

# Applications of antibacterial materials in biomedicine

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**Abstract.** The application of antibacterial materials is essential in the post COVID-19 era since the public has realized the importance of their enormously contributing role in dealing against the COVID-19 and various kinds of antibacterial materials have been synthesized with different preparation methods. At present, natural organic antibacterial materials, metal ion antibacterial materials and metal oxide antibacterial materials are the most widely used and studied in biomedical field. This research introduces various types of antibacterial materials including inorganic antibacterial materials, organic antibacterial materials and composite antibacterial materials and analyzes their application mechanism. Then this research cites examples of latest application of antibacterial medical materials, and summarizes the direction of development and research of antibacterial materials in the future.

**Keywords:** Antibacterial materials, Mechanism, Applications, Biomedicine.

## 1. Introduction

Antimicrobial materials mainly refer to materials that have antibacterial properties or can be antibacterial after antibacterial treatment. The chemical components in the materials are highly sensitive to microorganisms including bacteria, molds and viruses, and kill or preventing microorganisms growing on the surface through chemical reaction and physical action, thus play an antibacterial role. So early as ancient times, people found that some substances have natural antibacterial and safety and applied in the medical treatment. At that time, the ancient Egyptians were aware of covering the wound with thin silver sheets to avoid bacterial infection and expedite wound healing. The large-scale application of modern antibacterial materials began during the Second World War. The German army wore military uniforms processed with antibacterial finishing to reduce the bacterial infection of the wounded. The application of antibacterial materials entered a rapid development stage in the 1980s. At first, the application was mainly concentrated in daily necessities and household appliances, and has rapidly expanded to building materials and fiber products in recent years [1].

Interest in medical antimicrobial materials is booming in the recent time with the highly increasing need of people for medical well-being. Nowadays, there are three kinds of antibacterial materials: natural, organic and inorganic antibacterial materials. Generally speaking, natural antibacterial materials come from natural extracts, such as chitosan, chitin, juniper, Artemisia, aloe and other refined products, which have the advantages of high safety, but they generally have short service life, poor heat resistance and are not easy to reprocess, leading to narrow application range; Organic synthetic antibacterial materials are mainly made with quaternary ammonium, pyridine, guanidine and halogenated amine, which have the advantages of wide antibacterial range and fast sterilization speed. But they often lose antibacterial properties due to heating or dissolution and have relatively large toxic and side effects, easy hydrolysis and short service life; Inorganic antibacterial materials include metal ion materials and oxide photocatalytic materials. After made into nanoscale, they can better adsorb microorganisms due to the increase of specific surface area, so they have better antibacterial effect [2-4].

From the beginning of 2020, China and other counties successively broke out a large-scale epidemic of COVID-19, thus the demand for relevant medical apparatus and instruments further increased. During the epidemic, masks, forehead temperature guns, disinfectants and other products were all out of stock and the demand for such medical apparatus that are not valued by people at

ordinary times greatly increased. The emergence of the COVID-19 has vastly stimulated the development of the medical instruments market, and after the epidemic, related company will surely put more investment in researching and developing novel medical antimicrobial materials to manufacture instruments that performance better in the respond to COVID-19 and other diseases that may occur in the future [5].

Despite the intensive and considerable development achieved by biologists and material scientists, the problems that medical workers may face the risk getting infected during treating time because of the disqualification or inconformity of the medical instruments and implants still stay troublesome. Such medical device common adverse events frequently occur in the clinical situation, especially when using protective passive medical devices. Such medical devices are widely used in clinical diagnosis and treatment, including masks, gloves, protective clothing, protective articles for medical staff and hands. The occurrence of adverse events will often affect the medical work. It has a direct impact on the health of the patient and the clinical use process. In particular, in the hospital environment, bacteria are easy to cause infection through the clothing, gloves and other items of medical personnel. Nearly 100000 people die of such infection in the United States every year. The sewing and bonding between the components of such product are not tight, or the material itself is damaged or not performances well for the new clinical situation may usually count for the reasons why such medical common adverse events constantly appear. Therefore, the urge to develop novel and more effective kind of medical antimicrobial materials is desperately called when faced with the worldwide pandemic.

For this reason, this research will introduce a diverse of different antibacterial materials, including inorganic antibacterial materials, organic antibacterial materials and some composite antibacterial materials. The application of these antibacterial materials will be systematically analyzed in this research, and propose the direction of development and research of antibacterial materials in the future.

## 2. Inorganic antibacterial materials

Inorganic antibacterial materials are antibacterial products that take inorganic materials as carriers and are compounded with ions, oxides or photocatalytic materials of transition metals such as silver, copper and zinc with antibacterial properties, most of which are nanomaterials with large specific surface area with the purpose of achieving excellent antibacterial effect, as shown in Figure 1. At present, the most widely used are the metal  $Ag^+$  ion type and the photocatalytic type represented by  $TiO_2$ .

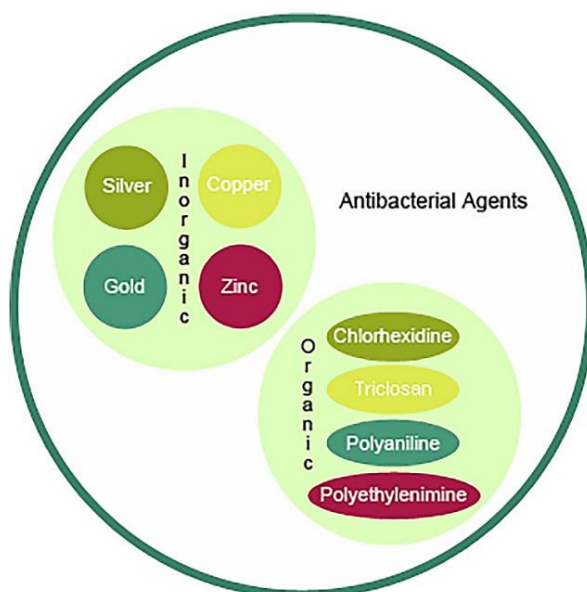


Figure 1. The types of the used inorganic antibacterial materials [6]

Inorganic antibacterial materials mainly function in two mechanisms. One is that metal elements directly contact the bacteria, act on the cell membrane and cell wall of the bacterial, slowly release trace ions, firmly adsorb on the cell membrane by Colombian gravity, and then penetrate the cell wall into the cell to solidify the bacterial protein. The cell then dies of the inability to divide and proliferate, so as to achieve the antibacterial effect. Besides, metal ions also can destroy the microbial electronic transport system, respiratory system and transport system. After the activity of bacteria is lost, the ions then are separated out of the bacteria and sterilized repeatedly, therefore, its antibacterial effect is long-lasting. Some of the mental ion, like  $\text{Ag}^+$ , has the ability to quickly combine with the sulfhydryl group(-SH) of enzyme protein in the bacteria, so that some enzymes relying on sulfhydryl group as the necessary group cannot survive, ameliorating to kill bacteria, repair tissues and promote wound healing, and at the same time also serving as the role of treating and preventing bacteria and fungi.

The other one is that active oxygen sterilization of nanomaterials, mainly using  $\text{TiO}_2$  and  $\text{ZrO}_2$ , catalyzes and activates its own oxygen and water to react under illumination to produce  $\text{O}_2$  or OH with high chemical activity. When these microorganisms are contacted by these free radicals, the organic matter in them will be oxidized into water and carbon dioxide, thus killing the microorganisms in a short time.

## 2.1. Metal antibacterial materials

In terms of metal antibacterial materials, ionic antibacterial agent is currently the most widely used for research and application and  $\text{Ag}^+$ -based antibacterial material has the most sweeping range, as shown in Table 1.

**Table 1.** The characteristics of common silver-based antibacterial materials [7]

Types	Mechanism	Advantages	Drawbacks	Applications
Silver-zeolite material	Metal ion contact sterilization and catalytic sterilization	Strong affinity	Easy to discolor, high expenditure, unstable antibacterial property	Medical treatment, stainless steel coating, fabric and water treatment
Silver-phosphate material	Slow-release effect and photocatalysis	Powerful adsorption, large specific surface area, non-toxic		
Silver-soluble glasses material	Slow-release sterilization	Long-term effective treatment		

Besides, Japanese scientists have made stainless steel medical instruments containing silver nanomaterials, such as antibacterial stainless-steel knives, antibacterial stainless-steel clips and other instruments. When the antibacterial effect was tested, the results showed that the stainless-steel utensils with silver nanomaterials on the surface had excellent antibacterial performance. When the bacteria contacted the above experimental objects for 24 hours, the residual bacteria on the stainless-steel surface  $<5$  cfu/25cm, that is, 99% of the bacteria were killed. Antibacterial surgical instruments, such as scalpels, forceps, forceps, needles and plates, can be manufactured by similar methods. At the same time, it can also produce antibacterial kitchen utensils, such as knives, spoons, shovels, etc. Other domestic tools, like stainless-steel antibacterial cup and stainless-steel antibacterial hand washing basin can also be made. At present, Japan's Kawasaki iron and steel company has put nano silver series stainless steel appliances on the market [8].

## 2.2. Metal oxide antibacterial material

Many nano-antibacterial materials made from metal oxides can not only penetrate into cells and destroy substances in cells, achieving antibacterial effect, but act on biomass through catalytic oxidation to achieve sterilization. The two antibacterial mechanisms are sometimes related, so the catalytic oxidation antibacterial material can also be metal oxide antibacterial material. For example, the photocatalysis mechanisms for the antibacterial material ZnO can be seen as two methods. The first method is that electron on the valence band of ZnO is stimulated under illumination and then transfers to conduction band, leaving positive hole. Electron and hole react with  $O_2$ ,  $-OH$  and  $H_2O$  adsorbing on the material surface, and then produce  $OH^-$ ,  $O_2^-$  and  $H_2O_2$ , decomposing different components in microorganisms, realizing the goal of sterilization. The other one is dissolution mechanism of  $Zn^{2+}$ . The free  $Zn^{2+}$  acts on protein and the physiological activity of bacterial cells is destroyed. When the bacteria are eliminated,  $Zn^{2+}$  dissociate out of the cells and then the above process repeats.

As shown in Figure 2, Fan et al. pretreated the PP nonwovens with silane coupling agent KH-560, and loaded the silver pyro silicate titanium dioxide ( $Ag_6Si_2O_7-TiO_2$ ) photocatalyst synthesized by deposition method on the surface of the treated PP nonwovens. The composite photocatalyst  $Ag_6Si_2O_7-TiO_2/PP$  produced catalytic oxidation reaction under visible light, which can kill more than 99% of *Escherichia coli* and *Staphylococcus aureus*.

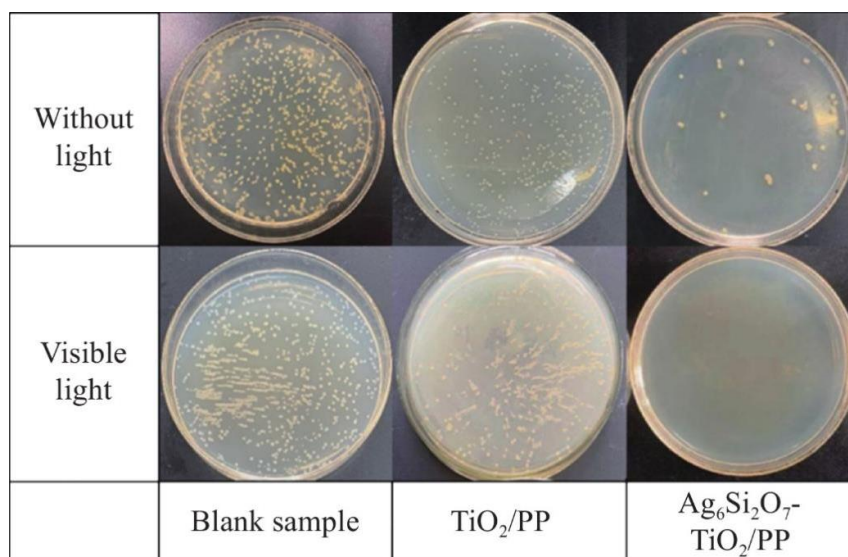


Figure 2. Antibacterial activity of the prepared antibacterial materials [9]

## 3. Organic antibacterial materials

Organic synthetic antibacterial materials are materials equipped with organic antibacterial agent, such as chitosan quaternary ammonium, pyridine, guanidine. At present, the most widely used organic antibacterial are those made with quaternary ammonium (phosphonium) salt, haloamines and chitosan.

The working principle of organic antibacterial material vary from the kind of the organic antibacterial agent the material is with, but mainly include adsorption-penetration-membrane-breaking, contact sterilization, release active bactericidal substance and destroy the cell function.

According to the molecular weight or synthesis method of additives, organic antibacterial materials can be classified into natural organic antibacterial materials, low molecular organic antibacterial materials and high molecular organic antibacterial materials.

### 3.1. Natural organic antibacterial material

Natural organic antibacterial material is made with organic antibacterial agent, most widely used of which is chitosan. Usually extracted from the shells of shrimp and crab, chitosan is a kind of natural macromolecule material with low price and strong active amino group. It has broad-spectrum antibacterial property, especially effective against mold and bacteria, and is non-toxic and non-irritating to human body. However, the antibacterial properties of chitosan can be easily affected by pH, relative molecular weight and degree of deacetylation. Generally, chitosan has the best antibacterial property at pH 5.5-6.5 and relative molecular mass between 10000-100000, and the extreme value appears as the increase of deacetylation degree.

It is speculated that there are two antibacterial mechanisms. The first one is that the cell absorbs the  $-NH_3^+$  in chitosan molecules and then a layer of polymer membrane is formed on the surface, preventing nutrients being transported to the cell. It can also disturb the electron charges on the cell wall and cell membrane, thus destroy the synthesis and dissolution balance of the cell wall, achieving the goal of bacteriostasis and sterilization. The second hypothesis of the mechanism is that chitosan molecules penetrate into cells, adsorb anionic substances in cells, disturb normal physiological activities of cells, and kill bacteria. Chitosan has outstanding membrane property and human body can easily absorb it through hydrolysis, making it an ideal drug carrier. It can form composite materials with high molecular substances like sodium alginate, cellulose and sodium polyacrylate to make composite drug loaded microspheres, thus improving the drug loading. However, natural organic antibacterial agents are lack of stable heat resistance, so they are not suitable to be used in plastics and other industries that require high heat resistance.

Besides, modification of the molecule can improve its antibacterial properties and broaden the antibacterial field and the antibacterial activity increased with the increase of alkyl chain. Sun Yun et al. Introduced chitosan oligomer (COS) branch chain into sodium alginate (SA) by two steps. The experiment showed that SA-COS contained only 1.8% cos can reduce *Staphylococcus aureus* by 99.19%. This antibacterial alginate can be cross-linked with multivalent metal ions to form hydrogels of various shapes. The wound covering made of this hydrogel can not only maintain the humidity conducive to wound healing, but also prevent bacterial infection [10-11].

### 3.2. Organic antibacterial materials based on low molecular mass (OAM-LMM)

OAM-LMM mainly include quaternary ammonium salts, quaternary phosphonium salts, biguanides, alcohols, phenols, organic metals, pyridines, imidazoles, etc. Its antibacterial mechanism is mainly combined with the anions on the cell membrane surface of bacteria and molds, or reacted with sulfhydryl groups to destroy the synthesis system of protein and cell membrane, so as to inhibit the reproduction of bacteria and molds. And the most emblematic organic antibacterial material is quaternary ammonium salt.

Quaternary ammonium salt antibacterial material has been widely studied and used because of their low price and fast sterilization speed. The general rule that the antibacterial ability and toxicity of this kind of antibacterial agents change with the structure is that the toxicity of the same kind of quaternary ammonium salt antibacterial agents with short alkyl chain is greater than that with long alkyl chain; At the same alkyl chain length, the toxicity of benzyl group is less than that of methyl group; Monoalkyl is more toxic than dialkyl. When the number of carbon atoms in the alkyl chain is less than 10 or more than 16, the killing effect of antibacterial agents on bacteria is small; When the number of carbon atoms is 14, the antibacterial activity of the antibacterial agent is the largest.

In the solution, the microbial cell membrane can be dissociated by the positive charge carried by the quaternary nitrogen atom in quaternary ammonium salt. Due to the electronegativity of phosphorus is weaker than that of nitrogen, quaternary phosphonium salt can better adsorb bacterial cells than quaternary ammonium salt, and has higher antibacterial activity. As strongly alkaline, Guanidine and its derivatives can attract negatively charged bacteria, restrict their free activities, and result in "contact death". Besides, under the electric field force, the negative charges on the cell wall and cell membrane are deformed because of uneven distribution, resulting in physical rupture,

resulting in the overflow of water, protein and other substances in the cell, resulting in the “bacterial lysosome” phenomenon and death. The antibacterial active components of low molecular weight antibacterial agents are cationic groups, but poor heat resistance and high toxicity are the important reasons for their limited application [12-13].

### 3.3. Organic antibacterial materials based on high molecular mass (OAM-HMM)

Compared with OAM-LMM, OAM-HMM have more stable performance, non-volatile, long service life, easy processing, easy storage, and will not penetrate into human or animal epidermis. Therefore, there have been many studies in recent years. The relative molecular weight increases and the charge density rises when the monomers with antibacterial functional groups are polymerized, while the microbial cells, phospholipids in the cell membrane and some membrane proteins are hydrolyzed with negative charges. Moreover, inorganic and organic antibacterial groups can be flexibly introduced during the process of modification to make disparate antibacterial agents and prepare polymer organic antibacterial materials with high performance and high selectivity. However, due to the poor compatibility of most OAM-HMM, their application is limited, so it is of great importance to construct new core-shell polymer antibacterial material. As shown in Figure 3, Ji et al. synthesized a new PVF-g-QA sponge, which show a high antibacterial activity for both *S. aureus* and *E. coli* bacteria strains [14].

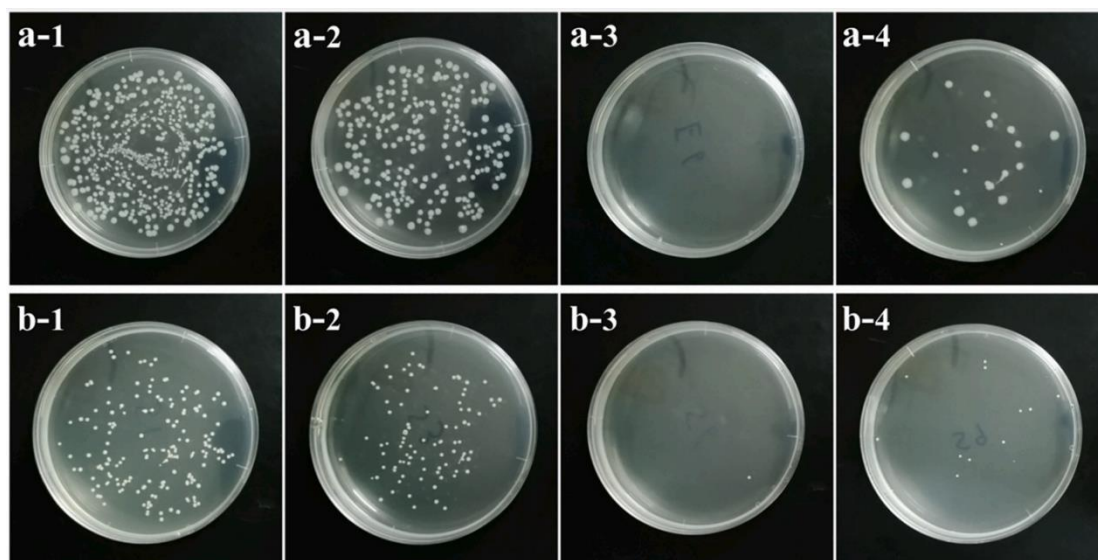


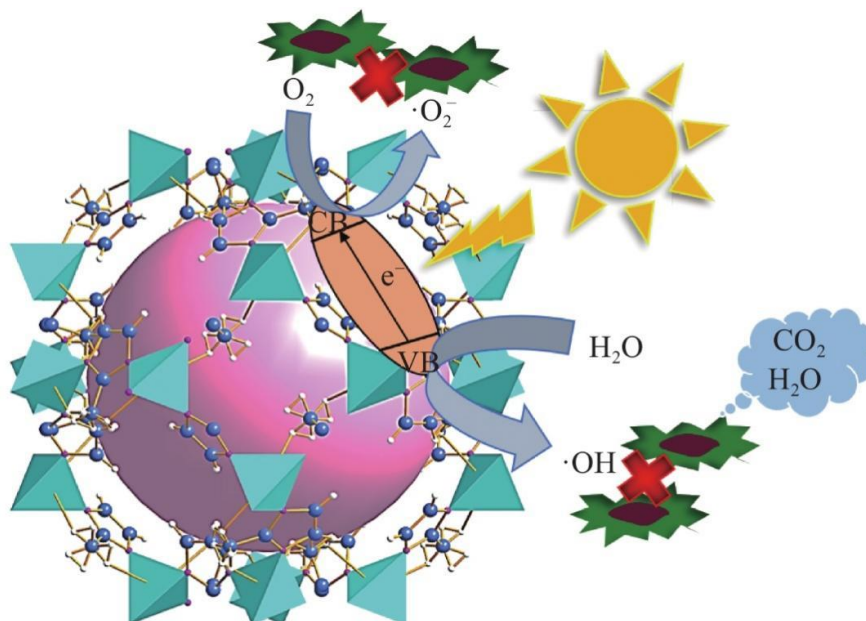
Figure 3. Antibacterial activity of the PVF-g-QA sponges [14]

## 4. Other antibacterial materials

Recently, considering the drawback and instability of single kind of antibacterial material, composite antibacterial materials have become the focus of current research. There are generally two kinds of research directions in this field. One is to use antibacterial materials, combining inorganic antibacterial materials with organic antibacterial materials, and the other is to combine inorganic antibacterial materials on cellulose.

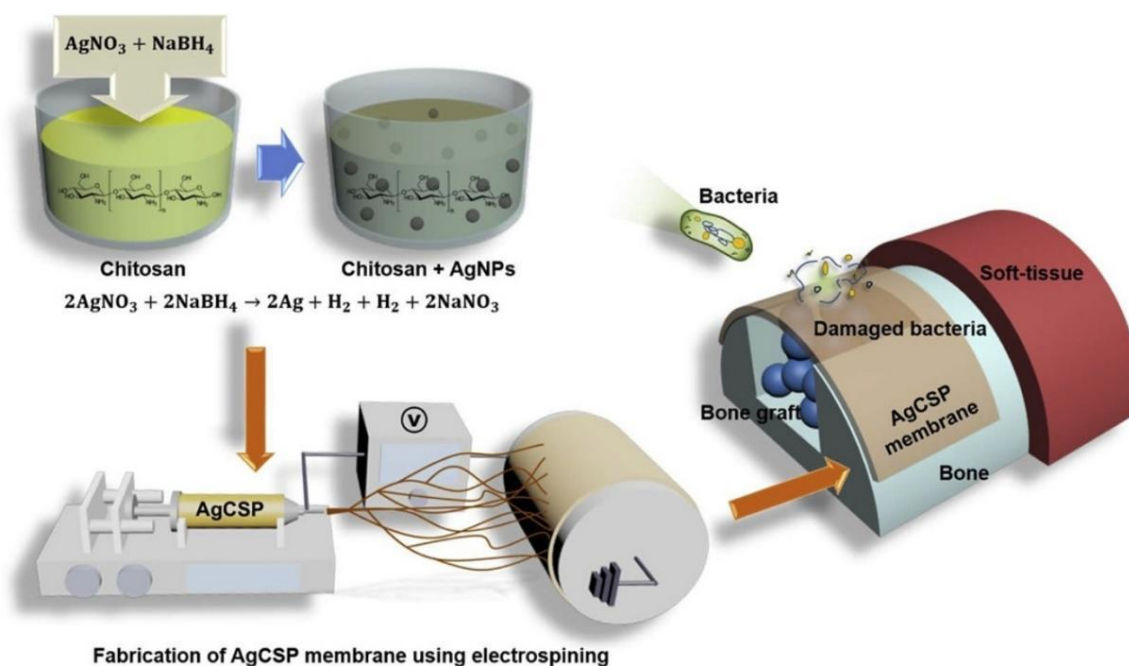
The antibacterial material with metal organic framework is a kind of antibacterial material with biocompatibility, high porosity and large specific surface area. Because of the integration of a variety of antibacterial methods, the antibacterial performance is strengthened. The metal ions contained in the material can contact with the cell membrane, making the permeability of the cell membrane change and rupture, so that the substances in the cell flow out and kill the cell; The metal elements contained in the material can penetrate the cell membrane, interact with DNA and protease in the cell, inhibit cell growth or kill cells. Some metals contained in the material are semiconducting, which can produce a

photocatalytic process under the action of light, oxidize oxygen or water in the air into reactive oxygen species (ROS), thus producing antibacterial effect, as shown in Figure 4.



**Figure 4.** Photocatalytic antibacterial mechanism of the used antibacterial material [15]

Combining chitosan with metal ions with antibacterial activity can not only exert their antibacterial effect, but also reduce the cytotoxicity of metal ions. At present, Ag nanoparticles/chitosan composites are common [16]. Lee et al. used electrospinning technology to prepare AgNPs embedded in chitosan film with good biocompatibility against *Brucella* and *Porphyromonas gingivalis* up to 2 cm, as shown in Figure 5. Raghavendra et al. used the reducing agent chitosan and add AgNPs to prepare a composite film with excellent antibacterial and environmental protection against *Staphylococcus aureus* and *E. coli* [18]. A new cellulose-based antibacterial material using cotton linter cellulose as raw material was prepared and its properties of antibacterial effect was also investigated [19].



**Figure 5.** Application of the prepared antibacterial material [17]

## 5. Conclusion

The development and application of antibacterial materials have a good development prospect. In recent years, especially under the influence of the COVID-19, people began to pay more and more attention to antibacterial and antiviral in food, clothing, housing and transportation. Under the current background of paying attention to health and advocating environmental protection, the antibacterial material industry is bound to make great achievements in the field of clinical medicine and environmental conservation. This research outlines the applications of different kinds of antibacterial materials in biomedical field. In order to improve the antibacterial effect, composite antibacterial materials have become the current development trend, and some new composite antibacterial agents can be developed in the future. These composite antibacterial agents can show a better antibacterial property at low concentration. In addition, considering the environmental friendliness and human safety requirements of the materials, a low-cost, green and safe antibacterial agent is still our most sought goal.

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