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Review Article

Antibacterial Behavior of Oxygen-Generating Nanomaterial for Medical Applications

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Abstract
There are significant challenges for the development of an efficient antibacterial agent for the prevention or treatment of post-surgical infections, especially with synthetic scaffolds for surgical implants. This problem has been further exacerbated by the extensive use of antibiotics in healthcare settings, which has led to an increased incidence of multidrug-resistant bacteria. Despite several successes in the development of novel antibacterial agents, there are ongoing efforts to find effective and safe antibacterial agents. Recently, the development of oxygen-generating nanomaterials has been proposed as a possible choice for antibacterial materials. The preliminary investigation demonstrated that such materials could exhibit strong antibacterial activity, minimize postsurgery-induced hypoxia, and prevent infections. Regenerative medicine is a multibillion-dollar industry, and the lack of suitable materials as 3D scaffolds has hindered its application in clinical settings. A critical review of the different kinds of oxygen-generating reagents, as well as their mechanisms of oxygen release and antimicrobial potential, is presented, following an appraisal of the literature.

Keywords: Antibacterial Agents, Nosocomial Infections, Post-Surgical Infections, Oxygen-Generating Biomaterials
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Introduction

Infectious diseases are caused by organisms such as bacteria, viruses, fungi and parasites. Many microorganisms naturally colonize the human body and are harmless or even beneficial under normal physiological conditions.[1] However, under specific conditions, such as immune suppression or environmental imbalance, commensal or opportunistic pathogens can cause infectious diseases.[2] A hospital-acquired infection (HAI), also known as a "nosocomial infection," refers to an infection that develops in patients during hospitalization, typically after 48 hours of admission, and represents a major cause of morbidity and mortality worldwide.[3-5] The Centers for Disease Control and Prevention (CDC), through the National Healthcare Safety Network (NHSN), classifies HAIs into 13 major categories encompassing over 50 infection sites. The most common sites include urinary tract infections (UTIs), surgical and soft tissue infections, gastroenteritis, meningitis and respiratory infections. The incidence and severity of HAIs are further influenced by immunocompromised conditions and advanced clinical interventions such as chemotherapy, organ transplantation, and immunotherapy.[6] A wide variety of microbes can result in nosocomial infections in healthcare settings. Bacteria are responsible for approximately 90% of these infections, while viruses, protozoa, and fungi account for a smaller proportion.[7] The most common bacteria typically involved in nosocomial infections include *Streptococcus* spp., *Acinetobacter* spp., *Enterococci*, *Pseudomonas aeruginosa*, coagulase-negative *Staphylococci*, *Staphylococcus aureus*, *Bacillus cereus*, *Legionella* and *Enterobacteriaceae* family members such as *Proteus mirabilis*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Serratia marcescens*.[8-11] Since the discovery of penicillin in 1928, antibiotics have revolutionized the prevention and treatment of infectious diseases. However, the overuse and misuse of antibiotics in both clinical and agricultural settings have resulted in an increased incidence of multidrug-resistant (MDR) bacteria. MDR bacteria include a group of gram-positive and gram-negative pathogens known as ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*,

Pseudomonas aeruginosa, and *Enterobacter* spp.).[12-17]

These ESKAPE organisms are responsible for many hospital-acquired infections in the United States and Europe, posing a significant challenge to global public health and infection control efforts.[18-20] Consequently, there is an urgent need for novel antibacterial agents and alternative treatment strategies capable of combating infections caused by these multidrug-resistant pathogens.[21-23]

Regenerative medicine offers great potential for the repair and replacement of damaged tissues and organs. However, its progress toward clinical application is hindered by the lack of suitable biomaterials that can form three-dimensional (3D) scaffolds supporting cell growth while preventing post-implantation infections. These infections can compromise tissue healing and remain a major barrier to the successful clinical translation of regenerative therapies.[21,24-27]

The rise of antimicrobial resistance is outpacing the development of new antibiotics. As a result, clinicians increasingly resort to last-resort agents, such as silver-based biocidal compounds, which may pose cytotoxic risks, are costly, and are often less effective than standard antibiotics. Patients with resistant infections frequently experience prolonged hospitalization, delayed recovery, or increased mortality.[28,29] Several alternative strategies, including inhibition of resistance enzymes and efflux pumps, gene silencing, antivirulence approaches, probiotic therapy, and bacteriophage-based treatments, have have been explored to mitigate antimicrobial resistance.[30,31] Nanotechnology-based antimicrobial strategies have recently gained attention, particularly the use of inorganic and metallic nanoparticles (e.g., silver, copper, and metal oxides such as TiO_2, CuO, Al_2O_3, MgO, and ZnO), which exhibit potent and broad-spectrum antibacterial activity. Their nanoscale dimensions, surface tunability, and chemical stability make them promising candidates for infection control. However, their long-term biosafety and cytocompatibility remain under investigation, underscoring the need for a universal, biocompatible antibacterial material suitable for diverse implant applications.[32-35] More recently, oxygen-generating biomaterials (OGBs) have been developed to address hypoxia at implantation sites. Interestingly, these materials not only supply oxygen to support cell viability but also display broad-spectrum antibacterial activity, making them promising candidates for next-generation implantable and tissue-engineered constructs.[36] Tissue engineering aims to repair or replace damaged organs using biomaterials, stem cells, and bioactive factors. The fundamental building blocks of engineered tissues are three-dimensional (3D) scaffolds that mimic the extracellular matrix and support cell attachment, proliferation, and vascularization. Adequate oxygen and nutrient diffusion throughout these scaffolds is essential for tissue viability, remodeling, and growth. However, insufficient oxygen supply remains one of the primary causes of failure in large 3D constructs, particularly in the central regions of engineered tissues cultivated *in vitro* or implanted *in vivo*. To enhance oxygen delivery, several design parameters have been proposed, such as maintaining a minimum pore diameter of approximately 100 μm in scaffold architecture to facilitate diffusion and vascular ingrowth.[37-42]

It is well established that cells experience hypoxia when migrating toward the scaffold core, leading to apoptosis and tissue necrosis. Oxygen deficiency typically occurs when the diffusion distance between cells and nearby blood vessels exceeds 100–200 μm, which restricts cell migration, angiogenesis, and tissue integration.[36,43] To mitigate this limitation, numerous studies have focused on promoting angiogenesis to enhance oxygen and nutrient supply. Endothelial cells and vascular endothelial growth factor (VEGF) have been employed to accelerate neovascularization, demonstrating significant improvements in both angiogenic responses and the survival of transplanted cells.[44-46] Additional approaches have sought to minimize post-implantation hypoxia through direct oxygen delivery using carriers such as silicone oils and cross-linked hemoglobin.[44-46] Effective oxygen diffusion becomes especially critical for scaffolds implanted in defects exceeding a few millimeters, where sustained oxygen release is required until host neovascularization develops. Therefore, an ideal system should provide a controlled and adequate oxygen supply for a defined period to maintain tissue viability.[47-50]

A distinct and promising strategy involves the use of OGBs, a subclass of oxygen-releasing biomaterials (ORBs) designed to alleviate hypoxia by producing molecular oxygen *in situ*. OGBs continuously release oxygen to surrounding cells, thereby supporting stem cell survival and function under hypoxic conditions.[36,47,51] Despite their potential, several challenges remain, including the risks of transplant rejection and uncontrolled oxygen release. The oxygen generation rate is influenced by factors such as pH, temperature, and the purity and solubility of peroxide compounds. To achieve prolonged and controlled release, OGBs have been incorporated into various polymeric matrices and fabricated in different forms, including microspheres,[36] films,[52] electrospun nanofibers,[52] and 3D scaffolds.[53] Beyond oxygen delivery, recent studies have shown that OGBs also exhibit broad-spectrum antibacterial properties, highlighting their dual function as both regenerative and antimicrobial biomaterials.

In this review, we critically examine the properties of oxygen-generating nanobiomaterials, elucidate their oxygen release mechanisms, and explore their antimicrobial potential.

Oxygen-Generating Mechanisms

The primary compounds employed for oxygen supply in

artificially engineered constructs, particularly within tissue engineering and biomedical contexts, encompass solid inorganic peroxides, liquid peroxides, and fluorinated compounds. Sodium percarbonate,[54] magnesium peroxide (MgO_2), hydrogen peroxide (H_2O_2),[55] calcium peroxide (CaO_2),[56] and fluorinated materials[57,58] are the most common OGBs.

All these materials produce hydrogen peroxide (H_2O_2) upon exposure to an aqueous environment and subsequently decompose into oxygen (Figure 1). The release rate of oxygen from OGBs directly influences their cytotoxicity, antibacterial activity, and generally their effectiveness on healing of the defect. One of the main challenges in the use of these materials is the burst release of oxygen, which may lead to high cytotoxicity against human cells. Therefore, the mechanism of oxygen release should be adjusted to provide a sustained release and avoid cytotoxicity. Many factors such as pH, temperature, type of medium, and amount of peroxide affect the decomposition of OGBs and oxygen release rate.[59-61]

$$\textit{(Calcium Peroxide)} \quad CaO_2(s) + 2H_2O \rightarrow Ca(OH)_2(s) + H_2O_2$$

$$\textit{(Magnesium Peroxide)} \quad MgO_2(s) + 2H_2O \rightarrow Mg(OH)_2(s) + H_2O_2$$

$$\textit{(Sodium Percarbonate)} \quad (Na_2CO_3)_2 + 3H_2O_2 \rightarrow 4Na^+ + 2CO_3^{-2} + 3H_2O_2$$

$$\textit{(Catalase)} \quad 2H_2O_2 \rightarrow O_2 + 2H_2O$$

Figure 1. The OGBs Decompose into Oxygen, and Catalase Converts Hydrogen Peroxide into Water and Oxygen.

Among solid inorganic peroxides, such as calcium peroxide (CaO_2),[56] magnesium peroxide (MgO_2),[54] and sodium peroxide ($Na_2CO_3 \cdot 1.5H_2O$), which release oxygen via hydrolytic decomposition upon aqueous exposure, CaO_2 demonstrates the highest oxygen generation yield, whereas MgO_2 exhibits the lowest due to its limited solubility and consequent slow reaction kinetics. A significant challenge with these peroxides, however, is the potential for cytotoxic burst release of oxygen and the generation of reactive oxygen species (ROS). Alternatively, liquid peroxides like hydrogen peroxide (H_2O_2) offer rapid oxygen release facilitated by high water solubility, yet their decomposition can yield cytotoxic free radicals such as hydroxyl radicals in the absence of native enzymes like catalase.[55] In contrast, fluorinated compounds, including perfluorocarbons (PFCs) like perfluorodecalin and specific surfactants (e.g., perfluoromethyl-cyclohexyl piperidine), function primarily as oxygen carriers, releasing dissolved oxygen through diffusion mechanisms, and are frequently formulated into aqueous emulsions or encapsulated within polymeric biomaterials to mitigate hypoxia in applications ranging from cardiovascular tissue engineering to tumor therapy.[62] Therefore, the mechanism of oxygen release should be adjusted to provide a sustained release and avoid cytotoxicity. Many factors such as pH, temperature, type of medium, and amount of peroxide affect the decomposition of OGBs and oxygen release rate.[47,59,60,63,64]

The provision of a sustained and controlled oxygen supply is imperative in tissue engineering to mitigate the cytotoxic effects associated with abrupt oxygen release and to promote cellular viability during angiogenesis. Typically, a range of materials, such as ceramics and polymers, have been employed for the purpose of drug release.[65,66] In tissue engineering applications, polymers are frequently preferred over ceramics due to their higher biodegradability. Polymers utilized in drug release encompass both synthetic and natural variants, and their combinations. To address this, bio-degradable polymeric matrices are frequently employed as carriers for oxygen-generating compounds, offering tunable release kinetics and biocompatibility. Current research explores advanced platforms such as hydrogels, including gelatin methacryloyl (GelMA) and gellan gum, which facilitate both oxygen delivery and cell encapsulation.[67-69] Innovations in this domain have led to the development of materials like a self-healing hyaluronic acid-perfluorocarbon hydrogel ("Oxygel"), capable of sustaining oxygen release for over 90 hours, thereby demonstrating significant potential for enhancing regenerative outcomes in hypoxic environments.[70]

Among the OGBs, CaO_2 has been shown to have a higher rate of oxygen generation.[56] Low solubility and slow reaction rate cause MgO_2 to decompose into oxygen very slowly. Addition of OGBs in polymeric composites, or encapsulation in hydrophobic materials, decreases the oxygen release rate.[54] The most important challenge in using such materials *in vivo* is the burst release of oxygen and production of free radicals that are toxic to host cells. An alternative strategy for overcoming such a challenge is encapsulating OGBs in catalase-containing polymeric materials. Catalase is a cellular enzyme found in living cells that decomposes hydrogen peroxide into oxygen and water.[55,59,71,72] Efforts to minimize the cytotoxic effects of OGBs are ongoing. A comparative summary of the main OGBs, their oxygen release mechanisms, and antibacterial

activities is presented in Table 1. This table highlights the physicochemical characteristics and bactericidal mechanisms of various OGBs reported in the literature.

Antibacterial Properties

Figure 2. Schematic illustration of the dual-action mechanism of oxygen-generating biomaterials (OGBs). The hydrolysis of peroxides releases hydrogen peroxide (H_2O_2), which decomposes into oxygen to alleviate tissue hypoxia. Concurrently, the generation of reactive oxygen species (ROS) disrupts bacterial membranes and degrades the extracellular polymeric substance (EPS) of biofilms. Because the oxygen-generating mechanism involves the decomposition of hydrogen peroxide in the majority of OGBs, it is possible to take advantage of the incomplete conversion of peroxide to oxygen for other applications.

Table 1. Summary of Oxygen-Generating Nanomaterials and their Antibacterial Mechanisms in Biomedical Applications

Material / System	Oxygen-generating	Form / Carrier	Antibacterial mechanism	Target bacteria	Key findings	References
Calcium peroxide (CaO_2)	Hydrolysis → H_2O_2 → O_2 + $Ca(OH)_2$	Nanofiber / scaffold / hydrogel	Release of H_2O_2 and ROS, production of $Ca(OH)_2$ with antibacterial effect	*E. coli, S. epidermidis, E. faecalis*	Strong antibacterial activity due to burst H_2O_2 release; Ascorbic acid addition reduces cytotoxicity	(36,63,73)
Magnesium peroxide (MgO_2)	Slow hydrolysis → $Mg(OH)_2$ + O_2	Powder, coating on textile fibers	ROS generation and Mg^+ release damage bacterial membranes	*S. aureus, E. coli*	Enhanced antibacterial effect with increasing MgO_2 concentration; biocompatible and sustained release	(52,74,75)
Sodium percarbonate ($Na_2CO_3 \cdot 1.5H_2O$)	Decomposition in aqueous media → H_2O_2 + O_2	Polymer composite	H_2O_2-mediated oxidative stress	*Broad-spectrum* (Gram+ / Gram–)	Sustained O_2 release; antibacterial activity coupled with oxygen supply	(52,58)
Hydrogen peroxide (H_2O_2)	Self-decomposition → O_2 + H_2O (catalyzed by catalase)	Liquid / incorporated in scaffold	Oxidative stress, DNA damage, inhibition of biofilm formation	*S. aureus, E. coli, B. subtilis*	Strong bactericidal and biofilm inhibition effects; local administration reduces toxicity	(76–81)
Fluorinated oxygen carriers	Fluorinated nano-hydroxyapatite releasing O_2	Hydrogel / nanoparticle	ROS-mediated antibacterial activity + O_2 delivery	*E. coli, S. aureus*	Dual oxygenation and antibacterial effects promoting bone regeneration	(82)
Cu-peroxide nanodots (CuO_2)	Self-catalyzed chemodynamic reaction → O_2 generation	Fibrous membrane	ROS and Cu^+ release for antibacterial and angiogenic effects	*S. aureus, P. aeruginosa*	Effective in wound healing under hypoxic conditions	(83)
Catalase-loaded OGBs	Catalytic decomposition of H_2O_2 → controlled O_2 release	Polymer encapsulation	Modulated ROS release reducing cytotoxicity	-	Sustained oxygenation with reduced burst effect	(50,84)

The adhesive property of bacteria to biomaterials and devices can lead to infections; approximately one million such cases are reported annually in the United States.[85,86] Opportunistic bacteria colonize after adhering to biomedical devices and develop biofilms resistant to multiple classes of antibacterial agents. The resolution of device-related infections requires removal of the device from the transplanted site. The increased risk of infections associated with biomedical devices has become one of the most important hurdles to consider when using such materials as tissue substitutes.[87,88] Numerous efforts have been made to develop strategies to overcome such challenges.[24,25,30,89] The amount of bacterial adhesion to various devices can be decreased by physical or chemical modifications of implant surfaces. For example, Chen et al.[90] blocked protein adsorption to the device by PEGylation, leading to decreased microbial adhesion. Gottenbos et al.[91] used positively charged polymers with antibacterial properties to overcome the challenge. A wide variety of studies have reported on the efficacy of coating the surface of devices with silver or silver-doped materials as widespread antimicrobial agents.[90] Despite the effectiveness of such strategies, there are still some problems associated with using these methods. For example, devices that are non-adherent to bacteria are expected to have low bioactivity.[92] The use of silver-derived materials has shown various degrees of effectiveness, depending on the situation.[93]

Therefore, there is a need for an efficient strategy to decrease the colonization of bacteria while retaining the bioactivity of devices. Hydrogen peroxide not only holds great promise as an oxygen supplier but also has strong antimicrobial activity. H_2O_2 restrains the development of biofilms, even at low concentrations, through repression of genes regulating glycolysis and biofilm formation.[76] Increased levels of H_2O_2 lead to the production of free radicals, showing strong biocidal activity that could also affect

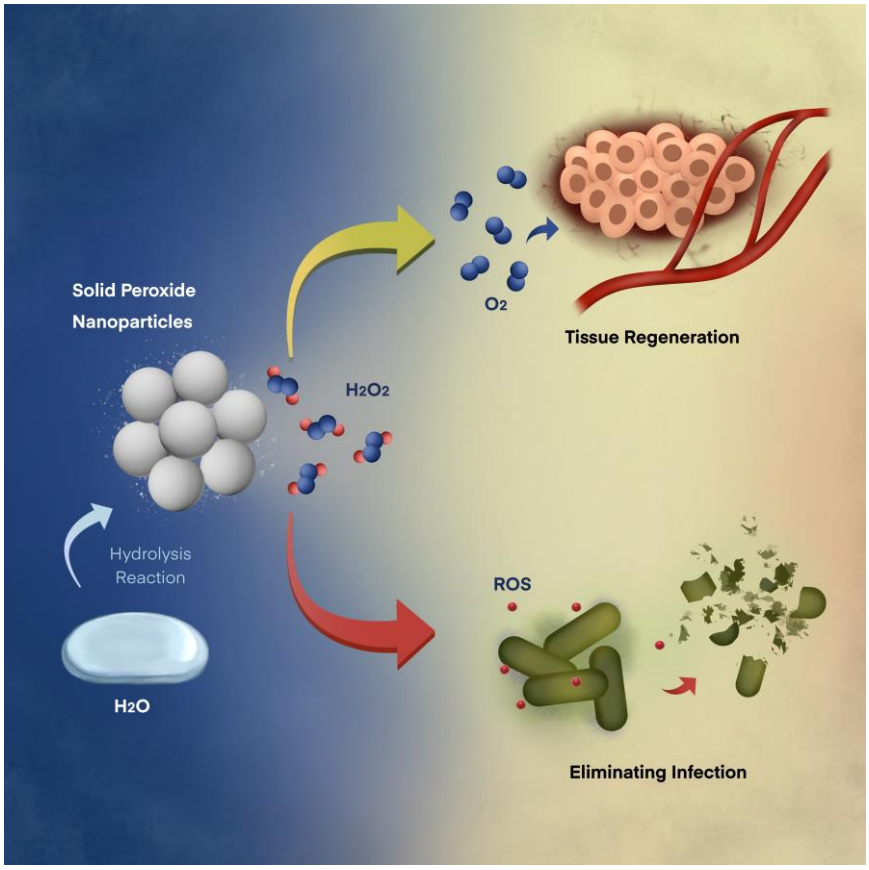

Figure 2. Dual-Action Mechanism of OGBs. Hydrolysis of inorganic peroxides (CaO_2, MgO_2) releases H_2O_2 and O_2, supporting two pathways: (1) tissue regeneration, where O_2 alleviates hypoxia to support cell viability; and (2) antibacterial activity, where ROS-induced oxidative stress disrupts bacterial membranes and penetrates biofilm EPS to degrade proteins and DNA in planktonic and quiescent cells.

human cell survival.[80,81] Local administration of H_2O_2, especially in orthopedics, could minimize side effects associated with systemic toxicity.[94] As previously described above, H_2O_2 is a byproduct generated after decomposition of certain OGBs such as calcium peroxide (CaO_2), sodium percarbonate ($Na_2CO_3 \cdot 1.5H_2O$), and magnesium peroxide (MgO_2). Beyond simple membrane damage, ROS generated by OGBs can penetrate the protective extracellular polymeric substance (EPS) matrix of biofilms. At the molecular level, hydroxyl radicals (•OH) and superoxide anions (O_2^-) induce oxidative stress that damages intracellular proteins, lipids, and DNA of quiescent bacteria within the biofilm, targets that traditional antibiotics often fail to reach due to limited diffusion.[74,78,79]

In their study on various peroxide systems, Wang et al.[73] successfully fabricated electrospun nanofibers made of calcium peroxide/polycaprolactone (PCL)/ascorbic acid. They incorporated different ratios of calcium peroxide into polycaprolactone to confer antibacterial activity to the resulting compounds. Ascorbic acid, as a cell protector, was also added to reduce oxidative stress caused by hydrogen peroxide release.[73] It has been found that the nanofibrous scaffold had antibacterial properties against *Escherichia coli* and *Staphylococcus epidermidis* due to the burst release of hydrogen peroxide. The ascorbic acid-incorporated scaffold not only alleviated the cytotoxic effect of hydrogen peroxide against human osteoblast cells but also increased its burst release due to elevated scaffold pore size, leading to increased antibacterial activity of the resultant scaffold[73] (Figure 3). This strategy could potentially be used for the prevention of device-related bacterial infections as well as serve as a sustained oxygen delivery system. Calcium hydroxide, a byproduct of CaO_2 decomposition, has also been reported to be an antibacterial agent. Chai et al.[95] investigated the susceptibility of Enterococcus faecalis biofilm to different antibiotics (co-trimoxazole, ampicillin, erythromycin, vancomycin, oxytetracycline, vancomycin, and gentamicin) and calcium hydroxide. According to their results, only two antibiotics (oxytetracycline and erythromycin) and calcium hydroxide were 100% effective in biofilm elimination.

MgO_2 produces various forms of reactive species, such as superoxide anions (O−) and ROS, upon decomposition and exhibits broad-spectrum antibacterial activity against both gram-positive and gram-negative bacteria.[74] In a study conducted by Navik and coworkers, different concentrations of MgO_2 (0.2 and 0.4 M) were applied to cotton fibers using the pad-dry-cure method to fabricate a textile product with

strong antibacterial activity against *S. aureus* and *E. coli*. They showed that the antibacterial activity of MgO_2 was associated with the release of reactive oxygen species and Mg ions.[75]

Endogenous H_2O_2 endows broad-spectrum antibacterial properties to honey. It was shown that the antibacterial activity of honey depends on the concentration of endogenous H_2O_2. Brudzynski studied the antibacterial effects of 42 Canadian honeys against standard strains of *E. coli* and *Bacillus subtilis* before and after removal of H_2O_2 by catalase. It was revealed that there is a significant non-peroxide antibacterial activity in honeys after the removal of H_2O_2 by catalase.[77] In another study, honey H_2O_2 showed bactericidal and bacteriostatic effects through oxidative damage and bacterial DNA degradation, but its antibacterial activity was modulated by other honey components.[78] A synergistic antibacterial activity of H_2O_2 in combination with sodium hypochlorite was also reported against *P. aeruginosa* biofilms.[79] To further compare the performance of different oxygen-generating systems, Table 2 provides a concise overview of their oxygen release kinetics, cytotoxicity levels, and antibacterial efficiency. This comparative evaluation emphasizes the trade-off between antibacterial potency and biocompatibility among various OGBs.

Table 2. Comparative Analysis of Oxygen Release Kinetics, Cytotoxicity, and Antibacterial Performance

Material / System	Oxygen release profile	Cytotoxicity to mammalian cells	Antibacterial efficiency	Sustained release capability	References
Calcium peroxide (CaO_2)	Fast initial burst; moderate sustained release	Moderate (reduced by ascorbic acid)	High	Medium	(36,63,73)
Magnesium peroxide (MgO_2)	Slow, long-term release	Low	Moderate to High	High	(52,75)
Sodium percarbonate ($Na_2CO_3{\cdot}1.5H_2O$)	Moderate, controllable via encapsulation	Low to Moderate	Moderate	Medium	(52,58)
Hydrogen peroxide (H_2O_2)	Immediate, short-lived	High (dose-dependent)	Very High	Low	(76,80,81)
Fluorinated carriers	Sustained via hydrophobic control	Low	High	High	(36,64)
Cu-peroxide nanodots	Steady catalytic release	Moderate	High	Medium	(58)
Catalase-loaded OGBs	Controlled and sustained	Very Low	Moderate	High	(50,84)

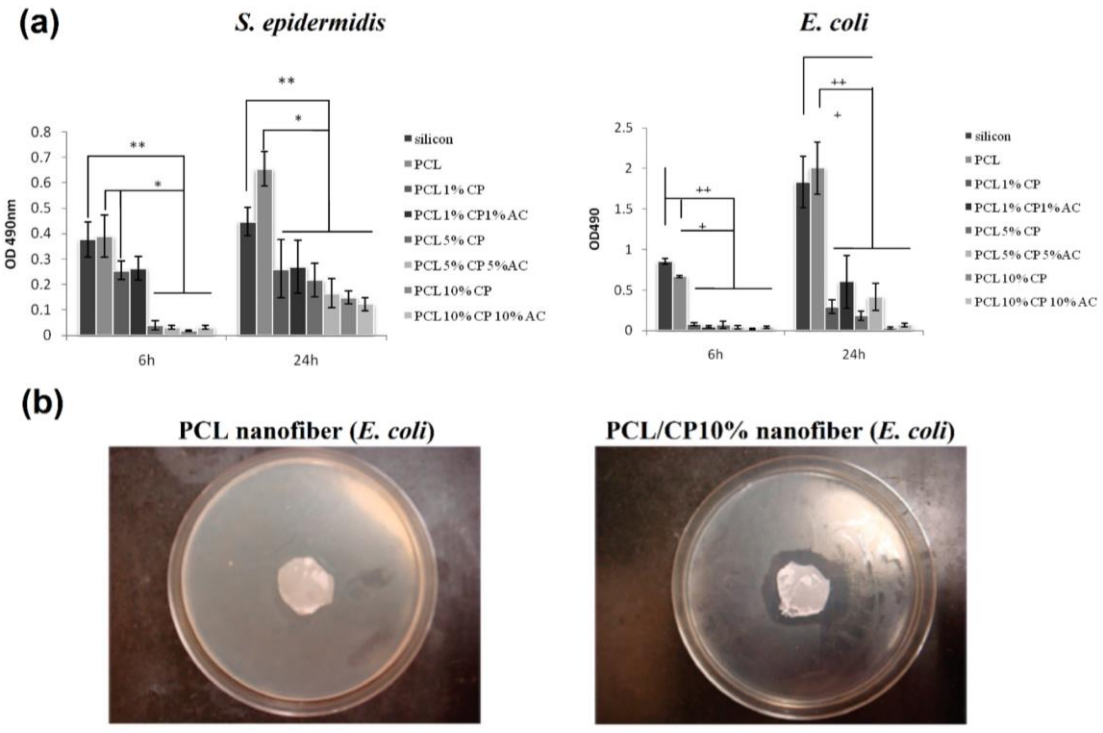

Figure. 3. (a) *Staphylococcus epidermidis* and *Escherichia coli* grown on PCL nanofibers with different concentrations of calcium peroxide (CP) and ascorbic acid (AC). PCL/10%CP showed the highest antibacterial activity among the samples. (b) *E. coli* growth inhibition zone formed around the PCL nanofibers and PCL/CP10% nanofiber. The inhibition zone around PCL/CP10% is clearly visible after 24 h of incubation at 37 °C (reproduced with permission from reference (73)).

Conclusion and Future Perspectives

The post-implantation infections caused by nosocomial bacteria have been a major concern in healthcare settings. On the other hand, the prevalence of multidrug-resistant bacteria is increasing, and so an alternative strategy along with common antibacterial therapy is required for full success in tissue implantation. A broad variety of studies have demonstrated that oxygen-generating biomaterials can feasibly be used for consistent delivery of oxygen to implanted engineered tissues to avoid hypoxia, especially in large tissue constructs. More recently, it has been shown that OGBs also have broad-spectrum antibacterial activity, which has made such materials very interesting for biomedical and biotechnology applications. Although OGBs require further modification to achieve more sustained release of oxygen and reduced cytotoxicity, these materials hold significant promise for future clinical translation as multifunctional platforms capable of simultaneously mitigating hypoxia and preventing implant-associated infections. Despite the promising antibacterial and regenerative potential of oxygen-generating biomaterials, several challenges must be addressed before their successful clinical translation. Regulatory considerations include the standardization of material composition, precise control over oxygen release kinetics, and comprehensive safety evaluations to comply with regulatory agency requirements. In addition, large-scale manufacturing of oxygen-generating systems presents challenges related to batch-to-batch reproducibility, long-term storage stability, and adherence to Good Manufacturing Practice (GMP) guidelines. Overcoming these regulatory and scalability barriers will be essential for translating laboratory-scale oxygen-generating biomaterials into clinically approved and commercially viable medical products. Future work must prioritize long-term biocompatibility and *in vivo* studies, focusing on developing targeted delivery systems to optimize the balance between achieving high antibacterial potency and maintaining low cytotoxicity. Specific attention should be paid to tuning oxygen release kinetics, particularly for addressing infections caused by ESKAPE pathogens in large tissue constructs.

Authors' Contributions

MF: Writing and editing; FM: Writing, review, editing, and preparation of graphical figures and tables; KS: Writing and preparation of tables; MS: Writing and preparation of tables; MG: Writing, review, editing, and data analysis; MG: Supervision, review and project management.

Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

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