

The use of silver hydrogel in wound treatment as an alternative to reduce antibiotic-resistant pathogens

O uso de hidrogel de prata no tratamento de feridas como alternativa para reduzir patógenos resistentes a antibióticos

El uso de hidrogel de plata en el tratamiento de heridas como alternativa para reducir los patógenos resistentes a los antibióticos

Received: 09/01/2022 | Reviewed: 09/08/2022 | Accept: 09/09/2022 | Published: 09/18/2022

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Abstract

Medical science is currently at an early stage for effectively controlling skin damage. One of the main barriers to good wound healing is bacterial infection, which poses a risk of long-term harmful effects. A clean wound, free of bacterial infections, is essential for the quick and effective regeneration of the skin. Hydrogel is one of the best biomaterials for antibiotic delivery in wound areas due to its high hydrophilicity, distinctive three-dimensional network, good biocompatibility, and cell adherence. Although many antibiotics are successful in treating infected wounds, improper or repetitive use of these medications may cause germs to become resistant. Notoriously, antimicrobial resistance in pathogenic bacteria is already considered a serious global public health issue. Recently, the use of silver associated with nanotechnology has been reconsidered as an important alternative to reduce the spread of antibiotic-resistant pathogens. Silver hydrogel dressings have become effective agents in wound management, substituting the use of antibiotics. The objective of this review is to show the importance of hydrogels in wound treatments, as well as the antibacterial properties of silver hydrogels and their implications in wound care.

Keywords: Hydrogel; Silver; Antimicrobial resistance; Bacteria; Wound; Antibiotic; Infection; Biomedicine; Biomaterial; Medical treatment.

Resumo

A ciência médica está atualmente em um estágio inicial para controlar efetivamente os danos à pele. Uma das principais barreiras para uma boa cicatrização de feridas é a infecção bacteriana, que apresenta um risco de efeitos nocivos a longo prazo. Uma ferida limpa, livre de infecções bacterianas, é essencial para a regeneração rápida e eficaz da pele. O hidrogel é um dos melhores biomateriais para administração de antibióticos em áreas de feridas devido à sua alta hidrofiliabilidade, rede tridimensional distinta, boa biocompatibilidade e aderência celular. Embora muitos antibióticos sejam bem-sucedidos no tratamento de feridas infectadas, o uso impróprio ou repetitivo desses medicamentos pode fazer com que os germes se tornem resistentes. Notoriamente, a resistência antimicrobiana em bactérias patogênicas já é considerada um grave problema de saúde pública global. Recentemente, o uso de prata associado à nanotecnologia tem sido reconsiderado como uma importante alternativa para reduzir a disseminação de patógenos resistentes a antibióticos. Os curativos de hidrogel de prata tornaram-se agentes eficazes no manejo de feridas, substituindo o uso de antibióticos. O objetivo da revisão é demonstrar a importância dos hidrogéis no tratamento de feridas, bem como as propriedades antibacterianas dos hidrogéis de prata e suas implicações no tratamento de feridas.

Palavras-chave: Hidrogel; Prata; Resistência antimicrobiana; Bactérias; Feridas; Antibiótico; Infecção; Biomedicina; Biomaterial; Tratamento médico.

Resumen

La ciencia médica se encuentra actualmente en una etapa temprana para controlar eficazmente el daño de la piel. Una de las principales barreras para una buena cicatrización de heridas es la infección bacteriana, que presenta un riesgo de efectos nocivos a largo plazo. Una herida limpia, libre de infecciones bacterianas, es fundamental para la regeneración rápida y eficaz de la piel. El hidrogel es uno de los mejores biomateriales para la administración de antibióticos en las áreas de heridas debido a su alta hidrofiliabilidad, red tridimensional distintiva, buena biocompatibilidad y adherencia celular. Aunque muchos antibióticos tienen éxito en el tratamiento de heridas

infectadas, el uso inadecuado o repetitivo de estos medicamentos puede hacer que los gérmenes se vuelvan resistentes. Notoriamente, la resistencia a los antimicrobianos en bacterias patógenas ya se considera un grave problema de salud pública mundial. Recientemente, el uso de plata asociada a la nanotecnología se ha reconsiderado como una alternativa importante para reducir la propagación de patógenos resistentes a los antibióticos. Los apósitos de hidrogel de plata se han convertido en agentes eficaces en el tratamiento de heridas, sustituyendo el uso de antibióticos. El propósito de la revisión es demostrar la importancia de los hidrogeles en el tratamiento de heridas, así como las propiedades antibacterianas de los hidrogeles de plata y sus implicaciones en el cuidado de heridas.

Palabras clave: Hidrogel; Plata; Resistencia antimicrobiana; Bacterias; Herida; Antibiótico; Infección; Biomedicina; Biomaterial; Tratamiento médico.

1. Introduction

The skin is unquestionably the organ of the human body most vulnerable to injury, scrapes, and burns. Notoriously, the damaged epithelium and connective structures weaken the human body's capability to protect the outer environment. Consequently, it is essential to remodel a healthy epidermis or even additional skin layers. When the healing process takes longer, the wound's typical microbiota alters and hosts more aggressive bacteria (Serra et al., 2015). Gram-positive bacteria, primarily *Staphylococcus aureus*, are more prevalent in the early stages of chronic wound development (García-Pérez et al., 2018; Serra et al., 2015). Gram-negative organisms (e.g., *Escherichia coli* and *Pseudomonas* spp.) are more prevalent and more prone to infiltrating the deeper layers of the skin in advanced stages, negatively impacting the tissues (Lyczak et al., 2000; Petkovšek et al., 2009). To combat the health problem caused by wound infections, different types of wound dressings have been created to protect the wound from bacterial contamination and to hasten the wound healing process (e.g., sponges, hydrogels, films, hydrocolloids, and hydrofiber mats) (Ahmed & Boateng, 2018; Capanema et al., 2017; Koehler et al., 2018; Yao et al., 2017; Ye et al., 2018). Recent studies have focused on incorporating bacteriostatic or bactericidal antibiotics into the wound dressings to assist wound healing (e.g., quinolones, tetracyclines, aminoglycosides, and cephalosporins) (Anjum et al., 2016; Liu et al., 2018; Michalska-Sionkowska et al., 2018; Rădulescu et al., 2016). Although many antibiotics are effective in the treatment of infected wounds, repeated or incorrect use of these drugs might lead to bacterial resistance (Rai et al., 2016). Notoriously, at least one of the most widely used antibiotics cannot effectively treat 70% of the bacteria that cause wound infections (Friedman et al., 2016). For example, strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa* were both considerably resistant to antibiotic treatment, according to a study done on 470 samples of wound secretions with bacterial identification (Pirvanescu et al., 2014). The abusive and inappropriate use of antibiotics has brought the crisis of resistant bacteria to light. Such a situation is considered a global threat and one of the main problems that science and medicine currently face (French, 2010; Hawkey, 2008). According to the World Health Organization (WHO), by 2050, antimicrobial-resistant bacteria will cause the death of more than 10 million people per year (Kraker et al., 2016). In this scenario, it is necessary to seek alternatives to help fight against antibiotic-resistant bacteria.

In antiquity, silver was widely used to treat infections precisely because of its bactericidal and fungicidal potential against more than 650 pathogenic microorganisms (Möhler et al., 2018). Hippocrates was the first physician to record the use of silver powder to treat ulcers and heal wounds (Adams, n.d.). Recently, the use of silver associated with nanotechnology has been reconsidered as an important alternative to mitigate the increase of antibiotic-resistant pathogens (Alavi & Rai, 2019; Beg et al., 2017; Chaudhuri & Chandela, 2016; Lima et al., 2019; Sánchez et al., 2016). Importantly, silver nanoparticles (AgNPs) stand out among the metallic nanoparticles due to their proven anti-inflammatory and antimicrobial activity (Abdelghany et al., 2018; Kasithevar et al., 2017). Several studies have already shown the effectiveness of AgNPs against antibiotic-resistant bacteria such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Streptococcus pyogenes*, *Klebsiella pneumoniae*, among others (Gupta et al., 2019; Lara et al., 2010; Liao et al., 2019; Lopez-Carrizales et al., 2018; Nanda & Saravanan, 2009). Moreover, AgNPs are proving to be effective antimicrobial agents due to the various mechanisms of

sterilization, albeit no definitive conclusions regarding these mechanisms have been reached (Rafael et al., 2019; Vetten et al., 2014). Unfortunately, AgNPs tend to agglomerate and sediment when in an aqueous medium, which causes the antimicrobial action to decrease gradually, harming the applications of AgNPs (Berdous & Ferfera-Harrar, 2016; Mekkawy et al., 2017; Sevgi et al., 2013). To solve this issue, AgNPs must be suspended in a support substrate that prevents particles from agglomerating and maintains long-term stability (Inoue et al., 2019; Mekkawy et al., 2017). Systems using hydrogels are among the main strategies to keep AgNPs stable. Hydrogels are three-dimensional polymeric compounds formed by cross-links that can absorb a large amount of liquid (Zhang & Khademhosseini, 2017). The hydrogel membrane with AgNPs is widely used in treating chronic wounds, adding the hydrogel's benefits with silver's antimicrobial action (Boonkaew et al., 2013; Nesovic & Miskovic-Stankovic, 2020; Varaprasad et al., 2011).

2. Methodology

The current study is an integrated literature review that synthesizes information on the use of silver hydrogel in wound treatment as an alternative to reduce antibiotic-resistant pathogens and incorporates the relevance of important research findings in practice. A literature review from bibliographic research in reliable scientific databases such as Science Direct, Scopus, Wiley Online Library, and Scielo was done between July and September 2022. To search for scientific articles, terms such as “silver hydrogel,” “wound treatment,” “antibiotic-resistant pathogens,” “biomedicine,” “infection,” and “medical treatment” were used. Criteria such as articles mostly in English, open-access availability, and preferably published between 2012 to 2022 were adopted for the selection of the most relevant publications on the use of silver hydrogel in wound treatment as an alternative to reduce antibiotic-resistant pathogens. However, it is important to note that although a few articles used in this review were published before 2012, they were still included in the present study due to their scientific importance, and most have a more reasonable number of citations. This review did not include dissertations, thesis, or information found on web pages.

3. Results and Discussion

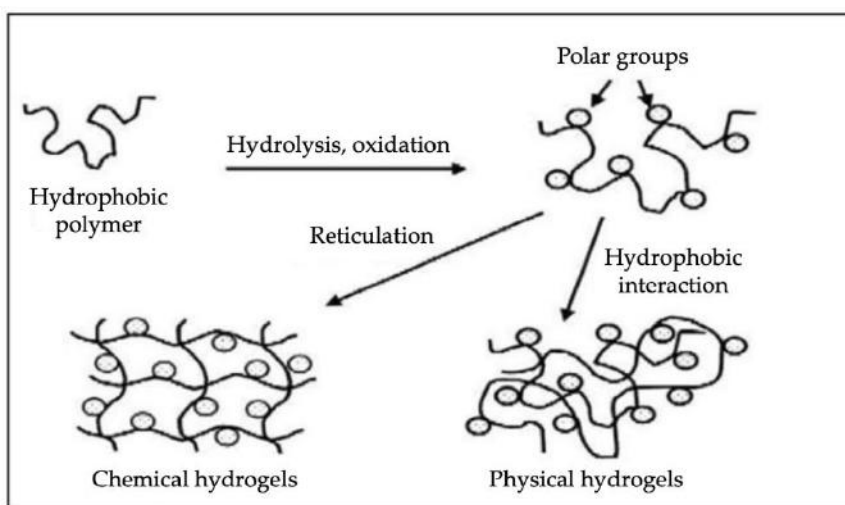
3.1 Hydrogel: Morphology and classification

The synthesis of poly (hydroxyethyl methacrylate) in 1960 is considered the beginning of modern hydrogel research (Wichterle & Lím, 1960). In this context, Wichterle and Lim sought to develop such polymeric matrices for biomedical purposes, with potential application to the human body. According to Kokabi, in 1989, Rosiak implemented the use of hydrogels as a basic material for the manufacture of wound dressings (Kokabi et al., 2007). And since then, there has been considerable progress in the synthesis and applications of hydrogels in the most diverse areas of knowledge. Hydrogels are cross-linked polymeric networks with a three-dimensional configuration capable of absorbing large amounts of water or biological fluids without suffering structural damage. This characteristic of hydrogels is attributed to the presence of hydrophilic groups, such as -OH, -COOH, -CONH, -CONH₂, and -SO₃H, in polymers that form the structures of hydrogels (Hamidi et al., 2008; Ullah et al., 2015).

Hydrogels are classified according to the method of formation, the ionic charge, and how the networks are reticulated (Nascimento & Lombello, 2016). Concerning the formation of chains, hydrogels are classified as homopolymers when only one type of monomer is used; copolymers when more than one type of monomer is used; and interpenetrating polymers when the polymeric chains of a given hydrogel penetrate and entangle with the chains of another hydrogel, forming blends (Nascimento & Lombello, 2016). Regarding the ionic charge, hydrogels are classified as neutral when they do not present ionizable groups (e.g., methyl methacrylate); cationic when they have groups capable of forming cations by changing the pH of

the reaction medium; and anionic when the hydrogel presents anion-forming groups, also due to the pH variation of the reaction medium (Nascimento & Lombello, 2016). Interestingly, the polymeric chains of a hydrogel can be chemically or physically linked, leading to permanent or reversible gels (Figure 1). Chemical hydrogels are formed by different macromolecular chains that are permanently joined through covalent bonds and can also be obtained by cross-linked polymers in the dry state or solution. On the other hand, physical hydrogels originate through electrostatic attraction, ionic bonds, hydrogen bonds, or hydrophobic interactions between polymer chains. They are often reversible and can be dissolved by changing the environmental conditions of the solution, such as pH, ionic strength, or temperature (Hoffman, 2012).

Figure 1. Methods for preparing hydrogels of physical and chemical origin.



Source: Goulart, D. B.

Physical crosslinking, more specifically, ionotropic gelation, also allows the encapsulation of the most diverse materials in hydrogels, such as cells, drugs and enzymes. This method produces microparticles, which are generated by extrusion of the polymeric dispersion containing the material to be encapsulated. The hydrogel spheres are produced when the solution containing the polymer is dripped onto the crosslinking solution, responsible for forming intra and intermolecular crosslinks, leading to a three-dimensional network (Bulmer et al., 2012; Prezotti et al., 2014). Ionotropic gelation is a simple, fast, and economical technique. On the other hand, hydrogels formed by this type of gelation present difficulties in controlling the release rate of the encapsulated material for a long period (Yeo et al., 2001).

3.2 Applications of hydrogel

In the last 20 years, scientific research on hydrogels has intensified. Countries such as the U.S., China, Japan, South Korea, Germany, and the United Kingdom stand out in conducting studies to develop and improve techniques for synthesizing and characterization of these polymer matrices, thus expanding the scope of their applications (Mahinroosta et al., 2018). The advantages of using these matrices include ease of preparation, use of natural products, biodegradability, biocompatibility, prolonged stability, and ease of biochemical modification of the formed structures (Ischakov et al., 2013). Such properties determine the application of the hydrogel in the fields of tissue engineering (Pensaifini et al., 2017), wound dressings (Rakhshaei & Namazi, 2017), biosensors (Jonášová & Stokke, 2016), pharmaceuticals (Treenate & Monvisade, 2017), agriculture (Guilherme et al., 2015a), adsorption of contaminants such as acid dyes in the textile industry (Khan & Lo, 2017), wastewater treatments (Mohammadzadeh Pakdel & Peighambaroust, 2018), and enzyme encapsulation (Martín et al., 2019).

Table 1. Main applications of hydrogels in different areas.

Field	Application	Reference
Agriculture	Controlled release of nutrients and pesticides, soil conditioners	(Guilherme et al., 2015b; Rizwan et al., 2021)
Food Science	Protection of aromatic compounds, encapsulation and controlled release of vitamins and minerals, food coating	(Farris et al., 2009; Shewan & Stokes, 2013)
Biomaterial	Optical devices, batteries, sensors, capacitors, hydro-absorbent materials, incorporation of macromolecules	(Kopeček, 2007; Kopeček & Yang, 2007)
Cosmetic	Foundations for skin, release of cosmetic actives	(Mitura et al., 2020; Morales et al., 2009)
Pharmacy	Controlled release of drugs and proteins, encapsulation of active principles	(McKenzie et al., 2015; Wanzke et al., 2020)
Biomedicine	Wound dressings, intraocular contact lenses, filling of cancellous bones, cartilage replacement, ultrasound, substrate for cell culture, artificial muscles	(Kamoun et al., 2017; Liang et al., 2021)

Source: Authors.

3.2.1 Hydrogel as wound dressings

Most modern wound care solutions ensure a warm and moist environment, widely acknowledged as crucial in promoting quick healing (Hu et al., 2018; Tan et al., 2019). The formation of the granulation tissue and the facilitation of skin cell division are best supported by a moist healing environment, which further promotes complete wound healing (Rowan et al., 2015). Thus, an ideal dressing is able to maintain high humidity levels at the wound site while simultaneously removing surplus exudates; it also needs to be non-toxic, non-allergenic, comfortable, and affordable, allow for oxygen and water vapor exchange, and provide protection against microbial invasion (Negut et al., 2018; Nischwitz et al., 2019). Modern wound dressings serve as vehicles for delivering therapeutic drugs at the wound site and include nanofibrous mats (Unnithan et al., 2016; Zou et al., 2020), sponges (Feng et al., 2019; Ma et al., 2019), films (Axibal & Brown, 2019; Ezzelarab et al., 2019), foams (Erring et al., 2019; Song et al., 2017), and hydrogels (Koehler et al., 2018; Pan et al., 2019; L. Zhang et al., 2019). Importantly, the cooling action and low tissue adhesion of hydrogel-based dressings help treated patients experience less pain compared to the other wound dressings (Madaghiele et al., 2014; Sood et al., 2014).

The hydrogel model used as a wound dressing was first developed by Rosiak and consists of water, poly(N-vinyl-2-pyrrolidone) (PVP), poly(ethylene glycol) (PEG), and agar, the last used as a pre-molding (Rosiak et al., 1989). Hydrogels can be used as dressings to keep the wound bed moist, facilitating the body's intrinsic enzymes to break down necrotic or non-viable tissue and promote cell regeneration (Wang et al., 2007). The properties that turn hydrogels into biomaterials are (1) their high water content (around 90% water and 10% natural or synthetic polymers) , which contributes to their biocompatibility; (2) low interfacial tension, which improves its ability to adhere to organic tissues and absorb proteins and tissue fluids; (3) physical properties similar to organic tissues, represented by its softness and elasticity, which minimizes mechanical irritation to friction; and (4) porous structure that allows the diffusion of metabolites and good oxygen permeability (Patel & Mequanint, 2011). Hydrogels can also be applied as a matrix for controlled release of active ingredients and antimicrobial agent (Hoque et al., 2018). The incorporation of therapeutic substances in the hydrogel membranes and the release of these agents in the wound result from a series of factors defined by the degree of crosslinking produced by irradiation (Maitra & Shukla, 2014). Hydrogels generated through radioactivity exhibit a strong reducing power, so gamma radiation has been used to reduce metal ions to synthesize nanoparticles in solution, especially silver nanoparticles (Shin et al., 2004). Radiation is used in manufacturing hydrogels to facilitate crosslinking and simultaneous sterilization, resulting in a product free of toxic residues, simplifying the manufacturing process, and lowering production costs (Benamer et al., 2006).

3.3 Sterilization of hydrogels for biomedical applications

Given the increasing complexity and diversity of biomaterials, in particular hydrogels, it is necessary to develop and validate new, safe and reproducible sterilization methods that allow them to be sterilized effectively after their manufacture, without compromising their properties and without high associated costs. Interestingly, the sterilizing process in hydrogels has been the subject of very few scholarly works in the previous ten years—less than 0.3% of all papers on the Web of Science portal—despite its significance from a scientific, clinical, and economic perspective. The sterilization of polymeric materials, such as hydrogels, must be carried out with special care. Under certain conditions, sterilization may cause degradation, discoloration, embrittlement, odor generation, promoting additional cross-linking, or even inducing toxic effects in materials subjected to the process (Ahmed et al., 2013; Murray et al., 2013; Phillip et al., 2013; Vanichvattanadecha et al., 2010). For instance, the simultaneous occurrence of the cross-linking and polymeric chain scission processes during gamma irradiation makes it challenging to interpret the benefits of the process (Zajko & Klimant, 2013). Importantly, sterilization at high temperatures generally leads to two main events: main chain reaction, which can result in breakage or further cross-linking; and side chain reaction, which can result in group elimination or cyclization (David, 1975). Regarding the oxidative processes, the polymers can be oxidized, partially degraded, or subjected to additional cross-linking. This exposure is characterized by an induction period during which the polymer may not show obvious changes. Nevertheless, the production of hydroperoxides may have long-term consequences (Rabek, 1975).

3.4 The importance of AgNPs in the treatment of wound infections

Treating wound infections caused by antimicrobial-resistant bacteria is a challenging task owing to the inability of conventional antibiotics to treat such infections (Rai et al., 2009). Metal nanoparticles (NPs) are viewed as potential alternatives to commonly used antibiotics since they have independently shown bactericidal effectiveness against numerous diseases, have the ability to reduce adverse drug reactions, and do not cause microbial resistance (Yang et al., 2017). NPs achieve their bactericidal effect by releasing toxic metal ions or by producing reactive oxygen species (ROS) when it comes into contact with a bacterial cell wall (Kumar et al., 2018). Moreover, NPs can also damage mitochondria, disrupt metabolic pathways, enter the cell wall, and impact proton efflux pumps by altering pH and disrupting the surface charge of membranes (Kumar et al., 2018; Wang et al., 2017).

Silver is a metal obtained largely as a by-product of lead mining, it is often associated with copper, and its medicinal properties have been used for over 2000 years (Alexander, 2009). Nanocrystalline silver was introduced as a wound dressing in 1998, with the claim that it reduces the occurrence of infection and provides an opportunity to improve clinical practice in wound care. Although the Greeks and Romans have used silver as a bactericidal agent since ancient times, colloidal silver only began to arouse interest in researchers after the emergence of bacterial resistance to antibiotics and advances in nanotechnology (Nowack et al., 2011). AgNPs have received extensive consideration by the scientific community owing to their inhibitory action towards approximately 650 different microbe species and against antimicrobial resistant bacteria (Boonkaew et al., 2013; Durán et al., 2016; Inoue et al., 2019; Raghavan et al., 2016; Sondi & Salopek-Sondi, 2004; Vyshnava et al., 2016). The exact mechanism of action of AgNPs is not clearly understood, which has generated discussion within the scientific community (Baptista et al., 2018; Franci et al., 2015). Importantly, a number of variables, including size, shape, size distribution, coating, agglomeration, surface electrical charge, concentration of nanoparticles, and release of Ag⁺ ions, are crucial for the antibacterial activity of AgNPs (Dakal et al., 2016; Durán et al., 2016; Ouay & Stellacci, 2015; Pareek et al., 2018a; Ramalingam et al., 2016). It has been observed that using silver nanoparticles to raise the surface-to-volume ratio effectively improves the bactericidal effectiveness of the silver ions (Nam et al., 2015). Increased contact area with the bacteria occurs concurrently with an improvement in surface-to-volume ratio (Nam et al., 2015). The silver must be in its ionic form to

function as an antibacterial agent. Thus, the nanoparticles' increased surface area allows for the production of more silver ions, which can interact with bacteria in a variety of ways (Bondarenko et al., 2013). For example, AgNPs smaller than 10 nm have demonstrated a more effective antibacterial effect than larger particles (Durán et al., 2016). AgNPs' size is a key determinant of their antibacterial effectiveness; the smaller the particle, the greater the surface area and interaction with bacterial surfaces and intracellular structures (Pareek et al., 2018a, 2018b). The main consequences of these interactions are DNA base mismatches and consequent inhibition of replication (Manna et al., 2015), denaturation of enzymes and structural proteins (Yuan et al., 2013), and inhibition of translation signals (Vyshnava et al., 2016). Moreover, AgNPs adhere to the bacterial cell membrane and cause structural changes that affect its permeability and transport, leading the cell to an imbalance in cellular respiration and consequently death (Dakal et al., 2016; Khalandi et al., 2017; Sondi & Salopek-Sondi, 2004). Silver is a soft acid, so its ions have a natural predisposition to interact with soft bases. Several bacterial cell structures are composed of sulfur and phosphorus, which are soft bases. Since bacterial DNA contains sulfur and phosphorus as its main components, the interaction with ions impairs DNA structure and function, causing bacterial death (Khalandi et al., 2017).

3.4.1 Concerns with the use of AgNPs

Several aspects influence the toxicity of AgNPs in hydrogels, including concentration and particle characteristics such as synthesis method, size, shape, surface electrical charge, and coating (Zhang et al., 2014). Researchers found that silver is cytotoxic to human dermal fibroblast cells in a concentration-dependent manner (Anisha et al., 2013). Studies have suggested that the use of hydrogel dressings with AgNPs may harm human health (e.g., potential cytotoxic effect on organic tissues) (Boonkaew et al., 2014) and the environment (Rezvani et al., 2019; Saleem Khan et al., 2015; Yu et al., 2013); however, this fact is not fully understood and is relatively unexplored. Importantly, as nanotechnology developed, experts were able to create a therapeutic window that increases the antibacterial capabilities of silver, lowers its minimum inhibitory concentration, and lessens its toxicity to healthy human cells (Nam et al., 2015). As a result, many wound dressings containing silver (e.g., Acticoat, Bactigrass, Tegaderm, Fucidin, and PolyMem Silver) have been approved for market introduction by the U.S. Food and Drug Administration (FDA) (Verma et al., 2016). When applying wound dressings to the wound site, cytotoxicity and antibacterial activity must be balanced. Even though the efficiency of silver ions has been clinically tested, caution should be exercised in using this treatment since unanticipated adverse effects may emerge in some circumstances. It is important to note that the limited efficacy of silver ion release, the limited number of silver species, the inability of silver ions to reach the wound bed, and the fast consumption of silver ions may require higher concentrations of silver compounds within the wound treatment, which could be fatal to healthy host cells (Atiyeh et al., 2007).

AgNPs can potentially harm the environment, particularly the soil microbiota, by killing the bacteria responsible for denitrification, impairing the nitrogen cycle, and, consequently, affecting soil nitrification, essential for plant growth (Yu et al., 2013). Toxic effects can also extend to aquatic environments where silver ions can interact with fish gills affecting fish osmoregulation (Rajkumar et al., 2016). Oxidative stress and lipid peroxidation have also been observed in fish brain tissue due to exposure to silver nanoparticles (Afifi et al., 2016; Saleem Khan et al., 2015). Oxidative stress develops through the formation of reactive oxygen species (ROS) and damage to cellular components, such as DNA, depletion of antioxidant molecules, binding and deactivation of proteins, and damage to the cell membrane (McShan et al., 2014; Zhang et al., 2016).

3.4.2 Synthesis of AgNPs

Two approaches are used to obtain metallic nanoparticles, including AgNPs top-down and bottom-up methods. The top-down method consists of successively breaking the metal into its conventional size until it reaches nanometric size, while the bottom-up method consists of building nanomaterials by grouping atoms and subatomic particles (Lee & Jun, 2019;

Mukherji et al., 2019; Tri Handok et al., 2018). AgNP synthesis commonly employs physical and chemical techniques; however, biological synthesis or biosynthesis research has gained notoriety (Beyene et al., 2017).

Among the physical techniques used in the synthesis of AgNPs, those that use evaporation (e.g., condensation) and laser ablation processes stand out. The evaporation/condensation processes are based on the formation of silver vapors and consequent cooling; however, this technique requires large energy expenditures to keep the heating system stable and above 1,000 °C (Harra et al., 2015). The laser ablation method involves “cutting” the silver to its conventional size with nanometrically calculated laser beams (Zhang et al., 2017). Both techniques require high cost and maintenance equipment, making the synthesis by chemical and biological routes more economically viable.

Compared to physical techniques, the synthesis of AgNPs by chemical methods offer a wider range of technologies and lower prices. The main methods include chemical reduction, microemulsion, photoreduction, electrochemical synthesis, and microwave irradiation (Iravani et al., 2014). The most widely used is chemical reduction, which consists of using chemical agents (e.g., sodium borohydride, sodium citrate, and ascorbic acid) to reduce silver ions (Ag^+) to reduced silver (Ag^0), with consequent aggregation and formation of AgNPs (Praveena et al., 2016; Zain et al., 2014). However, AgNPs synthesized by this method have high instability and a high aggregation probability, requiring surfactants (amines, acids, alcohols, and thiols) to ensure stability and prevent AgNPs from settling (Toh et al., 2015).

The synthesis of AgNPs using physical and chemical methods require equipment with high operating costs, chemical reagents with high toxicity, and the generation of by-products with polluting potential (Bilal et al., 2017). Given these negative points, the use of organisms and their bio compounds emerge as an alternative for synthesizing silver nanoparticles, a process known as biosynthesis, nanobiotechnology, or green synthesis (Ebrahimezhad et al., 2017). The biological synthesis of silver nanoparticles employs biomolecules of diverse origin, especially those from bacteria, yeasts, filamentous fungi, mushrooms, and plants (Table 2) (Keat et al., 2015). In this type of synthesis, the approach used is of the bottom-up type, where the reduction of silver ions (from an aqueous solution of silver nitrate) to AgNPs occurs by the action of enzymes and phytochemicals (Abdelghany et al., 2018; Siddiqi & Husen, 2016). In addition to reducing silver, these bio compounds also act in stabilizing AgNPs, reducing the possibility of aggregation and maintaining the biological activity of these nanomaterials (Raghavan et al., 2016).

Table 2. Organisms responsible for the biological synthesis of silver nanoparticles.

Organism	Species	Reference
Bacteria	<i>Bacillus brevis</i>	(Saravanan et al., 2018)
	<i>Nostoc</i> spp.	(Sonker et al., 2017)
	<i>Streptomyces exfoliatus</i>	(Iniyan et al., 2017)
Yeast	<i>Candida lusitanae</i>	(Eugenio et al., 2016)
	<i>Cryptococcus laurentii</i>	(Fernández et al., 2016)
	<i>Pichia fermentans</i>	(Chauhan et al., 2015)
	<i>Saccharomyces cerevisiae</i>	(Korbekandi et al., 2016)
Filamentous fungus	<i>Aspergillus flavus</i>	(Manimozhi & Anitha, 2014)
	<i>Cladosporium sphaerospermum</i>	(I. I. Abdel-Hafez et al., 2016)
	<i>Fusarium solani</i>	(Vijayan et al., 2016)
	<i>Penicillium nalgiovense</i>	(Maliszewska et al., 2014)
	<i>Phoma sorghina</i>	(Sonar et al., 2017)
Mushroom	<i>Ganoderma aplanatum</i>	(Mohanta et al., 2016)
	<i>Lactarius piperatus</i>	(Vamanu, 2017)
	<i>Lentinus edodes</i>	(Lateef & Adeeyo, 2015)
	<i>Pleurotus ostreatus</i>	(Al-Bahrani et al., 2017)
Plant	<i>Aloe vera</i>	(Tippayawat et al., 2016)
	<i>Morinda citrifolia</i>	(Suman et al., 2013)
	<i>Vitis vinifera</i>	(Gnanajobitha et al., 2013)

Source: Authors.

3.5 Applications of hydrogels based on silver for wound dressings

Despite the fact that a moist environment is necessary at the wound site, it may also raise the danger of microbial infections, which will lengthen the wound and/or slow down the healing process (Joshi Navare et al., 2020). Microbial colonization is undesirable because it may lead to major infections that may cause illness, septicemia, or even death (Zhang et al., 2021). Importantly, when wounds are colonized by opportunistic bacteria, the normal reparative and regenerative stages included in the healing process fail to occur (Simões et al., 2018). *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* are the most frequent microbial strains present in infected wounds (Cardona & Wilson, 2015). To prevent and treat infections, modern medicine relies on antimicrobial drugs like antibiotics, which work by either eliminating germs or preventing their growth (Abhishek Gupta et al., 2020). Therefore, hydrogels with antibacterial properties have enormous potential for use in clinical settings (Yang et al., 2018). Antimicrobial agents are typically divided into two categories: organic substances, such as antibiotics and organic mineral salts, and inorganic substances, such as silver (Banerjee et al., 2019), zinc (H. Liu et al., 2018), and copper (Mohandas et al., 2018). Wound dressings with incorporated antimicrobial compounds have emerged as a practical alternative in recent years for reducing wound microbial colonization and infection and enhancing the healing process (Negut et al., 2018).

The hydrogel membrane with silver nanoparticles represents one of the alternatives used in the treatment of chronic wounds (Shi et al., 2019). This type of coverage adds the benefits of the hydrogel with the antimicrobial action of silver. Clinical guidelines recommend that silver nanoparticle dressings be used on wounds where the infection is already established or on wounds with an excessive microbial load (Paladini et al., 2013). The most typical and inevitable impediment to wound healing is the development of an infection, which is relatively common in chronic wounds (Negut et al., 2018). Patients are heavily burdened and have a lower quality of life due to frequent dressing changes, repeated hospital admissions, and physical restrictions frequently associated with chronic wounds (Koehler et al., 2018). Hydrogel dressings with silver nanoparticles

have a broad spectrum of antimicrobial activities (Dai et al., 2018). Importantly, the application of antimicrobial hydrogels as dressings combines hydrogel properties with the bactericidal action of silver and constitutes a good option for treating chronic wounds.

In vitro studies have demonstrated the hydrogel dressings with AgNPs' bactericidal activity in multidrug-resistant bacteria, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella* spp., and *Candida albicans* (Bowler et al., 2004). Wu and collaborators studied novel silver-containing thermoplastic hydrogel membranes' synthesis, processing, and antimicrobial behavior (Wu et al., 2009). Antimicrobial activity was examined using exposure to *Escherichia coli*. Nanofiber hydrogels containing silver exhibited exceptional prominence against biofilm resistance in bacterial cultures (Wu et al., 2009). In another study, the hydrogels based on 2-hydroxyethyl acrylate and itaconic acid were synthesized by Vuković and collaborators and used for silver ions incorporation (Vuković et al., 2020). The hydrogels showed promising antibacterial activity against methicillin-sensitive *Staphylococcus aureus* (MSSA) and MRSA, indicating that they could be used to treat the potentially fatal illnesses (Vuković et al., 2020). Studies on chitosan hydrogel-based wound dressing formulations that contain and release nano-Ag and AgNPs have recently received attention (Hanif et al., 2016; Higa et al., 2016; Jaiswal et al., 2016; M.Y. et al., 2016; Nešović et al., 2017). Chitosan is a natural polysaccharide with hemostatic, bacteriostatic, and fungistatic properties suitable for medical applications (Koehler et al., 2018). To illustrate it, spherical AgNPs ranging from 10 to 30 nm were inserted into nanofiber surfaces to treat wounds (Wu et al., 2014). With 99% or more reduction in *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, this nanostructure showed significant antibacterial activity and supported the growth of epidermal cells without cytotoxicity effects (Wu et al., 2014). Other researchers used coated polyester-nylon wound dressings with AgNPs to lower the incidence of exogenous wound-related infections (Radulescu et al., 2016). *In vitro* and *in vivo* studies showed improved inhibitory activity against bacterial colonization and biofilm formation, particularly against *Pseudomonas aeruginosa*, and fibroblast cells could grow normally (Radulescu et al., 2016).

3.5.1 Hydrogels based on silver for the treatment of burn

Burns are described as skin damage brought on by high temperatures or acidic substances, the two most typical causes (Butko et al., 2019; Jeschke & Gauglitz, 2020). Burn injuries interfere with the normal skin barrier and a number of other infection-preventing defensive processes (Mofazzal Jahromi et al., 2018). As a result, burn patients continue to be susceptible to a variety of invasive microbial infections until complete epithelialization occurs (Parikh et al., 2005). Silver nanoparticles are frequently used in wound therapy to provide therapeutically desirable qualities and an optimal environment for quick and efficient burn healing. Acticoat™ and PolyMem Silver®, two available silver-containing dressings to treat burns, were compared to a novel silver hydrogel dressing by Boonkaew and collaborators (Boonkaew et al., 2014). After 24 hours, most of the examined microbial strains were below the detection threshold, and bacterial viability was decreased by 94 to 99% (Boonkaew et al., 2014). Acticoat™ Flex 3 was tested on a fibroblast cell culture *in vitro* and on a real partial thickness burn patient (Rigo et al., 2013). According to the findings collected by cellular staining techniques, the AgNPs lowered mitochondrial activity without lysing skin cells or jeopardizing the integrity of the skin cells' nuclei (Rigo et al., 2013). The reduction in mitochondrial activity suggests a decrease in the number of bacteria, thus supporting the antibacterial properties of the silver-based hydrogel dressing (Rigo et al., 2013). In another investigation, a thermo-sensitive methylcellulose (MC) hydrogel containing silver oxide nanoparticles (NPs) was created via one-pot synthesis in which a silver acetate precursor salt (CH₃COOAg) causes a salt-out effect in the MC solution (Kim et al., 2018). Interestingly, the MC hydrogel containing silver oxide NPs demonstrated remarkable antimicrobial activity and burn wound healing (Kim et al., 2018). Another study suggested a novel method for promoting vascularization in burn wounds (Banerjee et al., 2019). Contact burn wounds on the

dorsum of the rats and were infected with *Pseudomonas aeruginosa* and treated with PEGylated fibrin hydrogel containing 50 mgs of silver sulfadiazine loaded chitosan microsphere (SSD-CSM-FPEG) (Banerjee et al., 2019). The proposed sequential treatment for infected burn wounds reduced bacterial infection while encouraging neovascularization and enhanced matrix remodeling (Banerjee et al., 2019).

4. Conclusion

There are still numerous obstacles to be addressed in the field of wound care. In order to treat non-healing wounds brought on by infection, cutting-edge materials that could be employed as wound dressings must be designed. Recent research has made it possible to create hydrogel wound dressings for delivering therapeutic molecules and medications to the wound site. The use of silver hydrogel dressing in wound treatment to prevent bacterial infection contribute to the improvement of wound management by creating an ideal environment for maximum wound recovery. Despite the large number of hydrogel-based solutions already on the market, the creation or improvement of advanced hydrogel dressings continues to be a significant topic of study to further enhance skin healing in reports to particular therapeutic applications. Antimicrobial hydrogels are a crucial subset of macromolecular antimicrobial substances that have shown notable effectiveness in both the prevention and treatment of drug-resistant illnesses.

References

- Abdelghany, T. M., Al-Rajhi, A. M. H., Al Abboud, M. A., Alawlaqi, M. M., Ganash Magdah, A., Helmy, E. A. M., & Mabrouk, A. S. (2018). Recent advances in green synthesis of silver nanoparticles and their applications: About future directions. A review. *BioNanoSci.*, 8, 5–16. <https://doi.org/10.1007/s12668-017-0413-3>
- Adams, F. (n.d.). *Works by Hippocrates-On ulcers*. Written 400 B.C.E. Retrieved August 20, 2022, from <http://classics.mit.edu/Hippocrates/ulcers.html>
- Afifi, M., Saddick, S., & Abu Zinada, O. A. (2016). Toxicity of silver nanoparticles on the brain of *Oreochromis niloticus* and *Tilapia zillii*. *Saudi J. Biol. Sci.*, 23, 754–760. <https://doi.org/10.1016/j.sjbs.2016.06.008>
- Ahmed, A., & Boateng, J. (2018). Calcium alginate-based antimicrobial film dressings for potential healing of infected foot ulcers. *Ther. Deliv.*, 9, 185–204. <https://doi.org/10.4155/tde-2017-0104>
- Ahmed, M., Punshon, G., Darbyshire, A., & Seifalian, A. M. (2013). Effects of sterilization treatments on bulk and surface properties of nanocomposite biomaterials. *J. Biomed. Mater. Res. - B Appl. Biomater.*, 101, 1182–1190. <https://doi.org/10.1002/jbm.b.32928>
- Al-Bahrani, R., Raman, J., Lakshmanan, H., Hassan, A. A., & Sabaratnam, V. (2017). Green synthesis of silver nanoparticles using tree oyster mushroom *Pleurotus ostreatus* and its inhibitory activity against pathogenic bacteria. *Mater. Lett.*, 186, 21–25. <https://doi.org/10.1016/j.matlet.2016.09.069>
- Alavi, M., & Rai, M. (2019). Recent advances in antibacterial applications of metal nanoparticles (MNPs) and metal nanocomposites (MNCs) against multidrug-resistant (MDR) bacteria. *Expert Rev. Anti-Infect. Ther.*, 17, 419–428. <https://doi.org/10.1080/14787210.2019.1614914>
- Alexander, J. (2009). History of the medical use of silver. *Surg. Infect.*, 10, 289–292. <https://doi.org/10.1089/sur.2008.9941>
- Anisha, B., Biswas, R., Chennazhi, K., & Jayakumar, R. (2013). Chitosan–hyaluronic acid/nano silver composite sponges for drug resistant bacteria infected diabetic wounds. *Int. J. Biol. Macromol.*, 62, 310–320. <https://doi.org/10.1016/j.ijbiomac.2013.09.011>
- Anjum, S., Arora, A., Alam, M. S., & Gupta, B. (2016). Development of antimicrobial and scar preventive chitosan hydrogel wound dressings. *Int. J. Pharm.*, 508, 92–101. <https://doi.org/10.1016/j.ijpharm.2016.05.013>
- Atiyeh, B. S., Costagliola, M., Hayek, S. N., & Dibo, S. A. (2007). Effect of silver on burn wound infection control and healing: Review of the literature. *Burns*, 33, 139–148. <https://doi.org/10.1016/j.burns.2006.06.010>
- Axibal, E., & Brown, M. (2019). Surgical dressings and novel skin substitutes. *Dermatol. Clin.*, 37, 349–366. <https://doi.org/10.1016/j.det.2019.03.005>
- Banerjee, J., Seetharaman, S., Wrice, N. L., Christy, R. J., & Natesan, S. (2019). Delivery of silver sulfadiazine and adipose derived stem cells using fibrin hydrogel improves infected burn wound regeneration. *PLoS ONE*, 14, 1–22. <https://doi.org/10.1371/journal.pone.0217965>
- Baptista, P. V., McCusker, M. P., Carvalho, A., Ferreira, D. A., Mohan, N. M., Martins, M., & Fernandes, A. R. (2018). Nano-strategies to fight multidrug resistant bacteria-"A Battle of the Titans". *Front. Microbiol.*, 9, 1–26. <https://doi.org/10.3389/fmicb.2018.01441>
- Beg, M., Maji, A., Mandal, A. K., Das, S., Aktara, M. N., Jha, P. K., & Hossain, M. (2017). Green synthesis of silver nanoparticles using *Pongamia pinnata* seed: Characterization, antibacterial property, and spectroscopic investigation of interaction with human serum albumin. *J. Mol. Recognit.*, 30, 1–8. <https://doi.org/10.1002/jmr.2565>

- Benamer, S., Mahlous, M., Boukrif, A., Mansouri, B., & Youcef, S. L. (2006). Synthesis and characterisation of hydrogels based on poly(vinyl pyrrolidone). *Nucl. Instrum. Methods Phys. Res. B*, 248, 284–290. <https://doi.org/10.1016/j.nimb.2006.04.072>
- Berdous, D., & Ferfera-Harrar, H. (2016). Green synthesis of nanosilver-loaded hydrogel nanocomposites for antimicrobial application. *Inter. J. of Bio. Biomol. Agricul. Food and Biotech. Eng.*, 10, 529–536.
- Beyene, H. D., Werkneh, A. A., Bezabh, H. K., & Ambaye, T. G. (2017). Synthesis paradigm and applications of silver nanoparticles (AgNPs), a review. *Sustain. Mater. Technol.*, 13, 18–23. <https://doi.org/10.1016/j.susmat.2017.08.001>
- Bilal, M., Rasheed, T., Iqbal, H., Hu, H., & Zhang, X. (2017). Silver nanoparticles: biosynthesis and antimicrobial potentialities. *Int. J. Pharmacol.*, 13, 832–845.
- Bondarenko, O., Ivask, A., Käkinen, A., Kurvet, I., & Kahru, A. (2013). Particle-cell contact enhances antibacterial activity of silver nanoparticles. *PLoS ONE*, 8, e64060. <https://doi.org/10.1371/journal.pone.0064060>
- Boonkaew, B., Kempf, M., Kimble, R., Supaphol, P., & Cuttle, L. (2014). Antimicrobial efficacy of a novel silver hydrogel dressing compared to two common silver burn wound dressings: Acticoat™ and PolyMem Silver®. *Burns*, 40, 89–96. <https://doi.org/10.1016/j.burns.2013.05.011>
- Boonkaew, B., Suwanpreuksa, P., Cuttle, L., Barber, P., & Supaphol, P. (2013). Hydrogels containing silver nanoparticles for burn wounds show antimicrobial activity without cytotoxicity. *J. Appl. Polym. Sci.*, 131. <https://doi.org/10.1002/app.40215>
- Bowler, P., Jones, S., Walker, M., & Parsons, D. (2004). Microbicidal properties of a silver-containing hydrofiber dressing against a variety of burn wound pathogens. *J. Burn Care Rehabil.*, 25, 192–196. <https://doi.org/10.1097/01.bcr.0000112331.72232.1b>
- Bulmer, C., Margaritis, A., & Xenocostas, A. (2012). Production and characterization of novel chitosan nanoparticles for controlled release of rHu-Erythropoietin. *Biochem. Eng. J.*, 68, 61–69. <https://doi.org/10.1016/j.bej.2012.07.007>
- Butko, Y., Tkachova, O., Ulanova, V., Sahin, Y., Levashova, O., & Tishakova, T. (2019). Immune histochemical study of KI-67 level and ribonucleic acid in the process of healing of burn wounds after treatment with drugs containing dexpanthenol and ceramide. *Biointerface Res. Appl. Chem.*, 9, 4586–4590. <https://doi.org/10.33263/BRIAC96.58659>
- Capanema, N., Mansur, A., Carvalho, S., Mansur, L., Ramos, C., Lage, A., & Mansur, H. (2017). Physicochemical properties and antimicrobial activity of biocompatible carboxymethylcellulose-silver nanoparticle hybrids for wound dressing and epidermal repair. *J. Appl. Polym. Sci.*, 135, 45812. <https://doi.org/10.1002/app.45812>
- Cardona, A. F., & Wilson, S. E. (2015). Skin and soft-tissue infections: A critical review and the role of telavancin in their treatment. *Clin. Infect. Dis.*, 61, S69–S78. <https://doi.org/10.1093/cid/civ528>
- Chaudhuri, S., & Chandela, S. (2016). Plant mediated green synthesis of silver nanoparticles using tecomella undulata leaf extract and their characterization. *Nano Biom. Eng.*, 8, 1–8. <https://doi.org/10.5101/NBE.V8I1.P1-8>
- Chauhan, R., Reddy, A., & Abraham, J. (2015). Biosynthesis of silver and zinc oxide nanoparticles using Pichia fermentans JA2 and their antimicrobial property. *Appl. Nanosci.*, 5, 63–71. <https://doi.org/10.1007/s13204-014-0292-7>
- Dai, T., Wang, C., Wang, Y., Xu, W., Hu, J., & Cheng, Y. (2018). A nanocomposite hydrogel with potent and broad-spectrum antibacterial activity. *ACS Appl. Mater. Interfaces*, 10, 15163–15173. <https://doi.org/10.1021/acsami.8b02527>
- Dakal, T. C., Kumar, A., Majumdar, R. S., & Yadav, V. (2016). Mechanistic basis of antimicrobial actions of silver nanoparticles. *Front. Microbiol.*, 7, 1–17. <https://doi.org/10.3389/fmicb.2016.01831>
- David, C. (1975). Thermal degradation of polymers. *Comprehensive Chemical Kinetics*, 14, 1–173. [https://doi.org/10.1016/S0069-8040\(08\)70333-9](https://doi.org/10.1016/S0069-8040(08)70333-9)
- de Kraker, M. E. A., Stewardson, A. J., & Harbarth, S. (2016). Will 10 million people die a year due to antimicrobial resistance by 2050? *PLoS Med*, 13, 1–6. <https://doi.org/10.1371/journal.pmed.1002184>
- Durán, N., Durán, M., Jesus, M., Seabra, A., Fávoro, W., & Nakazato, G. (2016). Silver nanoparticles: A new view on mechanistic aspects on antimicrobial activity. *Nanomed.: Nanotechnol. Biol. Med.*, 12, 789–799. <https://doi.org/10.1016/j.nano.2015.11.016>
- Ebrahiminezhad, A., Zare-Hoseinabadi, A., Sarmah, A., Taghizadeh, A., Ghasemi, Y., & Berenjian, A. (2017). Plant-mediated synthesis and applications of iron nanoparticles. *Mol. Biotechnol.*, 60, 154–168. <https://doi.org/10.1007/s12033-017-0053-4>
- Erring, M., Gaba, S., Mohsina, S., Tripathy, S., & Sharma, R. (2019). Comparison of efficacy of silver-nanoparticle gel, nano-silver-foam and collagen dressings in treatment of partial thickness burn wounds. *Burns*, 45, 1888–1894. <https://doi.org/10.1016/j.burns.2019.07.019>
- Eugenio, M., Muller, N., Frases, S., Almeida-Paes, R., Lima, L., Lemgruber, L., Farina, M., Souza, W., & SantAnna, C. (2016). Yeast-derived biosynthesis of silver/silver chloride nanoparticles and their antiproliferative activity against bacteria. *RSC Adv.*, 6, 9893–9904. <https://doi.org/10.1039/C5RA22727E>
- Ezzelarab, M. H., Nouh, O., Ahmed, A. N., Anany, M. G., Rachidi, N. G. El, & Salem, A. S. (2019). A randomized control trial comparing transparent film dressings and conventional occlusive dressings for elective surgical procedures. *Open Access Maced. J. Med. Sci.*, 7, 2844–2850. <https://doi.org/10.3889/oamjms.2019.809>
- Farris, S., Schaich, K. M., Liu, L. S., Piergiovanni, L., & Yam, K. L. (2009). Development of polyion-complex hydrogels as an alternative approach for the production of bio-based polymers for food packaging applications: a review. *Trends Food. Sci. Technol.*, 20(8), 316–332. <https://doi.org/10.1016/j.tifs.2009.04.003>

- Feng, Y., Li, X., Zhang, Q., Yan, S., Guo, Y., Li, M., & You, R. (2019). Mechanically robust and flexible silk protein/polysaccharide composite sponges for wound dressing. *Carbohydr. Polym.*, *216*, 17–24. <https://doi.org/10.1016/j.carbpol.2019.04.008>
- Fernández, J. G., Fernández-Baldo, M. A., Berni, E., Camí, G., Durán, N., Raba, J., & Sanz, M. I. (2016). Production of silver nanoparticles using yeasts and evaluation of their antifungal activity against phytopathogenic fungi. *Process Biochem.*, *51*, 1306–1313. <https://doi.org/10.1016/j.procbio.2016.05.021>
- Franci, G., Falanga, A., Galdiero, S., Palomba, L., Rai, M., Morelli, G., & Galdiero, M. (2015). Silver nanoparticles as potential antibacterial agents. *Molecules*, *20*, 8856–8874. <https://doi.org/10.3390/molecules20058856>
- French, G. (2010). The continuing crisis in antibiotic resistance. *Int. J. Antimicrob. Agents*, *36*, S3–S7. [https://doi.org/10.1016/S0924-8579\(10\)70003-0](https://doi.org/10.1016/S0924-8579(10)70003-0)
- Friedman, N., Temkin, E., & Carmeli, Y. (2016). The negative impact of antibiotic resistance. *Clin. Microbiol. Infect.*, *22*, 416–422. <https://doi.org/10.1016/j.cmi.2015.12.002>
- García-Pérez, A. N., de Jong, A., Junker, S., Becher, D., Chlebowicz, M. A., Duipmans, J. C., Jonkman, M. F., & van Dijl, J. M. (2018). From the wound to the bench: Exoproteome interplay between wound-colonizing staphylococcus aureus strains and co-existing bacteria. *Virulence*, *9*, 363–378. <https://doi.org/10.1080/21505594.2017.1395129>
- Gnanajobitha, G., Paulkumar, K., Vanaja, M., Rajeshkumar, S., Malarkodi, C., Annadurai, G., & Kannan, C. (2013). Fruit-mediated synthesis of silver nanoparticles using *Vitis vinifera* and evaluation of their antimicrobial efficacy. *J. Nanostructure Chem.*, *3*(1). <https://doi.org/10.1186/2193-8865-3-67>
- Guilherme, M. R., Aouada, F. A., Fajardo, A. R., Martins, A. F., Paulino, A. T., Davi, M. F. T., Rubira, A. F., & Muniz, E. C. (2015a). Superabsorbent hydrogels based on polysaccharides for application in agriculture as soil conditioner and nutrient carrier: A review. *Eur. Polym. J.*, *72*, 365–385. <https://doi.org/10.1016/j.eurpolymj.2015.04.017>
- Guilherme, M. R., Aouada, F. A., Fajardo, A. R., Martins, A. F., Paulino, A. T., Davi, M. F. T., Rubira, A. F., & Muniz, E. C. (2015b). Superabsorbent hydrogels based on polysaccharides for application in agriculture as soil conditioner and nutrient carrier: A review. *European Polymer Journal*, *72*, 365–385. <https://doi.org/10.1016/j.eurpolymj.2015.04.017>
- Gupta, A., Mumtaz, S., Li, C.-H., Hussain, I., & Rotello, V. (2019). Combatting antibiotic-resistant bacteria using nanomaterials. *Chem. Soc. Rev.*, *48*, 415–427. <https://doi.org/10.1039/c7cs00748e>
- Gupta, Abhishek, Briffa, S. M., Swingler, S., Gibson, H., Kannappan, V., Adamus, G., Kowalczyk, M., Martin, C., & Radecka, I. (2020). Synthesis of silver nanoparticles using curcumin-cyclodextrins loaded into bacterial cellulose-based hydrogels for wound dressing applications. *Biomacromolecules*, *21*, 1802–1811. <https://doi.org/10.1021/acs.biomac.9b01724>
- Hamidi, M., Azadi, A., & Rafiei, P. (2008). Hydrogel nanoparticles in drug delivery. *Adv. Drug. Deliv. Rev.*, *60*, 1638–1649. <https://doi.org/10.1016/j.addr.2008.08.002>
- Hanif, M., Juluri, R., Fojan, P., & Popok, V. (2020). Polymer films with size-selected silver nanoparticles as plasmon resonance-based transducers for protein sensing. *Biointerface Res. Appl. Chem.*, *6*, 1564–1568.
- Harra, J., Juuti, P., Haapanen, J., Sorvali, M., Roumeli, E., Honkanen, M., Vippola, M., Yli-Ojanperä, J., & Mäkelä, J. M. (2015). Coating of silica and titania aerosol nanoparticles by silver vapor condensation. *Aerosol. Sci. Technol.*, *49*, 767–776. <https://doi.org/10.1080/02786826.2015.1072263>
- Hawkey, P. M. (2008). The growing burden of antimicrobial resistance. *J. Antimicrob. Chemother.*, *62* Suppl 1, 1–9. <https://doi.org/10.1093/jac/dkn241>
- Higa, A., Mambrini, G., Hausen, M., Strixino, F., & Leite, F. (2016). Ag-nanoparticle-based nano-immunosensor for anti-glutathione S-transferase detection. *Biointerface Res. Appl. Chem.*, *6*, 1053–1058.
- Hoffman, A. (2012). Hydrogels for biomedical applications. *Adv. Drug Deliv. Rev.*, *64*, 18–23. <https://doi.org/10.1016/j.addr.2012.09.010>
- Hoque, J., Bhattacharjee, B., Prakash, R. G., Paramanandham, K., & Haldar, J. (2018). Dual function injectable hydrogel for controlled release of antibiotic and local antibacterial therapy. *Biomacromolecules*, *19*, 267–278. <https://doi.org/10.1021/acs.biomac.7b00979>
- Hu, S., Bi, S., Yan, D., Zhou, Z., Sun, G., Cheng, X., & Chen, X. (2018). Preparation of composite hydroxybutyl chitosan sponge and its role in promoting wound healing. *Carbohydr. Polym.*, *184*, 154–163. <https://doi.org/10.1016/j.carbpol.2017.12.033>
- I. I. Abdel-Hafez, S., A. Nafady, N., R. Abdel-Rahim, I., M. Shaltout, A., & A. Mohamed, M. (2016). Biogenesis and Optimisation of Silver Nanoparticles by the Endophytic Fungus *Cladosporium sphaerospermum*. *IJNC*, *2*, 11–19. <https://doi.org/10.18576/ijnc/020103>
- Iniyar, A. M., Kannan, R. R., Joseph, F. J. R. S., Mary, T. R. J., Rajasekar, M., Sumy, P. C., Rabel, A. M., Ramachandran, D., & Vincent, S. G. P. (2017). In vivo safety evaluation of antibacterial silver chloride nanoparticles from *Streptomyces exfoliatus* ICN25 in zebrafish embryos. *Microb. Pathog.*, *112*, 76–82. <https://doi.org/10.1016/j.micpath.2017.07.054>
- Inoue, A., Sugimoto, H., & Fujii, M. (2019). Silver nanoparticles stabilized with a silicon nanocrystal shell and their antimicrobial activity. *RSC Adv.*, *9*, 15171–15176. <https://doi.org/10.1039/c9ra02559f>
- Iravani, S., Korbekandi, H., Mirmohammadi, S. V., & Zolfaghari, B. (2014). Synthesis of silver nanoparticles: Chemical, physical and biological methods. *Res. Pharm. Sci.*, *9*, 385–406. <http://www.ncbi.nlm.nih.gov/pubmed/26339255%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4326978>
- Ischakov, R., Adler-Abramovich, L., Buzhansky, L., Shekhter, T., & Gazit, E. (2013). Peptide-based hydrogel nanoparticles as effective drug delivery agents. *Bioorg. Med. Chem.*, *21*, 3517–3522. <https://doi.org/10.1016/j.bmc.2013.03.012>
- Jaiswal, M., Koul, V., & Dinda, A. (2016). In vitro and in vivo investigational studies of a nanocomposite- hydrogel-based dressing with a silver-coated chitosan wafer for full-thickness skin wounds. *J. Appl. Polym. Sci.*, *133*, 43472. <https://doi.org/10.1002/app.43472>

- Jeschke, M., & Gauglitz, G. (2020). Pathophysiology of burn injuries. In M. Jeschke, L.-P. Kamolz, F. Sjöberg, & S. Wolf (Eds.), *Handbook of Burns Volume I* (pp. 229–245). Springer.
- Jonášová, E. P., & Stokke, B. T. (2016). Bioresponsive DNA-co-polymer hydrogels for fabrication of sensors. *COCIS*, 26, 1–8. <https://doi.org/10.1016/j.cocis.2016.07.001>
- Joshi Navare, K., Eggermont, L., Rogers, Z., Mohammed, H., Colombani, T., & Bencherif, S. (2020). Antimicrobial hydrogels: Key considerations and engineering strategies for biomedical applications. In B. Li, T. Moriarty, T. Webster, & M. Xing (Eds.), *Racing for the Surface: Pathogenesis of Implant Infection and Advanced Antimicrobial Strategies* (pp. 511–542). Springer International Publishing.
- Kamoun, E. A., Kenawy, E. R. S., & Chen, X. (2017). A review on polymeric hydrogel membranes for wound dressing applications: PVA-based hydrogel dressings. *J. Adv. Res.*, 8, 217–233. <https://doi.org/10.1016/j.jare.2017.01.005>
- Kasithevar, M., Saravanan, M., Prakash, P., Kumar, H., Ovais, M., Barabadi, H., & Shinwari, Z. K. (2017). Green synthesis of silver nanoparticles using *Alysicarpus monilifer* leaf extract and its antibacterial activity against MRSA and CoNS isolates in HIV patients. *J. Interdiscip. Nanomed.*, 2, 131–141. <https://doi.org/10.1002/jin2.26>
- Keat, C. L., Aziz, A., Eid, A. M., & Elmarzugi, N. A. (2015). Biosynthesis of nanoparticles and silver nanoparticles. *Bioresour. Bioprocess.*, 2, 1–11. <https://doi.org/10.1186/s40643-015-0076-2>
- Khalandi, B., Asadi, N., Milani, M., Davaran, S., Abadi, A. J. N., Abasi, E., & Akbarzadeh, A. (2017). A review on potential role of silver nanoparticles and possible mechanisms of their actions on bacteria. *Drug. Res.*, 67, 70–76. <https://doi.org/10.1055/s-0042-113383>
- Khan, M., & Lo, I. (2017). Removal of ionizable aromatic pollutants from contaminated water using nano γ -Fe₂O₃ based magnetic cationic hydrogel: Sorptive performance, magnetic separation and reusability. *J. Hazard. Mater.*, 322, 195–204. <https://doi.org/10.1016/j.jhazmat.2016.01.051>
- Kim, M. H., Park, H., Nam, H. C., Park, S. R., Jung, J. Y., & Park, W. H. (2018). Injectable methylcellulose hydrogel containing silver oxide nanoparticles for burn wound healing. *Carbohydr. Polym.*, 181, 579–586. <https://doi.org/10.1016/j.carbpol.2017.11.109>
- Koehler, J., Brandl, F. P., & Goepferich, A. M. (2018). Hydrogel wound dressings for bioactive treatment of acute and chronic wounds. *Eur. Polym. J.*, 100, 1–11. <https://doi.org/10.1016/j.eurpolymj.2017.12.046>
- Kokabi, M., Sirousazar, M., & Hassan, Z. (2007). PVA–clay nanocomposite hydrogels for wound dressing. *Eur. Polym. J.*, 43, 773–781. <https://doi.org/10.1016/j.eurpolymj.2006.11.030>
- Kopeček, J. (2007). Hydrogel biomaterials: A smart future? *Biomaterials*, 28, 5185–5192. <https://doi.org/10.1016/j.biomaterials.2007.07.044>
- Kopecek, J., & Yang, J. (2007). Hydrogels as smart biomaterials. *Polym. Int.*, 56, 1078–1098. <https://doi.org/10.1002/pi.2253>
- Korbekandi, H., Mohseni, S., Jouneghani, R. M., Pourhossein, M., & Iravani, S. (2016). Biosynthesis of silver nanoparticles using *Saccharomyces cerevisiae*. *Artif. Cells Nanomed.*, 44, 235–239. <https://doi.org/10.3109/21691401.2014.937870>
- Kumar, M., Curtis, A., & Hoskins, C. (2018). Application of nanoparticle technologies in the combat against anti-microbial resistance. *Pharmaceutics*, 10, 1–17. <https://doi.org/10.3390/pharmaceutics10010011>
- Lara, H. H., Ayala-Núñez, N. V., del Turrent, L. C. I., & Padilla, C. R. (2010). Bactericidal effect of silver nanoparticles against multidrug-resistant bacteria. *World J. Microbiol. Biotechnol.*, 26, 615–621. <https://doi.org/10.1007/s11274-009-0211-3>
- Lateef, A., & Adeeyo, A. (2015). Green synthesis and antibacterial activities of silver nanoparticles using extracellular laccase of *Lentinus edodes*. *Not. Sci. Biol.*, 7, 405–411. <https://doi.org/10.15835/nsb.7.4.9643>
- Lee, S. H., & Jun, B. H. (2019). Silver nanoparticles: Synthesis and application for nanomedicine. *Int. J. Mol. Sci.*, 20, 865. <https://doi.org/10.3390/ijms20040865>
- Liang, Y., He, J., & Guo, B. (2021). Functional hydrogels as wound dressing to enhance wound healing. *ACS Nano*, 15, 12687–12722. <https://doi.org/10.1021/acsnano.1c04206>
- Liao, S., Zhang, Y., Pan, X., Zhu, F., Jiang, C., Liu, Q., Cheng, Z., Dai, G., Wu, G., Wang, L., & Chen, L. (2019). Antibacterial activity and mechanism of silver nanoparticles against multidrug-resistant *Pseudomonas aeruginosa*. *Int. J. Nanomed.*, 14, 1469–1487. <https://doi.org/10.2147/IJN.S191340>
- Lima, R., Del Fiol, F. S., & Balcão, V. M. (2019). Prospects for the use of new technologies to combat multidrug-resistant bacteria. *Front. Pharmacol.*, 10, 1–10. <https://doi.org/10.3389/fphar.2019.00692>
- Liu, H., Wang, C., Li, C., Qin, Y., Wang, Z., Yang, F., Li, Z., & Wang, J. (2018). A functional chitosan-based hydrogel as a wound dressing and drug delivery system in the treatment of wound healing. *RSC Adv.*, 8, 7533–7549. <https://doi.org/10.1039/c7ra13510f>
- Liu, X., Nielsen, L. H., Kłodzińska, S. N., Nielsen, H. M., Qu, H., Christensen, L. P., Rantanen, J., & Yang, M. (2018). Ciprofloxacin-loaded sodium alginate/poly (lactic-co-glycolic acid) electrospun fibrous mats for wound healing. *Eur. J. Pharm. Biopharm.*, 123, 42–49. <https://doi.org/10.1016/j.ejpb.2017.11.004>
- Lopez-Carrizales, M., Velasco, K. I., Castillo, C., Flores, A., Magaña, M., Martínez-Castanon, G. A., & Martínez-Gutierrez, F. (2018). In vitro synergism of silver nanoparticles with antibiotics as an alternative treatment in multiresistant uropathogens. *Antibiotics*, 7, 1–13. <https://doi.org/10.3390/antibiotics7020050>
- Lyczak, J. B., Cannon, C. L., & Pier, G. B. (2000). Establishment of *Pseudomonas aeruginosa* infection: Lessons from a versatile opportunist. *Microbes Infect.*, 2, 1051–1060. [https://doi.org/10.1016/S1286-4579\(00\)01259-4](https://doi.org/10.1016/S1286-4579(00)01259-4)

- El-Naggar, M., Gohar, Y., Sorour, M., Waheed, M. (2016). Hydrogel dressing with a nano-formula against methicillin-resistant staphylococcus aureus and pseudomonas aeruginosa diabetic foot bacteria. *J. Microbiol. Biotechnol.*, 26, 408–420. <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L608567592%0Ahttp://dx.doi.org/10.4014/jmb.1506.06048>
- Ma, R., Wang, Y., Qi, H., Shi, C., Wei, G., Xiao, L., Huang, Z., Liu, S., Yu, H., Teng, C., Liu, H., Murugadoss, V., Zhang, J., Wang, Y., & Guo, Z. (2019). Nanocomposite sponges of sodium alginate/graphene oxide/polyvinyl alcohol as potential wound dressing: In vitro and in vivo evaluation. *Compos. Part B Eng.*, 167, 396–405. <https://doi.org/10.1016/j.compositesb.2019.03.006>
- Madaghiele, M., Demitri, C., Sannino, A., & Ambrosio, L. (2014). Polymeric hydrogels for burn wound care: Advanced skin wound dressings and regenerative templates. *Burns Trauma*, 2, 153–161. <https://doi.org/10.4103/2321-3868.143616>
- Mahinroosta, M., Farsangi, Z., Allahverdi, A., & Shakoory, Z. (2018). Hydrogels as intelligent materials: A brief review of synthesis, properties and applications. *Mater. Today Chem.*, 8, 42–55. <https://doi.org/10.1016/j.mtchem.2018.02.004>
- Maitra, J., & Shukla, V. K. (2014). Cross-linking in hydrogels - A review. *Am. J. Polym. Sci.*, 4, 25–31. <https://doi.org/10.5923/j.ajps.20140402.01>
- Maliszewska, I., Juraszek, A., & Bielska, K. (2014). Green synthesis and characterization of silver nanoparticles using Ascomycota fungi *Penicillium nalgiovense* AJ12. *J. Clust. Sci.*, 25, 989–1004. <https://doi.org/10.1007/s10876-013-0683-z>
- Manimozhi, R., & Anitha, R. (2014). Mycosynthesis of silver nanoparticles using aqueous extract of *Aspergillus Flavus* Mycelium and its characterization. *IJPDA*, 2, 734–739. www.ijpda.com
- Manna, D., Mandal, A., Sen, I., Maji, P., Chakraborti, S., Chakraborty, R., & Islam, S. (2015). Antibacterial and DNA degradation potential of silver nanoparticles synthesized via green route. *Int. J. Biol. Macromol.*, 80, 455–459. <https://doi.org/10.1016/j.ijbiomac.2015.07.028>
- Martín, M., López, O., Ciolino, A., Morata, V., Villar, M., & Ninago, M. (2019). Immobilization of enological pectinase in calcium alginate hydrogels: A potential biocatalyst for winemaking. *Biocatal. Agric. Biotechnol.*, 18, 91–101. <https://doi.org/10.1016/j.bcab.2019.101091>
- McKenzie, M., Betts, D., Suh, A., Bui, K., Kim, L. D., & Cho, H. (2015). Hydrogel-based drug delivery systems for poorly water-soluble drugs. *Molecules*, 20, 20397–20408. <https://doi.org/10.3390/molecules201119705>
- McShan, D., Ray, P. C., & Yu, H. (2014). Molecular toxicity mechanism of nanosilver. *J. Food Drug Anal.*, 22, 116–127. <https://doi.org/10.1016/j.jfda.2014.01.010>
- Mekkawy, A., El-Mokhtar, M., Nafady, N., Yousef, N., Hamad, M., El-Shanawany, S., Ibrahim, E., & Elsabahy, M. (2017). In vitro and in vivo evaluation of biologically synthesized silver nanoparticles for topical applications: Effect of surface coating and loading into hydrogels. *Int. J. Nanomed.*, 12, 759–777. <https://doi.org/10.2147/IJN.S124294>
- Michalska-Sionkowska, M., Kaczmarek, B., Walczak, M., & Sionkowska, A. (2018). Antimicrobial activity of new materials based on the blends of collagen/chitosan/hyaluronic acid with gentamicin sulfate addition. *Mater. Sci. Eng. C Mater. Biol. Appl.*, 86, 103–108. <https://doi.org/10.1016/j.msec.2018.01.005>
- Mitura, S., Sionkowska, A., & Jaiswal, A. (2020). Biopolymers for hydrogels in cosmetics: Review. *J. Mater. Sci.: Mater. Med.*, 31, 1–14. <https://doi.org/10.1007/s10856-020-06390-w>
- Mofazzal Jahromi, M. A., Sahandi Zangabad, P., Moosavi Basri, S. M., Sahandi Zangabad, K., Ghamarypour, A., Aref, A. R., Karimi, M., & Hamblin, M. R. (2018). Nanomedicine and advanced technologies for burns: Preventing infection and facilitating wound healing. *Adv. Drug Deliv. Rev.*, 123, 33–64. <https://doi.org/10.1016/j.addr.2017.08.001>
- Mohammadzadeh Pakdel, P., & Peighambaroust, S. J. (2018). A review on acrylic based hydrogels and their applications in wastewater treatment. *Journal of Environmental Management*, 217, 123–143. <https://doi.org/10.1016/j.jenvman.2018.03.076>
- Mohandas, A., Deepthi, S., Biswas, R., & Jayakumar, R. (2018). Chitosan based metallic nanocomposite scaffolds as antimicrobial wound dressings. *Bioact. Mater.*, 3, 267–277. <https://doi.org/10.1016/j.bioactmat.2017.11.003>
- Mohanta, Y. K., Singdevsachan, S. K., Parida, U. K., Panda, S. K., Mohanta, T. K., & Bae, H. (2016). Green synthesis and antimicrobial activity of silver nanoparticles using wild medicinal mushroom *Ganoderma applanatum* (Pers.) Pat. from Similipal Biosphere Reserve, Odisha, India. *IET Nanobiotechnol.*, 10, 184–189. <https://doi.org/10.1049/iet-nbt.2015.0059>
- Möhler, J. S., Sim, W., Blaskovich, M. A. T., Cooper, M. A., & Ziora, Z. M. (2018). Silver bullets: A new lustre on an old antimicrobial agent. *Biotechnol. Adv.*, 36, 1391–1411. <https://doi.org/10.1016/j.biotechadv.2018.05.004>
- Morales, M., Gallardo, V., Clarés, B., Carcía, M., & Ruiz, M. (2009). Study and description of hydrogels and organogels as vehicles for cosmetic active ingredients. *J. Cosmet. Sci.*, 60, 627–636.
- Mukherji, S., Bharti, S., Shukla, G., & Mukherji, S. (2019). Synthesis and characterization of size- and shape-controlled silver nanoparticles. *Phys. Sci. Rev.*, 4, 20170082. <https://doi.org/10.1515/psr-2017-0082>
- Murray, K., Kennedy, J., McEvoy, B., Vrain, O., Ryan, D., Cowman, R., & Higginbotham, C. (2013). Effects of gamma ray and electron beam irradiation on the mechanical, thermal, structural and physicochemical properties of poly (ether-block-amide) thermoplastic elastomers. *J. Mech. Behav. Biomed. Mater. EHAV Biomed Mater.*, 17, 252–268. <https://doi.org/10.1016/j.jmbbm.2012.09.011>
- Nam, G., Rangasamy, S., Purushothaman, B., & Song, J. M. (2015). The application of bactericidal silver nanoparticles in wound treatment. *Nanomater. Nanotechnol.*, 5(1). <https://doi.org/10.5772/60918>
- Nanda, A., & Saravanan, M. (2009). Biosynthesis of silver nanoparticles from *Staphylococcus aureus* and its antimicrobial activity against MRSA and MRSE.

Nanomed.: Nanotechnol. Biol. Med., 5, 452–456. <https://doi.org/10.1016/j.nano.2009.01.012>

Nascimento, M., & Lombello, C. (2016). Hyaluronic acid and chitosan based hydrogels for cartilage tissue engineering. *Polymers*, 26, 360–370. <https://doi.org/10.1590/0104-1428.1987>

Negut, I., Grumezescu, V., & Grumezescu, A. M. (2018). Treatment strategies for infected wounds. *Molecules*, 23, 1–23. <https://doi.org/10.3390/molecules23092392>

Nešović, K., Kojić, V., Rhee, K. Y., & Mišković-Stanković, V. (2017). Electrochemical synthesis and characterization of silver doped poly(vinyl alcohol)/chitosan hydrogels. *Corrosion*, 73, 1437–1447. <https://doi.org/10.5006/2507>

Nesovic, K., & Miskovic-Stankovic, V. (2020). A comprehensive review of the polymer-based hydrogels with electrochemically synthesized silver nanoparticles for wound dressing applications. *Polym. Eng. Sci.*, 60, 1393–1419. <https://doi.org/10.1002/pen.25410>

Nischwitz, S., Hofmann, E., & Kamolz, L.-P. (2019). The ideal wound dressing — Beyond the ideal: A short comment on ‘Properties of an ideal burn dressing: A survey of burn survivors and front-line burn healthcare providers’ by T. Carta, J.P. Gawaziuk et al. *Burns*, 45, 1485–1486. <https://doi.org/10.1016/j.burns.2018.11.023>

Nowack, B., Krug, H. F., & Height, M. (2011). 120 years of nanosilver history: Implications for policy makers. *Environ. Sci. Technol.*, 45, 7593–7595. <https://doi.org/10.1021/es2017895>

Ouay, B., & Stellacci, F. (2015). Antibacterial activity of silver nanoparticles: A surface science insight. *Nanotoday*, 10, 339–354. <https://doi.org/10.1016/j.nantod.2015.04.002>

Paladini, F., Meikle, S., Cooper, I., Lacey, J., Perugini, V., & Santin, M. (2013). Silver-doped self-assembling di-phenylalanine hydrogels as wound dressing biomaterials. *J. Mater. Sci. Mater. Med.*, 24, 2461–2472. <https://doi.org/10.1007/s10856-013-4986-2>

Pan, H., Fan, D., Duan, Z., Zhu, C., Fu, R., & Li, X. (2019). Non-stick hemostasis hydrogels as dressings with bacterial barrier activity for cutaneous wound healing. *Mater. Sci. Eng. C*, 105, 110118. <https://doi.org/10.1016/j.msec.2019.110118>

Pareek, V., Gupta, R., & Panwar, J. (2018a). Do physico-chemical properties of silver nanoparticles decide their interaction with biological media and bactericidal action? A review. *Mater. Sci. Eng. C*, 90, 739–749. <https://doi.org/10.1016/j.msec.2018.04.093>

Pareek, V., Gupta, R., & Panwar, J. (2018b). Do physico-chemical properties of silver nanoparticles decide their interaction with biological media and bactericidal action? A review. *Materials Science and Engineering C*, 90(November 2017), 739–749. <https://doi.org/10.1016/j.msec.2018.04.093>

Parikh, D. V., Fink, T., Rajasekharan, K., Sachinvala, N. D., Sawhney, A. P. S., Calamari, T. A., & Parikh, A. D. (2005). Antimicrobial silver/sodium carboxymethyl cotton dressings for burn wounds. *Text. Res. J.*, 75, 134–138. <https://doi.org/10.1177/004051750507500208>

Patel, A., & Mequanint, K. (2011). Hydrogel biomaterials. In R. Fazel-Razai (Ed.), *Biomedical Engineering – Frontiers and Challenges*. IntechOpen. <https://doi.org/10.5772/24856>

Pensaifini, M., Ehret, A., Studeli, S., Marino, D., Kaech, A., Reichmann, E., & Mazza, E. (2017). Factors affecting the mechanical behavior of collagen hydrogels for skin tissue engineering. *J. Mech. Behav. Biomed. Mater.*, 69, 85–97. <https://doi.org/10.1016/j.jmbbm.2016.12.004>

Petkovšek, Ž., Eleršič, K., Gubina, M., Žgur-Bertok, D., & Erjavec, M. S. (2009). Virulence potential of Escherichia coli isolates from skin and soft tissue infections. *J. Clin. Microbiol.*, 47, 1811–1817. <https://doi.org/10.1128/JCM.01421-08>

Phillip, E., Murthy, N., Bolikal, D., Narayanan, P., Kohn, J., Lavelle, L., Bodnar, S., & Pricer, K. (2013). Ethylene oxide’s role as a reactive agent during sterilization: Effects of polymer composition and device architecture. *J. Biomed. Mater. Res. Part B*, 101, 532–540. <https://doi.org/10.1002/jbm.b.32853>

Pirvanescu, H., Balasoiu, M., Ciurea, M. E., Balasoiu, A. T., & Manescu, R. (2014). Wound infections with multi-drug resistant bacteria. *Chirurgia*, 109, 73–79.

Praveena, S. M., Han, L. S., Than, L. T. L., & Aris, A. Z. (2016). Preparation and characterisation of silver nanoparticle coated on cellulose paper: evaluation of their potential as antibacterial water filter. *J. Exp. Nanosci.*, 11, 1307–1319. <https://doi.org/10.1080/17458080.2016.1209790>

Prezotti, F., Cury, B., & Evangelista, R. (2014). Mucoadhesive beads of gellan gum/pectin intended to controlled delivery of drugs. *Carbohydr. Polym.*, 113, 286–295. <https://doi.org/10.1016/j.carbpol.2014.07.021>

Rabek, J. (1975). Oxidative degradation of polymers. *Comprehensive Chemical Kinetics*, 14, 425–538. [https://doi.org/10.1016/S0069-8040\(08\)70336-4](https://doi.org/10.1016/S0069-8040(08)70336-4)

Radulescu, M., Andronescu, E., Dolete, G., Popescu, R. C., Fufă, O., Chifiriuc, M. C., Mogoantă, L., Bălșeanu, T. A., Mogoșanu, G. D., Grumezescu, A. M., & Holban, A. M. (2016). Silver nanocoatings for reducing the exogenous microbial colonization of wound dressings. *Materials*, 9, 1–15. <https://doi.org/10.3390/ma9050345>

Rădulescu, M., Holban, A. M., Mogoantă, L., Bălșeanu, T. A., Mogoșanu, G. D., Savu, D., Popescu, R. C., Fufă, O., Grumezescu, A. M., Bezirtoglou, E., Lazar, V., & Chifiriuc, M. C. (2016). Fabrication, characterization, and evaluation of bionanocomposites based on natural polymers and antibiotics for wound healing applications. *Molecules*, 21, 2–14. <https://doi.org/10.3390/molecules21060761>

Rafael, D., Andrade, F., Martinez-trucharte, F., & Basas, J. (2019). Sterilization procedure for temperature-sensitive hydrogels loaded with silver nanoparticles for clinical applications. *Nanomaterials*, 9, 2–14. <https://doi.org/10.3390/nano9030380>

Raghavan, D., Zewde, B., Ambaye, A., Stubbs III, J., & Raghavan, D. (2016). A review of stabilized silver nanoparticles – Synthesis, biological properties, characterization, and potential areas of applications. *JSM Nanotechnol Nanomed*, 4, 1043.

Rai, M., Kon, K., Gade, A., Ingle, A., Nagaonkar, D., Paralikar, P., & Silva, S. (2016). Antibiotic resistance: Can nanoparticles tackle the problem? In

Antibiotic Resistance: Mechanisms and New Antimicrobial Approaches (pp. 121–143). Elsevier. <https://doi.org/10.1016/B978-0-12-803642-6.00006-X>

Rai, M., Yadav, A., & Gade, A. (2009). Silver nanoparticles as a new generation of antimicrobials. *Biotechnol. Adv.*, 27, 76–83. <https://doi.org/10.1016/j.biotechadv.2008.09.002>

Rajkumar, K. S., Kanipandian, N., & Thirumurugan, R. (2016). Toxicity assessment on haematology, biochemical and histopathological alterations of silver nanoparticles-exposed freshwater fish *Labeo rohita*. *Appl. Nanosci.*, 6, 19–29. <https://doi.org/10.1007/s13204-015-0417-7>

Rakhshaei, R., & Namazi, H. (2017). A potential bioactive wound dressing based on carboxymethyl cellulose/ZnO impregnated MCM-41 nanocomposite hydrogel. *Mater. Sci. Eng. C Mater. Biol. Appl.*, 73, 456–464. <https://doi.org/10.1016/j.msec.2016.12.097>

Ramalingam, B., Parandhaman, T., & Das, S. (2016). Antibacterial effects of biosynthesized silver nanoparticles on surface ultrastructure and nanomechanical properties of Gram-negative bacteria viz. *Escherichia coli* and *Pseudomonas aeruginosa*. *ACS Appl. Mater. Interfaces*, 8, 4963–4976. <https://doi.org/10.1021/acsami.6b00161>

Rezvani, E., Rafferty, A., McGuinness, C., & Kennedy, J. (2019). Adverse effects of nanosilver on human health and the environment. *Acta Biomater.*, 94, 145–159. <https://doi.org/10.1016/j.actbio.2019.05.042>

Rigo, C., Ferroni, L., Tocco, I., Roman, M., Munivrana, I., Gardin, C., Cairns, W. R. L., Vindigni, V., Azzena, B., Barbante, C., & Zavan, B. (2013). Active silver nanoparticles for wound healing. *Int. J. Mol. Sci.*, 14, 4817–4840. <https://doi.org/10.3390/ijms14034817>

Rizwan, M., Rubina Gilani, S., Iqbal Durani, A., & Naseem, S. (2021). Materials diversity of hydrogel: Synthesis, polymerization process and soil conditioning properties in agricultural field. *J. Adv. Res.*, 33, 15–40. <https://doi.org/10.1016/j.jare.2021.03.007>

Rosiak, J., Rucinska-Reybas, A., & Pekala, W. (1989). *Method of manufacturing of hydrogels dressing* (Patent No. 871). 4.

Rowan, M. P., Cancio, L. C., Elster, E. A., Burmeister, D. M., Rose, L. F., Natesan, S., Chan, R. K., Christy, R. J., & Chung, K. K. (2015). Burn wound healing and treatment: Review and advancements. *Crit. Care*, 19, 1–12. <https://doi.org/10.1186/s13054-015-0961-2>

Saleem Khan, M., Jabeen, F., Aziz Qureshi, N., Saleem Asghar, M., Shakeel, M., & Noureen, A. (2015). Toxicity of silver nanoparticles in fish: A critical review. *J. Biodivers. Environ. Sci.*, 6, 211–227. <http://www.innspring.net>

Sánchez, G. R., Castilla, C. L., Gómez, N. B., García, A., Marcos, R., & Carmona, E. R. (2016). Leaf extract from the endemic plant *Peumus boldus* as an effective bioproduct for the green synthesis of silver nanoparticles. *Mater. Lett.*, 183, 255–260. <https://doi.org/10.1016/j.matlet.2016.07.115>

Saravanan, M., Barik, S. K., MubarakAli, D., Prakash, P., & Pugazhendhi, A. (2018). Synthesis of silver nanoparticles from *Bacillus brevis* (NCIM 2533) and their antibacterial activity against pathogenic bacteria. *Microb. Pathog.*, 116, 221–226. <https://doi.org/10.1016/j.micpath.2018.01.038>

Serra, R., Grande, R., Butrico, L., Rossi, A., Settimo, U., Caroleo, B., Amato, B., Gallelli, L., & Franciscis, S. (2015). Chronic wound infections: the role of *Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Expert Rev. Anti. Infect. Ther.*, 13, 605–613. <https://doi.org/10.1586/14787210.2015.1023291>

Sevgi, M., Toklu, A., Vecchio, D., & Hamblin, M. (2013). Topical antimicrobials for burn infections – An update. *Recent Pat. Antiinfect. Drug Discov.*, 8, 161–197. <https://doi.org/10.2174/1574891x08666131112143447>

Shewan, H. M., & Stokes, J. R. (2013). Review of techniques to manufacture micro-hydrogel particles for the food industry and their applications. *J. Food Eng.*, 119(4), 781–792. <https://doi.org/10.1016/j.jfoodeng.2013.06.046>

Shi, G., Chen, W., Zhang, Y., Dai, X., Zhang, X., & Wu, Z. (2019). An antifouling hydrogel containing silver nanoparticles for modulating the therapeutic immune response in chronic wound healing. *Langmuir*, 35, 1837–1845. <https://doi.org/10.1021/acs.langmuir.8b01834>

Shin, H. S., Yang, H. J., Kim, S. Bin, & Lee, M. S. (2004). Mechanism of growth of colloidal silver nanoparticles stabilized by polyvinyl pyrrolidone in γ -irradiated silver nitrate solution. *J. Colloid Interface Sci.*, 274, 89–94. <https://doi.org/10.1016/j.jcis.2004.02.084>

Siddiqi, K. S., & Husen, A. (2016). Fabrication of metal nanoparticles from fungi and metal salts: Scope and application. *Nanoscale Res. Lett.*, 11, 1–15. <https://doi.org/10.1186/s11671-016-1311-2>

Simões, D., Miguel, S. P., Ribeiro, M. P., Coutinho, P., Mendonça, A. G., & Correia, I. J. (2018). Recent advances on antimicrobial wound dressing: A review. *Eur. J. Pharm. Biopharm.*, 127, 130–141. <https://doi.org/10.1016/j.ejpb.2018.02.022>

Sonar, H., Nagaonkar, D., Ingle, A., & Rai, M. (2017). Mycosynthesized silver nanoparticles as potent growth inhibitory agents against selected waterborne human pathogens. *Clean - Soil Air Water*, 45, 1600247. <https://doi.org/10.1002/clean.201600247>

Sondi, I., & Salopek-Sondi, B. (2004). Silver nanoparticles as antimicrobial agent: A case study on *E. coli* as a model for Gram-negative bacteria. *J. Colloid Interface Sci.*, 275, 177–182. <https://doi.org/10.1016/j.jcis.2004.02.012>

Song, E. H., Jeong, S. H., Park, J. U., Kim, S., Kim, H. E., & Song, J. (2017). Polyurethane-silica hybrid foams from a one-step foaming reaction, coupled with a sol-gel process, for enhanced wound healing. *Mater. Sci. Eng. C*, 79, 866–874. <https://doi.org/10.1016/j.msec.2017.05.041>

Sonker, A. S., O. R., Pathak, J., O. R., Kannaujia, V. K., & Sinha, R. P. (2017). Characterization and in vitro antitumor, antibacterial and antifungal activities of green synthesized silver nanoparticles using cell extract of *Nostoc* sp. strain HKAR-2. *Can. J. Biotech.*, 1, 26–37. <https://doi.org/10.24870/cjb.2017-000103>

Sood, A., Granick, M., & Tomaselli, N. (2014). Wound dressings and comparative effectiveness data. *Adv. Wound Care*, 3, 511–529. <https://doi.org/10.1089/wound.2012.0401>

Suman, T. Y., Radhika Rajasree, S. R., Kanchana, A., & Elizabeth, S. B. (2013). Biosynthesis, characterization and cytotoxic effect of plant mediated silver nanoparticles using *Morinda citrifolia* root extract. *Colloids Surf. B Biointerfaces*, 106, 74–78. <https://doi.org/10.1016/j.colsurfb.2013.01.037>

- Tan, S., Winarto, N., Dosan, R., & Aisyah, P. (2019). The benefits of occlusive dressings in wound healing. *Open Dermatol. J.*, *13*, 27–33.
- Tippayawat, P., Phromviyo, N., Boueroy, P., & Chompoosor, A. (2016). Green synthesis of silver nanoparticles in aloe vera plant extract prepared by a hydrothermal method and their synergistic antibacterial activity. *PeerJ*, *2016*, 1–15. <https://doi.org/10.7717/peerj.2589>
- Toh, H., Jurkschat, D., & Compton, R. (2015). The influence of the capping agent on the oxidation of silver nanoparticles: nano-impacts versus stripping voltammetry. *Chem. Eur. J.*, *21*, 2998–3004. <https://doi.org/10.1002/chem.201406278>
- Treenate, P., & Monvisade, P. (2017). In vitro drug release profiles of pH-sensitive hydroxyethylacryl chitosan/sodium alginate hydrogels using paracetamol as a soluble model drug. *Int. J. Biol. Macromol.*, *99*, 71–78. <https://doi.org/10.1016/j.ijbiomac.2017.02.061>
- Tri Handok, C., Huda, A., & Gulo, F. (2018). Synthesis pathway and powerful antimicrobial properties of silver nanoparticle: A critical review. *Asian J. Sci. Res.*, *12*, 1–17. <https://doi.org/10.3923/ajsr.2019.1.17>
- Ullah, F., Othman, M., Javed, F., Ahmad, Z., & Akil, H. (2015). Classification, processing and application of hydrogels: A review. *Mater. Sci. Eng.*, *57*, 414–433. <https://doi.org/10.1016/j.msec.2015.07.053>
- Unnithan, A. R., Ghavami Nejad, A., Sasikala, A. R. K., Thomas, R. G., Jeong, Y. Y., Murugesan, P., Nasseri, S., Wu, D., Park, C. H., & Kim, C. S. (2016). Electrospun zwitterionic nanofibers with in situ decelerated epithelialization property for non-adherent and easy removable wound dressing application. *Chem. Eng. J.*, *287*, 640–648. <https://doi.org/10.1016/j.cej.2015.11.086>
- Vamanu, E. (2017). Bioactive capacity of some Romanian wild edible mushrooms consumed mainly by local communities. *Nat. Prod. Res.*, *32*, 440–443. <https://doi.org/10.1080/14786419.2017.1308365>
- Vanichvattanadecha, C., Supaphol, P., Nagasawa, N., Tamada, M., Tokura, S., Furuike, T., Tamura, H., & Rujiravanit, R. (2010). Effect of gamma radiation on dilute aqueous solutions and thin films of N-succinyl chitosan. *Polym. Degrad. Stab.*, *95*, 234–244. <https://doi.org/10.1016/j.polymdegradstab.2009.10.007>
- Varaprasad, K., Mohan, Y., Vimala, K., & Raju, K. (2011). Synthesis and characterization of hydrogel-silver nanoparticle-curcumin composites for wound dressing and antibacterial application. *J. Appl. Polym. Sci.*, *121*, 784–796. <https://doi.org/10.1002/app.33508>
- Verma, J., Kanoujia, J., Parashar, P., Tripathi, C., & Saraf, S. (2016). Wound healing applications of sericin/chitosan-capped silver nanoparticles incorporated hydrogel. *Drug Deliv. Transl. Res.*, *7*, 77–88. <https://doi.org/10.1007/s13346-016-0322-y>
- Vetten, M., Yah, C., Singh, T., & Gulumian, M. (2014). Challenges facing sterilization and depyrogenation of nanoparticles: Effects on structural stability and biomedical applications. *Nanomed.: Nanotechnol. Biol. Med.*, *10*, 1391–1399. <https://doi.org/10.1016/j.nano.2014.03.017>
- Vijayan, S., Koilaparambil, D., George, T. K., & Manakulam Shaikmoideen, J. (2016). Antibacterial and cytotoxicity studies of silver nanoparticles synthesized by endophytic *Fusarium Solani* Isolated from *Withania somenifera* (L.). *J. Water Environ. Nanotechnol.*, *1*, 91–103. <https://doi.org/10.7508/jwent.2016.02.003>
- Vuković, J., Perić-Grujić, A., Mitić-Ćulafić, D., Nedeljković, B., & Tomić, S. (2020). Antibacterial activity of pH-sensitive silver(I)/poly(2-hydroxyethyl acrylate/itaconic acid) hydrogels. *Macromol. Res.*, *28*, 382–389. <https://doi.org/10.1007/s13233-020-8050-z>
- Vyshnava, S. S., Kanderi, D. K., Panjala, S. P., Pandian, K., Bontha, R. R., Goukanapalle, P. K. R., & Banaganapalli, B. (2016). Effect of silver nanoparticles against the formation of biofilm by *Pseudomonas aeruginosa* an in silico approach. *Appl. Biochem. Biotechnol.*, *180*, 426–437. <https://doi.org/10.1007/s12010-016-2107-7>
- Wang, L., Hu, C., & Shao, L. (2017). The antimicrobial activity of nanoparticles: Present situation and prospects for the future. *Int. J. Nanomed*, *12*, 1227–1249. <https://doi.org/10.2147/IJN.S121956>
- Wang, M., Xu, L., Hu, H., Zhai, M., Peng, J., Nho, Y., Li, J., & Wei, G. (2007). Radiation synthesis of PVP/CMC hydrogels as wound dressing. *Nucl. Instrum. Methods Phys. Res. B*, *265*, 385–389. <https://doi.org/10.1016/j.nimb.2007.09.009>
- Wanzke, C., Tena-Solsona, M., Rieß, B., Tebcharani, L., & Boekhoven, J. (2020). Active droplets in a hydrogel release drugs with a constant and tunable rate. *Mater. Horiz.*, *7*, 1397–1403. <https://doi.org/10.1039/c9mh01822k>
- Wichterle, O., & Lím, D. (1960). Hydrophilic gels for biological use. *Nature*, *185*, 117–118. <https://doi.org/10.1038/185117a0>
- Wu, J., Hou, S., Ren, D., & Mather, P. T. (2009). Antimicrobial properties of nanostructured hydrogel webs containing silver. *Biomacromolecules*, *10*, 2686–2693. <https://doi.org/10.1021/bm900620w>
- Wu, J., Zheng, Y., Song, W., Luan, J., Wen, X., Wu, Z., Chen, X., Wang, Q., & Guo, S. (2014). In situ synthesis of silver-nanoparticles/bacterial cellulose composites for slow-released antimicrobial wound dressing. *Carbohydr. Polym.*, *102*, 762–771. <https://doi.org/10.1016/j.carbpol.2013.10.093>
- Yang, K., Han, Q., Chen, B., Zheng, Y., Zhang, K., Li, Q., & Wang, J. (2018). Antimicrobial hydrogels: Promising materials for medical application. *Int. J. Nanomed.*, *13*, 2217–2263. <https://doi.org/10.2147/IJN.S154748>
- Yang, Y., Qin, Z., Zeng, W., Yang, T., Cao, Y., Mei, C., & Kuang, Y. (2017). Toxicity assessment of nanoparticles in various systems and organs. *Nanotechnol. Rev.*, *6*, 279–289. <https://doi.org/10.1515/ntrev-2016-0047>
- Yao, C. H., Lee, C. Y., Huang, C. H., Chen, Y. S., & Chen, K. Y. (2017). Novel bilayer wound dressing based on electrospun gelatin/keratin nanofibrous mats for skin wound repair. *Mater. Sci. Eng. C*, *79*, 533–540. <https://doi.org/10.1016/j.msec.2017.05.076>
- Ye, S., Jiang, L., Wu, J., Su, C., Huang, C., Liu, X., & Shao, W. (2018). Flexible amoxicillin-grafted bacterial cellulose Sponges for wound dressing: In vitro and in vivo evaluation. *ACS Appl. Mater. Interfaces*, *10*, 5862–5870. <https://doi.org/10.1021/acsami.7b16680>
- Yeo, Y., Baek, N., & Park, K. (2001). Microencapsulation methods for delivery of protein drugs. *Biotechnol. Bioprocess Eng.*, *6*, 213–230.

- Yu, S.-J., Yin, Y.-G., & Liu, J.-F. (2013). Silver nanoparticles in the environment. *Environ. Sci.: Process. Impacts*, 15, 78–92. <https://doi.org/10.1039/C2EM30595J>
- Yuan, Z., Li, J., Cui, L., Xu, B., Zhang, H., & Yu, C. P. (2013). Interaction of silver nanoparticles with pure nitrifying bacteria. *Chemosphere*, 90, 1404–1411. <https://doi.org/10.1016/j.chemosphere.2012.08.032>
- Zain, N. M., Stapley, A. G. F., & Shama, G. (2014). Green synthesis of silver and copper nanoparticles using ascorbic acid and chitosan for antimicrobial applications. *Carbohydr. Polym.*, 112, 195–202. <https://doi.org/10.1016/j.carbpol.2014.05.081>
- Zajko, Š., & Klimant, I. (2013). The effects of different sterilization procedures on the optical polymer oxygen sensors. *Sens. Actuators B: Chem.*, 177, 86–93. <https://doi.org/10.1016/j.snb.2012.10.040>
- Zhang, J., Chaker, M., & Ma, D. (2017). Pulsed laser ablation based synthesis of colloidal metal nanoparticles for catalytic applications. *J. Colloid Interface Sci.*, 489, 138–149. <https://doi.org/10.1016/j.jcis.2016.07.050>
- Zhang, L., Yin, H., Lei, X., Lau, J. N. Y., Yuan, M., Wang, X., Zhang, F., Zhou, F., Qi, S., Shu, B., & Wu, J. (2019). A Systematic review and meta-analysis of clinical effectiveness and safety of hydrogel dressings in the management of skin wounds. *Front. Bioeng. Biotechnol.*, 7, 1–16. <https://doi.org/10.3389/fbioe.2019.00342>
- Zhang, P., Zou, B., Liou, Y. C., & Huang, C. (2021). The pathogenesis and diagnosis of sepsis post burn injury. *Burns Trauma*, 9, 1–16. <https://doi.org/10.1093/burnst/tkaa047>
- Zhang, T., Wang, L., Chen, Q., & Chen, C. (2014). Cytotoxic potential of silver nanoparticles. *Yonsei Med. J.*, 55, 283–291. <https://doi.org/10.3349/ymj.2014.55.2.283>
- Zhang, X. F., Shen, W., & Gurunathan, S. (2016). Silver nanoparticle-mediated cellular responses in various cell lines: An in vitro model. *Int. J. Mol. Sci.*, 17, 1–26. <https://doi.org/10.3390/ijms17101603>
- Zhang, Y. S., & Khademhosseini, A. (2017). Advances in engineering hydrogels. *Science*, 356, 1–10. <https://doi.org/10.1126/science.aaf3627>
- Zou, P., Lee, W. H., Gao, Z., Qin, D., Wang, Y., Liu, J., Sun, T., & Gao, Y. (2020). Wound dressing from polyvinyl alcohol/chitosan electrospun fiber membrane loaded with OH-CATH30 nanoparticles. *Carbohydr. Polym.*, 232, 115786. <https://doi.org/10.1016/j.carbpol.2019.115786>