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A Systematic Review On Antimicrobial Hydrogel

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ABSTRACT

Pharmaceutical products made of hydrogels are a subset of polymeric materials. They have a greater capacity to absorb water. Excellent antibacterial properties, strong biocompatibility, water retention, swelling, high oxygen permeability, and other characteristics are all present in antibacterial hydrogel. bacterial and fungal illnesses caused by microbes. Hydrogels that possess antibacterial qualities can be used to combat germs. Antimicrobial hydrogels are used to stop the spread of diseases and stop bacterial development.

Hydrogels that are made to stop bacterial development and illnesses are known as antibacterial hydrogels. These hydrogels often contain antibacterial substances that function likes including by rupturing bacterial cell walls or preventing the action of bacterial enzymes. Several examples of frequently employed antibacterial substances, incorporating nanoparticles into antimicrobial hydrogels can enhance their efficacy. This article provides an overview about General characteristics, classification, material employed, preparation, application, advantages & disadvantages and future scopes of anti-microbial hydrogel.

Keywords: *Hydrogels, Microbial, Antimicrobial, Bacterial, Nanoparticles*

1. INTRODUCTION

The first reported hydrogel was introduce in 1960, when Wichterle and Lim synthesized poly(2-hydroxyethyl methacrylate) (PHEMA) and used it in the contact lens industry for its moisture absorption and network structure reinforcement, introducing the modern hydrogel[(1)]. Hydrogels are the polymer networks extensively swollen with water. Usually referred to as hydrogels, hydrophilic gels are networks of polymer chains that are often observed as colloidal gels with water acting as the dispersion medium. Antimicrobial hydrogel is used in diseases caused by bacteria, fungi and serious health problems, especially related to wound healing and contamination of biomedical implants. Antimicrobial hydrogel is one of the suitable biomaterials for drug delivery in the field of antimicrobials. The practical application of conventional hydrogel is limited because of its poor mechanical strength, single function and insensitivity to external stimuli, which leads to slow wound healing and infection [(2)]. The materials of in this brief review are primarily hydrogels, which are polymer networks extensively swollen with water. Hydrophilic gels that are usually known as hydrogels are networks of polymer chains that are sometimes found as colloidal gels in which water is the dispersion medium [(3)]. Anti-microbial hydrogel (AMHs) are classified by their different classes or criteria of AMHs. They are Delayed healing caused by wound infections in medical processes, especially surgery, has brought serious problems to clinicians [(4)]. In addition, bacterial resistance, which results from the overuse or misuse of inappropriate antibiotics in the treatment of infections, has become a persistent problem in global public health causing more than 10 million deaths each year. The most popular methods of treating this issue involve giving systemic antibiotic therapy or replacing out outdated materials, to which bacteria have grown resistant, with new ones. However, both of these methods lead to delayed healing, increased mortality and costs, and bacterial resistance [(5)].

Biomedical implant fouling and wound healing are two major health issues associated with microbial infections, which are caused by bacteria and fungus. Pathogens common to these kinds of infections include Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Pseudomonas aeruginosa, and Candida species. Depending on the degree of the infection, sepsis may develop as well as tissue morbidity from an extended or inhibited wound healing process. Regarding biomedical implants, infection at the implant-tissue interface can lead to implant failure, which necessitates implant removal and replacement [(6)]. Other devices, such as catheters, can act as vehicles for infection from the hospital environment to the patient. Various strategies have emerged to develop materials with antimicrobial activity for the prevention or treatment of wound infections, implants and device installations. Materials can be impregnated with antimicrobial agents that are released over time [(7)] or the surface of the material can be covalently modified to immobilize broad-spectrum antimicrobial agents such as antimicrobial peptides (AMP), silver ions or polycationic group.

Hydrogels are a useful starting point for the design of antimicrobial materials. They are a class of highly hydrated biomaterials, typically made from natural or synthetic polymers. Polysaccharides such as alginate, dextran and chitosan, as well as gelatine and fibrin proteins, are examples of natural polymers that form well-studied hydrogels. Synthetic polymers that create hydrogels include poly (vinyl alcohol) (PVA), polyethylene oxide (PEO), and poly (acrylic acid) (PAA). In addition, hydrogels can also be obtained from synthetic peptides and polypeptides. Many hydrogels are biocompatible and can be engineered to have mechanical properties similar to native tissues, and thus have been used in countless applications, including drug delivery, chronic and traumatic wound healing, implant coatings, cell encapsulation for three-dimensional tissues. Among these are tissue engineering and cell culture. Important to this review is the development of hydrogels with antimicrobial properties that further enhance the utility of this important class of biomaterials [(8,9)]. Herein, we will review on impart antimicrobial hydrogel.

2. GENERAL CHARACTERISTICS

Anti-microbial hydrogels possess distinctive characteristics that contribute to their effectiveness in combating microbial activity. Here are some general characteristics:

2.1 Biocompatibility: Anti-microbial hydrogels are designed to be biocompatible, ensuring minimal harm to host tissues·

2.2 Stained Release of Antimicrobial Agents: They exhibit controlled and sustained release of antimicrobial agents, contributing to prolonged efficacy [(10)].

2.3 Responsive to Environmental Stimuli: Some hydrogels respond to environmental stimuli, such as pH or temperature changes, allowing for targeted release of antimicrobial agents.

2.4 High Water Content: Hydrogels typically have high water content, mimicking the natural environment of biological tissues and promoting compatibility[(11)].

2.5 Ease of Application: They are often easy to apply and can conform to various surfaces, making them versatile for different applications.

2.6 Enhanced Wound Healing Properties: Anti-microbial hydrogels may promote wound healing in addition to their antimicrobial activity [(12)]

3. CLASSIFICATION

The materials utilized to make the hydrogels determine the classification of AMHs based on their origin: Proteins and other naturally occurring materials are the source of natural hydrogels, polysaccharides, and their mixtures; synthetic hydrogels are produced chemically by combining different crosslinking agents and monomers; and hybrid hydrogels combine the two to enhance formulations that already exist. As was indicated in the introduction, AMHs can be categorized using a variety of standards. Owing to the goal of this review, we will describe how the most widely used AMHs are categorized based on their makeup, enabling researchers and practitioners to choose the most suitable gel type for specific applications, considering factors such as antimicrobial spectrum, biocompatibility, stability, and desired release kinetics [(13)].

Classification of Antimicrobial Hydrogel are as follow:

3.1 BASED ON INFECTION TREATMENT [(14)]

Classification based on infection treatment have the following categories:

3.1.1 Hydrogels for the controlled release of antimicrobial agents

I. Hydrogels loaded with silver and gold nanoparticles

II. Hydrogels loaded with antibiotics

III. Hydrogels loaded with antimicrobials

3.1.2 Possessing inherent antimicrobial activity

I. Peptide-based hydrogels
II. Chitosan-containing hydrogels
III. Other polymer-derived hydrogels

3.2 BASED ON THE ANTIBACTERIAL MODE

Classification and Mechanism of Antibacterial Hydrogels Depending on the antibacterial mode, an antibacterial hydrogel can be divided into five categories:

3.2.1 Antibacterial hydrogel containing inorganic nanoparticles;

I. Antibacterial Hydrogel Containing Silver Nanoparticles
II. Antibacterial Hydrogel Containing Zinc Oxide Nanoparticles
III. Antibacterial Hydrogel Containing Titanium Dioxide Nanoparticles
IV. Antibacterial Hydrogel Containing Other Nanoparticles

3.2.2 Antibiotic loaded antibacterial hydrogel (which can directly kill cells for sterilization);

I. Aminoglycoside-Loaded Antibacterial Hydrogels
II. Glycopeptides-Loaded Antibacterial Hydrogels
III. Quinolones-Loaded Antibacterial Hydrogels

3.2.3 Hydrogel with inherent antimicrobial activity;

I. Antimicrobial peptide hydrogel
II. Chitosan antibacterial hydrogel
III. Amphoteric Ion Antibacterial Hydrogel

3.2.4 Photosensitive antibacterial hydrogel

3.2.5 Hydrogels with synergetic effects.

3.3 BASED ON THEIR COMPOSITION

3.3.1 Hydrogels with Inherent Antimicrobial Activity

I. Peptide-Based Hydrogels
II. Amphoteric Ion Hydrogels
III. Polysaccharide-Based Hydrogels

3.3.2 Antimicrobial Agent-Loaded Hydrogels.

I. Antibiotic-Loaded Hydrogels
II. Biological Extract-Loaded Hydrogels
III. Metal Nanoparticle-Loaded Hydrogels
IV. AMP-Loaded Hydrogels

Currently, most of the research concerns antibacterial hydrogels containing silver nanoparticles, chitosan hydrogels, and antibiotic hydrogels.

4. FORMULATION

1.1. MATERIAL EMPLOYED

1.1.1. Hydrogel loaded with metal nanoparticles.

Heavy metals have long been used against microbes. In the long run. All were said to be silver, gold, copper and zinc used in this field. The most common of these metals is silver used for its good antibacterial properties and relatively low toxicity but other metals, such as gold, copper and zinc, they have their own advantages and antibacterial spectrum.

I. Sliver nanoparticles (Ag NPs)

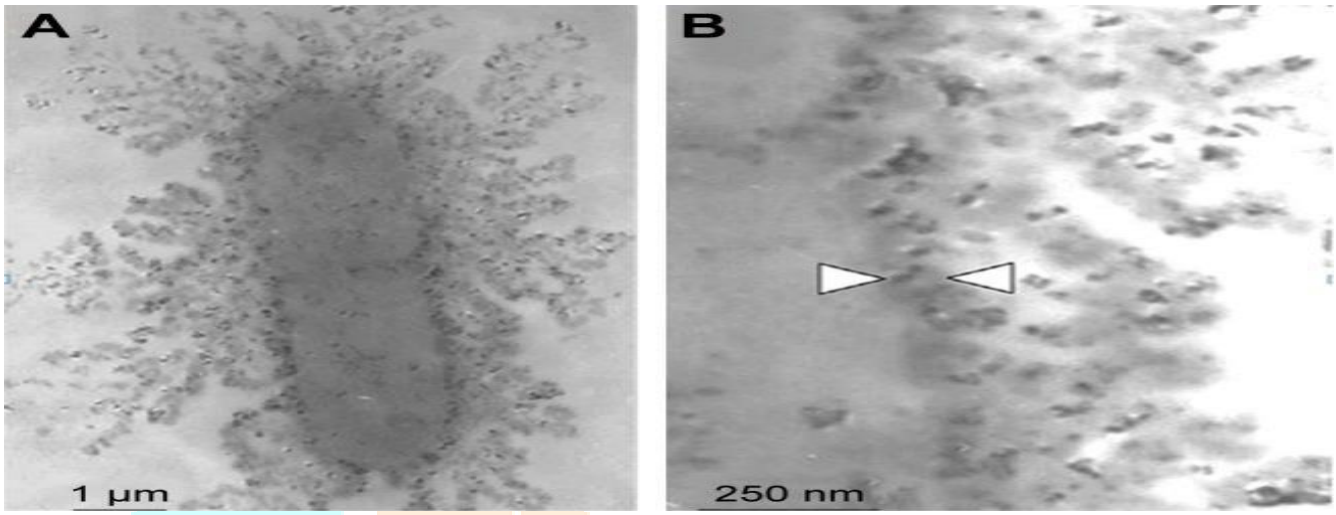

Fig 1: Transmission electron microscope image of *Escherichia coli* cells treated with silver nanoparticles in liquid Luria-Bertani medium: (A) membrane of *E. coli*; (B) nanoparticles accumulated in the membrane and penetrated the cell (arrows) [17]

Silver was considered an antimicrobial agent thousands of years before people knew the word "microorganisms". Silver bowls, water dishes, spoons and other vessels were used to store water, food and wine in good order [17] Silver powder was spread in wound healing and ulcer healing, which was the first documented by Hippocrates in the history of medicine. Silver Still silver it plays an important role in biomedical fields such as injuries bandages, textiles, bone implants etc,[18] thanks to the development of nanoscience and technology, silver is today used mainly in the form of nanoparticles Ag NPs have antimicrobial activity against many microbes (probably due to their multiple antimicrobial mechanisms action), including action against drug resistant bacteria, fungi (e.g. Candida albicans) and viruses Ag NPs are become effective antimicrobial agents because of them different sterilization mechanisms8, although not definitive mechanisms are inferred. Recent studies suggests that the main mechanism of antibacterial action Ag NPs must release silver ions (Ag).

A specific particle the activity of Ag NPs cannot be neglected, indicating that the mechanism of antibacterial action varies between Ag and Ag NPs The most widely accepted hypothesis is this Ag NPs released from Ag interact with cysteine regions of proteins on bacterial membranes that cause K a loss from within and disruption of cellular transport systems, which eventually leads to bacterial cell death [19]. & Mechanism shows in (fig. mechanism fig 1) Another study show that Ag interacts with cell wall proteins and the bacterial plasma membrane [20] Combination Ag^+ together the negatively charged membrane penetrates the Membrane therefore allows cytoplasmic contents to leak out of the cell and degrade H^+ gradient across the membrane and sometimes causes cell death, through the membrane and sometimes causes cell death. If the bacteria have not yet died, these contacts allow Ag^+ move through the cell wall and plasma membrane Finally, Ag works as an accessory an antimicrobial agent in the cytoplasm of a bacterial cell [21] despite the widespread use of Ag^+ bacterial resistance to Ag^+ is rare and slow to develop, especially in comparison to antibiotic resistance, making it a potential antimicrobial agent to address the problem of antibiotic resistance. Again, this is likely due to several mechanisms antimicrobial activity of Ag has been described previously, while antibiotics generally have only one mechanism of action, As it is Everyone knows that Ag NP based hydrogels have so many advantages that they worked better against gram-negative bacteria than Gram-positive bacteria, because gram-negative are compared to the low resistance of cell membranes Peptidoglycan cell walls of Gram-positive bacteria [22] But, it has also been suggested that there are fewer gram-negative bacteria more sensitive than Gram-positive bacteria to Ag, because Ag binds to negatively charged lipopolysaccharide (LPS). stronger than the outer membrane of gram-negative bacteria such as the peptidoglycan layer of gram-positive bacteria.

With this argument, Ag is captured by LPS and is less likely enter a gram-negative cell than a gram-positive cell [23].

However, serum albumin also reduces the antibacterial effect of Ag NP-embedded hydrogels [24] Genotoxicity Ag NPs and the balance between anti-reactive oxygen species (ROS) response and DNA damage have also been reported; and inhibition of mitosis and chromosomal instability, can they play an important role in silver-induced toxicity [25]. Therefore, the important questions are: improvement of the antimicrobial agent ability against gram-positive bacteria, gene minimization toxicity and lowering of serum albumin in the Design Ag NP-based hydrogels. More non-toxic and environmentally friendly synthetic processes like the idea Size-controlled synthesis of Ag NPs on tobacco mosaic virus (TMV) as a bio mediator without external reduction agents should be developed. Recent studies have found more hydrogels loaded with Ag NPs. Scientists they have better properties, such as strong antimicrobial activity properties and continuous release. All this development and improvements ensure the clinical potential of hydrogels [26].

II. Gold nanoparticles (Au NPs)

Gold is generally considered biologically inert, but Au NPs have various biological functions [27] Au NPs can be designed with different size and function with the desired polymers, in which case they are used as biocompatible materials Au NPs can be attached to bacteria membrane resulting in leakage of bacterial contents or penetration of the outer membrane and peptidoglycan layer that leads to the death of bacteria u NPs not only have an antibacterial effect. However, Au NP bound to ampicillin on the surface (Au NPAMP) killed several drug-resistant strains bacteria, including methicillin-resistant S. aureus (MRSA), P. aeruginosa, Enterobacter aerogenes and E. coli K-12 underscore DH5-alpha (pPCR-Script AMP SK) [28] Although isopropylacrylamide-based hydrogels contain Au NPs and pH-sensitive PMAA hydrogel.

Microcapsules containing Au NPs have already been reported [29,30], but their antimicrobial properties were not investigated until Gao et al showed that a hydrogel containing Au NP-stabilized liposomes for antimicrobial activity showed excellent antibacterial properties against S. aureus without skin. toxicity in a mouse model. In studies Ribeiro et. silk fibroin/nanohydroxyapatite hydrogel modified with in situ synthesized Au NPs showed antimicrobial activity. Compared with Ag NPs, not against toxicity osteoblastic cells were found, implying that Au NPs may be used for bone regeneration. [31] Additionally, acrylamide (AM) and wheat protein isolate (WPI) are used. To develop biodegradable gold nanocomposite hydrogels. The results showed that these biodegradable gold nanocomposite hydrogels can be used as potential candidates for antibacterial applications [32] With a combination of bimetallic (Ag, Au) hydrogel nanocomposites, took a step forward to improve its antimicrobial activity. [34]

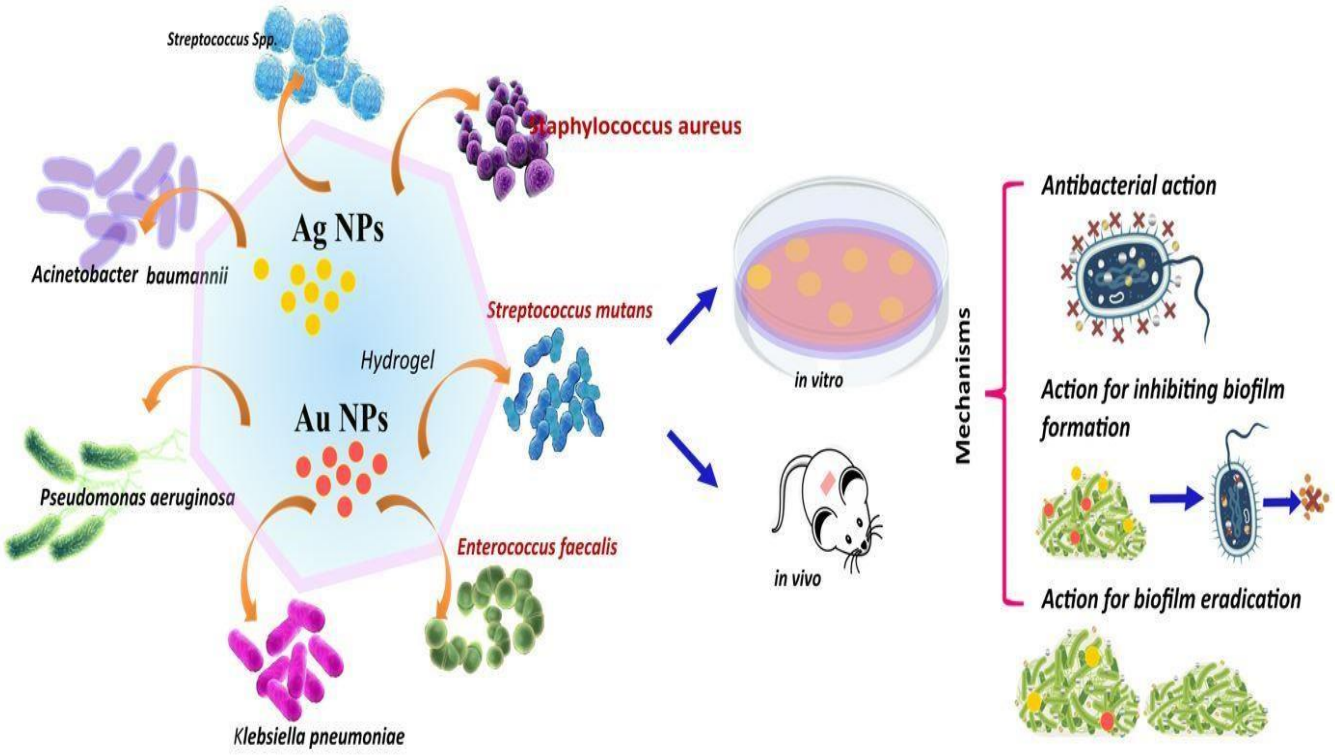

Figure 2. Mechanism of Ag NPs & Au NPs [33]

Even made of bimetal (Ag0-Au0) nanoparticles through a green process with mint leaf extract which showed significant antibacterial activity against Bacillus and E. coli. Although antimicrobial capacity Au NPs are weaker than Ag NPs, Au NPs are own interests' Antibacterial spectrum of Ag NPs is broad, including MRSA. In addition, hydrogels Au NPs showed negligible interference with bone regeneration. These properties of hydrogels containing Au NPs make them promising materials in clinical orthopaedic surgery [(35)].

III. Zinc oxide nanoparticles (ZnO NPs)

Besides silver and gold, there are also many other metal nanoparticles that have antimicrobial effects, but only just few are embedded in hydrogels. Zinc is one of them the most popular antimicrobial agent. ZnO NPs are used in many cosmetic materials because they are well known antibacterial activity and non-cytotoxicity in an appropriate manner concentration ZnO NPs fight microbes through several different means mechanisms Resistance to ZnO NPs has rarely been reported [(20)]

Some of the mechanisms are as follows:

I. ZnO NPs bind bacterial cell membranes tightly and destroy both lipids and membrane proteins cause membrane enlargement permeability and cell lysis;
II. ZnO NPs also cause Generation of Zn2+ ions and ROS, including hydrogen peroxide (H2O2) which damage the bacterial cell.

ZnO NPs are effective against both Gram-positive and Gram-negative bacteria Gram-negative bacteria due to its antibacterial effect with stands high temperatures and pressures bacterial spores [(36)] Similar to Ag NPs, ZnO NPs were added as PNIPAM antimicrobial hydrogel coatings, which proved to be promising candidates for new biomedical device coatings [(37)] synthesized CMC/ZnO nanocomposite hydrogel In situ formation of ZnO NPs in swollen CMC hydrogels which showed its antibacterial activity E. coli and S. aureus bacteria. Nanocomposite hydrogels Structure of IPN based on PEG- methyl ether methacrylate-modified ZnO (Zn O-PEGMA) and 4-azidobenzoagarose (AG-N3) showed increasing anti-adhesion property and bactericidal activity against gram-negative E. coli and Gram-positive Sauers [(38)] Furthermore, ZnO hydrogels has shown great potential in drug delivery and wound healing in some recent studies. CMC and CS hydrogels the use of ZnO as a hydrogel matrix has also been reported NPs, CMC hydrogels showed antibacterial activity against both gram-positive and gram-negative bacteria, and CS hydrogels were confirmed as a suitable wound dressing material, although the antibacterial capacity of ZnO NPs are relatively weak, low cytotoxicity is still shown that ZnO NPs have potential for clinical use. In addition, ZnO NPs have a positive effect on bone regeneration,109 which implies that ZnO NPs are promising materials in orthopaedics cutting [(39)].

1.1.2. Hydrogel loaded with micromolecular drugs

Micromolecular drugs encompass a range of antibiotic agents. These drugs have been clinically employed for their potent antimicrobial properties. Typically, they are administered systemically within hospital settings. When delivered via hydrogels, they can be applied directly to the affected area, offering an effective means to decrease the required dosage and mitigate the development of resistance.

Antibiotics – While antibiotics were discovered relatively late in human history compared to metal antimicrobial agents, they unquestionably hold the most prominent position. the most commonly used and most effective antimicrobial agents until now, [(40)] Antibiotic drug resistance is changing the biggest obstacle to development and implementation antibiotics There have been several in recent years new antibiotic approvals and new interest second and third line antibiotics mentioned earlier almost all recent antibiotic resistance appeared in the year when the resistant bacteria was found According to the latest research, only one antibiotic, tazobactam, does not have resistant bacteria. It is very effective against gram-positive bacteria. However, the antibacterial spectrum of tazobactam does not include Gram-negative bacteria, in addition, lack of choice In vitro resistance to tazobactam must be considered very cautious before widespread clinical use [(41)].

I. Ciprofloxacin
II. Gentamicin
III. Vancomycin
IV. Biological extracts
V. Synthetic antimicrobial drugs

I. Ciprofloxacin-

Ciprofloxacin is a fluoroquinolone antibacterial agent that is active in many Gram-positive and Gram-negative bacteria This is the gold standard for many topical applications such as eye and skin infections the mechanism of ciprofloxacin depends on blocking the bacterial DNA duplicates by binding to DNA gyrase, thus, causing double stranded breaks in bacterial chromosomes therefore resistance to this drug develops slowly.

Minimal toxicity the dose of ciprofloxacin depends on the dose, and excessive doses can do this causes tissue damage, while hydrogels can solve this problem as a topical delivery system Ciprofloxacin can be assembled with the tripeptide itself an antimicrobial nanostructured hydrogel that allows abundant the drug must be worn with an extended release [(42)] Personalized hydrogel coatings have been reported to prevent titanium implant related infections. Hydrogel obtained by polymerization of amino phenyl boronic acid in PVA with ciprofloxacin it has been reported to improve wound healing in diabetic patients diseases related to the colon have been reported because constipation can be treated with hydrogels containing indicated laxative psyllium and ciprofloxacin that ciprofloxacin-containing liposomal hydrogel improved maximum ocular availability through the albino rabbit cornea In a study by Zhou et al., complete inhibition of microorganism growth showed continuous tissue release. ciprofloxacin. Other researchers have used dextrin and polybasic hydrogel as a ciprofloxacin carrier and the results suggest that the hydrogel was a promising candidate for controlled release of ciprofloxacin [(43)] These studies show that ciprofloxacin-containing hydrogels have great potential for clinical use, especially in infectious diseases, due to their excellent antimicrobial properties and long-term effects.

II. Gentamicin

Gentamicin is a traditional broad-spectrum antibiotic used to treat skin and soft tissue infections. However, systemic toxicity, especially for kidney, and low plasma concentration hinder its application [(44)] To avoid the ADR effect, gentamicin is now often used topically, topically administration of functional gentamicin hydrogels gives an effective solution. Gentamicin-loaded PVA and PVA-AAm sterculia cross-linked hydrogels have many biomedical applications properties such as blood suitability, tensile strength, crack strength, water vapor permeability and oxygen diffusion. It can be a kind of powerful antimicrobial wound dressing [(45)] Super absorbable polysaccharide based on gentamicin hydrogel Pullulan derivatives also brought a broader view antimicrobial hydrogel. It can become one of the most important applications in the future and can expand 4000% of its volume [(46)], hydrogels have exceeded the limits of use of gentamicin because the effective dose can be reduced and other antibiotics with serious side effects are also used. in hydrogels. (Fig- 3)

III. Vancomycin

Vancomycin a macromolecular glycopeptide antibiotic, is considered the last line of defines against infection clinically, especially for methicillin-resistant staphylococcus but also now vancomycin-resistant Enterococcus (VRE) was discovered, in various fields. As previously mentioned, hydrogels such as the delivery system can protect and improve eligibility of vancomycin. Injectable plurone-α-cyclodextrin (CD) supramolecular gels crosslinked thiolate CS hydrogel dextrin grafted with maleic acid, thermosensitive hydrogel CS/gelatine/β-glycerol phosphate [(48)] Biocompatible Matrices Charged Copolymers Oligo(PEG-Fumarate)/Sodium Methacrylate (OPF/SMA) Hydrogel, Poly(β- Amino ester) (PBAE) hydrogels mixed with PEG (MW = 400) diacrylate (PEGDA) and diethylene glycol diacrylate (DEGDA) and hydrogels obtained by photo crosslinking methacrylic substances dextran and poly(l-glutamic acid)-g-hydroxyethyl methacrylate were all studied and showed excellent antimicrobial activity, properties and desired release capability [(49)]

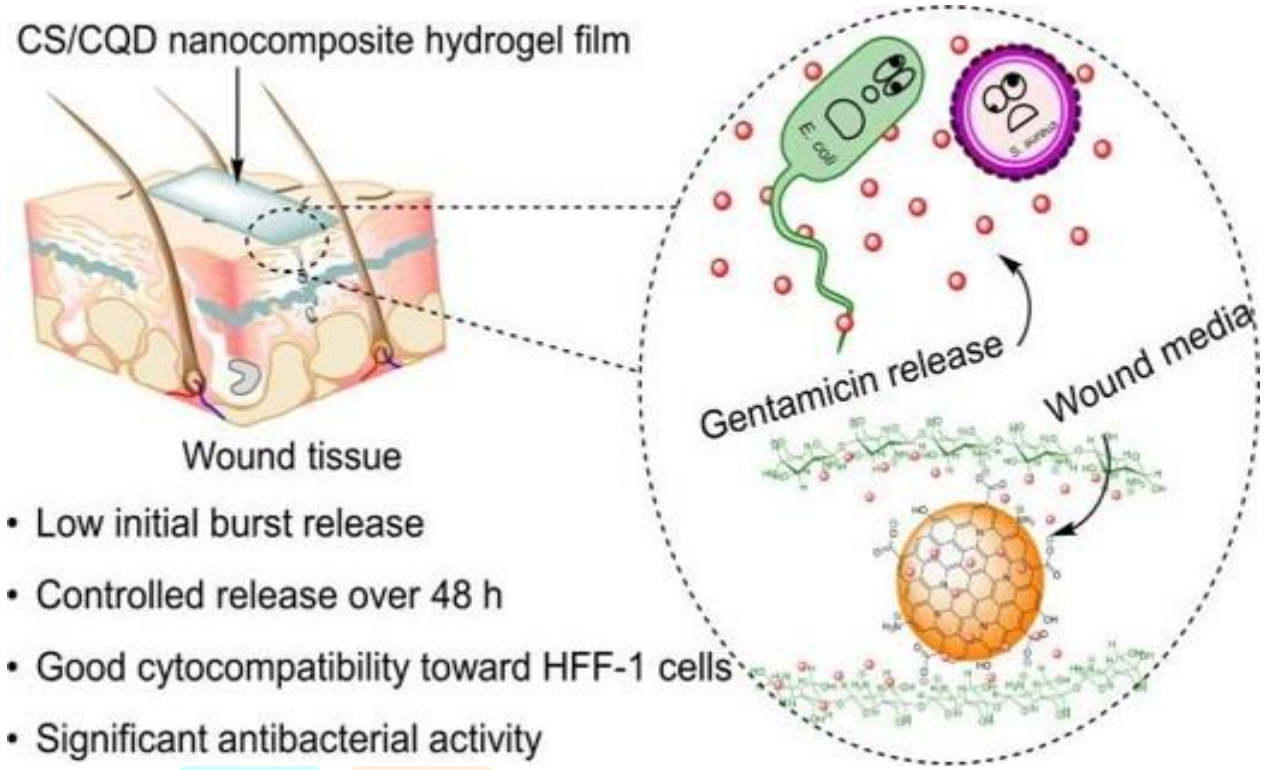

Figure 3: Working of Gentamicin [47]

The most common pathogen of osteomyelitis is S. aureus, especially MRSA. Vancomycin is always used to treat osteomyelitis because it is the most effective antibiotic against MRSA. The combination of hydrogels and vancomycin is a good material that can prevent osteomyelitis clinically. The release curve of vancomycin containing HA hydrogels is shown in Fig no: 4

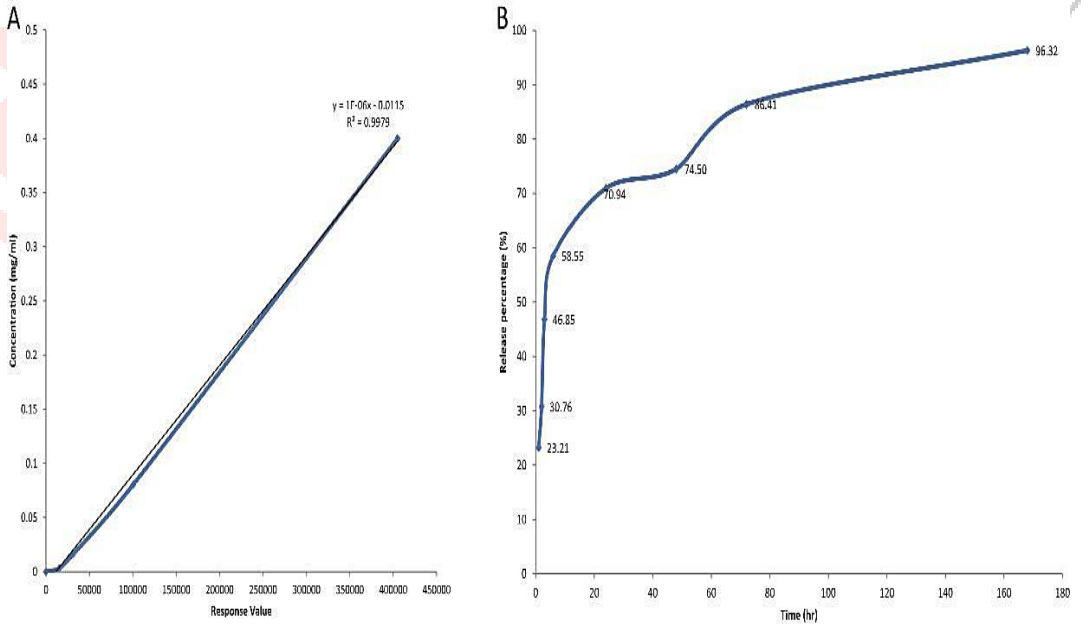

Figure 4. The release curve of vancomycin-containing HA hydrogels measured by high-performance liquid chromatography [50].

1.2. PREPARATION

The continuous release of antimicrobial agents in hydrogels is mainly achieved by structural changes in the hydrogels. Antimicrobial hydrogels have been divided into traditional sustained-release antimicrobial hydrogels and smart sustained hydrogels according to the release mechanism that corresponds to the biological microenvironment. Traditional hydrogels do not respond to changes in the microenvironment. The release of antimicrobial agents can only provide a local wound concentration and cannot precisely regulate the output concentration of antimicrobial agents according to the physical conditions of the wound. (as the strength of the local wound inflammatory response). Intelligent hydrogels can respond differently to the organism's microenvironment, self-assemble to form ordered supramolecular structures, and finally form hydrogels with special three-dimensional structures [51,52]

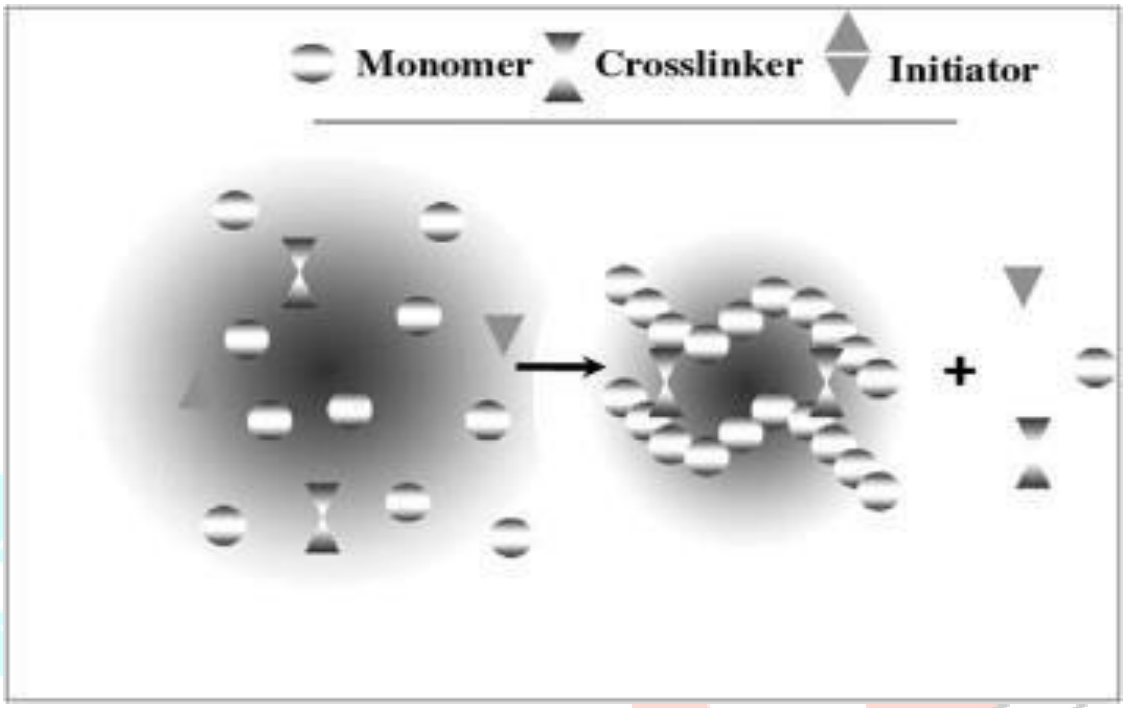

Figure 5: Schematic diagram of hydrogel preparation [2]

Antimicrobial hydrogels can be synthesized by various technical means methods, because it is too extensive an approach to synthesis is not the focus of this article, a brief introduction covers it all. (Show in fig 5:) Based on the different characteristics of the reaction process, it can be divided into three categories: crosslink polymerization monomer, graft copolymerization and polymer polymerization[53].

I. Crosslinking polymerization of monomers

Cross-linking polymerization refers to the production method polymeric hydrogel materials by free radical homo polymerization or copolymerization of monomers initiated in the presence of chemical initiators or radioactive cross-linking agents [54] In the polymerization process, the polymerization efficiency and properties of hydrogel materials can be controlled by adding initiators, chelating agents or chain transfer agents. Common monomers currently used in crosslinked polymer hydrogels include acrylic acid, acrylate, acrylamide, and ethylene derivatives reported a novel dual bionic adhesive hydrogel (DBAH) based on chitosan grafted with methacrylate (CS-MA), dopamine (DA) and N-hydroxymethyl acrylamide (NMA) by a simple radical polymerization process. This hydrogel has good suitability for wound healing and sealing in haemostasis and wound viscosity hydrogels can be modified by adjusting the ratio of CS-MA/DA forms a hydrogel by copolymerization of acrylamide (AM), and acrylic acid monomers (AA) in a glycerol-water binary solvent system This hydrogel is a promising material for self-adhesive bioelectronics to detect bio signals in cold or hot environments [55].

II. Graft copolymerization

Grafting hydrogel materials onto a substrate with a certain strength can greatly improve the mechanical properties of hydrogels and improve the shortcomings of traditional hydrogels with insufficient mechanical strength, Polymeric materials have several properties that can be modified by the type of copolymer, copolymerization reactivity, graft concentration, and graft distribution. The most efficient way to synthesize hydrogels by graft copolymerization is the covalent attachment of monomers to a support surface by means of free radical initiators (ammonium cerium nitrate, irradiation, peroxide) to form copolymers [56]. This method has several advantages such as a simple work procedure, shorter reaction time, milder conditions and high

reaction efficiency. Gingiva-based hydrogels prepared by radiation-induced graft copolymerization of N-vinyl imidazole on gingiva were determined along with evaluation of the release profile of the antibiotic levofloxacin. A slow release of the drug was observed without breaking the drug-loaded hydrogels. The polymers were found to be non-homolytic mucoadhesive and antioxidant in nature and could be offered as a gastrointestinal drug delivery system [57]. conducted studies on the equilibrium expansion of polymethacrylic acid-carboxymethyl starch (PMAA-CMS) hydrogel in enzyme-free form simulated gastric and intestinal fluids (SGF and SIF, respectively). In vitro release profiles show that the degradation of PMAA-CMS hydrogel synthesized by graft copolymerization in SIF was faster.

III. Crosslinking of polymers

Hydrogels can also be synthesized by adding crosslinking agents to aqueous polymer solutions or by electrostatic, ionic, hydrogen bonding, and chain winding [58]. One of the challenges in the production of hydrogels by crosslinking polymers is related to the control of crosslink density, which requires precise control of starting material concentrations or reaction parameters such as temperature or pH. prepared a novel pHsensitive poly (amino acid) hydrogel based on poly-γ-glutamic acid (γ-PGA) and ε-polylysine (ε-PL) mediated by carbodiimide (EDC) and N -hydroxysuccinimide (NHS). The results of the mechanical properties showed that the PGA/PL hydrogels were soft and elastic. In addition, PGA/PL hydrogels showed excellent biocompatibility in cell proliferation experiments [59].

Other synthesis method:

Synthetic Methods	Species of Hydrogels	Materials	Antimicrobial Capability	Application	Reference
Chemical crosslinking	Acacia gum-PVA hydrogel. Silk fibroin crosslinked glycyrrhizin acid and silver hydrogels.	Acacia gum, PVA, glutaraldehyde, salicylic. SF, Ag, GA.	Against Bacillus subtilis, P. aeruginosa, E. coli and S. aureus. Against S. aureus, P. aeruginosa.	Wound dressing	**(60)**
Physical crosslinking	PVA-TA hydrogel. AA-Al3+-MGA-[VBIm]Br hydrogel. Antibacterial chitosan/silver bionanocomposite	Arabic, AlCl3 PVA, TA. AA, 1-vinyl-3-butylimidazolium, COOH-modified gum. STPP, chitosan, AgNPs	Against E. coli and S. aureus. Against E. coli, S. aureus, and C. albicans. The antibacterial activity against E. coli and S. aureus lasted for 1 week.	Biomedical fields. Wound dressing. Drug carrier	**(61)**
Freezingthawing cycles	Nano-TiO2/CMCS/PVA composite hydrogel. AgNPs and PVA/CH hydrogel	PVA, CMCS, Nano-TiO2 AgNPs, PVA, CH.	Against E. coli and S. aureu. Against gram + ve and gram − ve bacteria.	Cosmetics, medical dressings. Wound dressing.	**(62)**
Solution polymerization	Poly (DMA-co-AAc) hydrogel	DMA, AAc, ammonium persulfate	Inhibit the growth of S. aureus.	Antibacterial materials	**(63)**
Photoinduction	Chitosan-PEG hydrogels	Chitosan derivatives, PEG	100% inhibition of the E. coli and S. aureus	Biofunctional materials	**(64)**

Chemical–physical crosslinking	Chitosan/PV A-based hydrogels	CS, PVA	Against S. aureus and K. pneumonia	Oral dressing	**(65)**

5. APPLICATION

- Antibacterial Hydrogels for Drug Delivery.
- Antibacterial Hydrogels for Wound Dressing.
- Antibacterial Hydrogels for Tissue Engineering.
- Chitosan Based Hydrogels for Antifungal and Antibiofilm Activity.
- Chitosan-Based Hydrogels for Antifungal Applications.

Type of antimicrobial gels	Nanoparticle	Application	Reference
Loaded with drugs:	Silver NPs Gold NPs Antibiotics Antimicrobial agents	Wound dressings and surface coatings. Antibiotics. Wound dressings and implant coatings. Wound dressings and surface coatings.	(66)
Inherently active based on:	Peptides Chitosan Polymers	Wound dressings and surface coatings. Wound dressings and surface coatings. Surface coatings.	(67)

6. ADVANTAGES

- High water swell ability.
- High oxygen permeability.
- Improved biocompatibility
- Conventional antibiotics.
- Targeted drug delivery.
- Sustained release.
- Reduced resistance development.
- Increased efficacy.
- Improved patient compliance.
- Reduced risk of allergic reactions. (68)

7. DISADVANTAGES

- Bacterial resistance and short-term antibacterial activity, prone to degradation and instability.
- Potential hypersensitivity.
- Difficult to extract and enrich.
- Sensitive to the pH, temperature and ionic strength of solution (69).

CONCLUSION & FUTURE SCOPES

The future of anti-microbial hydrogels appears promising, with ongoing research focusing on several key aspects. Innovations may include improved biocompatibility, sustained release of antimicrobial agents, and customization for specific applications. Additionally, advancements in 3D printing and nanotechnology may contribute to precise fabrication and enhanced properties, expanding the potential for use in medical settings, wound care, and beyond. As technology progresses, anti-microbial hydrogels could become more versatile and widely adopted in various healthcare and biotechnological applications.

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