on anaerobe removal, as it influenced the flow volume and oxygen content of the discharge: the greater the number of nozzles, the greater the flow volume, oxygen content, and efficacy of anaerobe removal.

Vasiliu S, Racovita S, Gugoasa IA, Lungan MA, Popa M, Desbrieres J. The benefits of smart nanoparticles in dental applications. Int J Mol Sci. 2021;22(5):1–24.

Abstract

Dentistry, as a branch of medicine, has undergone continuous evolution over time. The scientific world has focused its attention on the development of new methods and materials with improved properties that meet the needs of patients. For this purpose, the replacement of so-called "passive" dental materials that do not interact with the oral environment with "smart/intelligent" materials that have the capability to change their shape, color, or size in response to an externally stimulus, such as the temperature, pH, light, moisture, stress, electric or magnetic fields, and chemical compounds, has received much attention in recent years. A strong trend in dental applications is to apply nanotechnology and smart nanomaterials such as nanoclays, nanofibers, nanocomposites, nanobubbles, nanocapsules, solid-lipid nanoparticles, nanospheres, metallic nanoparticles, nanotubes, and nanocrystals. Among the nanomaterials, the smart nanoparticles present several advantages compared to other materials, creating the possibility to use them in various dental applications, including preventive dentistry, endodontics, restoration, and periodontal diseases. This review is focused on the recent developments and dental applications (drug delivery systems and restoration materials) of smart nanoparticles.

Yamaguchi H, Ishida Y, Hosomichi J, Suzuki JI, Hatano K, Usumi-Fujita R, et al. Ultrasound microbubble-mediated transfection of NF-κB decoy oligodeoxynucleotide into gingival tissues inhibits periodontitis in rats in vivo. PLoS One. 2017;12(11):1–15.

Abstract

Periodontitis is a chronic infectious disease for which the fundamental treatment is to reduce the load of subgingival pathogenic bacteria by debridement. However, previous investigators attempted to implement a nuclear factor kappa B (NF-κB) decoy oligodeoxynucleotide (ODN) as a suppressor of periodontitis progression. Although we recently reported the effectiveness of the ultrasound-microbubble method as a tool for transfecting the NF-κB decoy ODN into healthy rodent gingival tissue, this technique has not yet been applied to the pathological gingiva of periodontitis animal models. Therefore, the aim of this study was to investigate the effectiveness of the technique in transfecting the NF-κB decoy ODN into rats with ligature-induced periodontitis. Micro computed tomography (micro-CT) analysis demonstrated a significant reduction in alveolar bone loss following treatment with the NF-κB decoy ODN in the experimental group. RT-PCR showed that NF-κB decoy ODN treatment resulted in significantly reduced expression of inflammatory cytokine transcripts within rat gingival tissues. Thus, we established a transcutaneous transfection model of NF-κB decoy ODN treatment of periodontal tissues using the ultrasound-microbubble technique. Our findings suggest that the NF-κB decoy ODN could be used as a significant suppressor of gingival inflammation and periodontal disease progression.

Tablas base de datos: Google Scholar

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	La necesidad de buscar alternativas antimicrobianas en odontología.
BASE DE DATOS	Google Schoolar
artículos preseleccionados Referencia -estilo Vancouver y abstract	

Ammons M. Anti-Biofilm Strategies and the Need for Innovations in Wound Care. Recent Pat Antiinfect Drug Discov. 2009;5(1):10–7.

Abstract: With an aging and obese population, chronic wounds such as diabetic ulcers, pressure ulcers, and venous leg ulcers are of an increasingly relevant medical concern in the developed world. Identification of bacterial biofilm contamination as a major contributor to non-healing wounds demands biofilm-targeted strategies to treat chronic wounds. While the current standard of care has proven marginally effective, there are components of standard care that should remain part of the wound treatment regime including systemic and topical antibiotics, antiseptics, and physical debridement of biofilm and devitalized tissue. Emerging anti-biofilm strategies include novel, non-invasive means of physical debridement, chemical agent strategies, and biological agent strategies. While aging and obesity will continue to be major burdens to wound care, the emergence of wounds associated with war require investigation and biotechnology development to address biofilm strategies that manage multi-drug resistant bacteria contaminating the chronic wound. The article presents some of the recent patents related to anti-biofilm strategy in wound care.

Marston HD, Dixon DM, Knisely JM, Palmore TN, Fauci AS. Antimicrobial resistance. JAMA - J Am Med Assoc. 2016;316(11):1193–204.

ABSTRACT

IMPORTANCE The development of antibiotics is considered among the most important advances of modern science. Antibiotics have saved millions of lives. However, antimicrobial resistance (AMR) threatens this progress and presents significant risks to human health.

OBJECTIVE To identify factors associated with AMR, the current epidemiology of important resistant organisms, and possible solutions to the AMR problem.

DATA SOURCES, STUDY SELECTION, AND DATA SYNTHESIS PubMed (2000-2016), NIH REPORTER, and ClinicalTrials.gov databases were searched for articles and entries related to AMR, focusing on epidemiology, clinical effects of AMR, discovery of novel agents to treat AMR bacterial infections, and nonpharmacological strategies to eliminate or modify AMR bacteria. In addition to articles and entries found in these databases, selected health policy reports and public health guidance documents were reviewed. Of 217 articles, databases, and reports identified, 103 were selected for review.

RESULTS The increase in AMR has been driven by a diverse set of factors, including inappropriate antibiotic prescribing and sales, use of antibiotics outside of the health care sector, and genetic factors intrinsic to bacteria. The problem has been exacerbated by inadequate economic incentives for pharmaceutical development of new antimicrobial agents. A range of specific AMR concerns, including carbapenem- and colistin-resistant gram-negative organisms, pose a clinical challenge. Alternative approaches to address the AMR threat include new methods of antibacterial drug identification and strategies that neutralize virulence factors.

CONCLUSIONS AND RELEVANCE Antimicrobial resistance poses significant challenges for current clinical care. Modified use of antimicrobial agents and public health interventions, coupled with novel antimicrobial strategies, may help mitigate the effect of multidrug-resistant organisms in the future

Matthews L, Kanwar RK, Zhou S, Punj V, Kanwar JR. Applications of nanomedicine in antibacterial medical therapeutics and diagnostics. Open Trop Med J. 2010;3(1):1–9.

Abstract: The need for new and effective/efficient antibacterial therapeutics and diagnostics is necessary if we want to be able to maintain and improve the protection against pathogenic bacteria. Bacteria are becoming increasingly resistant to traditionally used antibiotics and as a result are a major health concern. The number of deaths and hospitalizations due to bacteria is increasing. Current methods of bacterial diagnostics are inefficient as they lack speed and ultra sensitivity and cannot be performed on site. This is where nanomedicine is playing a vital role. The discovery of new and innovative materials through the improvement in fabrication techniques has seen the establishment of an influx of novel antibacterial therapeutics and diagnostics. The goal of this review is to highlight the research that has been done through the implementation of nanomaterials and nanotechnologies for antibacterial medical therapeutic and diagnostic.

Marsh PD. Dental plaque as a microbial biofilm. Caries Res. 2004;38(3):204–11.

Abstract: New technologies have provided novel insights into how dental plaque functions as a biofilm. Confocal microscopy has confirmed that plaque has an open architecture similar to other biofilms, with channels and voids. Gradients develop in areas of dense biomass over short distances in key parameters that influence microbial growth and distribution. Bacteria exhibit an altered pattern of gene expression either as a direct result of being on a surface or indirectly as a response to the local environmental heterogeneity within the biofilm. Bacteria communicate via small diffusible signalling molecules (e.g. competence-stimulating peptide, CSP; autoinducer 2); CSP induces both genetic competence and acid tolerance in recipient sessile cells. Thus, rates of gene transfer increase in biofilm communities, and this is one of several mechanisms (others include: diffusion-reaction, neutralization/inactivation, slow growth rates, novel phenotype) that contribute to the increased antimicrobial resistance exhibited by bacteria in biofilms. Oral bacteria in plaque do not exist as independent entities but function as a co-ordinated, spatially organized and fully metabolically integrated microbial community, the properties of which are greater than the sum of the component species. A greater understanding of the significance of dental plaque as a mixed culture biofilm will lead to novel control strategies.

Naskar A, Kim KS. Nanomaterials as delivery vehicles and components of new strategies to combat bacterial infections: Advantages and limitations. Microorganisms. 2019;7(9).

Abstract: Life-threatening bacterial infections have been well-controlled by antibiotic therapies and this approach has greatly improved the health and lifespan of human beings. However, the rapid and worldwide emergence of multidrug resistant (MDR) bacteria has forced researchers to find alternative treatments for MDR infections as MDR bacteria can sometimes resist all the present day antibiotic therapies. In this respect, nanomaterials have emerged as innovative antimicrobial agents that can be a potential solution against MDR bacteria. The present review discusses the advantages of nanomaterials as potential medical means and carriers of antibacterial activity, the types of nanomaterials used for antibacterial agents, strategies to tackle toxicity of nanomaterials for clinical applications, and limitations which need extensive studies to overcome. The current progress of using different types of nanomaterials, including new emerging strategies for the single purpose of combating bacterial infections, is also discussed in detail.

Giau V Van, An SSA, Hulme J. Recent advances in the treatment of pathogenic infections using antibiotics and nano-drug delivery vehicles. Drug Des Devel Ther. 2019;13:327–43.

Abstract: The worldwide misuse of antibiotics and the subsequent rise of multidrug-resistant pathogenic bacteria have prompted a paradigm shift in the established view of antibiotic and bacterial–human relations. The clinical failures of conventional antibiotic therapies are associated with lengthy detection methods, poor penetration at infection sites, disruption of indigenous microflora and high potential for mutational resistance. One of the most promising strategies to improve the efficacy of antibiotics is to complex them with micro or nano delivery materials. Such materials/vehicles can shield antibiotics from enzyme deactivation, increasing the therapeutic effectiveness of the drug. Alternatively, drug-free nanomaterials that do not kill the pathogen but target virulent factors such as adhesins, toxins, or secretory systems can be used to minimize resistance and infection severity. The main objective of this review is to examine the potential of the aforementioned materials in the detection and treatment of antibiotic-resistant pathogenic organisms.

Rios AC, Moutinho CG, Pinto FC, Del Fiol FS, Jozala A, Chaud M V., et al. Alternatives to overcoming bacterial resistances: State-of-the-art. Microbiol Res [Internet]. 2016;191:51–80. Available from: http://dx.doi.org/10.1016/j.micres.2016.04.008

ABSTRACT: Worldwide, bacterial resistance to chemical antibiotics has reached such a high level that endangers public health. Presently, the adoption of alternative strategies that promote the elimination of resistant microbial strains from the environment is of utmost importance. This review discusses and analyses several (potential) alternative strategies to current chemical antibiotics. Bacteriophage (or phage) therapy, although not new, makes use of strictly lytic phage particles as an alternative, or a complement, in the antimicrobial treatment of bacterial infections. It is being rediscovered as a safe method, because these biological entities devoid of any metabolic machinery do not possess any affinity whatsoever to eukaryotic cells. Lysin therapy is also recognized as an innovative antimicrobial therapeutic option, since the topical administration of preparations containing purified recombinant lysins with amounts in the order of nanograms, in infections caused by Gram-positive bacteria, demonstrated a high therapeutic potential by causing immediate lysis of the target bacterial cells. Additionally, this therapy exhibits the potential to act synergistically when combined with certain chemical antibiotics already available on the market. Another potential alternative antimicrobial therapy is based on the use of antimicrobial peptides (AMPs), amphiphilic polypeptides that cause disruption of the bacterial membrane and can be used in the treatment of bacterial, fungal and viral infections, in the prevention of biofilm formation, and as antitumoral agents. Interestingly, bacteriocins are a common strategy of bacterial defense against other bacterial agents, eliminating the potential opponents of the former and increasing the number of available nutrients in the environment for their own growth. They can be applied in the food industry as biopreservatives and as probiotics, and also in fighting multi-resistant bacterial strains. The use of antibacterial antibodies promises to be extremely safe and effective. Additionally, vaccination emerges as one of the most promising preventive strategies. All these will be tackled in detail in this review paper

Kanwar I, Sah AK, Suresh PK. Biofilm-mediated Antibiotic-resistant Oral Bacterial Infections: Mechanism and Combat Strategies. Curr Pharm Des. 2017;23(14):2084–95.

Abstract: Oral diseases like dental caries and periodontal disease are directly associated with the capability of bacteria to form biofilm. Periodontal diseases have been associated to anaerobic Gram-negative bacteria forming a subgingival plaque (Porphyromonas gingivalis, Actinobacillus, Prevotella and Fusobacterium). Biofilm is a complex bacterial community that is highly resistant to antibiotics and human immunity. Biofilm communities are the causative agents of biological developments such as dental caries, periodontitis, peri-implantitis and causing periodontal tissue breakdown. The review recapitulates the latest advancements in treatment of clinical biofilm infections and scientific investigations, while these novel anti-biofilm strategies are still in nascent phases of development, efforts dedicated to these technologies could ultimately lead to anti-biofilm therapies that are superior to the current antibiotic treatment. This paper provides a review of the literature focusing on the studies on biofilm in the oral cavity, formation of dental plaque biofilm, drug resistance of bacterial biofilm and the antibiofilm approaches as biofilm preventive agents in dentistry, and their mechanism of biofilm inhibiti.

Fatima F, Siddiqui S, Khan WA. Nanoparticles as Novel Emerging Therapeutic Antibacterial Agents in the Antibiotics Resistant Era. Biol Trace Elem Res. 2020;

Abstract: Microorganisms are highly resistant to the antibiotics that are commonly used and thus are becoming serious public health problem. There is an urgent need for new approaches to monitor microbial behavior, and hence, nanomaterial can be a very promising solution. Nanotechnology has led to generation of novel antimicrobial agents such as gold, silver, zinc, copper, poly-£- lysine, iron, and chitosan which have shown remarkable potential, demonstrating their applicability as proficient antibiotic agents against various pathogenic bacterial species. The antimicrobial nanoproduct physically kills the organism's cell membranes that prevent the production of drug-resistant microorganisms. These nanosized particles can also be used as diagnostic agents, targeted drug delivery vehicle, noninvasive imaging technologies, and in vivo visual monitoring of tumors angiogenesis. These nanomaterials provide a promising platform for diagnostics, prognostic, drug delivery, and treatment of diseases by means of nanoengineered products/devices. This owes to their small size, prolonged antimicrobial efficacy with insignificant toxicity creating less environmental hazard or toxicity. Scientists address several problems such as health, bioethical problems, toxicity risks, physiological, and pharmaceutical concerns related with the usage of NPs as antimicrobial agents as current research lack adequate data and information on the safe use of certain tools and materials.

Davies D. Understanding biofilm resistance to antibacterial agents. Nat Rev Drug Discov. 2003;2(2):114–22.

Abstract: According to a public announcement by the US National Institutes of Health, ''Biofilms are medically important, accounting for over 80% of microbial infections in the body''. Yet bacterial biofilms remain poorly understood and strategies for their control remain underdeveloped. Standard antimicrobial treatments typically fail to eradicate biofilms, which can result in chronic infection and the need for surgical removal of afflicted areas. The need to create effective therapies to counter biofilm infections presents one of the most pressing challenges in antibacterial drug development. In this article, the mechanisms that underlie biofilm resistance to antimicrobial chemotherapy will be examined, with particular attention being given to potential avenues for the effective treatment of biofilms.

Rello J, Bunsow E, Perez A. What if there were no new antibiotics? A look at alternatives. Expert Rev Clin Pharmacol [Internet]. 2016;9(12):1547–55. Available from: http://dx.doi.org/10.1080/17512433.2016.1241141

Abstract

Introduction: bacterial resistance to antibiotics is increasing worldwide, due to the emergence of multidrug-resistant strains. With this panorama, there is a serious danger that we may be entering the "post-antibiotic era". Areas covered: we assess why so few new classes of antibiotics have been developed in the past years and discuss a variety of treatments that may be able to replace antimicrobials: monoclonal antibodies, bacteriophages, stem cells and anti-virulence agents such as liposomes.

Expert Commentary: there are a series of economic, scientific-research and regulatory reasons for the scarcity of new antimicrobials. New approaches are needed to combat infections. Innovative strategies like Eco-Evo drugs and innovative delivery methods such as aerosol or nanoparticle administration require a new management paradigm, in combination with rapid molecular diagnostic tests. Biopharma, clinical researchers, regulatory agencies, governments and investors must work together in the attempts to achieve effective treatment for infections caused by MDR organisms.

Huang R, Li M, Gregory RL. Bacterial interactions in dental biofilm. Virulence. 2011;2(5):435–44.

Abstract: Biofilms are masses of microorganisms that bind to and multiply on a solid surface, typically with a fluid bathing the microbes. The microorganisms that are not attached but are free-floating in an aqueous environment are termed planktonic cells. Traditionally, microbiology research has addressed results from planktonic bacterial cells. However, many recent studies have indicated that biofilms are the preferred form of growth of most microbes and particularly those of a pathogenic nature. Biofilms on animal hosts have significantly increased resistance to various antimicrobials compared to planktonic cells. These microbial communities form microcolonies that interact with each other using very sophisticated communication methods (i.e., quorum-sensing). The development of unique microbiological tools to detect and assess the various biofilms around us is a tremendously important focus of research in many laboratories. In the present review, we discuss the major biofilm mechanisms and the interactions among oral bacteria.

Kouidhi B, Al Qurashi YMA, Chaieb K. Drug resistance of bacterial dental biofilm and the potential use of natural compounds as alternative for prevention and treatment. Microb Pathog [Internet]. 2015;80:39–49. Available from: http://dx.doi.org/10.1016/j.micpath.2015.02.007

Abstract: Oral diseases, such as dental caries and periodontal disease are directly linked with the ability of bacteria to form biofilm. The development of dental caries involves acidogenic and aciduric Gram-positive bacteria colonizing the supragingival biofilm (Streptococcus, Lactobacillus and Actinomycetes). Periodontal diseases have been linked to anaerobic Gram-negative bacteria forming a subgingival plaque (Porphyromonas gingivalis, Actinobacillus, Prevotella and Fusobacterium). Cells embedded in biofilm are up to 1000- fold more resistant to antibiotics compared to their planctonic ones. Several mechanisms have been proposed to explain biofilms drug resistance. Given the increased bacterial resistance to antibiotics currently used in dentistry, a great importance is given to natural compounds for the prevention of oral bacterial growth, adhesion and colonization. Over the past decade, interest in drugs derived from medicinal plants has markedly increased. It has been well documented that medicinal plants and natural compounds confer considerable antibacterial activity against various microorganisms including cariogenic and periodontal pathogens. This paper provides a review of the literature focusing on the studies on (i) biofilm in the oral cavity, (ii) drug resistance of bacterial biofilm and (iii) the potential use of plant extracts, essential oils and natural compounds as biofilm preventive agents in dentistry, involving their origin and their mechanism of biofilm inhibition.

Kuang X, Chen V, Xu X. Novel Approaches to the Control of Oral Microbial Biofilms. Biomed Res Int. 2018;2018.

ABSTRACT

Efective management of bioflm-related oral infectious diseases is a global challenge. Oral bioflm presents increased resistance to antimicrobial agents and elevated virulence compared with planktonic bacteria. Antimicrobial agents, such as chlorhexidine, have proven efective in the disruption/inhibition of oral bioflm. However, the challenge of precisely and continuously eliminating the specifc pathogens without disturbing the microbial ecology still exists, which is a major factor in determining the virulence of a multispecies microbial consortium and the consequent development of oral infectious diseases.Terefore, several novel approaches are being developed to inhibit bioflm virulence without necessarily inducing microbial dysbiosis of the oral cavity. Nanoparticles, such as pH-responsive enzyme-mimic nanoparticles, have been developed to specifcally target the acidic niches within the oral bioflm where tooth demineralization readily occurs, in efect controlling dental caries. Quaternary ammonium salts (QAS) such as dimethylaminododecyl methacrylate (DMADDM), when incorporated into dental adhesives or resin composite, have also shown excellent and durable antimicrobial activity and thus could efectively inhibit the occurrence of secondary caries. In addition, custom-designed small molecules, natural products and their derivatives, as well as basic amino acids such as arginine, have demonstrated ecological efects by modulating the virulence of the oral bioflm without universally killing the commensal bacteria, indicating a promising approach to the management of oral infectious diseases such as dental caries and periodontal diseases. Tis article aims to introduce these novel approaches that have shown potential in the control of oral bioflm. Tese methods may be utilized in the near future to efectively promote the clinical management of oral infectious diseases and thus beneft oral health

Aimetti M. Nonsurgical periodontal treatment. Int J Esthet Dent. 2014;9(2):251–67.

Abstract: An increasing number of patients have become aware of the detrimental effects of periodontal disease and tooth-loss and they seek periodontal care. The cornerstone of management of chronic periodontitis is the non-surgical periodontal treatment. The primary goal of periodontal therapy is to preserve the natural dentition by achieving and maintaining a healthy functional periodontium. Many adjunctive treatment modalities have been introduced lately to enhance the therapeutic outcome of periodontal treatment. The aim of this review is to search for systematic reviews which evaluate these therapeutic modalities and discuss their efficacy. The databases of Medline via Ovid, Embase and the Cochrane Database of Systematic Reviews were searched for up to date systematic reviews in English language. The results and conclusions of the systematic reviews found in the periodontal literature are discussed in this paper. The efficacy of different oral hygiene regimens in maintaining and improving gingival health, the efficacy of the nonsurgical periodontal treatment, the full mouth disinfection, the systematic antimicrobial therapy, the local adjunctive therapies, the host modulation treatment, the Photodynamic and laser therapy are discussed. It appears that there is no certain magnitude of initial probing pocket depth where nonsurgical periodontal therapy is no longer effective. Some of the aforementioned modalities have been found to offer statistical significant benefit in clinical outcomes than the scaling and root planning alone. If this statistical significance is clinically significant needs to be critically assessed by the clinician upon the treatment planning and decision making.

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	Generalidades de las nanoburbujas
BASE DE DATOS	Google Scholar
artículos preseleccionados Referencia -estilo Vancouver y abstract	

Chan CU, Chen L, Arora M, Ohl CD. Collapse of surface nanobubbles. Phys Rev Lett. 2015;114(11).¡

ABSTRACT

Surface attached nanobubbles populate surfaces submerged in water. These nanobubbles have a much larger contact angle and longer lifetime than predicted by classical theory. Moreover, it is difficult to distinguish them from hydrophobic droplets, e.g., polymeric contamination, using standard atomic force microscopy. Here, we report fast dynamics of a three phase contact line moving over surface nanobubbles, polymeric droplets, and hydrophobic particles. The dynamics is distinct: across polymeric droplets the contact line quickly jumps and hydrophobic particles pin the contact line, while surface nanobubbles rapidly shrink once merging with the contact line, suggesting a method to differentiate nanoscopic gaseous, liquid, and solid structures. Although the collapse process of surface nanobubbles occurs within a few milliseconds, we show that it is dominated by microscopic dynamics rather than bulk hydrodynamics.

Petsev ND, Shell MS, Leal LG. Dynamic equilibrium explanation for nanobubbles' unusual temperature and saturation dependence. Phys Rev E - Stat Nonlinear, Soft Matter Phys. 2013;88(1).

ABSTRACT

The dynamic equilibrium model suggests that surface nanobubbles can be stable due to an influx of gas in the vicinity of the bubble contact line, driven by substrate hydrophobicity, that balances the outflux of gas from the bubble apex. Here, we develop an alternate formulation of this mechanism that predicts rich behavior in agreement with recent experimental measurements. Namely, we find that stable nanobubbles exist in narrow temperature and dissolved gas concentration ranges, that there is a maximum and minimum possible bubble size, and that nanobubble radii decrease with temperature.

Luu TQ, Hong Truong PN, Zitzmann K, Nguyen KT. Effects of Ultrafine Bubbles on Gram-Negative Bacteria: Inhibition or Selection? Langmuir. 2019;35(42):13761–8.

ABSTRACT: Ultrafine bubbles exist in all liquids and are naturally stable. As their properties are not entirely known, it is unclear how they impact the surrounding solution and comparable-sized particles within it. It is essential to further investigate the properties of ultrafine bubbles in order to expand their industrial application. In this regard, the effect of ultrafine bubbles on bacterial development is of particular interest. Our current study, using optical density measurements and fluorescence microscopic images has demonstrated that ultrafine gas bubbles impact the morphology and phenotype of Escherichia coli and Pseudomonas aeruginosa. Specifically, Fourier transform infrared spectroscopic measurements indicated a thickening of bacterial membranes in samples exposed to ultrafine bubbles. The study also confirmed that ultrafine bubbles can inhibit bacterial cell growth. This study signifies the role of surface phenomena in bacterial culture, which is crucial in the upstream processes of recombinant DNA technology applications.

Ushikubo FY, Furukawa T, Nakagawa R, Enari M, Makino Y, Kawagoe Y, et al. Evidence of the existence and the stability of nano-bubbles in water. Colloids Surfaces A Physicochem Eng Asp [Internet]. 2010;361(1–3):31–7. Available from: http://dx.doi.org/10.1016/j.colsurfa.2010.03.005

ABSTRACT

Although micro- and nano-bubble technology has been attracting attention in many fields, the state of water after the introduction of those bubbles is still not clear. In this study, the existence and stabilization of nano-bubbles after the generation of bubbles were investigated. The presence of nano-sized particles was detected through dynamic light scattering for days, when pure oxygen was used to generate the bubbles, and for less than 1 h, in the case of air bubbles. NMR spin–lattice relaxation time increased with the introduction of micro- and nano-bubbles in manganese ions solution, indicating the presence of a gas–liquid interface which adsorbed the manganese ions. Furthermore, the zeta potential measured in the water after the introduction of oxygen micro- and nano-bubbles was in the range from −45 mV to −34 mV and from −20 mV to −17 mV in water bubbled with air, indicating the presence of stable electrically charged particles. This study suggested a strong possibility of the existence of nano-bubbles in water for a long time. The stability of nano-bubbles is supported by the electrically charged liquid–gas interface, which creates repulsion forces that prevent the bubble coalescence, and by the high dissolved gas concentration in the water, which keeps a small concentration gradient between the interface and the bulk liquid.

Guan M, Guo W, Gao L, Tang Y, Hu J, Dong Y. Investigation on the temperature difference method for producing nanobubbles and their physical properties. ChemPhysChem. 2012;13(8):2115–8.

ABSTRACT

In recent years, the possibility of nanobubbles at the solid– liquid interface has drawn wide attention in the scientific community and industry. Thus the search for evidences for the existence of nanobubbles became a scientific hotspot. To produce interfacial nanobubbles, a systematic experiment, called the temperature difference method, is carried out by replacing low temperature water (LTW) with high temperature water (HTW) at the highly-oriented pyrolytic graphite (HOPG)–water interface. When LTW (4 8C) is mixed with HTW (25–40 8C), nanobubbles are observed by atomic force microscopy (AFM), and their size, density and total volume per square micrometer are measured. Furthermore, pancake-like gas layers and the coexistence of nanobubbles on top of the pancake layers are also observed.

Fang CK, Ko HC, Yang CW, Lu YH, Hwang IS. Nucleation processes of nanobubbles at a solid/water interface. Sci Rep [Internet]. 2016;6(December 2015):1–10. Available from: http://dx.doi.org/10.1038/srep24651

ABSTRACT

Experimental investigations of hydrophobic/water interfaces often return controversial results, possibly due to the unknown role of gas accumulation at the interfaces. Here, during advanced atomic force microscopy of the initial evolution of gas-containing structures at a highly ordered pyrolytic graphite/ water interface, a fluid phase first appeared as a circular wetting layer ~0.3nm in thickness and was later transformed into a cap-shaped nanostructure (an interfacial nanobubble). Two-dimensional ordered domains were nucleated and grew over time outside or at the perimeter of the fluid regions, eventually confining growth of the fluid regions to the vertical direction. We determined that interfacial nanobubbles and fluid layers have very similar mechanical properties, suggesting low interfacial tension with water and a liquid-like nature, explaining their high stability and their roles in boundary slip and bubble nucleation. These ordered domains may be the interfacial hydrophilic gas hydrates and/or the long-sought chemical surface heterogeneities responsible for contact line pinning and contact angle hysteresis. The gradual nucleation and growth of hydrophilic ordered domains renders the original homogeneous hydrophobic/water interface more heterogeneous over time, which would have great consequence for interfacial properties that affect diverse phenomena, including interactions in water, chemical reactions, and the self-assembly and function of biological molecules.

Calgaroto S, Wilberg KQ, Rubio J. On the nanobubbles interfacial properties and future applications in flotation. Miner Eng [Internet]. 2014;60(January 2016):33–40. Available from: http://dx.doi.org/10.1016/j.mineng.2014.02.002

ABSTRACT

Nanobubbles, generations forms, basic studies and applications constitute a growing research area, included their usage in advanced mineral flotation. Yet, there are investigation needs for sustainable generation procedures, stability and understanding the nanobubbles interfacial properties and structures. Results proved that a reduction in pressure makes the super-saturated liquid suffers cavitation and nanobubbles were generated. Medium pH and solutions tested were adjusted, in the air saturation vessel, before the nanobubbles were formed, and this allowed to control (in situ) the surface charge/zeta potential-size of the forming nanobubbles. Measurements obtained with a ZetaSizer Nano equipment showed zeta potential values, in the presence of 102 mol L1 NaCl, displaying sigmoidal pH behaviour between pH 2 (+26 mV) and 8.5 (28 mV); an isoelectric point was attained at pH 4.5 and were positively charged (up to 23 mV) in acidic medium, a phenomenon which has not been previously observed. In alkaline medium, bubbles were highly negative zeta potential (59 mV) at pH 10. The double layers appear to play a role in the formation of stable nanobubbles providing a repulsive force, which prevents inter-bubble aggregation and coalescence. Accordingly, the sizes of the nanobubbles depended on their charge and increased with pH, reaching a maximum (720 nm) around the isoelectric point (±5 mV). Highly charged and small nanobubbles (approximately 150–180 nm) were obtained in the presence of surfactants (104 mol L1 of alkyl methyl ether monoamine or sodium dodecyl sulphate); the zeta potential values in these experiments followed a similar trend of other reported values, validating the technique used with the nanobubbles sizes varying with pH from 150 to 400 nm. Thus, charged and uncharged stable nanobubbles can be tailor-made with or without surfactants and it is expected that their use will broaden options in mineral flotation especially if collectors coated nanobubbles (‘‘bubble-collectors’’) were employed. A detailed and updated review on factors involving stability, longevity and coalescence of nanobubbles was made. It is believed that future trend will be on sustainable formation and application of nanobubbles at industrial scale contributing to widen applied research in mineral, materials processing and liquid effluent treatment by advanced flotation.

Stride E. Physical principles of microbubbles for ultrasound imaging and therapy. Cerebrovasc Dis. 2009;27(SUPPL. 2):1–13.

Abstract: Microbubble ultrasound contrast agents have been in clinical use for more than two decades, during which time their range of applications has increased to encompass echocardiography, Doppler enhancement, perfusion studies and molecular imaging, as well as a number of therapeutic applications including drug delivery, gene therapy, high-intensity focused ultrasound treatments and sonothrombolysis. The aim of this article is to review the different types of microbubble agent, their physical behaviour and the mechanisms underlying their effectiveness in imaging and therapeutic applications.

Zhang XH, Maeda N, Craig VSJ. Physical properties of nanobubbles on hydrophobic surfaces in water and aqueous solutions. Langmuir. 2006;22(11):5025–35.

ABSTRACT

In recent years there has been an accumulation of evidence for the existence of nanobubbles on hydrophobic surfaces in water, despite predictions that such small bubbles should rapidly dissolve because of the high internal pressure associated with the interfacial curvature and the resulting increase in gas solubility. Nanobubbles are of interest among surface scientists because of their potential importance in the long-range hydrophobic attraction, microfluidics, and adsorption at hydrophobic surfaces. Here we employ recently developed techniques designed to induce nanobubbles, coupled with high-resolution tapping-mode atomic force microscopy (TM-AFM) to measure some of the physical properties of nanobubbles in a reliable and repeatable manner. We have reproduced the earlier findings reported by Hu and co-workers. We have also studied the effect of a wide range of solutes on the stability and morphology of these deliberately formed nanobubbles, including monovalent and multivalent salts, cationic, anionic, and nonionic surfactants, as well as solution pH. The measured physical properties of these nanobubbles are in broad agreement with those of macroscopic bubbles, with one notable exception: the contact angle. The nanobubble contact angle (measured through the denser aqueous phase) was found to be much larger than the macroscopic contact angle on the same substrate. The larger contact angle results in a larger radius of curvature and a commensurate decrease in the Laplace pressure. These findings provide further evidence that nanobubbles can be formed in water under some conditions. Once formed, these nanobubbles remain on hydrophobic surfaces for hours, and this apparent stability still remains a well-recognized mystery. The implications for sample preparation in surface science and in surface chemistry are discussed.

Taverna D, Kociak M, Stéphan O, Fabre A, Finot E, Décamps B, et al. Probing physical properties of confined fluids within individual nanobubbles. Phys Rev Lett. 2008;100(3):1–4.

ABSTRACT

Spatially resolved electron energy-loss spectroscopy (EELS) in a scanning transmission electron microscope (STEM) has been used to investigate a He fluidic phase in nanobubbles embedded in a metallic Pd90Pt10 matrix. Using the 1s ! 2p excitation of the He atoms, maps of the He density and pressure in bubbles of different diameters have been realized, to provide an indication of the bubble formation mechanism. Detailed local variations of the He K-line characteristics have been measured and interpreted as modifications of the electromagnetic properties of the He atom close to a metallic interface, which affects a correct estimation of the densities within the smallest bubbles.

Borkent BM, Dammer SM, Schönherr H, Vancso GJ, Lohse D. Superstability of surface nanobubbles. Phys Rev Lett. 2007;98(20):1–5.

ABSTRACT

Shock wave induced cavitation experiments and atomic force microscopy measurements of flat polyamide and hydrophobized silicon surfaces immersed in water are performed. It is shown that surface nanobubbles, present on these surfaces, do not act as nucleation sites for cavitation bubbles, in contrast to the expectation. This implies that surface nanobubbles are not just stable under ambient conditions but also under enormous reduction of the liquid pressure down to −6MPa. We denote this feature as superstability.

Agrahari V, Mitra AK. Therapeutic Delivery. Ther Deliv. 2016;7(2):117–38.

ABSTRACT

In recent decades ultrasound-guided delivery of drugs loaded on nanocarriers has been the focus of increasing attention to improve therapeutic treatments. Ultrasound has often been used in combination with microbubbles, micron-sized spherical gasfilled structures stabilized by a shell, to amplify the biophysical effects of the ultrasonic field. Nanometer size bubbles are defined nanobubbles. They were designed to obtain more efficient drug delivery systems. Indeed, their small sizes allow extravasation from blood vessels into surrounding tissues and ultrasound-targeted site-specific release with minimal invasiveness. Additionally, nanobubbles might be endowed with improved stability and longer residence time in systemic circulation. This review will describe the physico-chemical properties of nanobubbles, the formulation parameters and the drug loading approaches, besides potential applications as a therapeutic tool.

Eklund F. Nanobubbles in water - how to identify them and why they are stable Department of Physics. 2019. 57 p.

ABSTRACT

Gas bubbles smaller than 1 micrometer in water, commonly referred to as nanobubbles, is a growing field of research and innovation. Applications range from medical imaging and drug delivery to mining industry and environmental remediation. There are many possibilities but important questions remain – how is it possible for small gas bubbles to be stable against dissolution and how can they be detected and differentiated from solid particles and oil droplets ? In this work we demonstrate that several common nanobubble generation methods can generate contamination particles which can be mistaken for bubbles and that with sufficient cleanliness, neither particles, droplets or bubbles are generated. Theories on nanobubble stability that does not include impurities can thus be dismissed. (Paper 1). Lipid stabilization and the dynamic equilibrium model based on hydrophobic dirt particles appear to be the only valid models for nanobubble stability at present. We furthermore demonstrate Holographic Nanoparticle Tracking Analysis (HNTA) as a powerful new method to detect and differentiate between nanobubbles and nanoparticles in the same solution (Paper 2). As H-NTA determines the refractive index of tracked objects, bubbles will differ very significantly from solid particles or oil droplets. The refractive index of a bubble also indicates the amount of adsorbed material as well as possible clustering of multiple bubbles. The method also powerfully enables detection of different particle populations close in size and refractive index in a dispersion. The size range is 0.3-0.4 µm to 1.5 µm.

Shende PK, Desai D, Gaud RS. Role of solid-gas interface of nanobubbles for therapeutic applications. Crit Rev Ther Drug Carrier Syst. 2018;35(5):469–94.

ABSTRACT: The development of nanoscale particles offers tremendous potential for the formulation of nanobubbles, an area of great interest in therapeutic ultrasound, detection, diagnosis, and drug delivery systems. This review compiles information for designing nanobubbles tailored to various applications such as color Doppler imaging, multidrug-resistant treatment, cosmeceuticals, gene therapy, cancer treatment, water treatment, and so forth. Nanobubbles also extend a path for convenient and eco-friendly systems for cleaning conducting surfaces. We anticipate that this review will provide insights into nanobubble formulation, applications, and future approaches. It also focuses on newer technologies and formulation of gases, polymers, and excipients. Nanobubbles emerge as novel biocompatible, nontoxic carriers for clinical and commercial applications in healthcare but have yet to be explored in other fields

Serizawa Professor Emeritus A, Mai C. Fundamentals and Applications of Micro/Nano Bubbles. 2017;(Ishpmnb). Available from: http://webs.rmutl.ac.th/assets/upload/files/2017/01/20170106155252_97638.pdf

Temesgen T, Bui TT, Han M, Kim T il, Park H. Micro and nanobubble technologies as a new horizon for water-treatment techniques: A review. Adv Colloid Interface Sci [Internet]. 2017;246:40–51. Available from: http://dx.doi.org/10.1016/j.cis.2017.06.011

ABSTRACT

This review article organizes the studies conducted on the areas of microbubbles and nanobubbles with a special emphasis on water treatment. The basic definitions of bubble types and their size ranges are also presented based on the explanations of different researchers. The characterization parameters with state-of-the-art measuring and analysis techniques of microbubble and nanobubble technologies are summarized. Some major applications of these technologies in water-treatment processes are reviewed and briefly discussed. Based on the reviews, various potential areas for research and bubble application gaps in water and wastewater treatment technologies are identified for further study. The article is prepared in such a way that it provides a step-by-step acquaintance to the subject matter with the objective of focusing on the application of microbubbles and nanobubbles in water-treatment technology.

FAN M, TAO D, HONAKER R, LUO Z. Nanobubble generation and its application in froth flotation (part I): nanobubble generation and its effects on properties of microbubble and millimeter scale bubble solutions. Min Sci Technol [Internet]. 2010;20(1):1–19. Available from: http://dx.doi.org/10.1016/S1674-5264(09)60154-X

ABSTRACT

A special nanobubble generation system has been developed for evaluating the effect of nanobubble on froth flotation. In this study, an eight-factor five-level Central Composite Experimental Design was conducted for investigating eight important parameters governing the median size and the volume of nanobubbles. These process parameters included surfactant concentration, dissolved oxygen (O2) content, dissolved carbon dioxide gas (CO2) content, pressure drop in cavitation tube nozzle, <50 nm hydrophobic particle concentration, <50 nm hydrophilic particle concentration, slurry temperature and the time interval after nano- bubble generation. The properties, stability and uniformity of nanobubbles were investigated. The study of the produced nanobubble's effects on the characteristics of microbubble solutions and millimeter scale bubble solutions was performed in a 50.8 mm column.

Argenziano M, Bessone F, Cavalli R. Nanobubbles: State of the Art, Features, and the Future. Handbook of Materials for Nanomedicine. 2020. p. 333–79.

Alheshibri M, Qian J, Jehannin M, Craig VSJ. A History of Nanobubbles. Langmuir. 2016;32(43):11086–100.

ABSTRACT: We follow the history of nanobubbles from the earliest experiments pointing to their existence to recent years. We cover the effect of Laplace pressure on the thermodynamic stability of nanobubbles and why this implies that nanobubbles are thermodynamically never stable. Therefore, understanding bubble stability becomes a consideration of the rate of bubble dissolution, so the dominant approach to understanding this is discussed. Bulk nanobubbles (or fine bubbles) are treated separately from surface nanobubbles as this reflects their separate histories. For each class of nanobubbles, we look at the early evidence for their existence, methods for the production and characterization of nanobubbles, evidence that they are indeed gaseous, or otherwise, and theories for their stability. We also look at applications of both surface and bulk nanobubbles.

Zhang X yu, Wang Q shuai, Wu Z xian, Tao D ping. An experimental study on size distribution and zeta potential of bulk cavitation nanobubbles. Int J Miner Metall Mater. 2020;27(2):152–61.

Abstract: Nanobubble flotation technology is an important research topic in the field of fine mineral particle separation. The basic characteristics of nanobubbles, including their size, concentration, surface zeta potential, and stability have a significant impact on the nanobubble flotation performance. In this paper, bulk nanobubbles generated based on the principle of hydrodynamic cavitation were investigated to determine the effects of different parameters (e.g., surfactant (frother) dosage, air flow, air pressure, liquid flow rate, and solution pH value) on their size distribution and zeta potential, as measured using a nanoparticle analyzer. The results demonstrated that the nanobubble size decreased with increasing pH value, surfactant concentration, and cavitation-tube liquid flow rate but increased with increasing air pressure and increasing air flow rate. The magnitude of the negative surface charge of the nanobubbles was positively correlated with the pH value, and a certain relationship was observed between the zeta potential of the nanobubbles and their size. The structural parameters of the cavitation tube also strongly affected the characteristics of the nanobubbles. The results of this study offer certain guidance for optimizing the nanobubble flotation technology.

Ramamoorty M. An Introduction to Thyristors and Their Applications. An Introd to Thyristors Their Appl. 1977;11(4):3–7.

ABSTRACT

Micro-bubbles gradually decrease in size due to the dissolution of interior gases by the surrounding liquid and eventually disappear, leaving some Nano-Bubbles. It has been proved that free radicals are generated during the collapsing of Micro-bubbles. The present introduction focuses on the biological application of Micro/Nano-bubbles, whose practical bioapplications, development of cell-level biological treatment, and concept of cell manipulating device in the next stage of the development are introduced. In addition, the future application of Micro/Nano-bubbles to Bio-computing systems is also discussed.

Bui TT, Nguyen DC, Han M. Average size and zeta potential of nanobubbles in different reagent solutions. J Nanoparticle Res. 2019;21(8).

Abstract: In the present study, we analyzed the average size and zeta potential of nanobubbles (NBs) in chemical reagent solutions. Here, we proposed the possible mechanisms for the size growth and for negative and positive NB creation. NBs were produced by dispersing a supersaturated air-water mixture in a mixing chamber, and then causing the breakup of microbubbles in a Teflon hose. The size and zeta potential of the NBs were measured by dynamic light scattering. The NB size had no dependency on pH and grew over time. The proposed mechanism of the NBs' size growth related to their coalescence in the solutions. The bubbles were charged negatively in the presence of glucose, ethylenediaminetetraacetic acid, and Na+ , while they were charged positively in the addition of dimethyldioctadecylammonium bromide, Al3+, and Fe3+. The NB zeta potential decreased in all solutions, while their pH increased from 2 to 12. Zeta potential values remained stable for 150 min, proving the longterm permanence of bubbles in the bulk solutions. The charged NBs were created from the adsorbed species such as OH– and DODA+ and possible aqueous speciation (through the addition of metal ions) on its surface. Our results indicate that the type of chemical reagent solution can influence both the sign of the surface charge and the size of NBs, allowing them to be applicable in many treatment processes for water treatment.

Jadhav AJ, Barigou M. Bulk Nanobubbles or Not Nanobubbles: That is the Question. Langmuir. 2020;36(7):1699–708.

ABSTRACT: Bulk nanobubbles are a novel nanoscale bubble system with unusual properties which challenge our understanding of bubble behavior. Because of their extraordinary longevity, their existence is still not widely accepted as they are often attributed to the presence of supramolecular structures or contaminants. Nonetheless, bulk nanobubbles are attracting increasing attention in the literature, but reports generally lack objective evidence that the observed nano-entities are indeed nanobubbles. In this paper, we use various physical and chemical analytical techniques to provide multiple evidence that the nano-entities produced mechanically in pure water by a continuous high-shear rotor-stator device or acoustic cavitation and spontaneously by water−ethanol mixing are indeed gas-filled domains. We estimate that the results presented here combined provide conclusive proof that bulk nanobubbles do exist and they are stable. This paper should help close the debate about the existence of bulk nanobubbles and, hence, enable the scientific community to rather focus on developing the missing fundamental science in this area.

Michailidi ED, Bomis G, Varoutoglou A, Efthimiadou EK, Mitropoulos AC, Favvas EP. Fundamentals and applications of nanobubbles. Vol. 30, Interface Science and Technology. 2019. 69–99 p.

Oh SH, Kim JM. Generation and Stability of Bulk Nanobubbles. Langmuir. 2017;33(15):3818–23.

ABSTRACT: Recently, extremely small bubbles, referred to as nanobubbles, have drawn increased attention due to their novel properties and great potential for various applications. In this study, a novel method for the generation of bulk nanobubbles (BNBs) was introduced, and stability of fabricated BNBs was investigated. BNBs were created from CO_2 gas with a mixing method; the chemical identity and phase state of these bubbles can be determined via infrared spectroscopy. The presence of BNBs was observed with a nanoparticle tracking analysis (NTA). The ATR-FTIR spectra of BNBs indicate that the BNBs were filled with CO_2 gas. Furthermore, the BNB concentration and its ζpotential were about 2.94 × 108 particles/mL and −20 mV, respectively (24 h after BNB generation with a mixing time of 120 min). This indicates the continued existence and stability of BNBs in water for an extended period of time.

Tan BH, An H, Ohl CD. How Bulk Nanobubbles Might Survive. Phys Rev Lett [Internet]. 2020;124(13):134503. Available from: https://doi.org/10.1103/PhysRevLett.124.134503

ABSTRACT

The existence of bulk nanobubbles has long been regarded with scepticism, due to the limitations of experimental techniques and the widespread assumption that spherical bubbles cannot achieve stable equilibrium. We develop a model for the stability of bulk nanobubbles based on the experimental observation that the zeta potential of spherical bubbles abruptly diverges from the planar value below 10 μm. Our calculations recover three persistently reported—but disputed—properties of bulk nanobubbles: that they stabilize at a typical radius of ∼100 nm, that this radius is bounded below 1 μm, and that it increases with ionic concentration.

Yasui K, Tuziuti T, Kanematsu W. Mysteries of bulk nanobubbles (ultrafine bubbles); stability and radical formation. Ultrason Sonochem [Internet]. 2018;48:259–66. Available from: https://doi.org/10.1016/j.ultsonch.2018.05.038

ABSTRACT

There are two main mysteries in bulk nanobubbles which are cavitation nuclei. One is the mechanism of stability of a bulk nanobubble. The other is the problem whether OH radicals are produced from bulk nanobubbles without a dynamic stimulus. For the former problem, several proposed models are briefly reviewed. The dynamic equilibrium model is discussed in details that a bulk nanobubble is stabilized by a partial coverage of the bubble surface by a hydrophobic material. The TEM images of bulk nanobubbles seem to support the dynamic equilibrium model. For the latter problem, numerical simulations of dissolution of an air nanobubble are reviewed, which suggest that no OH radical is produced from a dissolving nanobubble. A possible role of H_2O_2 generated during bulk nanobubble production using hydrodynamic cavitation is briefly discussed in relation to the experimental results of “OH radical” detection.2 Keywords: cavitation nuclei, dynamic equilibrium model, hydrophobic impurity, surface coverage, gas diffusion, Laplace pressure, numerical simulation

Nirmalkar N, Pacek AW, Barigou M. On the Existence and Stability of Bulk Nanobubbles. Langmuir. 2018;34(37):10964–73.

ABSTRACT: Bulk nanobubbles are a novel type of nanoscale bubble system. Because of their extraordinary behavior, however, their existence is not widely accepted. In this paper, we shed light on the hypothesis that bulk nanobubbles do exist, they are filled with gas, and they survive for long periods of time, challenging present theories. An acoustic cavitation technique has been used to produce bulk nanobubbles in pure water in relatively large numbers approaching 109 bubble·mL−1 with a typical diameter of 100−120 nm. We provide multiple evidence that the nanoentities observed in suspension are nanobubbles given that they disappear after freezing and thawing of the suspensions, their nucleation rate depends strongly on the amount of air dissolved in water, and they gradually disappear over time. The bulk nanobubble suspensions were stable over periods of many months during which time the mean diameter remained unchanged, suggesting the absence of significant bubble coalescence, bubble breakage, or Ostwald ripening effects. Measurements suggest that these nanobubbles are negatively charged and their zeta potential does not vary over time. The presence of such a constant charge on the nanobubble surfaces is probably responsible for their stability. The effects of pH, salt, and surfactant addition on their colloidal stability are similar to those reported in the literature for solid nanoparticle suspensions, that is, nanobubbles are more stable in an alkaline medium than in an acidic one; the addition of salt to a nanobubble suspension drives the negative zeta potential toward zero, thus reducing the repulsive electrostatic forces between nanobubbles; and the addition of an anionic surfactant increases the magnitude of the negative zeta potential, thus improving nanobubble electrostatic stabilization.

Meegoda JN, Aluthgun Hewage S, Batagoda JH. Stability of nanobubbles. Environ Eng Sci. 2018;35(11):1216–27.

Abstract With stable existence in liquids for over several weeks, nanobubbles have an extensive range of applications across many fields of science and engineering. For an effective and functional use of these bubbles, it is important to know the reason for their long-term stability. Therefore, a comprehensive laboratory investigation was performed to determine bubble size distributions and zeta potentials of nanobubbles, first with four different gases (test series I), then with different salt concentrations, pH levels, and temperatures of the solution (test series II). Experimental results from test series I showed that the average bubble size depended on the gas solubility in water, and zeta potential depended on the ability of the gas to generate OH- ions at the water/gas interface. Experimental results from test series II showed that bubbles with high negative zeta potentials can be generated in solutions of high pH, low temperatures, and low salt concentrations. The high pH solutions produced smaller but stable nanobubbles. Bubble diameter slightly increased with increasing salt concentration. However, bubble size did not show considerable dependence on solution temperature. Long-term tests showed that with time zeta potential of bubbles decreased while the bubble size increased. Even though bubble sizes are expected to decrease with time due to gas diffusion, results indicate increased bubble sizes. This is because of decrease in zeta potential and bubble movement due to Brownian motion which causes bubble coalescence over time to form larger bubbles

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	Nanoburbujas de ozono y su efecto bactericida en odontología
BASE DE DATOS	Google Schoolar
artículos preseleccionados Referencia -estilo Vancouver y abstract	

Singh B, Shukla N, Cho CH, Kim BS, Park MH, Kim K. Effect and application of micro- and nanobubbles in water purification. Toxicol Environ Health Sci [Internet]. 2021;13(1):9–16. Available from: https://doi.org/10.1007/s13530-021-00081-x

Abstract:

Objective and methods: The importance of water purifcation has increased due to the availability of several pollutants, such as chemicals, toxic metals, gases, and biological contaminants in the water. Commercial wastewater and domestic wastewater have commonly been treated using biological approaches. However, these approaches have limitations, such as high energy costs, low efciency, requirement of trained staf, expensive chemicals, and multistep processing. Therefore, to overcome these challenges, the development of advanced technologies is increasingly in demand. Micro- and nanobubbles with advantages such as small size, large specifc surface area, long residence time in the water, high mass transfer power, high zeta interface potential, and the capacity to produce hydroxyl radicals are considerably signifcant. Results and conclusions: In this study, we discuss the current applications of micro- and nanobubbles using traditional and advanced techniques, such as fotation, aeration, and ozonation, which are capable of eliminating contaminants and color, water disinfection, and the oxidation of organic pollutants. Bubble technology has emerged as a potential platform for the successful extraction of harmful contaminants from water using these techniques.

Batagoda JH, Hewage SDA, Meegoda JN. Nano-ozone bubbles for drinking water treatment. J Environ Eng Sci. 2018;14(2):57–66.

ABSTRACT

Safe drinking water is a key necessity, and ozonation is one of the common processes in drinking water preparation. The main drawbacks of using conventional ozone methods are the high-buoyancy-related low retention time and rapid decomposition of ozone eradicating residual ozone in water, which do not support prevention of regrowth of microorganisms in treated water. When ozone is delivered as nanobubbles, it increases the retention time due to the low-rising-velocity-related low buoyancy and increased higher specific area of nanobubbles compared to those of ordinary bubbles. The diffusion and concentration of ozone in the water are very important in the treatment process. Experimental results and theoretical calculations show that using nanobubbles leads to lower diffusion and higher ozone concentration compared to using ordinary bubbles. Decomposition of ozone in water generates oxygen where higher oxygen concentrations are obtained using nanobubbles. The oxygen formed during decomposition of ozone generates radicals that can oxidise pollutants. This paper summarises the methods of generating nanobubbles for drinking water treatment at the commercial scale and proposes a method of using ceramic diffusers in a treatment plant with increased efficiency. Moreover, the cost–benefit analysis presented highlights the benefits of using ozone as nanobubbles.

Jhunkeaw C, Khongcharoen N, Rungrueng N, Sangpo P, Panphut W, Thapinta A, et al. Ozone nanobubble treatment effectively reduced pathogenic Gram positive and negative bacteria in freshwater and safe for tilapia. bioRxiv. 2020;1–23.

Abstract:

High concentrations of pathogenic bacteria in water usually results in outbreaks of bacterial diseases in farmed fish. Here, we explored the potential application of an emerging nanobubble technology in freshwater aquaculture. Specifically, we aimed to determine if this technology was effective at reducing the concentration of pathogenic bacteria in the water, and to assess whether it was safe for fish. An ozone nanobubble (NB-O_3) treatment protocol was established based on examination of nanobubble size, concentration, disinfection property, and impact on fish health. A 10-min treatment with NB-O_3 in 50 L water generated approximately 2-3 × 10^7 bubbles with majority sizes less than 130 nm and ozone level of ~800 mV ORP. A single treatment with water contaminated with either *Streptococcus agalactiae* or *Aeromonas veronii* effectively reduced 96.11-97.92 % of the bacterial load. This same protocol was repeated 3 times with 99.93-99.99 % reduction in the bacterial concentration. In comparison, bacterial concentration the control tanks remained the same level during the experiments. In fish-cultured water with the presence of organic matter (e.g. mucus, feces, bacterial flora, feed, etc.), the disinfection property of NB-O_3 was reduced i.e bacterial concentration was reduced by 42.94 %, 84.94 % and 99.27 % after the first, second and third treatments, respectively. To evaluate the safety of NB-O_3 to fish, juvenile Nile tilapia were exposed to NB-O_3 treatment for 10 minutes. No mortality was observed during the treatment or 48 h post treatment. Gill histology examination revealed that a single NB-O_3 treatment caused no alteration morphology. However, damage in the gill filaments was noticed in the fish receiving two or three consecutive exposures within the same day. Results of all the experiments conducted in this study suggest that NB-O_3 technology is promising for controlling pathogenic bacteria in aquaculture systems, and may be useful at reducing the risk of bacterial disease outbreaks in farmed fish.

Saijai S, Thonglek V, Yoshikawa K. Sterilization effects of ozone fine (micro/nano) bubble water. Int J Plasma Environ Sci Technol. 2019;12(2):55–8.

Abstract: Effects of sterilization of fine (micro/nano) bubble (FB) water of ozone gas were studied in relating to treatment times. In the applications of FB water, since hydroxyl radicals (OH•) were observed to occur in the water, it is expected that ozone FB water can have strong and long-duration sterilization effects, which is a very important function, in particular, for food safety applications. In order to verify the effects, more comprehensive experiments were made to clarify for FB water of ozone gas. The results showed that fresh ozone fine bubbles (O3FB) water had the most effective inhibition of the growth of Escherichia coli when used right after 60 min generation. In the three days-storage O3FB water, no sterilization effect was observed. The results of this study suggest that the application of fresh O3FB water may be useful for sterilization process in the food industry.

Fernandes T, Bhavsar C, Sawarkar S, D'souza A. Current and novel approaches for control of dental biofilm. Int J Pharm [Internet]. 2018;536(1):199–210. Available from: https://doi.org/10.1016/j.ijpharm.2017.11.019

ABSTRACT

Insights in oral demographics have revealed that a significant percentage of population faces chronic incidences of oral diseases. The innervation of these oral manifestations is required because untreated conditions may lead to bone loss in the oral cavity and systemic complications. Conventional treatments include surgery of the affected area followed by its management and/or treatment with antibiotics. However, widely used antibiotics like Triclosan have serious side effects including down-regulation of oral keratinocytes and fibroblasts. Thus, novel treatments with more targeted approaches have been under investigation. Treatment modalities like Viral mediated gene delivery, liposomes, nanoparticles, and nanobubbles not only help in management of oral diseases but also aid in reducing the biofilm formed due to bacterial bioburden in the areas less accessible through oral and conventional means. This review focuses on the limitation of conventional treatments and highlights the recent investigations in the use of the novel treatment approaches in order to increase the patient compliance and alleviation of side effects. The authors have also tried to emphasize on the future perspectives of glucansucrase inhibitors, photodynamic therapy and probiotics as targeted drug delivery systems. However, further investigations are necessary for implementation of these novel approaches in the clinical setup

Tricarico G, Orlandin JR, Rocchetti V, Ambrosio CE, Travagli V, Orientale P. Ozone 3 2020. 2020;9071–93.

Abstract.

OBJECTIVE: The therapeutic application of ozone and its derivatives in the dental field has been used for many purposes. However, there has yet to be a consistent evaluation of the outcomes, due to the lack of standardization of the treatment operating procedures.

MATERIALS AND METHODS: The keywords "ozone", "ozonated", "ozonation" "ozonized", "ozonization", "dentistry", "periodontology", "oral surgery", "oxygen-ozone therapy" were used to perform a literature review using PubMed, Cochrane, Google Scholar, Zotero databases with the temporal restriction for manuscripts published between 2010 and 2020. Clinical trials and case reports of good, neutral, as well as negative results related to ozone treatment specifications were evaluated.

DISCUSSION: A better understanding of the mechanisms of action of this bio-oxidative therapy could open new horizons related to the personalization of treatments and the quality of dental care. The critical condition to achieve these goals is an improved knowledge of the qualitative/quantitative characteristics of ozone and its derivatives.

Jibu RM, Leslie Rani S, Geetha R V. Healozone: A new way to treat dental caries-a review. Ann Rom Soc Cell Biol. 2021;25(3):1267–81.

ABSTRACT

In most industrialized countries, dental caries (tooth decay) is a major oral health problem. Healozone is an oxygen generating system that adds ozone to the part of the tooth that is damaged by decay. A thorough literature search was performed using the database like PubMed, Google scholar, BioRxiv, MESH, Google Cochrane database using the keywords „healozone‟ and ‟ dental caries‟ with no date and year restrictions. The language is restricted to English. 16 articles with similar data have been found which were analyzed and have been included in this study. The recent articles discussed in this study help us in gaining further knowledge about „healozone‟ and their application in dental caries. The usage of healozone has been discussed in this article and has been widely used by dental practitioners with a 100% success rate. Healozone treatment is more in contrast to the current traditional therapeutic modalities as it is a minimally invasive and conservative approach, a very inexpensive, painless therapy that increases patient acceptance and compliance with minimal adverse effects. The main aim of the study is to fathom the application of healozone in the treatment of dental caries which is a significant area of focus in a majority of the countries since it affects the population on a vast scale.

Elizabeth PS, Néstor MM, David QG. Nanoparticles as dental drug-delivery systems. Nanobiomaterials Clin Dent. 2019;567–93.

Iliadis D, Millar BJ. Ozone and its use in periodontal treatment. Open J Stomatol. 2013;03(02):197–202.

ABSTRACT

Objectives: To evaluate the effects of ozone in periodontal treatment in dental practice.

Methods: An evaluation of the current state of knowledge regarding the application of ozone in periodontal treatment revealed limited available literature. Therefore an audit was conducted in dental practice in order to evaluate the effects of ozone in periodontal treatment. Twentyfive patients were treated with gaseous ozone after having had failed conventional periodontal treatment. BPE scores and the six deepest pockets were measured in each patient before and after the use of ozone.

Results: From the initial number of twenty-nine patients selected, twenty-five patients attended both follow up appointments. Based on BPE scores, twenty of the patients have overall improvement while five of the patients continued to have deterioration. Eight patients had an improvement in depths of periodontal pockets by three millimetres, sixteen patients had improvement by one to two millimetres and one patient did not improve. The depth of pockets after the use of ozone decreased significantly ($P < 0.001$).

Conclusion: The audit revealed that gaseous ozone significantly ($P < 0.001$) reduced the depth of pockets in patients with periodontal disease. The positive results encourage further investigation in the subject.

Ari G, Vijayaraj S, Rajendran S, Mahendra J, Priya K L. Role of ozone therapy in the management of periodontal diseases. IP Int J Periodontol Implantol. 2020;5(4):143–8.

ABSTRACT

Periodontitis is a destructive inflammatory infection of the supporting structures of teeth which is triggered by explicit microorganisms, leading to progressive destruction of the periodontal ligament and alveolar bone, subsequently causing pocket formation, gingival recession or both. Ozone has been applied in medicine for more than a century now, although its clinical implications in dentistry have only been recently investigated. The results of ozone therapy in any form (gaseous, water or oil), in the management of dental diseases such as caries, periodontitis, and hypersensitivity, have been explored and studied with promising outstanding outcomes. The use of ozone as an adjunctive therapy characterizes a novel method in the treatment of chronic periodontal disease. Owing to the antimicrobial and immunostimulating effects of ozone therapy, it is well established in the treatment of gingival and periodontal diseases. This review article outlines the clinical applications of ozone therapy in periodontal diseases.

TABLA 4. PRESELECCIÓN DE ARTÍCULOS POR TEMÁTICA	
TEMÁTICA	Perspectivas
BASE DE DATOS	Google Schoolar

artículos preseleccionados
Referencia -estilo Vancouver y abstract

Alheshibri M, Qian J, Jehannin M, Craig VSJ. A History of Nanobubbles. Langmuir. 2016;32(43):11086–100.

ABSTRACT: We follow the history of nanobubbles from the earliest experiments pointing to their existence to recent years. We cover the effect of Laplace pressure on the thermodynamic stability of nanobubbles and why this implies that nanobubbles are thermodynamically never stable. Therefore, understanding bubble stability becomes a consideration of the rate of bubble dissolution, so the dominant approach to understanding this is discussed. Bulk nanobubbles (or fine bubbles) are treated separately from surface nanobubbles as this reflects their separate histories. For each class of nanobubbles, we look at the early evidence for their existence, methods for the production and characterization of nanobubbles, evidence that they are indeed gaseous, or otherwise, and theories for their stability. We also look at applications of both surface and bulk nanobubbles.

Peng H, Birkett GR, Nguyen A V. Progress on the Surface Nanobubble Story: What is in the bubble? Why does it exist? Adv Colloid Interface Sci [Internet]. 2015;222:573–80. Available from: http://dx.doi.org/10.1016/j.cis.2014.09.004

ABSTRACT

Interfaces between aqueous solutions and hydrophobic solid surfaces are important in various areas of science and technology. Many researchers have found that forces between hydrophobic surfaces in aqueous solution are significantly different from the classical DLVO theory. Long-range attractive forces (non-DLVO forces) are thought to be affected by nanoscopic gaseous domains at the interfaces. This is a review of the latest research on nanobubbles at hydrophobic surfaces from experimental and simulation studies. The review focusses on non-intrusive optical view of surface nanobubbles and gas enrichment on solid surfaces by imaging and force mapping. By use of these recent experimental data in conjunction with molecular simulation work, all major theories on surface nanobubble formation and stability are critically reviewed. Even though the current body of research cannot comprehensively explain all properties of surface nanobubbles observed, the fundamental understanding has been significantly improved. Line tension has been shown to be incapable of explaining the contact angle of nanobubbles. Dense gas layer theory provides a new explanation on both large contact angle and long-time stability. The high density of gas in these domains may significantly affect the gas–water interface which is in line with some observation made on bulk nanobubbles. Along this line of inquiry, experimental and simulation effort should be focussed on measuring the density within surface nanobubbles and the properties of the gas water interface which may be the key to explaining the stability of these nanobubbles.

Arakawa S, Sugisawa M, Leewananthawet A. Application of Ozone Nanobubble Water (ONBW) to Peri-Implantitis Treatment. Dentistry. 2017;7(12):5–10.

ABSTRACT

In this case report, we investigated the effects of Ozone nanobubble water (ONBW) on peri-implantitis lesions with non-surgical treatment. ONBW preserves the ozone gas nucleus for more than 6 months although half life time of ozone water was almost 30 min. ONBW exerts anti-microbial activity towards several kinds of bacteria including periodontopathic bacteria and cariogenic bacteria. There was no cytotoxicity against oral epithelial and mucosa cells. The Advanced quick bonding (AQB) implants on 19 and 20 were placed on a patient 43 years old female four years ago. The chief complaint of her was swelling at the site of 20. The patient presented swollen at peri-implant area, Bleeding of probing (BOP), and probing depth (PD)=6 mm at buccal site of an implant of 20. There was no findings of mobility at concerned implant. The bone resorption and a radiolucent part around the implant was confirmed with periapical radiograph. The amount of bone loss was 5.0 and 6.5 mm at mesial and distal site of 20, respectively. This peri-implantitis was evaluated the case required surgical therapy. In addition to mechanical plaque control, the patient received regular professional oral hygiene treatment and irrigation with ONBW every week at 100 mL each. And also, regarding chemical plaque control, the irrigation for pockets was also performed at home by the patient at a frequency of three times a day every day. After 12 weeks, soft tissues of the peri-implant presented no clinical signs of inflammation and BOP, and PD was 3 mm. The bone levels did not change significantly as demonstrated by the follow-up roentgenography taken after 3 years. Microbiologically, the number of red-complex of periodontopathic bacteria have been decreased substantially. This case report supports that ONBW might be effective and predictable as an adjunctive therapy for peri-implantitis. To the best our knowledge, this is the first report on describing the peri-implantitis treatment with ONBW

Jibu RM, Leslie Rani S, Geetha R V. Healozone: A new way to treat dental caries-a review. Ann Rom Soc Cell Biol. 2021;25(3):1267–81.

ABSTRACT In most industrialized countries, dental caries (tooth decay) is a major oral health problem. Healozone is an oxygen generating system that adds ozone to the part of the tooth that is damaged by decay. A thorough literature search was performed using the database like PubMed, Google scholar, BioRxiv, MESH, Google Cochrane database using the keywords „healozone" and " dental caries" with no date and year restrictions. The language is restricted to English. 16 articles with similar data have been found which were analyzed and have been included in this study. The recent articles discussed in this study help us in gaining further knowledge about „healozone" and their application in dental caries. The usage of healozone has been discussed in this article and has been widely used by dental practitioners with a 100% success rate. Healozone treatment is more in contrast to the current traditional therapeutic modalities as it is a minimally invasive and conservative approach, a very inexpensive, painless therapy that increases patient acceptance and compliance with minimal adverse effects. The main aim of the study is to fathom the application of healozone in the treatment of dental caries which is a significant area of focus in a majority of the countries since it affects the population on a vast scale.

Issac A V, Joseph K, Soman RR, Samuel A, Chandy S, Nithin †, et al. the Implications of Using Ozone in General Dental Practice. :40–6.

ABSTRACT

Ozone water is successfully used in the treatment of different diseases. Gingival and periodontal diseases represent a major concern both in dentistry and medicine. Majority of the causes and etiologic agent can be treated with ozone water. Several known action of ozone water like antihypoxic, antimicrobial, immunostimulating action can beneficial in treating periodontal diseases and regeneration.

Kumar M. 'Ozone Nano Bubble Water: A Magic Wand for the Treatment of Periodontal Disease.' ARC J Dent Sci. 2016;1(3):1–2.

Abstract: Chronic periodontitis is a highly prevalent disease affecting mainly the middle aged population. Traditionally a lot of materials have been used as an adjunct to scaling and root planing for the treatment of periodontal disease with variable success. The present manuscript highlights the efficacy of a novel product, ozone nano bubble water (NBW3) in the treatment of periodontal disease, which could be a promising antimicrobial agent and may revolutionize the field of periodontology as well of pharmacy in the management of periodontitis.

Hayakumo S, Arakawa S, Takahashi M, Kondo K, Mano Y, Izumi Y. Effects of ozone nano-bubble water on periodontopathic bacteria and oral cells - In vitro studies. Sci Technol Adv Mater. 2014;15(5):1–7.

ABSTRACT

The aims of the present study were to evaluate the bactericidal activity of a new antiseptic agent, ozone nano-bubble water (NBW3), against periodontopathogenic bacteria and to assess the cytotoxicity of NBW3 against human oral cells. The bactericidal activities of NBW3 against representative periodontopathogenic bacteria, *Porphyromonas gingivalis* (*P. gingivalis*) and *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*) were evaluated using *in vitro* time-kill assays. The cytotoxicity of NBW3 was evaluated using three-dimensional human buccal and gingival tissue models. The numbers of colony forming units (CFUs)/mL of *P. gingivalis* and *A. actinomycetemcomitans* exposed to NBW3 dropped to below the lower limit of detection (<10 CFUs mL^{-1}) after only 0.5 min of exposure. There were only minor decreases in the viability of oral tissue cells after 24 h of exposure to NBW3. These results suggest that NBW3 possesses potent bactericidal activity against representative periodontopathogenic bacteria and is not cytotoxic to cells of human oral tissues. The use of NBW3 as an adjunct to periodontal therapy would be promising.

Moraschini V, Kischinhevsky ICC, Calasans-Maia MD, Shibli JA, Sartoretto SC, Figueredo CM, et al. Ineffectiveness of ozone therapy in

nonsurgical periodontal treatment: a systematic review and metaanalysis of randomized clinical trials. Clin Oral Investig. 2020;24(6):1877–88.

Abstract

Objective This systematic review (SR) aimed at assessing the adjunctive clinical effect of ozone therapy (OT) on nonsurgical periodontal treatment.

Materials and methods Articles published prior to September 2019 were electronically searched in four databases without any other date or language restrictions and manually searched in regular journals and in gray literature. This review was performed according to the PICO format. The eligibility criteria comprised randomized controlled trials (RCTs) that analyzed the adjunctive effect of OT on nonsurgical periodontal treatment.

Results Twelve studies published between 2010 and 2019 were included in this SR. A metaanalysis of ten reports showed that there was no statistically significant difference in the periodontal parameters analyzed when scaling and root planing (SRP) plus sulcus irrigation with ozonated water or sulcus insertion of ozonated gas were used when compared to SRP alone. Additionally, there was no significant difference when the effect of SRP plus ozonated water was compared with SRP plus 2% chlorhexidine gluconate (CLX). No studies reported significant microbiological differences when the use of ozone was compared with SRP alone.

Conclusions The results of this SR do not support the use of OT for nonsurgical periodontal treatment. However, due to the potential heterogeneity across the studies, the presence of confounding factors, and the short follow-up of some included RCTs, these results should not be considered definitive.

Clinical relevance The current evidence indicates that ozone has antimicrobial activity and good biocompatibility with periodontal cells and gingival fibroblasts. However, no evidence was found for a positive effect of OT as an adjunct to scaling and root planing.

Leewananthawet A, Arakawa S, Okano T, Daitoku Kinoshita R, Ashida H, Izumi Y, et al. Ozone ultrafine bubble water induces the cellular signaling involved in oxidative stress responses in human periodontal ligament fibroblasts. Sci Technol Adv Mater [Internet]. 2019;20(1):589–98. Available from: https://doi.org/10.1080/14686996.2019.1614980

ABSTRACT Periodontitis is a chronic inflammatory disease caused by oral microorganisms in the subgingival biofilm. Stable aqueous ozone ultrafine bubble water (OUFBW) has recently begun to be used as an antiseptic in the treatment of periodontitis. The effectiveness of OUFBW is thought to depend on the bactericidal actions of dissolved ozone exerted via its oxidizing effect. On the other hand, the effects of ozone on the periodontal tissues are largely unknown. In this paper we examined the cellular responses after OUFBW treatment. Human primary periodontal ligament fibroblasts (hPDLFs) or Ca9-22 human gingival epithelial cells were treated with OUFBW or UV-inactivated OUFBW. The production of reactive oxygen species (ROS), the activation of mitogen-activated protein kinase (MAPK) and the nuclear factor-kappa B (NF-κB) activation were analyzed. The transcript profiles of hPDLFs after OUFBW treatment were also analyzed by RNA sequencing (RNA-seq). Our results showed that OUFBW induces oxidative stress by generating ROS, which, in turn, activated the MAPK pathway. OUFBW triggered activation of c-Fos, a major component of the transcription factor activator protein 1 (AP-1), and also nuclear factor erythroid 2 (NF-E2)-related factor 2 (Nrf2), which possessed a high sensitivity to oxidative stress. The results of RNA-seq analysis revealed that the numerous genes involved in oxidative stress responses or MAPK signaling pathway were upregulated after OUFBW treatment. Investigation of the signaling pathways activated by OUFBW highlights another aspect of the biological roles of OUFBW, in addition to its bactericidal activity, in the treatment of periodontitis.

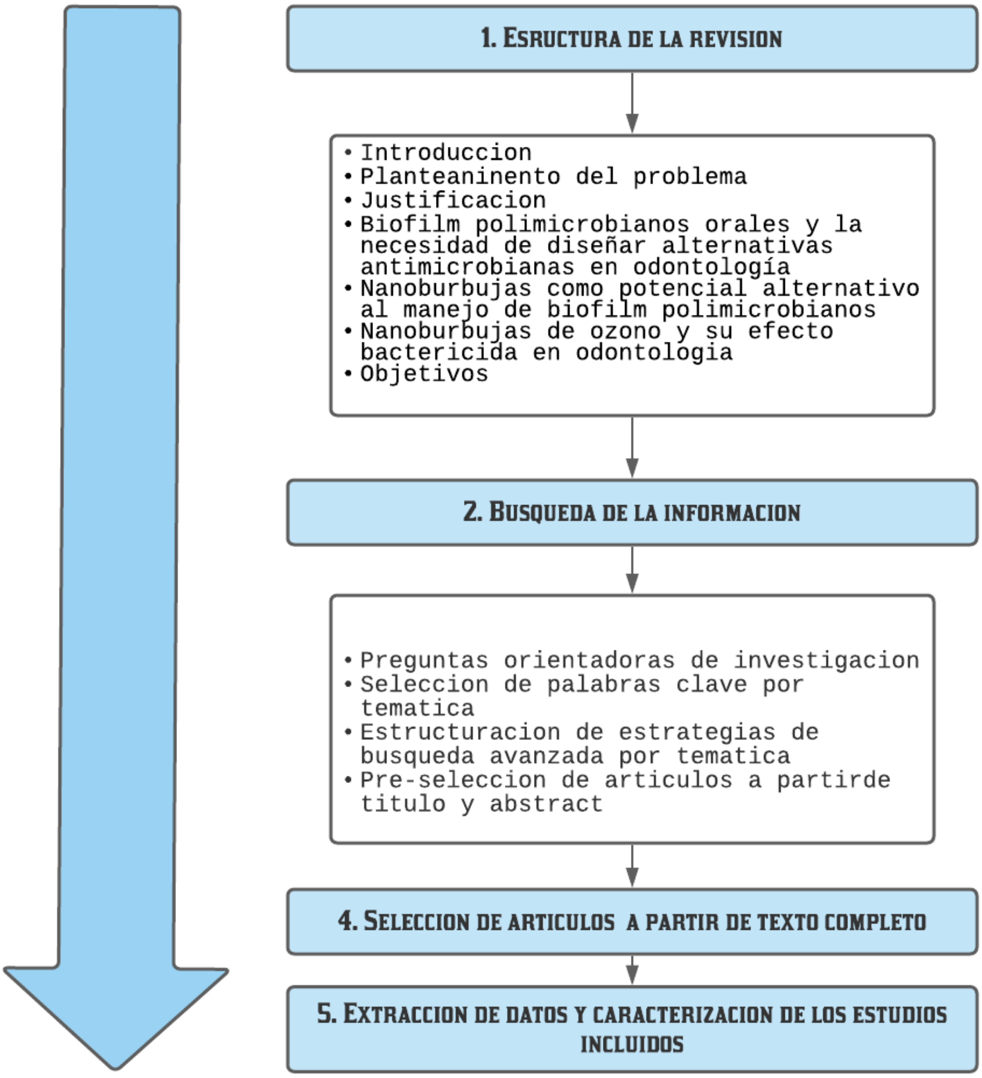
4. Selección de artículos por temática (criterios de selección e inclusión de artículos)

- Sin restricción de tiempo o periodo de publicación.
- Artículos disponibles en texto completo.
- Restricción de idioma de los artículos: inglés, español
- Tipos de estudio: revisiones de literatura, estudios de casos y controles in vivo e in vitro, reportes de caso, estudios observacionales y estudios experimentales.
- Artículos publicados en revistas científicas
- Bases de datos: Pubmed y Google Scholar

5. Proceso de extracción de información de artículos por temática Seguido del proceso de búsqueda, con los artículos seleccionados por temática y abstract, se elaboró una tabla de síntesis de la información para la extracción del contenido relevante de manera organizada, los datos que fueron seleccionados de cada artículo se describen a continuación:

- Base de datos.
- Título del artículo.
- Autor/Año/País de publicación.
- Revista en la cual fue publicado.
- Indicadores bibliométricos (Factor de impacto, índice H, cuartil, índice de citaciones).
- Tipo de estudio.
- Área de aplicación odontológica.
- Clasificación de nanoburbuja.
- Característica física o química de la nanoburbuja que se describe.
- Efecto antimicrobiano de la nanoburbuja de ozono.
- Definición de nanoburbuja.
- Zona anatómica.

6. Proceso de estructuración de la revisión.



7. CONSIDERACIONES EN PROPIEDAD INTELECTUAL

a. Sustento legal

Esta es una investigación sin riesgo ya que no se realizó ninguna intervención en humanos. Los derechos de autor fueron respetados teniendo como norma la ley 23 de 1982 la cual expresa que los autores de obras científicas tienen protección para las obras realizadas por ellos, bajo la presente ley y el derecho común. Todos los artículos fueron citados bajo el nombre o seudónimo del autor y el título original de los artículos. Además, se realizaron las citaciones correspondientes utilizando ideas importantes de los artículos, dándole un sentido razonable dando una reproducción simulada y sustancial, que redunde en perjuicio del autor de los artículos que serán utilizados. En cada cita se mencionó el nombre del autor y el año, además del título original de los artículos (*Congreso de La República Ley Número 23 de 1982 (28*, 1982).

8. RESULTADOS:

a. Resultados del proceso de búsqueda de información:

A partir de las temáticas propuestas y la selección de palabras clave por temática se generaron estrategias de búsqueda para ser implementadas en las bases de datos Pubmed y Google Scholar, de los cuales se pre seleccionaron 115 artículos; posteriormente al ser evaluados por expertos por título y abstract se redujo a 82 artículos en texto completo y en idioma inglés, que servirán de apoyo para la caracterización de la información de la extracción de información. La cantidad de artículos seleccionados por temática en las diferentes bases de datos se encuentra contenida en los siguientes flujogramas:

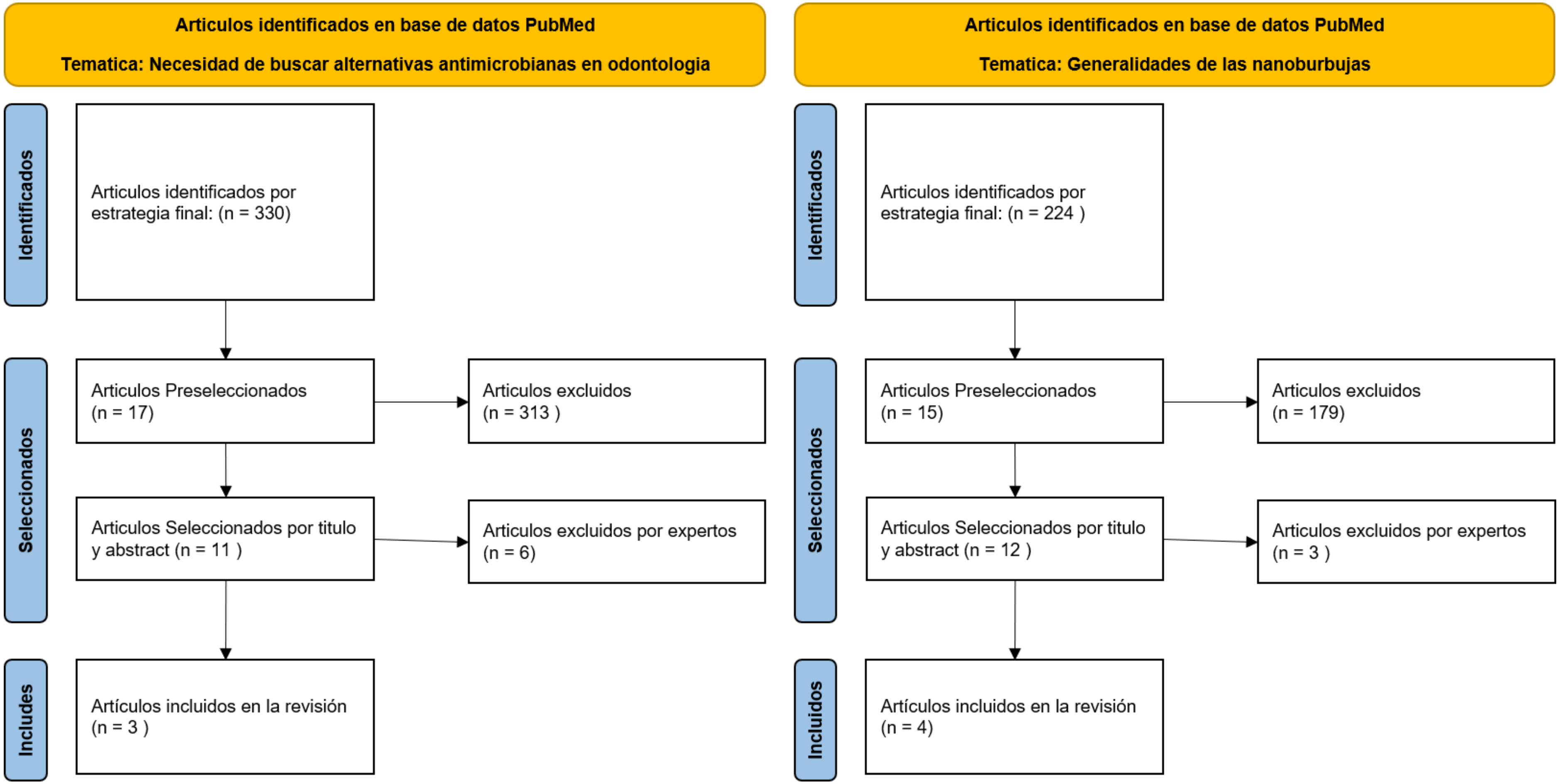


Figura 6 Flujogramas de Artículos seleccionados en la base de datos Pubmed para las temáticas de Necesidad de buscar alternativas antimicrobianas en odontología y Generalidades de las nanoburbujas

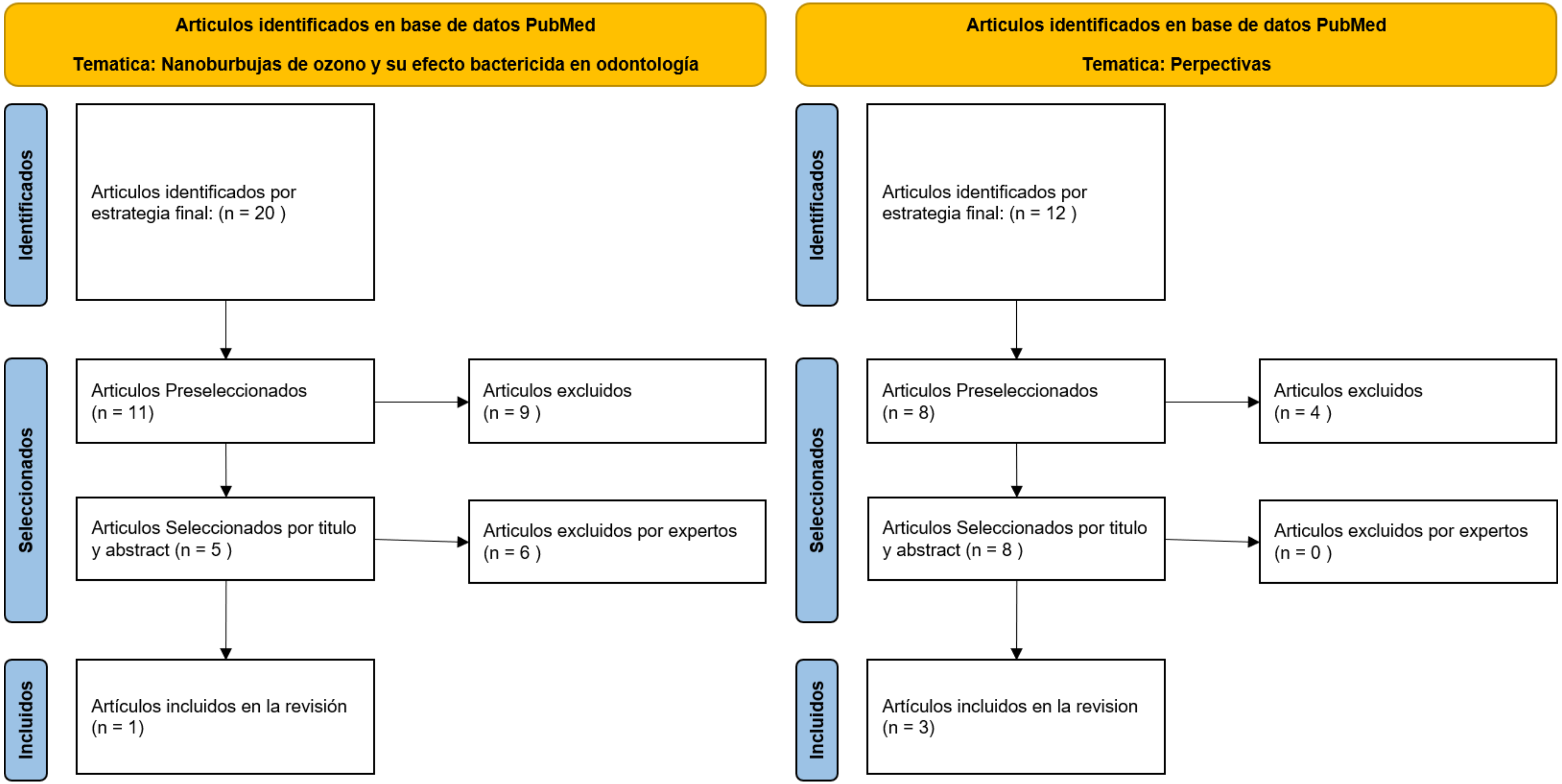


Figura 7 Flujogramas de artículos seleccionados en la base de datos Pubmed para las temáticas de Nanoburbujas de ozono y su efecto bactericida en odontología y Perspectivas

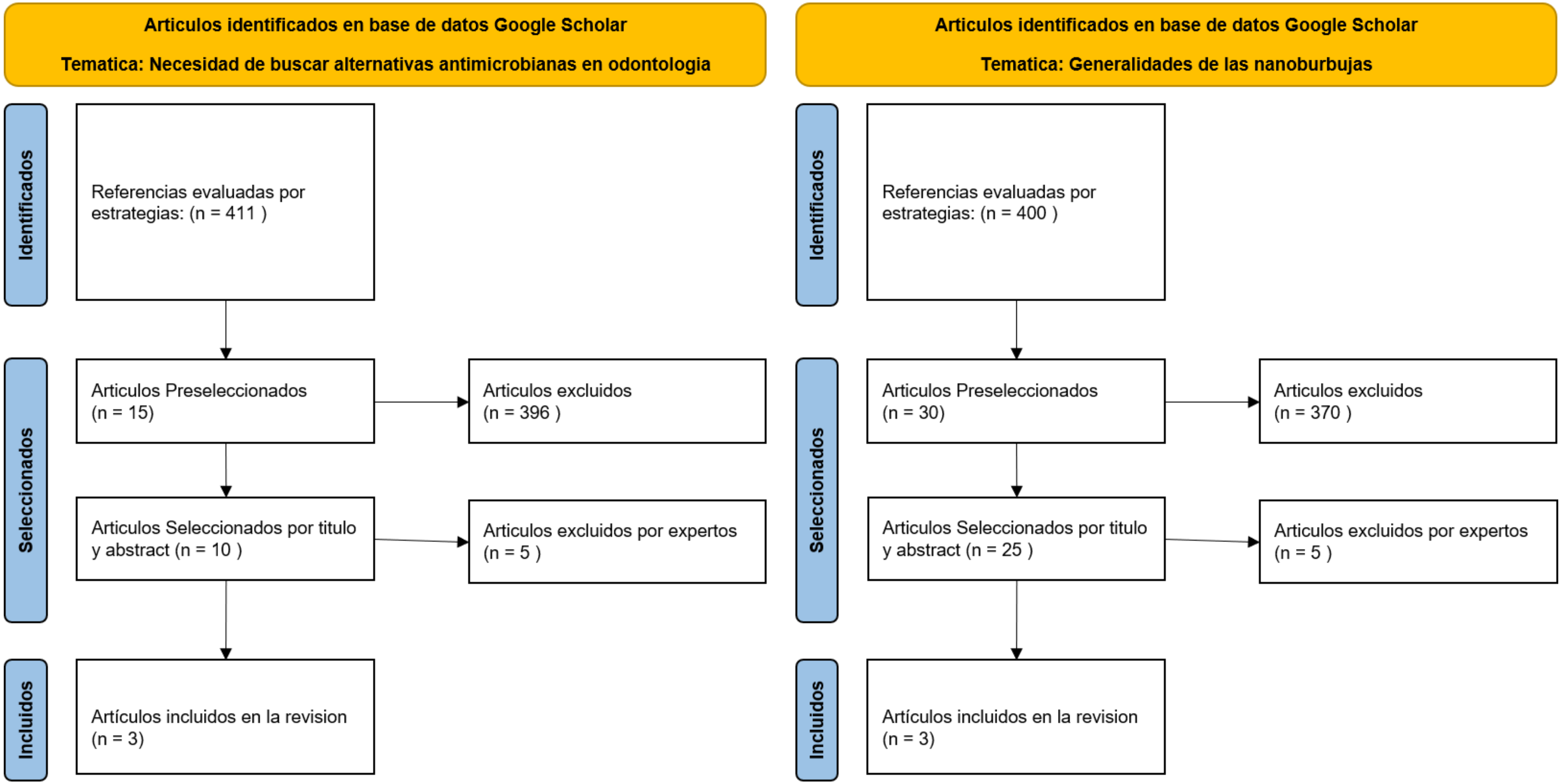


Figura 8 Flujogramas de artículos seleccionados en la base de datos Google Scholar para las temáticas de Necesidad de buscar alternativas antimicrobianas en odontología y Generalidades de las nanoburbujas.

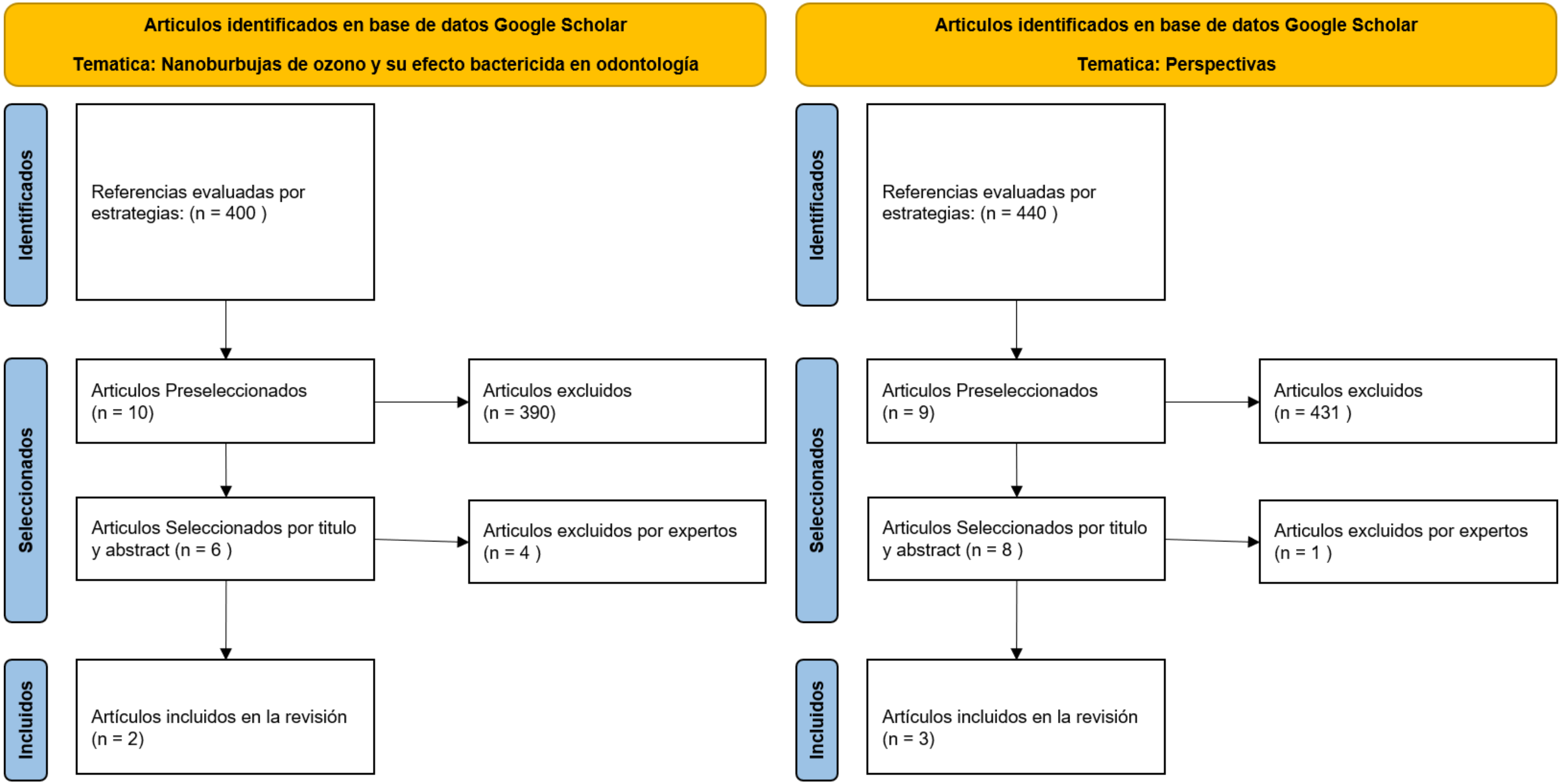


Figura 9 Flujogramas de artículos seleccionados en la base de datos Google Scholar para las temáticas de Nanoburbujas de ozono y su efecto bactericida en odontología y Perspectivas

Con base a los artículos seleccionados por título y abstract en las búsquedas realizadas en Pubmed y Google Scholar del total de artículos referente a la temática de necesidad de búsqueda de tratamiento se seleccionaron 21 artículos, de los cuales 17 de ellos fueron revisiones de literatura, 2 fueron estudios experimentales *in vitro*, 1 de ellos experimental *in vivo* y 1 reporte de caso.

Según la temática de generalidades de las nanoburbujas el total de artículos seleccionados fue de 34 artículos, donde 15 fueron revisiones de literatura, 1 estudio experimental *in vitro* y 18 artículos experimentales en ciencias básicas.

Para la temática de nanoburbujas de ozono y su efecto bactericida se seleccionaron 11 artículos, de los cuales 3 fueron artículos de revisión de literatura, 1 artículo de experimental *in vitro*, 2 de ellos experimentales *in vivo* y 5 artículos experimentales en ciencias básicas.

Por último, se seleccionaron 16 artículos para la temática de perspectivas siendo 6 artículos revisiones de literatura, 5 estudios experimentales *in vitro*, 4 estudios de experimentales *in vivo* y 1 reporte de caso.

Para un total de 41 artículos de revisiones de literatura, 9 estudios experimentales *in vitro*, 7 estudios experimentales *in vivo*, 23 artículos experimentales en ciencias basicas y 2 reportes de caso.

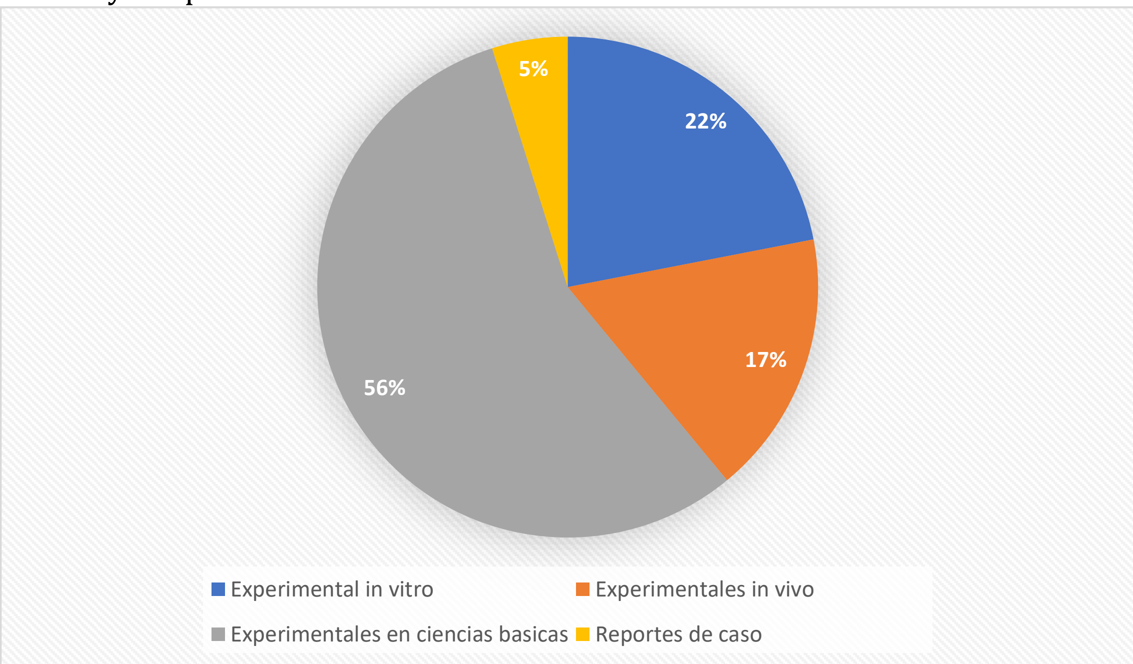


Figura 10 Porcentaje y tipo de artículos encontrados en las búsquedas realizadas en Pubmed y Google Scholar

En relación a los resultados de las tendencias actuales de las nanoburbujas y su utilización de distintas áreas del conocimiento según las métricas brindadas por las bases de datos Web of Science y Scopus para el termino de nanoburbuja, se evidencio de manera general que los artículos donde mayoritariamente son mencionadas las nanoburbujas son artículos referentes al estudio de las ciencias básicas (WoS = 60,8%/ Scopus = 61,3%), seguido de áreas de ingeniería (Scopus 20%) y desarrollo de tecnología de dispositivos (WoS = 20,2%), las publicaciones actualmente que se enfocan en las nanoburbujas para investigaciones clínicas corresponden a un 8.5% en Scopus y un 5,6% en WoS.

En el análisis de distribución de los reportes de nanoburbujas disponibles actualmente en el subgrupo de investigación clínica se evidencio que en Scopus la mayor proporción corresponde a medicina con un 4,66%, seguido de farmacología toxicología y farmacéutica con 3,17%, neurociencias 0,52% y con una proporción en el área odontológica de 0,05%. Y en Web of Science se observó una distribución correspondiente al 15,12% a investigación en medicina experimental, un 12,68% en el área oncológica, un 6,34% en neurología y neurociencias, y un 0,98% en odontología y medicina oral.

Al revisar la base de datos Clinical Trials.gov de la librería nacional de medicina de estados unidos utilizando el termino nanoburbuja, se encontraron 3 estudios donde solo 1 de ellos fue un reporte finalizado referente a el diagnostico de la malaria, y 2 artículos activos referentes a la esclerosis lateral amiotrófica y la artritis reumatoide.

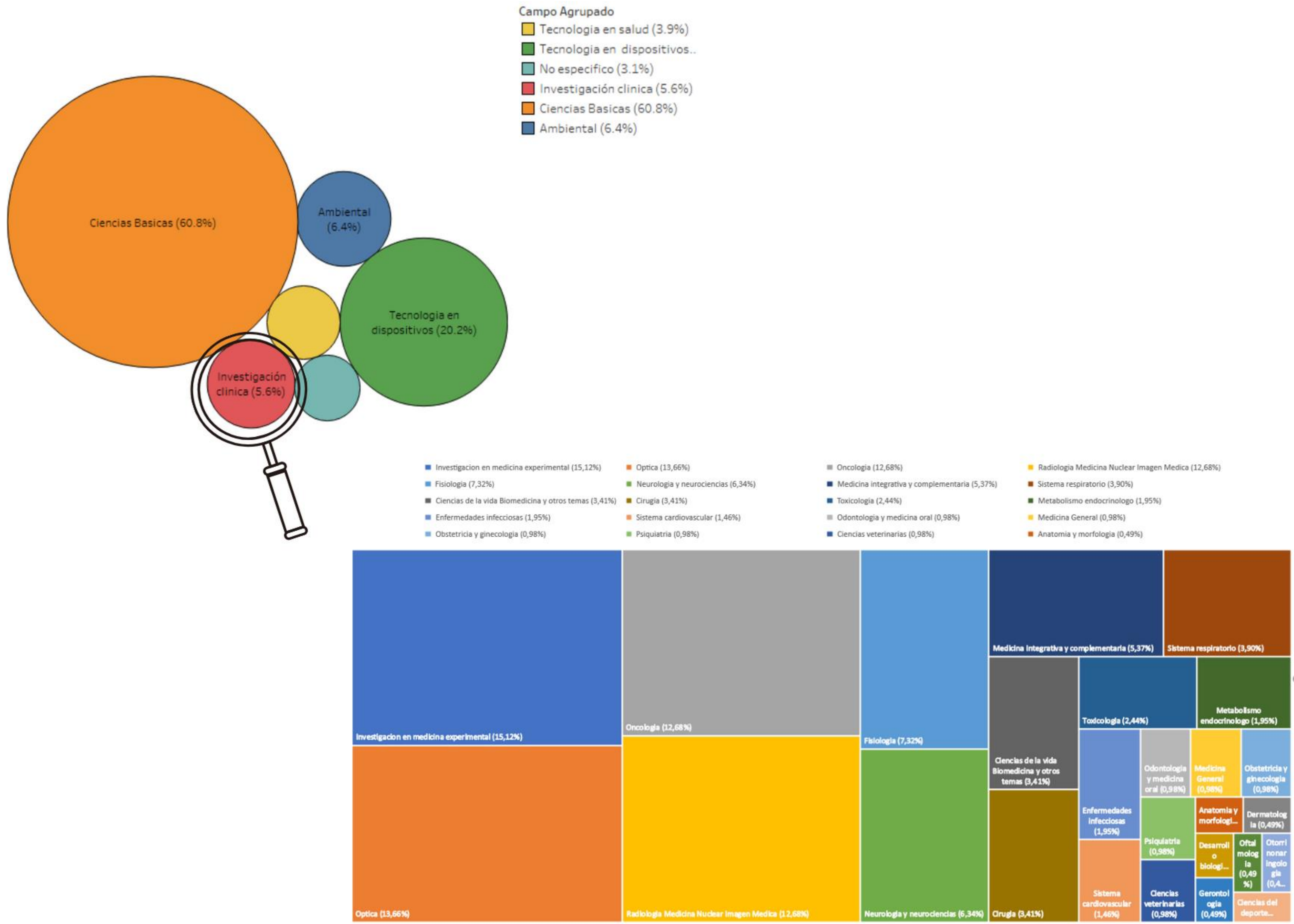


Figura 11 Visualización de datos tendencias actuales de las nanoburbujas según subgrupo de investigaciones clínicas en la base de datos Web of Science

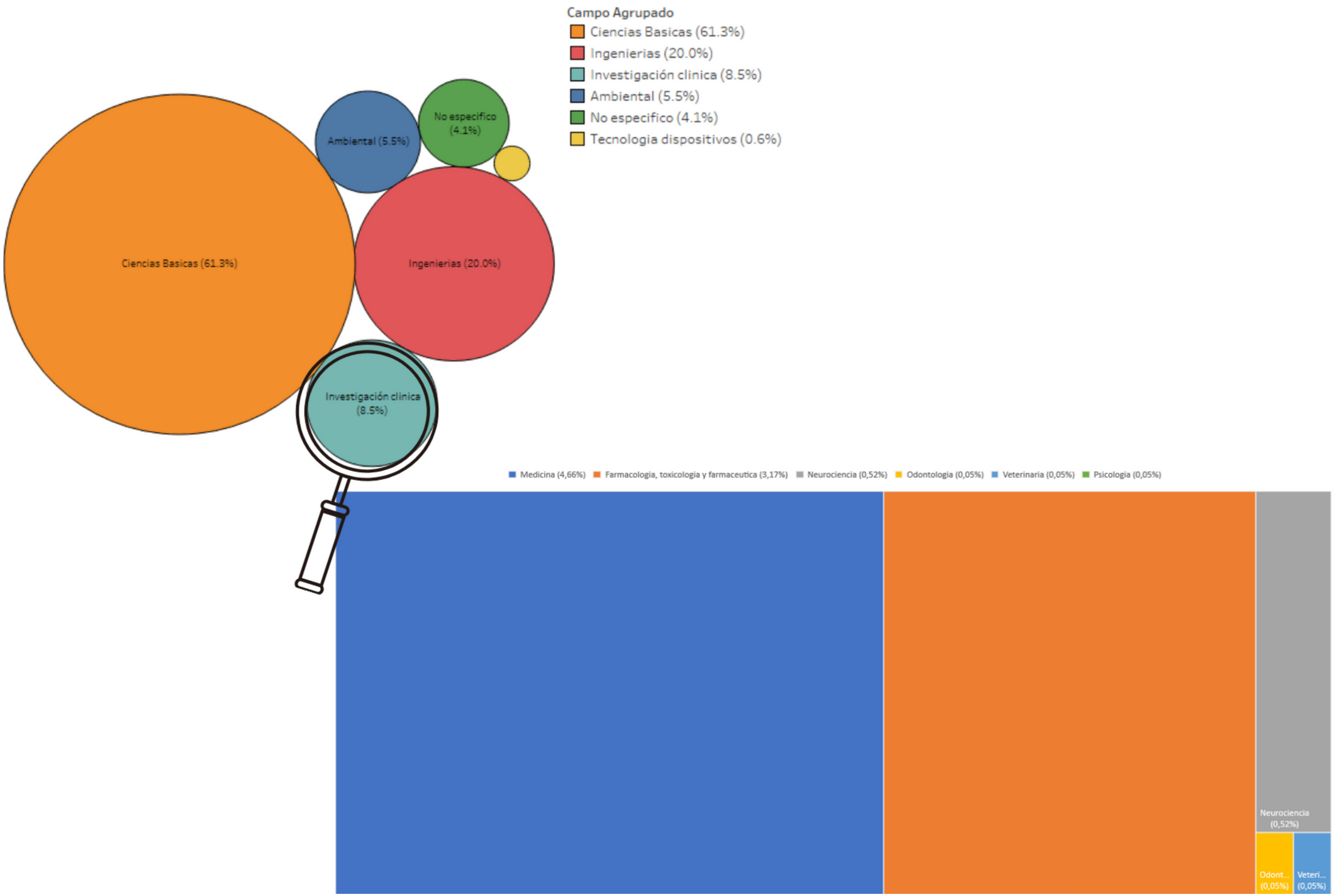


Figura 12 Visualización de datos tendencias actuales de las nanoburbujas según subgrupo de investigaciones clínicas en la base de datos Scopus

b. Resultados de proceso de extracción de información

1. Biofilms bacterianos como la principal causa de enfermedades orales

La habilidad de formar biofilms es común en procariotas (bacteria), un aspecto que cada vez toma mayor trascendencia en salud pública, pues las infecciones orquestadas por complejas comunidades microbianas y multiespecies, siguen siendo la principal causa de infecciones (Costalonga & Herzberg, 2014). Adicionalmente, ecosistemas tan diversos como la cavidad oral debido a la i) variedad de superficies dentales, mucosas; ii) y constante exposición a fluidos como la saliva y fluido crevicular, la hacen un reservorio ideal para más de 700 especies bacterianas y el desarrollo de enfermedades inflamatorias crónicas (Jr, 2015; Wade, 2013). La caries y enfermedad periodontal se posicionan como las infecciones de mayor prevalencia a nivel global, solo superado por el resfriado común (Ministerio de Salud y Protección Social, 2014). Algunas de las razones que explican la alta frecuencia de enfermedades de origen bacteriano a nivel global es: i) la baja tasa de efectividad de los antibióticos tradicionales y ii) el desarrollo de resistencia bacteriana (Ghernaout & Elboughdiri, 2020). *De esta manera la progresión de la enfermedad periodontal es favorecida por las características estructurales y micro ambientales que confiere el biofilm subgingival para el desarrollo de resistencia antimicrobiana.*

1.1 Características de un Biofilm periodonto patógeno y resistencia antimicrobiana.

La periodontitis es una infección bacteriana inducida en huéspedes susceptibles a un biofilm polimicrobiano subgingival en el que la inflamación y la disbiosis se refuerzan positivamente manteniendo la progresión de la periodontitis (Papapanou et al., 2018). Dicha inflamación es principalmente promovida por patógenos claves (*P. gingivalis, T. denticola y T. forsythia*) que integran complejos nichos con otras especies, mientras que la colonización de estos "patógenos clave" es facilitada por patógenos accesorios (patobiontes). Estos últimos son fundamentales, ya que inicialmente subvierten la respuesta del huésped hacia la disbiosis subgingival, inflamación y destrucción del tejido periodontal (Ximénez-Fyvie et al., 2000).

Gran parte de los desafíos actuales en el manejo de la periodontitis se originan a partir del complejo rol del biofilm en la progresión de la enfermedad. El biofilm subgingival es una compleja barrera fisicoquímica que le confiere a los microorganismos la evasión de la respuesta inmune y/o resistencia al efecto antimicrobiano de enjuagues y antibióticos, los cuales son usados generalmente en la terapia coadyuvante de la periodontitis (Access et al., 2017).

La resistencia es un importante aspecto que considerar en el biofilm subgingival, ya que confiere a las bacterias la capacidad de sobrevivir en presencia de agentes antimicrobianos y/o ante elevados niveles de este tipo de agentes (Rams et al., 2014). *Los principales mecanismos de resistencia asociados a la conformación de un biofilm polimicrobianos han sido descritos en torno a que cuenta con su propia matriz de sustancia polimérica extracelular (EPS), la modulación del metabolismo bacteriano favoreciendo lentas tasas de crecimiento bacteriano y por último la expresión de genes específicos para la supervivencia y resistencia bacteriana.*

1.1.1 La resistencia antimicrobiana y su rol a través de **EPS matriz, modulación del crecimiento y expresión génica**

Actualmente se ha demostrado el incremento significativo de bacterias resistentes a antibióticos en infecciones orales y maxilofaciales (Lebeaux et al., 2014). Dichos incrementos se pueden asociar a varios factores todos ellos relacionados con las propiedades que confiere el biofilm como la presencia de una barrera física, la alta densidad microbiana, la baja tasa de crecimiento bacteriano, la expresión de genes específicos para la resistencia, así como las alteraciones del microambiente (acidificación del pH, disminución en las tensiones de oxígeno, desbalance oxido-redox, etc) (Cox & Wright, 2013). De acuerdo con lo anterior, son diversos los mecanismos de resistencia bacteriana que se han descrito en el biofilm y que puede agruparse en:

- ***Baja penetración de antibióticos debido a la matriz EPS***: las características fisicoquímicas de la matriz extracelular que rodea a las células microbianas tienen la habilidad de repeler o retardar la penetración de los agentes antibióticos por las diferencias de cargas entre los antimicrobianos algunos con carga positiva y la matriz extracelular con carga negativa respectivamente (Obst et al., 1997). La presencia de esta matriz explica la lenta penetración de antibióticos como fluoroquinolonas y aminoglucósidos (Gordon et al., 1988; Mah & O'Toole, 2001), y además provee protección ante radiación UV y deshidratación (Lebeaux et al., 2014).

Otros factores físicos que disminuyen la efectividad de la antibioticoterapia, son la disminución en la tensión de oxígeno, sobre todo en biopelículas subgingivales, por lo que se genera una atmósfera anaerobia y de bajo pH adecuada para estos microorganismos, pero que le restan propiedades antimicrobianas a algunos antibióticos (Access et al., 2017).

- ***Baja tasa de crecimiento celular:*** Microorganismos con altas tasas de crecimiento son más susceptibles a agentes antimicrobiano, mientras que bajas tasas de crecimiento proveen resistencia bacteriana (Chemotherapy, 1853)**.** El crecimiento lento de microorganismos se produce debido a la disponibilidad limitada de nutrientes y sus gradientes, especialmente en zonas del biofilm que se denominan "zonas de fase estacionaria". La baja actividad metabólica bacteriana es más evidente a medida que madura el biofilm, acentuando cada vez más el desequilibrio entre la alta demanda de nutrientes y su limitada disponibilidad, principalmente en las comunidades bacterianas internas de la biopelícula (Chemotherapy, 1853).

Importantes enzimas tipo hidrolasas pueden modificar la molécula del antibiótico, especialmente ante el estrés bacteriano a causa de la deprivación de nutrientes. Se sabe que el déficit de nutrientes puede promover señales de supervivencia bacteriana como la lactona N-acilhomoserina (AHL), una señal también descrita en *P. gingivalis* a través de la expresión del gen LuxS (Lei et al., 2009), disminuyendo así la tasa de replicación y la proteostasis bacteriana(Kolenbrander, 2000). De esta manera, el stress se establece como un mecanismo de supervivencia, ya que la bacteria disminuye mucho sus procesos metabólicos y de replicación siendo así más resistente a los agentes antimicrobianos (Gutierrez et al., 2013).

- **Expresión de genes específicos**: Respecto a los patrones de expresión génica, estos difieren significativamente entre microorganismos planctónicos y microorganismos en biofilms polimicrobianos maduros (Rams et al., 2014). Mediante transcriptomica se ha demostrado que en la formacion in-vitro de biofilms multiespecies, 19.1% de los genes expresados por *P. gingivalis* fueron significativa y diferencialmente expresados (165 genes fueron sobreregulados y 200 subregulados), comparado con crecimientos plantónicos (Romero-Lastra et al., 2019). Estos genes fueron principalmente involucrados en funciones relacionadas a estrés oxidativo, envoltura celular, transposones y metabolismo, los cuales podrían incidir en bajar la tasa de crecimiento y aumentar la resistencia bacteriana. (Romero-Lastra et al., 2019).

2. Limitaciones de la terapia antimicrobiana tradicional en el manejo de la periodontitis:

Actualmente la prescripción sistémica de antibióticos es reconocida como una estrategia que podría beneficiar al paciente con periodontitis. Sin embargo, varios aspectos relacionados con la selección y prescripción empírica (sin previo análisis microbiológico), han hecho que la resistencia antimicrobiana a antibióticos y sus efectos adversos sean una problemática global en salud pública según declaraciones de distintas organizaciones como la Organización Mundial de la Salud (OMS) y la academia americana de periodoncia (Brinkac et al., 2017; Hetrick et al., 2009; Qasim et al., 2014; Rams et al., 2014).

En la última década, se han documentado altos niveles de resistencia antimicrobiana en diversas regiones geográficas alrededor del mundo, tales como España en el sur de Europa y Colombia en sur América (Rams et al., 2014). Este fenómeno ha sido asociado con el acceso cada vez menos controlado a antibióticos y su automedicación (Qasim et al., 2014). Adicionalmente, la composición multi-especie del biofilm subgingival en pacientes con periodontitis es otro agravante que contribuye significativamente a la baja susceptibilidad de los periodontopatógenos ante la terapia antibiótica (Brinkac et al., 2017).

Datos recientes reportan la alta frecuencia de la resistencia antibiótica en patógenos periodontales. El uso de antibióticos como doxiciclina y tetraciclina se ha asociado con un 55% y 46.9% de resistencia antimicrobiana en periodontopatógenos como *P. micra, P. intermedia/nigrescens, A. actinomycetemcomitans.* Datos similares también han sido observados para *P. gingivalis P. intermedia/ nigrescens,* y *F. nucleatum* asiladas de muestras subgingivales mostrando resistencia a amoxicilina, clindamicina y metronidazol(Rams et al., 2014). Este tipo de resultados incentive el uso complementario de diferentes espectros antimicrobianos como la combinación de amoxicilina y metronidazol. Esta práctica fue ampliamente usada para inhibir un mayor rango de periodontopatógenos(Van Winkelhoff et al., 1996). Sin embargo, especies resistentes a ambos antibióticos ya han sido reportadas tales como *Streptococcus* constellatus, entéricas/*pseudomonas*, *S. aureus*, *E. faecalis*, and *A. actinomycetemcomitans*, *P. intermedia/nigrescens*, lo cual acentúa aún más la dificultad en el manejo antimicrobiano de infecciones como la periodontitis, pues la prescripción sistémica de amoxicilina y metronidazol no ha sido efectiva en todos los pacientes, mostrando resultados muy similares al grupo placebo o control (Winkel et al., 2001) y que pueden ser explicados en gran parte por la protección adicional que les confiere el biofilm a los micoorganismos (Brinkac et al., 2017).

Se ha reportado que bacterias en embebidas en la placa bacteriana pueden ser hasta 1000 veces más resistentes comparado con sus contrapartes plantónicas (Hetrick et al., 2009). Por esta razón, la resiliencia bacteriana conlleva frecuentemente a la recuperación y reformación del biofilm, haciendo obsoletas las medidas antibióticas tradicionales, pues el 70% de las infecciones bacterianas a nivel hospitalario son resistentes para al menos uno de los antibióticos comúnmente usados (Qasim et al., 2014). De esta manera, es reconocible que la prevención, manejo y eliminación de la placa bacteriana disbiotica, es una problemática que requiere atención urgente no solamente a nivel odontológico sino biomédico; pues la resistencia antimicrobiana se traduce en mayores tasas de morbilidad y mortalidad capaz de incrementar los costos en los diferentes sistemas de salud pública a nivel global (Qasim et al., 2014).

3. Estrategias antimicrobianas diferentes a la antibioticoterapia para el manejo de la periodontitis

Tras conocerse que el uso tópico o sistémico de antibióticos trae consigo una serie de desventajas como la selectividad antimicrobiana, posible desarrollo de resistencia y riesgo de efectos adversos. El uso tópico a bajo costo de enjuagues antisépticos de amplio espectro con bajo potencial de reacciones adversas es cada vez más preferible en el manejo de la periodontitis. El agente coadyuvante más ampliamente usado en el manejo de la periodontitis es la clorhexidina(CHX), la cual es aplicada en concentraciones de 0.1% hasta 2% (Serra, 2016). Sin embargo, su uso prolongado puede causar varios efectos adversos como descamación epitelial, pigmentaciones dentales y/o linguales, así como alteraciones en el gusto (percepción de sabor amargo y/o metalizado) (Francisco Javier Manzano Moreno, Víctor Javier Costela Ruiz, Enrique García Recio, Rebeca Illescas Montes, Lucia Melguizo Rodríguez, 2013). Además, bajas concentraciones de CHX pueden ser toxicas en fibroblastos gingivales y osteoblastos, reduciendo la producción de proteínas colágenas y no colágenas, impidiendo así la adecuada reparación del periodonto (Francisco Javier Manzano Moreno, Víctor Javier Costela Ruiz, Enrique García Recio, Rebeca Illescas Montes, Lucia Melguizo Rodríguez, 2013; Mariotti & Rumpf, 1999). Además, el incremento en el número de reacciones alérgicas a la CHX incluyendo urticaria de contacto, asma ocupacional y shock anafiláctico, ha desmotivado su uso y prescripción clínica (Mariotti & Rumpf, 1999).

Considerando las limitaciones de la clorhexidina sobre todo en términos de seguridad, distintos estudios han revisado extensivamente los datos de efectividad de otras alternativas antimicrobianas como es el caso del triclosán. Por ejemplo, la revisión sistemática de 30 ensayos clínicos aleatorizados desde 1990 a 2012 donde se analizaron los datos de 14, 835 participantes permitió concluir que el triclosán es efectivo en prevenir gingivitis y sangrado gingival, además de sus propiedades anti-placa (Riley & Lamont, 2013). Siendo este un método seguro y sin ningún efecto adverso en humanos. No obstante, es insuficiente la evidencia que soporte su uso como agente antimicrobiano para la prevención o manejo de la periodontitis.

En términos generales, desarrollar alternativas de antisépticos que ofrezcan una mayor actividad antimicrobiana, un mejor perfil de seguridad y menor tasa de efectos adversos, siguen siendo un importante requerimiento en salud oral, ya que generarían una gran valor e impacto clínico para el tratamiento y resolución de la enfermedad periodontal, especialmente la periodontitis.

4. El ozono y las nanoburbujas como agente antimicrobiano en periodontitis

El ozono es un gas incoloro compuesto por 3 moléculas de oxígeno presente como una forma alotrópica del oxígeno y que se encuentra naturalmente en la atmosfera y especialmente a nivel de la estratosfera ayudando a la filtración de los rayos UV (Azarpazhooh & Limeback, 2008; Bansal & Lecturer, 2012). (Ver figura 13).

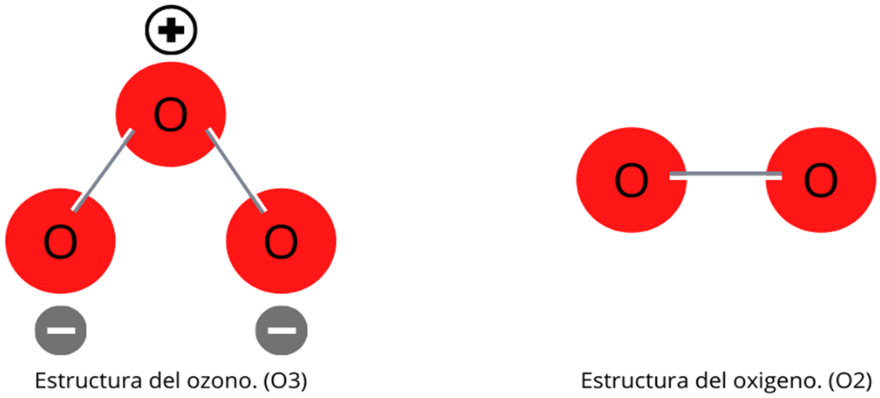


Figura 13 Estructura Molecular del Ozono y el Oxigeno

Las distintas terapias de ozono han demostrado beneficios como la estimulación de células inmunocompetentes y la síntesis de inmunoglobulinas, interleucinas y prostaglandinas que beneficiaran los procesos de inflamación y cicatrización, así mismo estimula la circulación y transporte de oxígeno promoviendo la secreción de vasodilatadores y aportando a la síntesis de proteínas (Seidler et al., 2008). Adicionalmente, se destacan los efectos antimicrobianos de las terapias de ozono actualmente descritas, un aspecto fundamental que puede significar el desarrollo de agentes antimicrobianos cargados con ozono como las nanoburbujas. No obstante, es indispensable establecer los pilares fundamentales de sus características y propiedades que definen actualmente a esta emergente tecnología, así como los hitos más importantes en su desarrollo y sus principales tendencias de investigación en salud.

Entre los distintos campos con potencial aplicación de las nanoburbujas se encuentra el de la salud donde juegan un papel fundamental para el desarrollo de nuevas terapias y estrategias que permitan la optimización y evolución en la solución de problemas médicos y odontológicos. Entre las aplicaciones encontramos preservación de tejidos, injuria isquémica, medicina regenerativa, agente de contraste en imágenes diagnósticas y teragnosis, además de poseer un efecto bactericida, entre otros (Michailidi et al., 2019). No obstante, es indispensable establecer los pilares fundamentales de sus características y propiedades que definen actualmente a esta emergente tecnología, así como los hitos más importantes en su desarrollo y sus principales tendencias de investigación en salud.

4.1 Las nanoburbujas y sus tendencias de investigación en salud

Actualmente en relación a la literatura de las nanoburbujas y su implementación en distintos campos de la salud, la mayor concentración de estudios son en ciencias básicas y ciencias aplicada como la nanoingieneria, así como ensayos clínicos, destacando su evaluación en disciplinas como oncología, farmacología y neurociencias. (Ver figura 14 y 15).

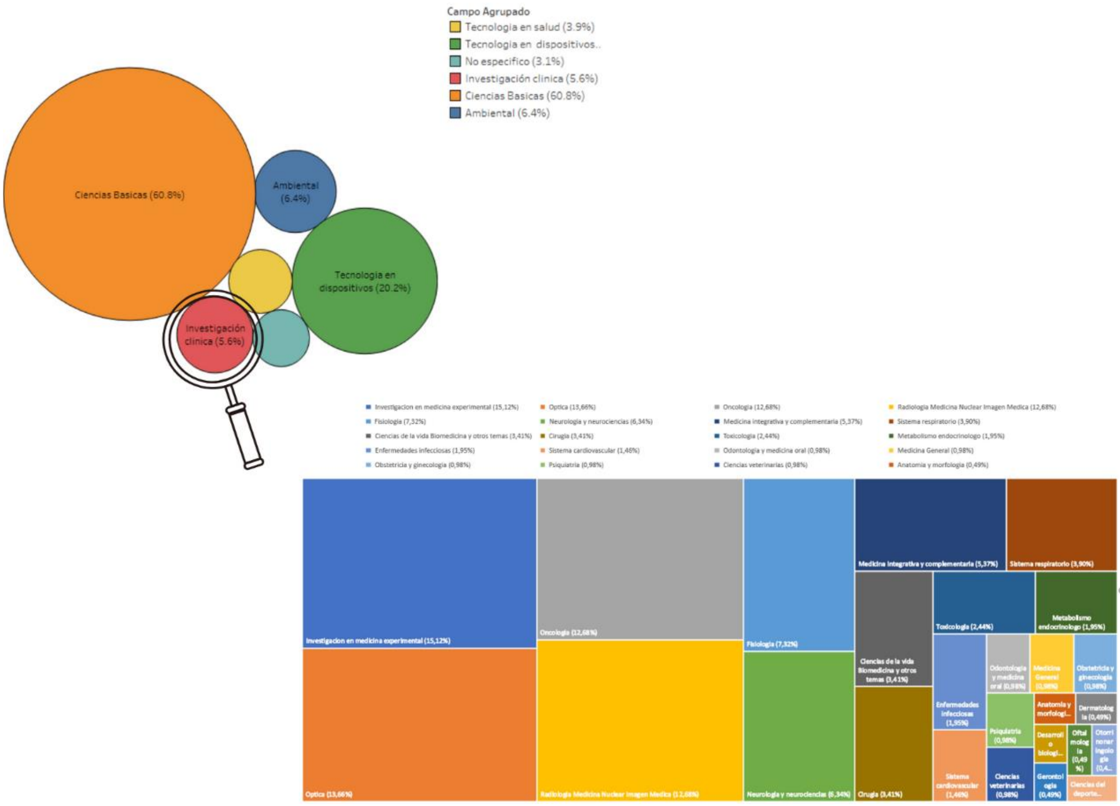


Figura 14 Visualización de datos tendencias actuales de las nanoburbujas según subgrupo de investigaciones clínicas en la base de datos Web of Science

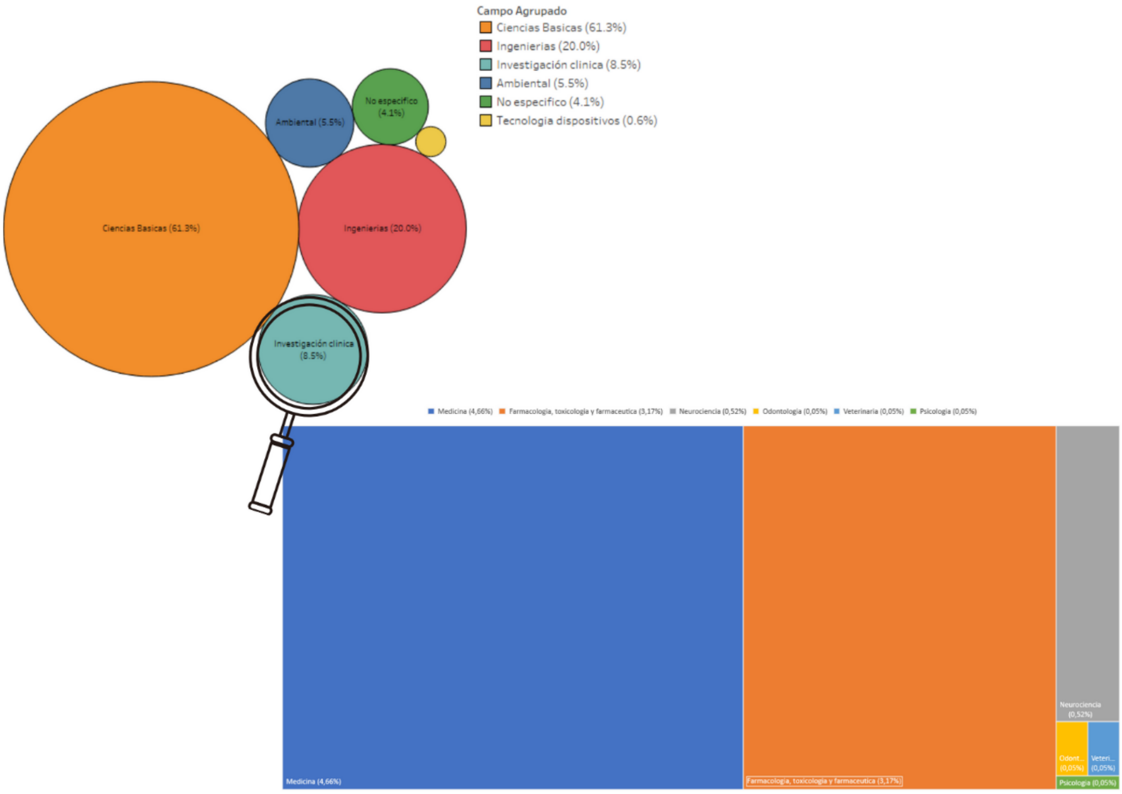


Figura 15 Visualización de datos tendencias actuales de las nanoburbujas según subgrupo de investigaciones clínicas en la base de datos Scopus

4.2 Definición y clasificación de las nanoburbujas.

La organización Internacional para la estandarización (ISO) ha realizado distintas definiciones referentes a las burbujas, determinando que una burbuja es un gas contenido en un medio rodeado por una interfaz (ISO 20480-1:2017). De acuerdo a su diámetro estas pueden ser clasificadas en burbujas finas (menor a 100 µm), microburbujas (mayores a 1 µm) y por ultimo las nano burbujas (menores a 1 µm).Este tipo de burbuja a su vez es clasificado en nanoburbujas tipo bulk o a granel y hace referencia a geometrías esféricas de nanoburbujas las cuales se mantienen en suspensión dentro de soluciones liquidas o de interfaz liquida (Alheshibri et al., 2016).

4.3 Características físicas, químicas y eléctricas de las nanoburbujas

El tamaño de una burbuja es la primer característica determinante para comprender sus propiedades, ya que una distribución de tamaño en escala nanométrica se asocia con mejor estabilidad, transferencia de masa, influyendo significativamente en su comportamiento y demás características fisicoquímicas y eléctricas dentro de un líquido (X. yu Zhang et al., 2020). (Ver figura 16).

Las burbujas son distribuidas en una solución mediante fuerzas de flotabilidad y por el movimiento al azar entre las moléculas que se encuentran suspendidas en un líquido (movimiento browniano). Las burbujas de mayor tamaño tienden a emerger mostrando una mayor fuerza de flotación y mientras que las nanoburbujas permanecen en el medio liquido por un mayor tiempo debido con un patrón de movimiento aleatorio o movimiento browniano (Azevedo et al., 2016).

Otra de las características físicas que hacen únicas a las nanoburbujas es la velocidad de ascenso, la cual va ligada a su estabilidad y vida media en suspensión. El diámetro de la burbuja y la viscosidad del líquido condicionan la velocidad de ascenso, siendo mayor para las macroburbujas (> 100µm) y menor para microburbujas (< 100 µm) y casi despreciable para las nanoburbujas (< 1 µm) (Azgomi et al., 2007).

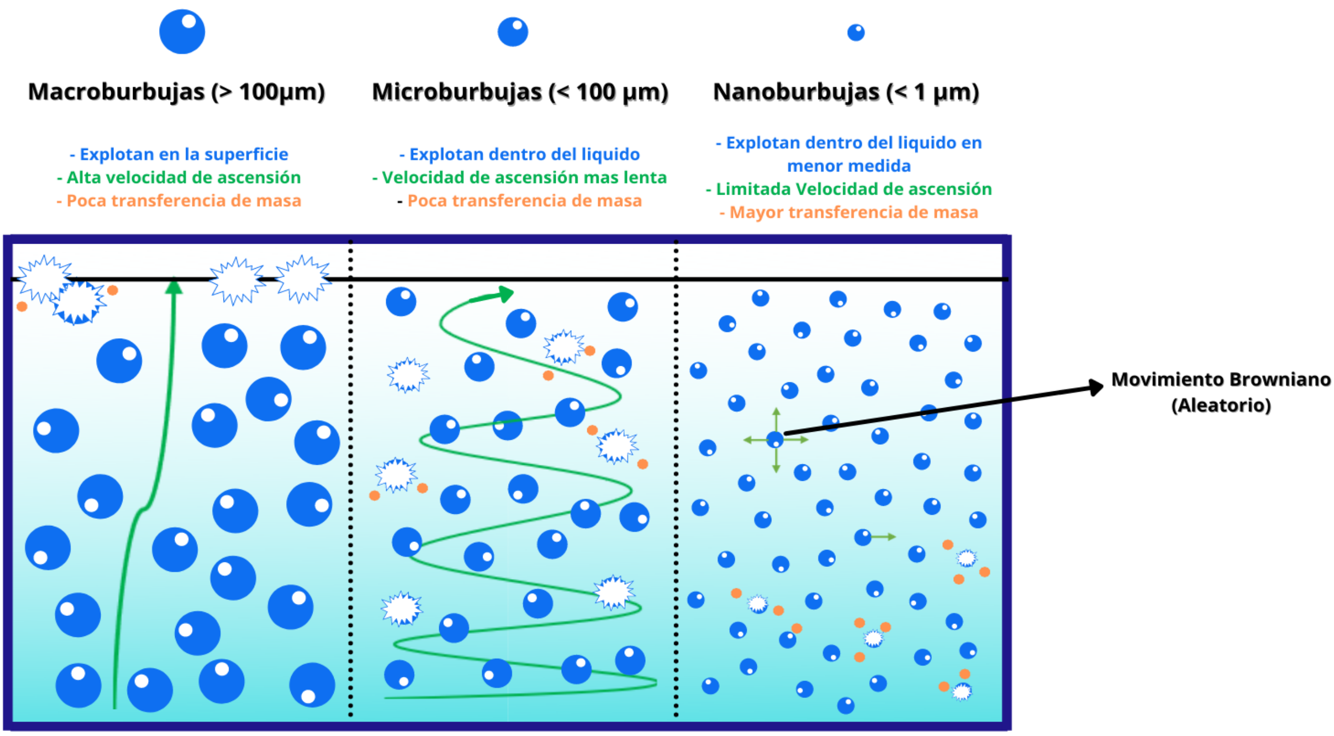


Figura 16 Descripción general de las características físicas de las macroburbujas, microburbujas y nanoburbujas.

Las nanoburbujas a diferencia de otras burbujas de mayor tamaño, también poseen características únicas como su carga de superficie que les confiere una vida media de hasta 6 meses en condiciones *in vitro* (Nirmalkar et al., 2018). Las nanoburbujas son consideradas partículas electrostáticas que se distribuyen a partir de iones de hidróxido (anión) sobre iones de hidrogeno (catión), formando puentes hidrógenos estables entre su interfaz, evitando la dispersión del gas que contiene y manteniendo un equilibro cinético frente a las altas presiones, lo que les ayuda a tener una vida media más prolongada (Allaker & Douglas, 2009).

Dentro de las características químicas de las nanoburbujas, se sabe que estas también son afectadas por el pH del medio en el que se encuentren. Diferentes reportes observaron que cambios en el pH no provocan cambios significativos en su tamaño y distribución, pero si influyen en su estabilidad. A pH alcalino, las nanoburbujas incrementaran su estabilidad gracias a su carga superficial volviéndose más negativas y por lo tanto más estable, mientras en una solución a pH acido, desciende su estabilidad al verse vulnerada la fuerza iónica de la solución en la que se encuentran (Hamamoto et al., 2018).

4.4 Estabilidad de las Nanoburbujas de Ozono

El potencial zeta se debe entender como el potencial que tiene una partícula en un plano de corte en la doble capa eléctrica de una solución, esta se representa como una medida de magnitud como parámetro electrostático de las partículas en un estado se suspensión, evaluando la estabilidad de la dispersión en un medio líquido, esta se puede medir por diferentes formas como técnicas de electroforesis y electroacústicas (Bibiana et al., 2012).

El potencial zeta de las nanoburbujas cambiara según el gas que contengan, siendo más alto para gases que presenten una mayor solubilidad como es el caso del ozono y el oxígeno debido a que generan radicales libres de grupos hidroxilo, aumentando así los valores de cargas negativas en la solución, destacando que el potencial zeta de una partícula con buena estabilidad coloidal se caracteriza por valores de potencial zeta cercanos a los -30 mV (milivoltios), valores muy similares a lo reportados en nanoburbujas de ozono entre 20 mV y 27 mV (Ushikubo et al., 2010).

4.5 Mecanismos del efecto antimicrobiano de las nanoburbujas de Ozono.

Los principales mecanismos antimicrobianos del ozono son explicados como resultado del daño a nivel de la membrana citoplasmática de los microorganismos, así como la oxidación de sus proteínas y en consecuencia perdida de función celular, El espectro de acción no es especifico, ni selectivo, no obstante es muy llamativo como no daña las células eucariotas debido a que cuentan con diferentes estrategias antioxidantes que les permite mantener el balance redox sin comprometer su función en células como neuronas y células epiteliales (Himuro, 2017; P. et al., 2013).

La acción antimicrobiana de las nanoburbujas de ozono es ejercida partir de los radicales libres que se generan al momento de la cavitación de las nanoburbujas (Fernandes et al., 2018), facilitando la disrupción de la membrana celular y citoplasmática de bacterias, oxidando las glicoproteínas, glicolípidos y demás biomoléculas, facilitando la lisis bacteriana (Ari et al., 2020). (Ver figura 17).

En odontología se ha evaluado la actividad bactericida de las nanoburbujas de ozono contra bacterias periodonto patógenas y su citotoxicidad contra células propias de

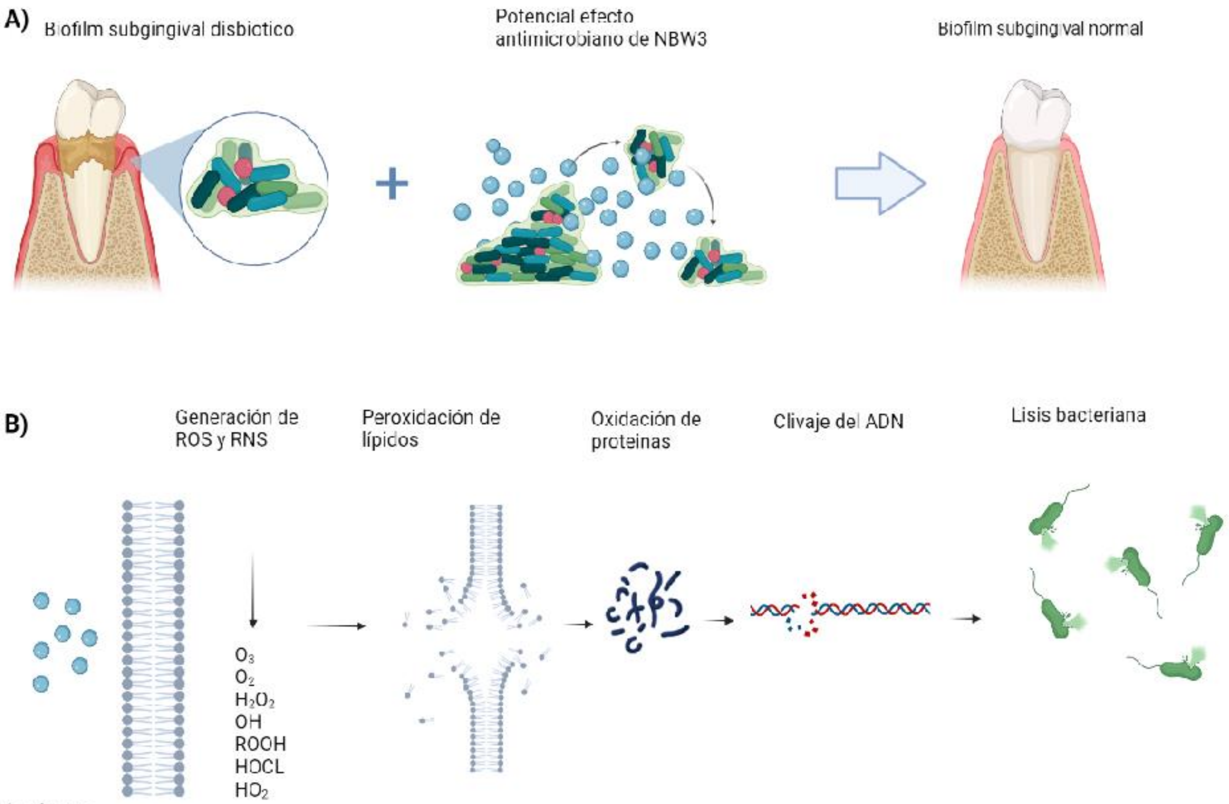


Figura 17 Mecanismo antibacteriano del ozono y sus subproductos para disminuir la viabilidad bacteriana.

cavidad oral; el efecto bactericida fue evaluado contra *Porphyromonas gingivalis* y *Aggregatibacter actinomycetemcomitans* en un estudio de experimental *in vitro*, demostrando una alta efectividad en su capacidad bactericida y nula citotoxicidad a las células propias de los tejidos de la cavidad oral (Hayakumo et al., 2014). Similares resultados también han sido reportados en pacientes con periodontitis en el que el uso de agua con nanoburbujas de ozono junto con la terapia mecánica periodontal, mostro los mejores resultados en términos de efectividad según análisis microbiológico, reduciendo significativamente el número de colonias de *P. gingivalis* y *T. forsythia* en la placa subgingival, disminuyendo el tamaño de la bolsa periodontal y mejorando los niveles de inserción periodontal (Hayakumo et al., 2013).

5. Las nanoburbujas y sus futuros desarrollos en salud:

Entre los distintos campos con potencial aplicación de las nanoburbujas se encuentra el de la salud donde juegan un papel fundamental para el desarrollo de nuevas terapias y estrategias que permitan la optimización y evolución en la solución de problemas médicos y odontológicos. Entre las otras aplicaciones que se proyectan como importantes desarrollos encontramos preservación de tejidos, injuria isquémica, medicina regenerativa, agente de contraste en imágenes diagnósticas, terapia génica, distribución de medicamentos, terapia anticáncer, terapia anti-inflamatoria, manejo de enfermedades neurodegenerativas y oxigenación de tejidos, teragnosis e ingeniería de tejidos, además de poseer un efecto bactericida, entre otros (Batchelor et al., 2020; Endo-Takahashi & Negishi, 2020; Khan et al., 2019; Khan, Hwang, Seo, et al., 2018; Meegoda et al., 2018; Michailidi et al., 2019; Oeffinger & Wheatley, 2004; Owen et al., 2016). Esta diversidad en sus aplicaciones es en parte argumentado tanto por la naturaleza de las propiedades físicas, químicas y eléctricas de las nanoburbujas, así como por la variedad de gases que puede contener en su interior, la versatilidad de los distintos métodos para la nano ingeniería de estas partículas y sus flexibles métodos de producción.

5.1 Nanoburbujas y Caries.

En odontología las nanoburbujas también han sido utilizadas contra flora bacteriana cariogenica en la eliminación de estos microrganismos , también se han realizado esfuerzos por utilizar nanoburbujas de ozono en estudios experimentales para la remoción de *Streptococcus mutans* y *Candida albicans* en aparatología ortodóntica de dientes extraídos, así como su utilización en superficies de prótesis totales de adultos en su desinfección por medio de un generador de nanoburbujas demostrando una efectiva eliminación de microorganismos en ambos casos (Lin, 2020; SUEISHI et al., 2020).

En el área endodóntica se ha utilizado agua con nanoburbujas como irrigante para la remoción del barrillo dentinal intraconducto y su eficacia como agente desinfectante en dientes porcinos demostrando ser más efectivo que el EDTA al 17% y permitiendo la infiltración de tetraciclina en el túbulo dentinal sugiriendo que el agua con nanoburbujas puede ser puede ser un complemento prometedor de los irrigantes y medicamentos en la terapia endodóntica (Shawli et al., 2020).

5.2 Nanoburbujas y Enfermedad Periodontal.

Adicional al estudio de nanoburbujas en el tratamiento y manejo de la periodontitis y sus propiedades antimicrobianas para *P. gingivalis T. forsythia y Aggregatibacter actinomycetemcomitans* (Hayakumo et al., 2013, 2014). También se proyecta su desarrollo en el manejo de perimplantitis, pues aunque la evidencia aún insuficiente para argumentar su efectividad antimicrobiana en este tipo de lesiones, reportes de caso empieza a dilucidar que el agua con nanoburbujas de ozono puede ser efectivo como terapia coadyuvante para la peri-implantitis, no obstante se requiere el diseño de ensayos clínicos controlados que permitan evaluar su efecto en comparación con otros agentes antimicrobianos (Arakawa et al., 2017).

9. CONCLUSIONES

El análisis realizado durante la revisión permitió concluir que el control de enfermedades infecciosas cobra cada día mayor relevancia en especial en enfermedades como la periodontitis debido a la aparición de nuevos microorganismos con capacidad de resistir a la terapia antibiótica, por lo que es necesario desarrollar alternativas para el desarrollo de terapias más efectivas como el uso de nanoburbujas de ozono, las cuales han demostrado en diferentes estudios su capacidad antimicrobiana y propiedades de citocompatibilidad al ser comparada con otro tipo de enjuagues como la clorhexidina, que actualmente es considerada el estándar de oro, pero que su uso crónico conlleva a problemas y efectos adversos sobre el paciente. La literatura encontrada sobre el uso de nanoburbujas en odontología actualmente es muy escasa y no corresponde a una mayoría con respecto al estado del arte y consideramos pertinente incentivar al desarrollo y creación de nueva literatura que pueda aplicar las propiedades de las nanoburbujas en el desarrollo de terapias que se apliquen en odontología.

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