Review Article

Ozone use in surface disinfection: an integrative review

O uso do ozônio na desinfecção de superfícies: revisão integrativa

El uso de ozono para la desinfección de superficies: revisión integradora

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Abstract

Objective: To analyze the scientific evidence regarding the effectiveness of using ozone to disinfect surfaces based on an integrative literature review.

Methods: A search was carried out in the SciELO, MEDLINE, LILACS, PubMed, Science Direct databases. Eleven articles published January 2010 to August 2021 were analyzed. All employed the experimental laboratory research model and achieved different levels of disinfection by O_3, however, with varied surfaces and products tested, in addition to different methodological procedures.

Results: The majority had an inhibition rate by O_3 equal to or greater than 90%, thus proving the effectiveness of this agent as a surface disinfectant, even with variations in parameter values such as concentration and exposure time, in all selected articles, even those that did not prove the effectiveness of $O_{3.}$

Conclusion: This review shows the inhibitory power that O_3 has on different pathogens, even if there are variables in the factors used for this purpose, highlighting it in front of other disinfectants. Thus, it corroborates the composition of surface disinfection protocols and decision-making among managers and committees about sanitizing technologies.

Resumo

Objetivo: Analisar as evidências científicas com relação à eficácia do uso do ozônio para desinfecção de superfícies a partir de uma revisão integrativa de literatura.

Métodos: Realizou-se busca nos bancos de dados eletrônicos: SciELO, MEDLINE, LILACS, PubMed, Sciense Direct. Foram analisados onze artigos, publicados no período de janeiro de 2010 a agosto de 2021. Todos empregaram o modelo de investigação experimental laboratorial e alcançaram diferentes níveis de desinfecção pelo O_3, no entanto, com variadas superfícies e produtos testados, além de diferentes procedimentos metodológicos.

Resultados: A maioria apresentou taxa de inibição pelo O_3 igual ou superior a 90%, comprovando assim a eficácia desse agente como desinfetante de superfícies, mesmo havendo variações de valores dos parâmetros como, concentração e tempo de exposição, em todos os artigos selecionados, até mesmo nos que não comprovaram a eficácia do $O_{3.}$

Conclusão: Essa revisão evidencia o poder inibitório que o O_3 possui sobre diferentes patógenos, mesmo que haja variáveis nos fatores utilizados para esse fim, destacando-o frente a outros desinfetantes. Corrobora, assim, na composição de protocolos de desinfecção de superfícies e na tomada de decisão entre gestores e comissões acerca de tecnologias saneantes.

Keywords
Desinfection; Disinfectants; Ozone; Cross infection; Infection control

Descritores
Desinfecção; Desinfetantes; Ozônio; Infecção hospitalar; Controle de infecções

Descriptores
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Conflicts of interest: nothing to declare.

Resumen

Objetivo: Analizar las evidencias científicas con respecto a la eficacia del uso del ozono para la desinfección de superficies a partir de una revisión integradora de la literatura.

Métodos: Se realizó una búsqueda en los bancos de datos electrónicos: SciELO, MEDLINE, LILACS, PubMed, Sciense Direct. Se analizaron 11 artículos, publicados en el período de enero de 2010 a agosto 2021. Todos utilizaron el modelo de investigación experimental laboratorial y obtuvieron distintos niveles de desinfección por O_3, pero utilizando distintas superficies y productos, además de distintos procedimientos metodológicos.

Resultados: La mayoría presentó una tasa de inhibición por O_3 igual o superior al 90 %, lo que comprueba la eficacia de ese agente como desinfectante de superficies, aunque existan variaciones en los valores de los parámetros, como concentración y tiempo de exposición, en todos los artículos seleccionados, incluso en los que no se comprobó la eficacia del O_3.

Conclusión: Esta revisión evidencia el poder inhibitorio que el O_3 presenta ante distintos patógenos, aunque existan variables en los factores utilizados para esa finalidad, por lo que se destaca ante otros desinfectantes. De esta forma, se confirma la composición de protocolos de desinfección de superficies y la toma de decisiones entre gestores y comisiones sobre tecnologías de desinfección.

Introduction

Healthcare-associated infections (HAIs) have proven to be a relevant public health problem.[1] In addition to burdening the State with costs, morbidity and mortality rates caused by HAIs are around 1.7 million and 99 thousand per year, respectively.[2] This situation requires an incessant search for preventive measures, as environmental contamination plays an important role in the transmission of various pathogens.[3]

In order to control and prevent these infections, as well as to inhibit the growth of microorganisms that are resistant to at least two classes of antibiotics, multidrug-resistant microorganisms (MRD),[4] studies indicate that routine cleaning and disinfection have a positive effect on the sanitization of surfaces in the hospital environment, since cleaning consists of eliminating dirt and, after the previously cleaned surface, the disinfection process removes the microbial load and multidrug-resistant strains.[5]

Traditionally, the infectants found in the market with chlorine, alcohols, aldehydes, among others, are used for the elimination of microbial load present on nosocomial surfaces [6] whose mechanism of action is by inhibition of growth and microbial lethal action. [7]

Nevertheless, it has recently been observed the search for new disinfection methods that assess the decontaminating effect of ozone (O_3) in water and air contaminated by *Staphylococcus aureus, Pseudomonas auriginosas, Escherichia coli* and *Streptococcus faecalis*, with positive results for the reduction of the contaminating potential of microorganisms, both in water and in the environment in the form of aerosols.[8]

O_3's oxidative effect arises as a safe and low-cost proposal in antimicrobial containment in different areas.[9] This gas stands out as a disinfectant compound, since O_3's bactericidal action is greater than that of chlorine, as it acts by causing the lysis of bacterial cells, viruses and fungi through the oxidation of the cell wall, cytoplasmic membrane and other components of the microbial cell structure.[10]

In this regard, due to its vast antimicrobial capacity, O_3 has proven to be an increasingly accessible, reliable and cost-effective choice for surface-related disinfection techniques, becoming a strong ally in the elimination of pathogenic agents, having the potential to act as a complementary element of cleaning and disinfection protocols.[11]

That said, given the advance of MRD that represent an important threat to health services and considering the low development of new antimicrobial agents, it is essential to develop new sanitizing technologies.[12] Therefore, this study aimed to highlight the effectiveness of using this agent for disinfecting surfaces, from scientific articles using integrative literature review.

Methods

This is an integrative literature review (ILR)[13] that followed six phases: in the 1st phase, the guiding question was elaborated; in the 2nd phase, the search or sampling of references took place; in the 3rd phase, data collection took place; in the 4th phase, there was a critical analysis of included studies; in the 5th phase, there was a discussion of results; in the 6th phase, the integrative review presentation was formulated.

The following question emerged: What is the scientific evidence of O_3 use in surface disinfection from January 2010 to August 2021? This question guided a bibliographic search, filtering the articles that were consistent with the object of the study.

A search was carried out in the Scientific Electronic Library Online (SciELO), Medical Literature Analysis and Retrieval System Online (MEDLINE), Latin American and Caribbean Literature in Health Sciences (LILACS), PubMed, ScienceDirect, all present in the Virtual Library in Health and Web of Science, using the descriptors: Disinfection, Ozone and Hospital Infection, associated with Boolean operators "AND, NOT and OR".

We found 340 articles, only 11 of which were used in the analysis of this study, since most belonged to the areas of dentistry, food industry and wastewater treatment, which did not corroborate with the theme proposed by this research. There was also a limitation of selected articles due to the lack of the descriptor "surface" in the Health Sciences Descriptors (DeCS) database.

We included complete articles, which covered the theme and objective of the study, published between 2010 and 2021, in Portuguese, English and Spanish.

We excluded duplicate articles, abstract-only publications, literature reviews, reflections, and reviews.

For article selection, the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) recommendations were followed, as shown in Figure 1.

Results

After applying the inclusion and exclusion criteria, we selected 11 articles that answered the central question of the research, which will be presented in Chart 1, according to classification, database, title, authors, year, country and objective of the study.

The studies' authors were allocated in different professional areas: medicine (A3, A4, A5, A8, A9,

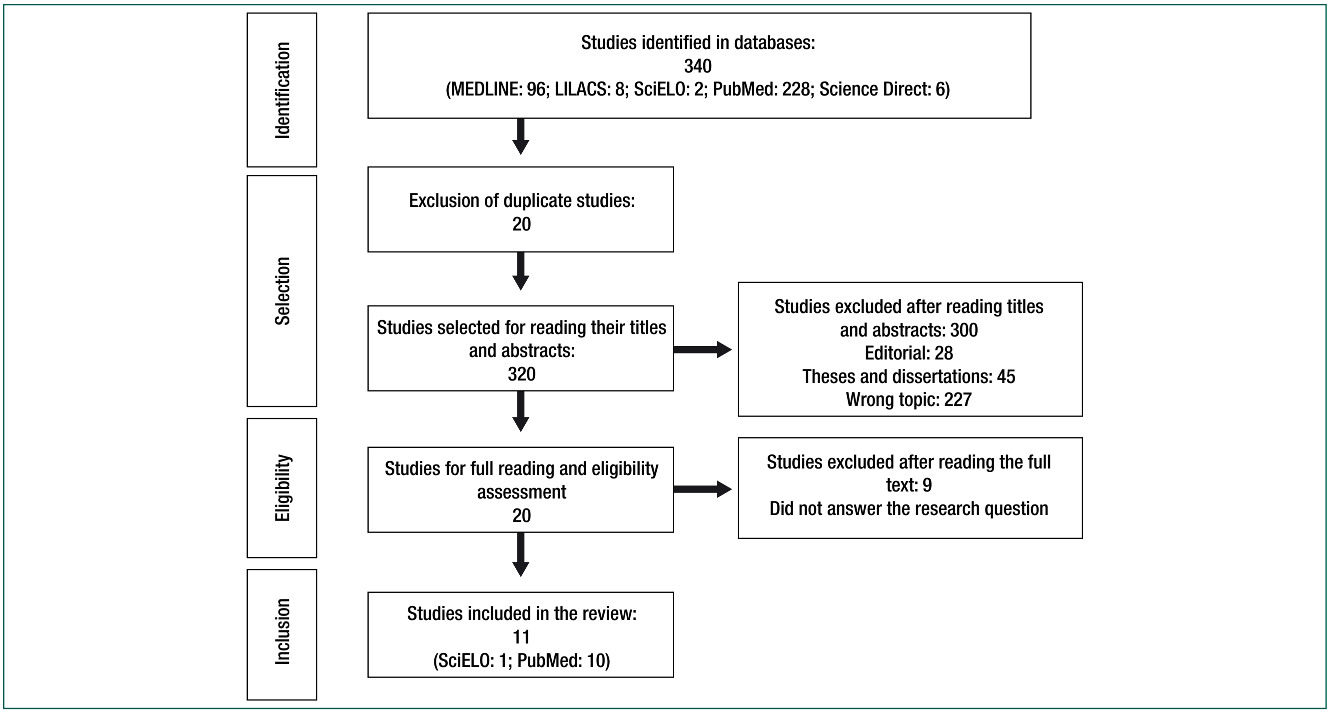

Figure 1. Flowchart for primary study selection, prepared based on the PRISMA recommendation

Chart 1. Review article synthesis

Classification	Database	Title	Authors/year	Objective
A1	SciELO	*Ação antimicrobiana do gás ozônio em superfícies e na aeromicrobiota*	Caetano, MH et al. (2021)[9], Brazil.	To assess O_3's antimicrobial action on surfaces and artificially acclimatized ambient air.
A2	PubMed	Pseudoviruses for the assessment of coronavirus disinfection by ozone	Zucker, I et al. (2021), [14] Israel.	To test using pseudoviruses as a model to assess O_3 disinfection of the coronavirus at ozone concentrations of 30, 100 and 1,000 ppmv.
A3	PubMed	Disinfection of Pseudomonas aeruginosa from N95 respirators with ozone: a pilot study	Manning, EP et al. (2021), [15] EUA.	To seek the necessary conditions for O_3 to disinfect N95 respirators for reuse and the effects of multiple exposure cycles.
A4	PubMed	Inactivation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by gaseous ozone treatment	Yano, H et al. (2020), [16] Japan.	To assess the effectiveness of O_3 for SARS-CoV-2 inactivation.
A5	PubMed	Development and improvement of an effective method for air and surfaces disinfection with ozone gas as a decontaminating agent	Moccia, G et al. (2020), [17] Italy.	To develop and implement a cleaning and sanitizing procedure for O_3 critical clinical environments to prevent hospital infections by eliminating all toxic and harmful microorganisms from the air and ensure safe use for operators and patients.
A6	PubMed	*Utilização de gás ozônio na desinfecção de resíduos de serviços de saúde*	Gonzaga, T. N., Kozusny-Andreani, D. I. (2018). [18] Brazil.	To assess the technical feasibility of applying O_3 as a bactericide and fungicide in samples of potentially infectious health care waste.
A7	PubMed	*Ozônio no controle de micro-organismos em resíduos de serviços de saúde*	Martins, C. C.; Kozusny-Andreani, D. I.; Mendes, E. C. B. (2015). [19] Brazil.	To verify the effectiveness of O_3 in the control of pathogenic microorganisms isolated from health service waste (RSW).
A8	PubMed	Inactivation of human coronavirus by FATHHOME's dry sanitizer device: rapid and eco-friendly ozone-based disinfection of SARS-CoV-2	Uppal, T et al. (2021), [20] USA.	To test the inactivation of human coronavirus by FATHHOM's O_3-based dry disinfection device.
A9	PubMed	Comparison of the effects of formaldehyde and gaseous ozone on HBV-contaminated hospital quilts	Guo, D et al. (2015), [21] China.	To investigate the clinical efficacy of formaldehyde and O_3 for the terminal cleaning of HBV-contaminated hospital quilts.
A10	PubMed	SARS-CoV-2 viability on different surfaces after gaseous ozone treatment: a preliminary evaluation	Percivalle, E et al. (2021), [22] Italy.	To report an investigation into O_3 use as a potentially effective hygiene method against the new coronavirus
A11	PubMed	Evaluation of the effectiveness of two automated room decontamination devices under real-life conditions	Knobling, B et al. (2021)[23], Germany	To assess the effectiveness of two automated room decontamination devices under real-life conditions.

A10 and A11), nursing (A1 and A7), interdisciplinary (A6) and chemistry (A2), between 2020 and 2021, developed in Brazil (A1, A6 and A7), Israel (A2), United States, (A3 and A8) Japan (A4) Italy (A5 and A10), China (A9) and Germany (A11). They used the experimental-laboratory research model and achieved different levels of disinfection by O_3, however, with various surfaces and products tested, in addition to different methodological procedures. Accordingly, A9 and A11 applied comparisons between O_3 and UV light, formaldehyde and hydrogen peroxide, respectively.

All studies used O_3 concentration ratios ranging from 0.5 to 1,000 ppm, exposure time between 10 and 320 minutes, temperature between 21°C and 55.8°C and relative humidity between 37 and 90%, with variation in the use of two or more of these parameters. Furthermore, rates of inhibition of microorganisms that alternate from 58 to 99% were related between the articles, representing the high or low effectiveness of O_3 in the elimination of pathological agents.

The microorganisms fought in these experiments differ between viruses and bacteria, including Hepatitis B virus (HBV), Influenza A (IAV), Respiratory Syncytial Virus (RSV), SARS-CoV-2, and *Pseudomonas auriginosa, Escherichia coli, Staphylococcus aureus, Salmonella enteriditis* and *Enterococcus faecium* bacteria. All viruses tested underwent freezing, thawing, dilution and/or centrifugation processes to finally be exposed to disinfectant O_3. It is noteworthy that all experimental steps followed biosafety protocols levels 2 and 3.

It was observed that most studies[16-20, 23,24] with significant inhibition results used in their method the exposure time with an average of 50 minutes, relative humidity above 50% and average temperature of 25°c, while the article with low inhibition result (A9)[21] used time of 10 to 20 minutes, relative humidity of 37% to 38% and room temperature, and time of 15, 30 and 60 minutes respectively, however, without reporting temperature and humidity.

The tested surfaces covered the wall, floor and benches of a clinical microbiology laboratory, offices, general surgery unit, high, medium and low criticality rooms, containing high-touch hospital furniture, such as doorknobs, beds, etc., glass, stainless steel, copper, aluminum alloy, nickel, acrylic, plastic, N95 respirators, surgical masks, disposable boots, safety overalls, fabric hoods, apron, face shield, hospital blankets and ambulance. Mask N95 was the most frequent study surface, appearing in four of the eleven selected surveys.

Regarding O_3 efficacy, A6[18] found that the control of microorganisms occurred through the application of O_3 dissolved in water and by exposure to different times, with greater effectiveness in bacteria, when compared to fungi, concluding that O_3 is efficient in the in vitro control of microorganisms isolated from HSW.

Furthermore, still in the aforementioned research, with respect to the virus, the UV light inhibition rate was 99% while O_3 was 58%, compared to the viruses under treatment. With regard to bacterium elimination, the result of elimination by UV light was less than the minimum detection by the technique. By contrast, disinfection by O_3 did not achieve significant results.

In a second analysis, A9[21] compared the disinfection potential of formaldehyde in relation to O_3 in hospital sheets, divided into two groups examined, tissue and cotton, contaminated with HBV. Formaldehyde was used in the form of liquid formalin at a concentration of 37%, and O_3 at a concentration of 30 mg/m^3, varying its fumigation time between 15, 30 and 60 minutes and concomitantly, there was a control group that did not suffer any exposure to disinfectants.

After the periods of exposure, it was found that, in relation to the group without disinfection, the number of HBV copies was significantly reduced after exposure to formaldehyde, while O_3 did not obtain a satisfactory result, since the amount of HBV copies remained similar both in the control group and in the group exposed to O_3.

Subsequently, A11[23] addressed O_3 compared to hydrogen peroxide in a typical patient room with adjacent bathroom and anteroom, where researchers produced two types of surfaces, high and low contamination, with *E. faecium* as the chosen microorganism.

The surface was exposed to O_3 at a concentration of 70 to 80 ppm for 15 minutes, with relative humidity of 80 to 90%, without reporting temperature parameters. Meanwhile, in the hydrogen peroxide-based device, nebulization time was 20 and 30 minutes. O_3 reached the reduction factor of > 5 log,[10] parameter used for demonstration of bactericidal efficacy[23-25] throughout the test room. The device that uses peroxide did not reach a relevant inhibition rate, and time and position adjustments had to be made to achieve an adequate rate reduction.

It is important to point out that the exposure time of hydrogen peroxide was initially 20 minutes and then there was an adjustment to 30 minutes, since the reduction of the microorganism was not satisfactory in the initial time. Furthermore, it should be noted that, despite not obtaining considerable results in high contamination, peroxide is capable of containing pathogens in realistic surface contamination, i.e., with low contamination.

Therefore, it was observed that nine articles presented an inhibition rate by O_3 equal to or greater than 90%, thus proving the effectiveness of this chemical substance as a surface disinfectant, even with variations in the concentration parameters, which ranged from 10 to 1,000 ppm.

Discussion

Ozone effectiveness in inhibiting different microorganisms

O_3 presents itself as an excellent disinfectant due to its high germicidal capacity and high penetration power, even acting as a sterilizing agent. Thus, due to its ability to eliminate protozoa, in addition to having bactericidal, fungicidal and virucidal properties, O_3 is a potent disinfectant, being recognized as one of the best antimicrobial agents.[25-27]

However, A9[21] did not attest to O_3 efficacy in relation to UV light and formaldehyde, as there was no significant difference between the control group and the one that was disinfected by O_3. However, the results in disinfection with formaldehyde were also unsatisfactory due to the side effects already listed in the literature, such as eye or skin irritation, which, at high levels, can induce squamous cell carcinomas in rats' nasal passages.[28] The author also recommends that, for the appropriate use of formaldehyde in hospital disinfection, the concentration levels and exposure time are low.[28] Therefore, measures such as ammonia use in water can eliminate formaldehyde residues, but there is a risk of secondary contamination.[29]

Factors and parameters related to disinfection

Regarding the parameters used in the disinfection process, literature states that O_3's antimicrobial action comes from factors such as concentration, exposure time, relative humidity and temperature.[30]

The percentage difference in inhibition rate is justified by A2[14] because there is a distinction in the behavior of the viruses in prolonged times due to the drying effect of the suspension, which prevented the effective verification of the potential of O_3 in longer times. This corroborates the other studies that were successful in disinfecting with exposure time of 10, 15 and 20 minutes (A8)[20] and 15 minutes.[10]

From this perspective, in a study on the bactericidal properties of O_3 on MRD, they found that the inhibition rate decreased significantly when using a concentration of 10 g mL-1 for 4 minutes, where there was no bacterial growth, in the readings taken at 48 hours and after 7 days, while at the concentrations of 4 g mL-1 and 3 g mL-1, there was bacterial growth, although to a lesser extent, attesting to the bactericidal action proportional to the concentration.[9]

Surfaces used for disinfection

It was observed that A3,[15] which sought to disinfect N95 respirators, used in its test O_3 at 450 ppm for 2 hours, finally obtaining a satisfactory result regarding disinfection without any damage or change in the integrity and quality of the respirators. The waste left by sanitizers, both on surfaces and in the air, can cause damage to the health of workers and users of these services, corroborating another research[14] that states that O_3 is a highly unstable gas, i.e., that it quickly returns to its original state as O_2 as well as having a half-life of only 40 to 45 minutes at 20ºC. Thus, it appears that O_3, in addition to being a potent disinfectant, has benefits that stand out from other sanitizing agents, such as not needing consumables to generate it, not leaving residues, being highly volatile, reaching areas that other products cannot reach,[10] such as corners and hinges.

Conclusion

Studies that scientifically evidenced O_3 use in the disinfection of surfaces were analyzed. The works pointed to this substance as a potent microbial inhibition technology. However, there was a need for more experiments on the subject so that parameters such as concentration, exposure time, humidity and temperature are adequate according to the needs and surfaces used.

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