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Antimicrobial Polymers Containing Ammonia Derivatives

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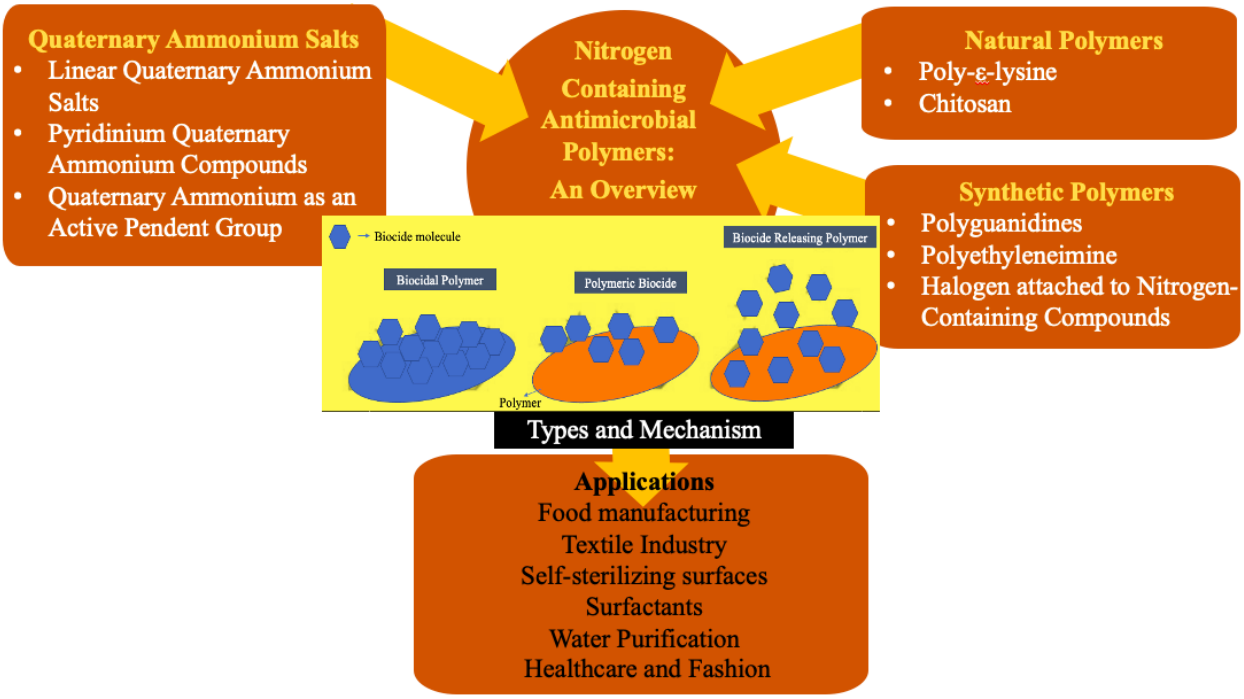
Abstract:

The ever increasing number of harmful pathogens and the implications of their spread pose a major issue for modern science. These infections can be a primary source of concern in many sectors including healthcare, pharmaceuticals, dental restorations, surgical instruments, medical equipment, and sanitation systems. Polymeric antimicrobials can destroy or prevent germs from developing on a surface or in the surrounding environment. They have recently garnered considerable attention owing to their higher efficacy, lesser toxicity, higher selectivity, sustainability, eco-friendly nature, and longer lifespans. In the face of the prevalence of antibiotic resistance, the development of new antimicrobial polymers with better efficacy has been a major priority. This review focuses on antimicrobial polymers containing nitrogen, the relationship between their activity and structure, their method of action, the effect of several parameters on antimicrobial potency, and their applications in various spheres including COVID-19.

Keywords:

Antimicrobial polymers, Biocides, Quaternary ammonium compounds, Bacterial growth inhibition, Cationic polymers



1. Introduction

Bacteria, fungi, and parasites, commonly known as "microbes," are living things that play a major part in the transmission of infections.[1] Pathogenic or harmful organisms are the fundamental cause of infectious illnesses, accounting for more fatalities than any other cause.[2] Antibacterial chemicals/disinfectants are used to stop the development of bacteria or restrict their proliferation. Myriad of infectious illnesses remain difficult to treat even though a number of antimicrobial medicines have been developed that can kill or suppress germs.[3,4]

Microorganisms produce biofilms on surfaces, which are primarily cells that cluster together and create an extracellular polymeric matrix to grow in. Biofilms are composed of polysaccharides and other components such as proteins and DNA that are secreted by the organism. Defective biofilms do not support microbial development and do not offer a suitable environment for microbial development. Treatments that decrease bacterial viability or adherence may be required for effective antimicrobial applications. For instance, heparin contains anti-adhesive and hydrophilic qualities that prevent the development of germs.[5] Biofilms are very difficult to remove and most biocides fail to have any effect on them. Instead of destroying bacteria, the methods to restrict biofilm development and decrease microbial adherence could be more effective at controlling infectious disease transmission.[6,7]

Antimicrobial Polymers

Antimicrobial polymers are materials that are able to eliminate or reduce the proliferation of bacteria on the surface or in the surrounding environment. The various antibacterial materials are categorized into distinct categories: those that have inherent antimicrobial activity; that acquire biocidal action through chemical modification; which integrate low- or high-molecular weight antimicrobial organic compounds and finally, those which integrate active inorganic systems.[8,9] Macromolecular antimicrobial structures can be polymers covalently linked to smaller antibacterial agents or that have inherent antimicrobial action.[9–12] The former type commonly functions by releasing microscopic molecular antibiotics.[13] However, antimicrobial polymers, namely those containing inherent antibacterial properties, may impede or prevent the development of drug-resistant microorganisms. Polymeric structures also boost the antimicrobial capacity of antimicrobial polymers. Antimicrobial polymers may

be distributed in solution as antibiotics or preservatives that undergo covalent bonding in order to deliver the antimicrobial polymer to the substrate for disinfection purposes. Controlled mobility antimicrobial polymers in solution kill bacteria with greater accessibility than those covalently bound to surfaces.[14]

2.1. Need for Antimicrobial Polymers

Various human health-related industrial sectors, including hospitals, water purification systems, dental equipment, household sanitation and food packaging are all vulnerable to microorganism contamination. The pathogens at these locations lead to a wide spectrum of diseases and ailments. Resistance to antibiotics grows fast, making the problem even worse.[15,16] As a result, keeping these areas free of pollutants and contaminants is crucial. Disinfectants like hypochlorite, hydrogen peroxide, reactive oxygen species, silver salts and quaternary ammonium compounds (QAC) along with methods like sterilization or ionization with heat have been used but they have only a short-term impact and cause environmental toxicity that restrict their utilisation.[17] While new polymers with antimicrobial properties were being developed, researchers were also experimenting with the structure of existing polymers in order to alter their physical and chemical properties to achieve the desired biological and physiochemical qualities.[13] Antimicrobial polymers have received increased interest in academic and industry research in the last half of the twentieth century. Numerous units, including amines (primary, secondary, and tertiary), sulfonium, quaternary pyridinium, quaternary ammonium, 1,3-thiazole, guanidinium/biguanide salt, phosphonium, quaternary imidazolium[18], 1,2,3-triazole[19]are combined to form antimicrobial polymers in a variety of ways.[20–22]

2.2. Mode of action and Mechanism

Antimicrobial polymers are broadly classified into biocidal polymers, polymeric biocides, and biocide-releasing polymers.[23][Figure 1] Biocidal polymers are polymers that have inherent antibacterial activity and the use of these polymers in the creation of antimicrobial surfaces is particularly advantageous since no harmful biocides are discharged into the environment. Polymeric biocides are polymer backbones that include biocide molecules and are synthesised by covalently linking a number of well-known biocide compounds to a polymer. Due to the steric barrier created by the polymer backbone, these materials usually possess lesser activity than their low molecular weight counterparts. Biocide-releasing polymers are polymeric matrices that contain biocide molecules incorporated in a variety of ways, or polymers that have biocides attached through cleavable linkages [6,24]. Owing to the high concentration of biocides obtained during the release and the close proximity of the biocide to the target cells, this antibacterial technique exhibits extraordinary effectiveness.

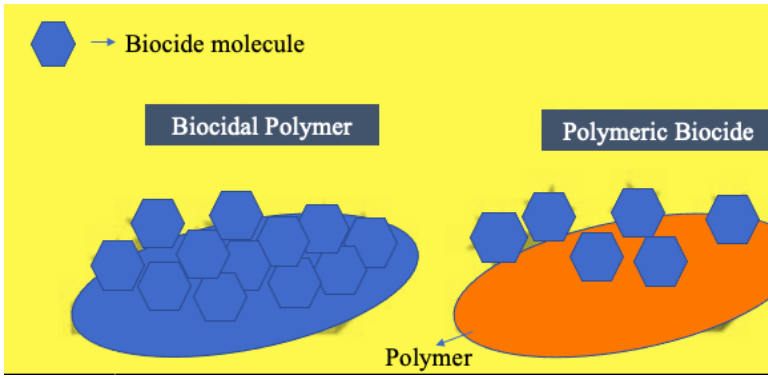


Figure 1: Working principle of the types of antimicrobial polymers (adapted from [25] under Creative Commons Attribution License)

Cells have an external membrane that is negatively charged and commonly have divalent cations, such as magnesium and calcium, added to stabilise it. Antimicrobial polymers first interact electrostatically with pathogen cell membranes (CM). They have the capability to disrupt the CM by forming pores, thereby increasing water/ion diffusion, causing additional damage to the structural organisation and integrity of the CM due to osmoregulation. The ions are supplied by teichoic or lipoteichoic acid molecules in gram-positive bacteria's cell wall (CW), lipopolysaccharides and phospholipids in gram-negative bacteria's outer membrane and the CM, which is composed of a phospholipid bilayer with embedded essential functional proteins, for example, enzymes. The cytoplasmic membrane is semi-permeable and thus regulates the movement of solutes and metabolites in and out of the cytoplasm of the cell.[26–29] Cationic hydrophilic–hydrophobic

macromolecular complexes within the cytoplasmic membrane act as a target site for the bulk of antibacterial polymers. Mammalian CM, which are rich in phosphatidylcholine, phosphatidylserine and cholesterol, are less negatively charged and more stable than bacteria's membranes, which are rich in phosphatidylethanolamine and phosphatidylglycerol but deficient in cholesterol, allowing antimicrobial polymers to distinguish pathogens from mammalian cells.[30,31]Structural organisation and integrity of CM is disrupted due to surface activity and adsorption/absorption capacity (surfactants), as well as high binding affinity for bacterial cells, which is heightened by a high lipophilicity.[13,32–34] Groups such as quaternary ammonium, quaternary phosphonium, guanidinium etc. are frequently found in these polymers.

When designing effective antimicrobial polymers, regardless of the type of polymeric system used, several important characteristics should be considered, including the conditions of the intended application, its biocidal activity against microbes, nontoxicity along with its stability over the required storage time and in long-term applications. This review focuses on the most notable advancements in the field of antimicrobial polymers with an emphasis on the mechanism and design of the action of polymers having nitrogen atom in their structure.

3. Antimicrobial Polymers with Quaternary Ammonium Salts

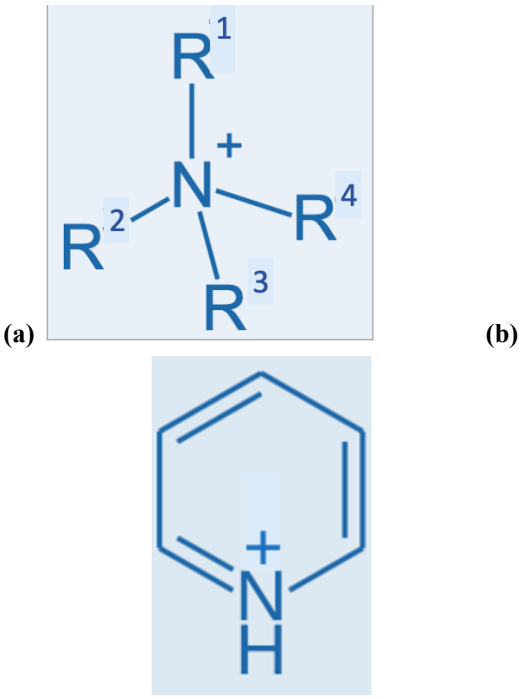


Figure 2: (a) Structure of Quaternary Ammonium and (b) Pyridinium

3.1. Linear Quaternary Ammonium Salts

The chemical composition of quaternary ammonium compounds (QACs) is made up of nitrogen (N) covalently bonded to four different groups. Its generic formula, $N^{+}R_1R_2R_3R_4.X^{-}$ is often accompanied by numerous functional groups such as hydrogens, alkyl groups, and alkyl groups that contain different substituents where R might be a hydrogen atom and X an anion (Figure 2a). This broad range of QAC contain 8–18 carbon atoms and they generally have good germicidal capability. The prominent members of this class include chlorides of benzalkonium, cetrimonium and stearalkonium.[35] Lipophilicity, being a function of N-alkyl chain length, affects the antimicrobial properties of QACs. Compounds containing 12-14 alkyls in their alkyl chain length have the best antibacterial action against gram-positive bacteria whereas alkyls with a carbon chain length of 14-16 have the best antibacterial activity against gram-negative bacteria.[28] First the QACs (which are positively charged) engage with negatively charged bacterial membranes by electrostatic contact. Then the QAC's hydrophobic tail is inserted into the bacteria's membrane core. Since the membrane core is hydrophobic in nature too, the tail denatures its structural proteins and enzymes. Moreover, QACs modify the ultrastructure

of antibiotic-resistant Escherichia coli (E. coli) in a dose and time-dependent manner.

The highest standard for protein-resistant coatings is set by poly(ethylene glycol) (PEG) cross-linked polymers. But due to their greatly enhanced resistance to acid-base and oxidation-reduction reactions, polymers functionalized with ammonium or phosphonium are more stable than PEG-based polymers. They might also be good candidates for protein-resistant medical equipment in biohazard separation systems or in systems that operate in harsh environments, thereby requiring chemical cleaning. Dynamic membrane protein fouling resistance and water transport performance were better in poly[trimethyl(4-vinylbenzyl)phosphonium bromide] than PEG for slightly cross-linked use. Biocide end group were formed on the polymeric backbone of antimicrobial polymers.[36]Cationic ring opening polymerization of 2-alkyl-1,3-oxazolines was carried out, after which the macromolecule was treated with a cationic surfactant[37] QACs have several uses across a variety of products such cosmetics, topical ointments, alcohol based hand lotions, antifouling building materials and mouthwash. A large number of quaternary ammonium nitrates (QANs) were employed in a variety of products such as dental resins, adhesives, sealants, and paints. Dental polymers created by Tiller's group include poly(2-alkyloxazoline) polymers containing antibacterial polymers. Poly(2-methyl oxazoline) and a quaternary ammonium end group were used to develop a contact-active antibacterial material, using a macromeric biocide called poly(2-methyl oxazoline). Utilizing a commercially available dental adhesive containing this polymer, microorganisms like Streptococcus mutants in the tubules of teeth were destroyed, along with human collagenases and gelatinases, two enzymes that contribute to periodontal tissue degradation.[38]

3.2. Pyridinium QACs

The heterocyclic rings (similar to QACs) containing a nitrogen atom that demonstrate germicidal effect are called quaternary pyridinium (figure 2b). They have a mechanism alike to that of QACs. The researchers found pyridinium-type polymers that were able to destroy gram-positive and gram-negative bacteria and yeast but failed to impede the growth of B. subtilis and fungi. Pyridinium groups inside the polymer chain operate as antibacterial agents. They attach or stick to bacteria while in their living or dead forms. With a median lethal dosage (LD 50) of 2330 mg/kg, these compounds have a low toxicity. [39]

Another type of antibacterial polymers, which include aromatic/heterocyclic groups, are known as the imidazole derivatives. Since free imidazole is capable of creating hydrogen bonds with medications and proteins but its alkylated form (imidazolium) loses this capacity, alkylated imidazole aggregates electrostatically. They are less susceptible to environmental hazards and more biodegradable[40]. For instance, copolymers of N-Vinyl imidazole and phenacyl methacrylate were synthesized and found to demonstrate significant antimicrobial properties against fungi, yeast and bacteria. [41]

3.3. Quaternary Ammonium as an Active Pendent Group

These are polymers that have no innate antimicrobial properties but may be altered to possess antimicrobial abilities by the inclusion of an active group or chemical. These polymers have active pendent groups and polymers containing antibacterial compounds that are bonded to either inorganic or organic molecules. Acrylic or methacrylic derivatives, such as 2(dimethylamino)ethyl methacrylate, including commercial methacrylic monomers, are the primarily known cationic quaternary polyelectrolytes utilised as antimicrobial polymers. These polymers have a high degree of structural flexibility because of their hydrophobicity, surface charge, and other properties. Polymethacrylate- and polymethacrylamide-based amphiphilic copolymers were created by Kuroda et al.[42] In order to construct a non-hemolytic antimicrobial polymer, the researchers performed a systematic process of adjusting hydrophobic groups, polymer composition and length of the polymer. Primary, secondary and quaternary amine groups were used in the side chains of each copolymer series to increase the cationic charge. This research showed that the hydrophobicity of polymers and the ability of amine side-chains to protonate reversibly played important roles in determining whether polymers possess antibacterial properties. [43,44]

Polysiloxanes are silicon oxide linear polymers that represent another prominent type of polymers. Owing to their considerable flexibility and amphiphilicity, these polymers have recently received interest as antibacterial polymers linked to quaternary ammonium groups. Amphiphilicity increases the concentration of quaternary groups near the microbe CW and flexibility helps in the interaction between quaternary groups and microorganisms. A study shows that block polysiloxane copolymers substituted with quaternary ammonium groups have substantial antibacterial properties against E. coli and Staphylococcus aureus (S.aureus). However, it was unable to distinguish between block type polymers and statistical copolymers in terms of polymer activity.[45] The biocidal efficiency of polysiloxanes containing quaternary ammonium ions and N,N-dialkylimidazolium groups was compared in a study performed by Mizerska et al. When polysiloxane-based quaternary ammonium salts were employed, a similar response was shown for these compounds against the pathogens Enterococcus hirae, Proteus vulgaris, E. coli, and P. aeruginosa. The compositions outperformed polysiloxane having quaternary ammonium groups when it comes to thermal stability.[46]

4.Based on Natural Polymers

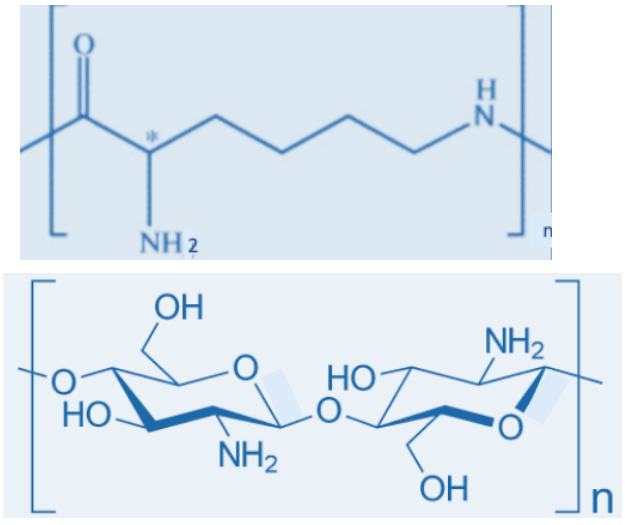


Figure 3: (a) Structure of Poly-ε-lysine and (b) Chitosan

4.1.Poly-ε-lysine

Poly-ε-lysine (ε-PL) is a cationic, naturally occurring homopolyamide of L-lysine (with 'n' ranging between 25 to 30), characterised by an amide connection between the α-carboxyl and ε-amino groups (figure 3a). It was discovered for the first time in the filamentous bacterium Streptomyces albulus during the screening of Dragendorff's reagent.[47] Later, it was revealed that species of Ergot fungi and Streptomycetaceae were instrumental for the generation of ε-PL.[48] ε-PL is a nontoxic, thermostable, biodegradable, water soluble and edible polymer. At alkaline pH, the ε -PL in the β-sheet conformation transforms to an antiparallel β-sheet when the pH exceeds the pKa of the alpha-amino group. But when the pH is acidic, an electrostatically extended conformation is observed. [49] On comparing it with α-poly-L-lysine ('n' = 50), which is primarily used for gene transfer, ε-PL is efficient against both gram-negative and gram-positive bacteria along with bacterial strains of Bacillus subtilis, Bacillus stearothermophilus and Bacillus coagulans. [50,51]

ε-PL's antimicrobial activity can be described by electrostatic adsorption on the surface of the microbial cell followed by membrane stripping, leading to physiological damage to the cells and eventual death of the bacterium.[52]The role of ε-PL in inhibiting human and porcine pancreatic lipase activity in the presence of bile salts and phosphatidylcholine-containing substrates was elaborated. ε-PL inhibits the absorption of dietary fat from the small intestine and is utilized by obese patients as a dietary intervention.[53]Research demonstrates its broad application in food preservation, microchip coating, medication, gene delivery, and as a nutritional agent, interferon inducer, super absorbent, mild emulsifier, hydrogel and disinfectant. For example, antimicrobial polymers such as hydrophobically modified ε-PL graft copolymers, have been examined as emulsifiers in the food sector. [53]

4.2. Chitosan

In 1859, Rouget developed Chitosan, a linear polycationic hetero polysaccharide copolymer and the biomedical field's most intensively researched polymer. It consists of 1,4-linked D-glucosamine and N-acetyl-D-glucosamine which is formed by partially N-deacetylating chitin in an alkaline medium (figure 3b). The quantity of amine groups in chitosan plays a vital role to tune physical, chemical and biological aspects of the biopolymer. Alterations in the amine

group enables it for greater application diversity.[54] [55,56] The broad-spectrum antibacterial action of chitosan was first proposed almost four decades back.[57] Since then, it has proven to be antimicrobial against a wide variety of bacteria, filamentous fungus and yeasts. Bacteria tend to be less susceptible to chitosan's antibacterial effect than fungi. [58,59] While chitosan possesses bactericidal action, its potency is reliant on features of the polymer, such as positive charge density, molecular weight, concentration, hydrophilic/hydrophobic characteristic, chelating capacity, and the polymer's physical state. Bacterial inactivation is further enhanced by other factors such as the ionic strength of the medium, the pH, the temperature, the reaction duration, and the sort of microbe.[60]

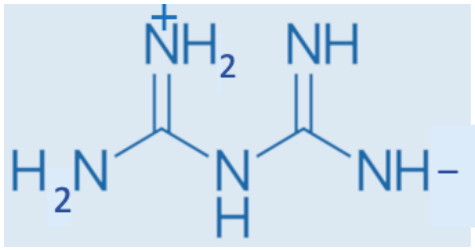
Myriad of mechanisms have been developed to explain the antibacterial activities of chitosan, including electrostatic interaction, hydrophobic and chelating effect. The protonation of amino groups takes place when the pH of the medium is less than pKa and the electrostatic interaction between the polymer and bacterial CW takes priority. When the pH is greater than pKa, there is no considerable protonation; the hydrophobic interaction and chitosan-chelation processes lead to antibacterial activity. These two processes represent the greater activity of neutral or higher pH chitosan than native chitosan. [60–62]

When compared to gram positive bacteria, gram negative bacteria are more susceptible to chitosan. Bacteria which are gram-negative have a greater negative surface charge. Divalent metal ions (sodium, potassium, etc.) sustain these charges, whereas gram-positive bacteria are mostly made up of lipoteichoic acid, which is polyanionic and serves to strengthen the CW. [63] Electrostatic interaction is an important mechanism for gram positive bacteria. Electrostatic contact in conjunction with chelation forms an antibacterial medium for gram-negative bacteria. Following a pathogen adherence, chitosan with different molecular weight shows different modes of action.[63–65] To find out if chitosan has antibacterial capabilities, researchers like Raafat et al. conducted several testing methods, including in vitro trials, cell-death studies, membrane permeability studies and leakage tests.[66] They hypothesised that when chitosan is bound to the CW, it induced secondary cellular effects, disrupted the energy of the membranes to generate pathways, impaired the chain of electron transportation and thereby forced cells to switch towards producing anaerobic energy, ultimately resulting in cellular dysfunction.

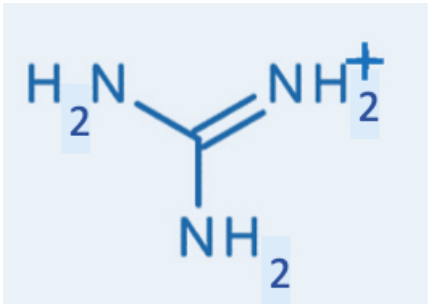
Recently, chitosan–pectin–TiO_2 dressing was generated by electrospinning chitosan with titanium dioxide or titania (TiO_2) nanoparticles in solution. While TiO_2 nanoparticles confer antibacterial activity against gram-positive bacteria and gram-negative bacteria, cell growth inhibition, and high corrosion resistance, pectin, a naturally occurring prophylactic substance, confers protection against toxic cation poisoning as well as curing properties. In another study, chitosan was effectively electrospun with nanocellulose, a biocompatible, biodegradable and sustainable biomaterial with a wide range of biotechnological applications, including wound dressing, tissue engineering, and drug delivery. When tested against E. coli and S. aureus, these membranes successfully killed 99.9 percent of the bacterial population.[67]

5. Based on Synthetic Polymers

5.1.Polyguanidines



(a)



(b)

Figure 4: (a) Structure of Biguanide and (b) Structure of Guanidium

Due to their high biocidal efficacy, water solubility, lack of toxicity and broad antibacterial spectrum, polyguanidines and polybiguanides are an important class of antimicrobial polymers (figure 4). Also,

owing to their electrostatic interaction with CM, acrylate monomers containing pendant biguanide groups exhibit significant antibacterial activity. Being antimicrobial in nature, they are more effective against gram-positive bacteria than gram-negative bacteria. Bacteria belonging to the gram-positive species have a more straightforward structure, making them more susceptible to polymeric biocides with a high molecular weight.[68]Polyhexamethylene guanidine stearate and polyhexamethylene biguanidine stearate were produced through a precipitation reaction. Polymers which remain stable at elevated temperatures and have a minimum inhibitory concentration (MIC) less than 200 g/mL are considered resistant.[69] Using polycondensation of guanidinium salts and four separate diamines, Albert et al. created many oligomeric guanidines. Antimicrobial activity was studied against a range of bacteria, including gram-positive, gram-negative, and antibiotic-resistant varieties. Effective antibacterial activity requires a molecular mass of roughly 800 Daltons. Cationic and anionic components are mixed to produce the right ratio of cationic to anionic particles.[70]

5.2.Polyethyleneimine (PEI)

Figure 5: Structure of Polyethyleneimine

The synthetic, nonbiodegradable, cationic polymer PEI has all three primary, secondary and tertiary amino functional groups (figure 5). Aziridine and 2-ethyl-2-oxazoline can be polymerized to linear and branched forms by ring-opening and acid-catalyzed polymerization, respectively[71,72] In the case of PEI, a number of beneficial chemical alterations may be carried out, due to the abundant reactive amino groups in the material. In the beginning, PEIs were tested to see whether they could prevent bacteria from adhering to glass by forming a covalent bond with it. However, the test was unsuccessful, because the number of bacteria on the untreated glass was exactly the same as the number on the PEI-treated glass. Alkyl groups were used to help hydrophobicity and positive charge density, but the antibacterial activity was limited.[73] Methods to bind N -alkyl-PEI on a range of inorganic and organic, artificial and natural, nanoscale and macroscopic, porous or monolithic surface materials, including commercial glass, plastics and textiles have also been undertaken by researchers. Air-borne, water-borne bacteria and fungi, including antibiotic-resistant and pathogenic and, were virtually 100% inactivated on these surfaces, with no signs of resistance development. A primary mechanism of antibacterial action is the breakdown of the CM.[74]

A number of N-alkylated PEI-impregnated fabrics, such as cotton, polyester, wool and viscose are also highly effective at destroying airborne gram-negative and gram-positive bacteria. PEI exhibits excellent antibacterial properties when it has a high molecular weight; however, the same properties do not apply when the molecular weight is low.[75] Substituted PEIs were also used to treat Candida albicans, which increases the risk of laryngectomy patient prosthesis degradation. These surfaces that are treated with dimethylaminoethyl methacrylate and PEI-bonded demonstrated a 92% decrease in bacterial growth, thereby being employed for medical coatings. [76] For example, in order to increase the overall efficiency of dental resin, quaternary ammonium PEI nanoparticles were impregnated in it to battle the Streptococcus mutans bacteria, as well as other elements such as silica.[77]

5.3. Halogen attached to Nitrogen-Containing Compounds

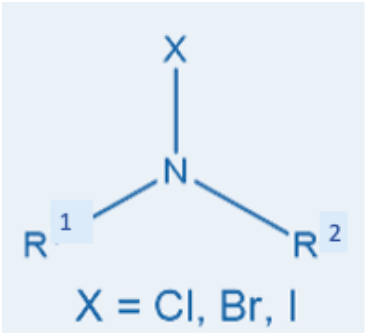


Figure 6: Structure of N-halamine

Affixed to the nitrogen atom, N-halamine compounds provide the stability and delayed release of free active halogen species into the environment by creating covalent nitrogen-halogen bonds.[59] In 1969, Kovacic and co-workers synthesised these compounds for the first time[58]. In these halogen compounds, although

chlorine is the most often utilised halogen, other halogens such as bromine and iodine have also been shown to perform (figure 6). Similarly, direct transportation of an active element to a biological target site is facilitated by the oxidising halogens. They also enhance dissociation of the active element into free halogen under aqueous circumstances. The free reactive halogens react with and hinder the growth of microorganisms.[60,62]

Both aqueous and dry environments are suitable for keeping N-halamines stable, which makes them preferred to inorganic halogens like bromine and chlorine. They are effective against a wide variety of bacteria, are environmentally acceptable, and are non-toxic to humans. To develop the N-halamine structure, N-halamine precursors are covalently attached to the target polymer and then halogenated to provide an antimicrobial N-halamine structure.[61,62] Usually, imidazolidine-2,4-dione (also known as hydantoin) and dimethylhydantoin N -halamines are used for this purpose. This is because they are renewable, allowing them to be charged repeatedly via interaction with chlorine or bromine donor chemicals like sodium hypochlorite, sodium dichlorocyanurate, sodium hypobromite or trichloroisocyanuric acid. After creating rechargeable N-halamine polymeric biocides with imidazolidin-4-one derivatives, they were treated with chlorine bleach which led them to portray antibacterial properties. This antibacterial substance proved to be more effective against E. coli.[78] To test the N-halamine biocide, it was applied on cotton fabric through layer-by-layer (LBL) method, thereafter, introducing household bleach to accomplish the introduction of biocidal activity. The coatings can withstand washes and ultraviolet radiation, killing S. aureus and E. coli bacteria fully in 15 minutes.[63] There are several uses for N-halogens, such as water purification, concrete tiles, paints, biocidal coatings and healthcare.[47] [64,6547,66]Recently, a LBL approach was used to fabricate an N-halamine-modified PGA multifilament. Due to the significant bactericidal activity of N-halamines, the resultant sutures were able to inactivate E. coli and S. aureus within 30 minutes of contact time.[79]

6. Applications of antimicrobial polymers

6.1. Food manufacturing

In today's society, food safety and the health of the customer are vital, and the food manufacturers have implemented a number of safety measures to protect consumers' health. Poly(butylene adipate), an aliphatic polyester that has been functionalized with a quaternary phosphonium group via an azide-alkyne reaction catalysed by copper, has been explored as a possible antimicrobial polymer for packaging material. This particular reaction has the significant advantage of being carried out under mild circumstances, preserving the polyester backbone's characteristics and chain length. The functionalized polyester was capable of greatly reducing all E. coli counts on the surface and in dispersion.[80]

Nisin is the only bacteriocin that has been authorised as a food preservative because of its positive properties of low toxicity and antibacterial activity[81]. Food packaging applications utilise a newly discovered method for making nisin-loaded chitosan/poly(L-lactic acid) antibacterial films. It is a spontaneous, endothermic process that gives rise to nisin in the finished film's diffusion process. The controlled release of nisin from the film demonstrates substantial antibacterial effect against S. aureus.[82] Antimicrobial packing films were created by combining low-density polyethylene and an ethylene vinyl acetate/potassium sorbate mix. A novel method for integrating preservatives into a polyolefin matrix was described, which used glycerol mono-oleate as a dispersant to provide homogeneous dispersions of the preservatives in the packing films, greatly increasing thermal stability with no viscosity decrease.[83]

6.2 Textile Industry

Textiles are favoured substrates for microbial growth under favourable circumstances, such as temperature and moisture. The availability of antimicrobial compounds has sparked the creation of new and previously unknown uses of textiles, many of which are entirely new to the textile industry. The antimicrobial textiles industry has shown considerable growth during the past two decades.

A modified sol-gel technique was employed to develop Ag:ZnO/chitosan nanocomposite coated

antimicrobial textiles. The synthesised hybrid nanocomposite demonstrated enhanced heat stability, whereas the chitosan and the hybrid nanocomposite had similar antibacterial characteristics. The effect was strengthened in the 50% polyester/50% cotton cotton/polyester hybrid textile mixture.[84] Microbe proliferation on textiles during usage and storage has a detrimental effect on both the wearer and the cloth. From branched PEI, a photosensitive hydrophobic polycationic salt was produced. The positive charges on the nucleophilic amino groups were increased by methylating them into quaternary ammonium groups, resulting in the photosensitive N-alkyl-PEI. After dipping the plain cotton cloth in a solution of the polymer in dichloroethylene, it was dried in the dark. UV light can be used to covalently attach the polymer to the cotton cloth. The coated-antimicrobial fabric's efficacy against E. coli and S. aureus was evaluated in phosphate buffered saline.[85]

6.3. Self-Sterilizing Surfaces

An increased risk of hospital-acquired infections can be contributed by the growth of harmful bacteria on medical device surfaces (catheters, implants, etc.). Bacterium start out by getting on the surface of the device, then germinate into a biofilm that is well-defended against antibiotics and the immune system of the host. To prevent this problem, antimicrobial metals (such as silver) that are permeable to the surrounding environment were utilized and the bacteria were to be killed by the leaching of these materials. Contaminated products containing antimicrobial agents have the potential of spreading into the environment and also have a limited shelf life since the antimicrobial ingredient quickly leaches out after the early stages of usage. Instead of solving this issue, additional options include the use of non-leaching biocide compounds or biocide molecules covalently linked to the glass, metals, or other materials.[86] Poly(4-vinyl-N-alkylpyridinium bromide) were bound to glass slides and used to test the antibacterial characteristics of covalently-bonded poly(4-vinyl-N-alkylpyridinium bromide) solutions. They applied an aqueous suspension of bacteria to the surface, allowed the solution to air-dry and then counted the number of living cells. Acylated amino glass slides were prepared via the method of cross-linking amino glass slides with acryl chloride and then copolymerizing it with 4-vinylpyridine. About 97% of the S. aureus cells put on a glass slide were destroyed when poly(4-vinylpyridine) was applied to the slide, followed by alkylation with hexyl bromide. The bacterial colonies decreased 100 times when comparing the hexyl-poly vinyl pyrrolidone slides to the original amino slides[87]While biofilm-tolerant, biofilm-preserving materials are desired for a range of applications, their creation is a tough task. Zwitter ionic poly(carboxybetaine methacrylate) (pCBMA) grafts on glass surfaces were examined for their long-term biofilm formation resistance in a study led by Cheng et al. According to the results, the pCBMA coating considerably limits the production of P. aeruginosa biofilm for up to 240 hours at 25°C, and for 64 hours at 37°C and further, suppresses the production of Pseudomonas putida biofilm for up to 192 hours at 30°C. CBMA coatings show promising potential for use in both biomedical and industrial applications, given their resistance to non-specific protein adsorption and the suppression of bacterial biofilms.[88]

Ye et al. and his colleagues devised a simple solvent-free grafting approach that resulted in self-sterilizing surfaces. They first made crosslinked poly(dimethylaminomethyl styrene-coethylene glycol diacrylate) (P(DMAMS-co-EGDA)) undergo vapour deposition, which was accompanied by in situ grafting of poly(dimethylaminomethyl styrene) (PDMAMS) from the P(DMAMS-co-EGDA) layer's reactive sites. Of all the various microorganisms, gram-positive Bacillus subtilis and gram-negative E. coli were 100% annihilated by PDMAMS/co-EGDA. In contrast to normal washing, the grafted coating kept its bactericidal effectiveness after being washed several times. [89] The fundamental limitation in the use of stainless steel implants in orthopaedic surgery is their susceptibility to microbial adherence. Tertbutyl aminoethyl methacrylate (TBAEMA) initiated polymerization with an initiator was conducted to form polyacrylate chains. The chain-grafting method of Ignatova et al. included the addition of polyacrylate chains to initiate a copolymerization of TBAEMA with acrylic acid (AA) monomers or mono-methyl ether of poly(ethylene oxide) methacrylate (PEOMA). Copolymerization of TBAEMA with either PEOMA or AA reduces fibrinogen adsorption by a ratio of

2–3. Poly(TBAEMA-co-AA) and Poly(TBAEMA-co-PEOMA) had 3 to 4 orders of magnitude less bacteria attached as compared to bare stainless steel, as shown by S. aureus adhesion tests. The phenomenon in orthopaedic surgery is enabled by a kind of polymer brush that may be chemisorbed onto stain-free steel surfaces.[90]

6.4. Surfactants

QACs found in polymers and surfactants have several uses, including shampoo, contact lens solutions hair colour and hair spray. A team of researchers led by Lenoir synthesised antimicrobial surfactants of PEB poly(ethylene-butylene) -b-PDMAEMA from diblock copolymers (PDB-b-PDMAEMA) by quaternizing the amino groups of the poly(ethylene-butylene)poly(2-(dimethylamino)ethyl methacrylate) (PEB-b-PDMAEMA) with octylbromide, whose activity has been shown to be equivalent to that of benzalkonium chloride.[91]It has also been explored using chitosan and its derivatives. In order to stabilise the emulsion, the adsorbed surfactant interacts with chitosan to form interfacial complexes. Electrostatic and steric repulsion between droplets is greatly increased by the double-layered highly charged surfaces, which reduces the likelihood of the droplets to coalesce. In this study, the creation of stable oil-in-water emulsions was shown to be possible at ideal circumstances, which include the use of surfactant-chitosan layers and droplets enclosed in surfactant-chitosan membranes. Using surfactant-chitosan layers to stabilise the emulsion allows for resilience to variations in ionic strength, temperature and pH. Ionic strength fluctuations, heat processing and freezing provide no challenge for emulsions stabilised using surfactant-chitosan layers.[92]However, the replacement was moderate, therefore the micelle became less stable. A strategy to make chitosan-based amphiphilic compounds with more densely packed hydrophobic substituents was found by reductive N-alkylation of chitosan with 3- O -dodecyl- D -glucose.[92]

An unusual sulfating agent ($N(SO_3Na)_3$) made from sodium bisulfite ($NaHS0_3$) and sodium nitrite ($NaN0_2$) was used to treat quaternary ammonium chitosan (which is also known as sodium alkyltrimethylammonium chloride) in a homogeneous aqueous environment to make quaternary ammonium chitosan sulphates of varying degrees of substitution. The anticoagulant activity was tested with an activated partial thromboplastin time assay, a prothrombin and thrombin time assay. In contrast to previous findings, this study found that quaternary ammonium chitosan sulphates provided an additional twelve to thirty percent more activated partial thromboplastin time and thrombin time. They showed that increasing the number of sulphate groups attached to the quaternary ammonium chitosan improved the anticoagulant effect. A statistical association was discovered between the anticoagulant properties of the compound and its concentration, substitution and molecular weight.[93]

6.5. Water Purification

Water-soluble disinfectants (or Chlorine) are used to sterilise water. The drawback of residual toxicity, in spite of proper concentrations of the agents being administered, is a factor when it comes to using soluble disinfectants.[78,94]Residues from these disinfectants and antibacterial chemicals cannot be avoided, and as a result, far worse side effects arise. Additionally, since they are already in the environment's food chain, their leftovers can be more widely distributed. While chlorinated organic compounds are unlikely to react with water to generate trihalomethane mimics that are carcinogenic, their utilisation should be avoided because of this. However, insoluble chemicals can be used to dissolve bacteria out of water.[13,95]Another method is to use insoluble contact disinfectants that kill or eradicate the target bacteria only by touching them. The adaptability and capacity to be rendered insoluble in water makes polymeric disinfectants well-suited for use in fibre disinfectants, surface coatings and hand-held water filters. Over the last few decades, several researchers have developed insoluble polymeric disinfectants for water treatment. Tyagi et al. developed a water-insoluble matrix using iodine-containing polymers (methyl methacrylate-co-N-vinyl-2-pyrrolidone).[96]This copolymer was made using a 1:1 (volume ratio) ratio of vinyl-2-pyrrolidone and methyl methacrylate (MMA), along with an AIBN (volume ratio) initiator at 0.5 percent (volume ratio) was present. Sieving was done to separate particles of 250 to 500 micrometres in size, and the material was treated with molecular resublimed iodine at 37 °C for 24 hours to

get the iodinated copolymer. Specially generated cartilage was used to evaluate this copolymer for its antibacterial characteristics. Some concentrations of microbial cells containing S. aureus, Candida spp. and E. coli were injected into the water reservoir. There were microbes present in the water at evenly spaced intervals. Grafting 4-vinylpyridine (4-VP) onto polypropylene (PP) nonwoven cloths and then quaternizing with a halohydrocarbon such as butyl bromide, benzyl bromide, benzyl chloride, ethyl bromide, hexadecyl bromide was carried out to synthesise nonwoven cloths treated with modified PP. The modified PP nonwoven cloths demonstrated that they were capable of trapping bacterial cells. Benzyl bromide quaternization was shown to be the most effective in eliminating E. coli.[95]

After being compared to the traditional and more conventional N-halamine molecules, the cyclic N-halamines displayed extraordinary characteristics, including longer-term stability, higher biocidal activity and the ability to refill when the efficacy has been exhausted. To produce crosslinked copolymers, copolymerization was carried out between vinylbenzyl chloride (which contained divinylbenzene as a crosslinker) and 2-chloromethylvinyl ether or methyl methacrylate, either of which also contained divinylbenzene. This type of quaternization was employed to further change the crosslinked copolymers by using triethylamine and triphenylphosphine. The antibacterial activity of the modified copolymers were then established against a variety of bacteria (C. albicans, S. aureus, B. subtilis, E. coli, F. oxysporum, and A. flavus).[97]

6.6. Healthcare and Medicine: Drug Delivery, Coatings, Dental Care

Most of the active drugs that have significant effects on the body's physiology are small-molecule compounds that rapidly cross all cell types and are regularly excreted from the body. Adverse side effects emerge when specificity is impaired, thus large and repeated dosages are necessary to maintain therapeutic action and when this occurs, the drugs tend to display a broad range of side effects. Pharmaceuticals that are embedded in macromolecular carriers, such as antibacterial medicines, have an effect on their body’s rate of excretion and permit a longer, controlled release. [98]Several controlled delivery systems increase the therapeutic effectiveness and safety of pharmaceuticals by providing drugs at the set rate specified by the physiological environment.[99] Using well-characterized medications covalently bonded to a macromolecular biodegradable or soluble framework, new polymeric pharmaceuticals can be synthesised. Unlike the traditional physical combination-based delivery method, which requires the polymeric drug to have pharmacological effect on its own while functioning as a carrier for the pharmaceutical component, the “polymeric drug" has the benefit of working in this way.

Polymeric medicines with strong antimicrobial activity have the potential to carry high local charge density because of the antimicrobial polymers' specific capacity to transport the active groups with high local charge density. An antimicrobial wound dressing was created by blending poly(ethylene-co-vinyl acetate) and poly(lactic acid)[100]. Quaternary ammonium cellulose derivatives are of special interest to the cosmetics industry because of their use as conditioners for skin and hair care products.[101] Poly(methyl methacrylate) bead-mediated gentamicin treatment offers a better concentration of gentamicin at the infection site than systemic treatment.[102] It was determined that the implant gave a high amount of antibiotics. For a period of five years, the beads stayed in situ. Gentamicin release tests, which had been in place for five years, found a residual amount of antibiotic that still remained in the device. Using gentamicin implants to treat local infections in sheep confirmed that the technology may be utilised in veterinary patients. Cross-linked high amylase starch (with varying amounts of antibiotic ciprofloxacin) was implanted into mice.[103]Local therapy and prevention of bone and soft tissue infections are supported by ciprofloxacin-containing implants with substantial promise. HEMA monomer was utilised to generate antimicrobial sutures made from PP monofilament.[96]Poly(HEMA) hydrogel sutures were used to immobilise an antibacterial drug called 8-hydroxy quinoline. It was discovered that the modified sutures have antibacterial properties against S. aureus. Dental restorative materials have recently been seen as having questionable therapeutic efficacy[104]. Research was conducted on several

occasions to try to enhance the bactericidal properties of the resin matrix phase or filler[105]. First, they explained the procedure to produce 1,2-methacryloyloxy-dodecylpyridinium bromide (MDPB), an antibacterial monomer. To create the monomer (MDPB), quaternary ammonium dodecylpyridinium was reacted with methacryloyl chloride, after which additional monomers were copolymerized to make the resin matrix. This combination of MDPB-based resin composites reduced dental plaque development on the surface and was still effective after being stored in a moist environment.[105]

Polyacrylate derivatives are among the most studied due to their low toxicity, ease of availability, simplicity of processing and wide range of functionalized monomers. The process of polymerizing polydimethylsiloxanes with 2-hydroxyethylacrylate/acrylic acid and the antibacterial surfactant cetyltrimethylammonium chloride lead to nanophase amphiphilic coatings that are covalently bound to glass and loaded with the antibacterial surfactant (CTAC). These coatings acted like contact-active surfaces that kill microorganisms on their surface and had activity similar to CTAC-loaded surfaces.

Researchers Liang et al. studied several quaternary ammonium salt siloxane copolymers and N-halamine siloxane's biocidal coating capabilities. To test the antimicrobial properties of the copolymers, the cotton swatches were coated along with the polymers and then exposed to E. coli and S. aureus. Only N-halamine functional groups are effective in fighting S. aureus, although N-halamine units are just as potent in stopping the growth of E. coli.

Many decades of scientific and clinical study have proven a relation between an increased risk of developing coronary heart disease and higher blood cholesterol levels. People who have this form of coronary heart disease are found to have a higher level of LDL (low-density lipoprotein) or triglyceride-containing lipoproteins, in particular, LDL-bound cholesterol. Hyperlipoproteinemia is considered to be a variant of hyperlipoproteinemia. When it comes to hyperlipoproteinemias, the first-line therapy is bile acid sequestrants (cholestyramine and colesevelam hydrochloride). Bile acid sequestrants such as cholestyramine and colesevelam hydrochloride are FDA-approved treatments for elevated plasma cholesterol levels. Bile acid sequestrants encapsulate bile acids in the small intestine lumen and perform as anion exchange resins. When the microsomal hydroxylase responsible for the rate-determining step in the conversion of cholesterol to bile acids is inhibited, it results in an increase in hepatic bile acid synthesis. The most proven and safest strategy for people with higher levels of low-density lipoprotein cholesterol is the use of bile acid sequestrants as these drugs are not absorbed by the intestines. Bile acid sequestrant can sequester negatively charged bile acids. They do not enter the bloodstream and are instead eliminated from the body via the digestive tract after binding with bile.

The introduction of a number of amino-functionalized polymers that are based on poly(epichlorohydrin) and poly(2-ehloroethylvinyl ether) resulted in the development of polyether-based amine-functional polymers. By employing hamsters as animal models, the amine functional polyethers showed impressive bile acid sequestration capabilities in vivo, showing the potential for a novel way to treating hypercholesterolemia. A few of these polymers function better than the commercial bile acid sequestrants. These innovative polyammonium gels may have the potential to help reduce cholesterol levels.

Dental composites were synthesised with quaternary ammonium PEI nanoparticles and commercially available composite resins were mixed with a synthetic polymer to create the dental composite. S. mutants was used to test for antimicrobial properties. Using S. variations in antimicrobial studies, researchers found that PEI nanoparticles were active at a concentration of as little as 1 percent against the bacteria that they were tested against. Without losing the original mechanical capabilities, a PEI-based nanoparticle composite resin kept its antibacterial capabilities for one month. Reducing the establishment of biofilms and secondary caries in composite resin restorations with the incorporation of antibacterial nanoparticles is a possible benefit.[106]

6.7. Stimuli-sensitive Coatings

Biomaterial coatings that release antimicrobials for orthopaedic joint prosthesis and central venous catheters are in high demand. Antimicrobial drugs placed into catheters often exhibit a quick release profile and reach efficacious concentrations within a few days after being implanted. This results in a fastened depletion of antimicrobial compounds, making them inaccessible for subsequent stages that are more susceptible to infection by the microbes. Taking this into careful consideration, temperature-sensitive antimicrobial releasing polymers were designed and programmed to release antimicrobial compounds on demand. Copolymers of n-butyl (meth)acrylate and styrene were employed as thermosensitive polymers containing chlorhexidine. When the temperature is raised above the glass transition temperature of this copolymer, the drug is released. [107]

6.8. Antimicrobial polymers to circumvent antibiotic resistance

Although many antimicrobial polymers exhibit superior bactericidal efficacy against a broad range of bacteria, they eventually succumb to microbial resistance. Conscious attempts are being made to overcome this limitation, for instance, a novel class of cationic, biodegradable, antimicrobial polycarbonates comprising hexyl and propyl side chains were quaternized with various nitrogen-containing heterocycles, such as imidazoles, pyridines etc. These polymers exhibit a broad spectrum of antimicrobial action against Candida albicans, Staphylococcus aureus, E. coli and P. aeruginosa. They exhibited a high selectivity for microorganisms over mammalian (rat) red blood cells in the hemolysis testing. These polymers work by membrane-lytic processes, which eliminates the possibility of resistance emergence. To further prevent the spread of antibiotic resistance, a naturally functionalized bacterial polyhydroxyalkanoate (PHACOS) was developed that inhibits the growth of methicillin-resistant S. aureus (MRSA) both in vivo and in vitro. Functionalized side chains containing thio-ester groups are thought to be responsible for its action. S. aureus biofilm formation was significantly reduced (3.2-fold) when PHACOS was used instead of the control poly(ethylene terephthalate) and poly(3-hydroxyoctanoate-co-hydroxyhexanoate).
However, no significant reduction in bacterial adhesion is found. Additionally, PHACOS possesses active surface killing effects when in contact with the bacteria.[108,109]

Table 1 lists some of the antimicrobial polymers and the respective target microorganisms.

Table 1: Table summarizing the antimicrobial polymer type and its target.

Polymer	Pathogen type	Reference
Pyridium-type polymers	Gram positive and Gram negative bacteria, yeast, fungi	[110]
Copolymers of Phenolic N-Vinylimidazole and Alkylated Phenacyl Methacrylate	Bacteria, yeast, fungi	[41]
Benzalkonium chloride, Cetrimonium chloride, Stearalkonium chloride	Gram positive and Gram negative bacteria (E. coli)	[28]
Quaternary ammonium compounds	E. coli	[111]
Poly(2-methyl oxazoline)	Micro-organisms like Streptococcus mutans	[38]
Block and Statistical Polysiloxanes substituted with quaternary ammonium groups	E. coli, S. aureus	[45]
Polysiloxanes containing quaternary ammonium groups, Polysiloxanes containing pendant	Enterococcus hirae, Proteus vulgaris, E. coli, and P. aeruginosa.	[46]

N,N -dialkylimidazolium		
Poly-ε-lysine	Ergot fungi species and Streptomycetaceae	[48]
Chitosan–pectin–TiO 2	E. coli, S. aureus	[67]
Guanidinium salt and diamine	Gram-positive and Gram-negative bacteria, Antibiotic-resistant varieties	[70]
N-alkylated PEI	E. coli, S. aureus	[73]
Substituted PEI	Candida albicans	[76]
Quaternary ammonium PEI nanoparticles	Streptococcus mutans, Silica	[77]
N-halamine with Imidazolidin-4-one derivatives	E.coli	[78]
N-halamines	E. coli, S. aureus	[112]
Poly-ε-lysine	Bacillus coagulans, Bacillus stearothermophilus, Bacillus subtilis	[113]
N-halamine-modified PGA	E. coli, S. aureus	[79]
Poly(butylene adipate)	E. coli	[80]
Nisin-loaded chitosan/poly(L-lactic acid)	S. aureus	[83]
N-alkyl-polyethylenimine in dichloroethylene	E. coli, S. aureus	[85]
Acryl chloride copolymerized with 4-vinylpyridine	S. aureus	[87]
Poly(carboxybetaine methacrylate)/pCBMA	P. aeruginosa	[88]
Poly(dimethylamino methyl styrene-coethylene glycol diacrylate)/ P(DMAMS-co-EGDA)	Gram-negative E. coli, Gram-positive Bacillus subtilis	[89]
Poly(TBAEMA-co-PEOMA) and Poly(TBAEMA-co-AA)	S. aureus	[90]
Methyl methacrylate-co-N-vinyl-2-pyrrolidone	E. coli, Candida spp., S. aureus	[96]
Vinylbenzyl chloride with 2-chloromethylvinyl ether or methyl methacrylate	S. aureus, E. coli, B. subtilis, A. flavus, F. oxysporum, C. albicans	[97]
Polypropylene with Benzyl bromide	E. coli	[95]
Poly(HEMA) hydrogel	S. aureus	[104]

7. Role of Antimicrobial Polymers in COVID-19 Pandemic

Antimicrobial polymers' usage in the development of critical and essential medical equipment also shed light on their role during the COVID-19 pandemic.[114] Due to the porous nature of 3D printed plastic components (6-8 m)[115] and the difficulties associated with sterilisation [116], using additive manufacturing to create critical medical equipment, particularly those exposed to high microbial loads, can be more problematic.[116] However, by adopting parameter settings that result in fused extruded layers and utilising commercially available antimicrobial materials [117], molecules as small as 0.282 nm may be blocked, which is far smaller than viruses such as coronaviruses (0.03+ 0.01 μm).[118] The recent discovery of thermoplastic blends containing antibacterial copper nanocomposites enables the production of antimicrobial thermoplastics in a practical and simple manner. According to a recent study, a commercially available antimicrobial additive manufacturing polymer (Copper3D PLACTIVETM 1% copper nanoparticles composite, Santiago, Chile) was effective against

methicillin-resistant E. coli and Staphylococcus aureus at a concentration of up to 99.99 percent.[117], Thus, the unusual need for biocidal polymers during a pandemic, along with the ease of access to additive printing ingredients and equipments, may drive the use of this technology to revolutionise the manufacturing of life-saving medical devices when the supply chain is insufficient. COVID-19 patients are at risk of developing pneumonia-like symptoms, like difficulty in breathing and an adequate supply of personal protective equipment and supportive care is the need of the hour.[119] A combination of antimicrobial polymers can be used to fabricate prototypes of critical medical equipment in order to expedite the production of the final device, such as ventilator connections, or as a finished product, that is, face masks. Additionally, sharing a single ventilator and recycling connections from other medical equipment may result in infection issues and air leakage. Antimicrobial polymers can aid in prototyping and clinical testing these connections with the objective of accelerating final product production using standard manufacturing methods (injection moulding). The connections' final result may successfully improve the capacity of a single machine to breathe four simulated COVID-19 respiratory failure patients. Previous research indicates that the high viral load retained in surgical masks may act as a source of viral transmission to both the patients as well as the health care worker using the mask. This can occur when healthcare professionals dispose of the mask improperly or touch their mask and then fail to wash their hands correctly. Thus, by incorporating antimicrobial polymers with additive manufacturing to make reusable face masks, the viral load remaining on the mask may be significantly reduced, protecting end users from infection during prolonged mask use. [120]
Research on antimicrobial polymeric materials is expanding, and it will continue to do so in the years to come. Despite this, researchers should take extra efforts to use standardised methodologies and microbe strains when they conduct their experiments in order to collect more significant and precise data that will help us to find out the mechanism through which the microorganisms function and how we might avoid or combat them.
The FDA has approved the use of benzalkonium chloride (BAC) in the formulation of healthcare worker hand massages in conjunction with isopropanol and ethanol. Recent study indicates, however, that BAC has a less consistent anti-coronavirus effect than any of the alcohols.[121] Apart from the usage of BAC as a hand sanitizer, Kampf and colleagues proved that it was ineffective at lowering the viral loading of HCoV (endemic human coronavirus) after 1 minute exposure at an active concentration of 0.04 percent w/v on a steel surface. This, together with the suspension assay result, has generated controversy and alarm, as QACs, notably BAC, are active ingredients in a variety of household disinfection wipes and sprays, as well as additives to a variety of soaps and nonalcohol-based hand sanitizers. This is because they have the potential to eliminate surface bacteria and common viruses such as influenza by disrupting their phospholipid membrane [122–127]. Pratelli's Zoonoses and Public Health research tested the efficacy of QACs against Canine Coronavirus (CCoV), another member of the Coronaviridae family. While these findings pertain to CCoV, they are related to SARS-CoV-2 and should aid in establishing the efficacy of QACs.[128,129]

The SARS-CoV-2 consists of negatively charged RNA wrapped within a positively charged protein capsid that is further covered with material generated from positive zeta-potential host cell membranes[130] According to Hathout and Kassem, positively charged chitosan polymers could be used to create positive, large surface area nanofibres. Following that, these nanofibres might be incorporated into textiles to provide protective apparel for healthcare professionals.[131–133] Electrostatic attraction between the chitosan nanofibres and the positively charged virus particles would result in a reduction in the viral load on the protective garments.[133,134] N-(2-hydroxypropyl)-3-trimethylammonium chitosan chloride, with an average molecular weight of 250 kDa and a degree of substitution ranging from 50% to 80%, exhibits substantial interaction with the recombinant HCoV S-protein ectodomain (human coronavirus, a SARS-CoV-2 analogue). This interaction stops the S-protein from binding to the host cell, hence preventing viral infection[135,136] N-palmitoyl-N-monomethyl-N,N-dimethyl-N,N-trimethyl-6-O-glycolchitosan at a dose of 10–100 g/ml was reported to significantly inhibit SARS-CoV-2

infection in A549ACE2+ human lung cells and Vero E6 cells (kidney epithelial cells from an African green monkey (Chlorocebus sp.) by 3–4 log values. This finding is explained by the virus's electrostatic interaction, which prevents the virus from infecting human airway epithelial cells. [137,138]

Similarly, N-halamine compounds like N-halamine 1-chloro-2,2,5,5-tetramethyl-4-imidazolidinone (MC) was employed to modify the PP nonwoven textiles by a simple soaking procedure and demonstrated complete inactivation (6 $\log_{10}$) of S. aureus and E. coli. [139]A similar soaking, padding and drying procedure was employed to coat PET fabric with a 5% (w/w) terpolymer, poly(hydantoinyl acrylamide-co-glycidyl methacrylate-co-2-(methacryloyloxy)ethyl trimethylammonium chloride). The material was halogenated with a 10% (w/w) Clorox solution (bleach) and demonstrated complete reduction of S. aureus and E. coli cells (6 $\log_{10}$ reduction) within two minutes of contact time [140]. In another study, specific N-halamine precursors like as methacrylamide and acrylamide were graft copolymerized to PP and further transformed into fibres via extrusion. Following that, the fibres were halogenated by immersing them in chlorine bleach, which resulted in a 100 percent reduction of E. coli within 30 minutes.[140141] N-halamine additives [chlorinated 5,5-dimethyl hydantoin (CDMH), chlorinated 2,2,5,5-tetramethyl-imidozalidin-4-one (CTMIO) and chlorinated 3-dodecyl-5,5-dimethyl hydantoin (CDDMH)] were also incorporated with nylon-6 and demonstrated to achieve complete E. coli and S. aureus reductions.[142]Unlike physical coating approaches, electrospinning's covalent connection and in situ inclusion exclude the chance of N-halamine escaping from the fabric surface. Despite the fact that very little study has been published on the leaching of N-halamine modified textiles into water, the direct release of N-halamine from fabric or face mask surfaces has not been explored to assess its effect on the skin. Due to the fact that these antimicrobial components are frequently deposited on the intermediary filtering layers of the face mask, direct contact with the skin is unusual. Despite the fact that studies have demonstrated that textiles including N-halamine have a high level of antibacterial activity, there is no published research on the use of this chemical in the development of antimicrobial face masks. Bacterial and viral filtration efficacy tests would demonstrate the practical utility of a face mask containing N-halamine during pandemics like COVID-19. [140–144]

Sanitised® T 99-19 (a commercially available QAC) was deposited on needled nonwoven polyester and melt-blown nonwoven PP and tested for the antibacterial effect. In comparison to melt-blown nonwoven polypropylene, needled nonwoven polyester demonstrates enhanced antibacterial activity against E. coli, S. aureus, Candida albicans (C. albicans), and Aspergillus niger due to the active component's increased migration to the fibre surface. [143,145,146] Perlite (volcanic glass) carriers have been shown in tests to enhance the hydrophilicity, antibacterial activity and adaptability of PP to bind with a variety of chemical agents. Alkylammonium microbicides (QAC compound) incorporated on perlite and bentonite (aluminosilicate base carriers), are referred to as bio-perlite and bio-bentonite, respectively, and were used to endow PP fibres with biocidal characteristics during melt blowing. Melt-blown PP containing 15% bio-perlite showed 96.8 percent bacterial filtration efficacy against E. coli and 74.1 percent against S. aureus, respectively.[147] A QAC-based Goldshield-5 solution (GS5, 1%) was sprayed onto a three-layered surgical mask and upon exposure for 60 minutes, there was significant reduction in Acinetobacter baumannii, Enterococcus faecalis, and S. aureus colonies.[148] However, spray coating would not guarantee complete penetration of the antimicrobial element into cracks or shadowed areas, demanding additional research into coating efficiency and longevity. Additionally, several QAC compounds are corrosive and have been linked to health concerns such as occupational asthma and skin rashes.[148]As a result, a comprehensive evaluation of biocompatibility is recommended before widespread use of QAC incorporated masks during a pandemic. Another study improved the antiviral activity of a commercial face mask by covering the replaceable cellulose filter layer with PEI. A novel filtration setup was created and authorised for the purpose of determining the efficiency of the filtering against the H5N2 virus. Two layers of these PEI modified nonwoven cellulosic fibre filters were found to be effective at

blocking the droplet/air-borne H5N2 virus. However, by employing antiviral tests, the inquiry might be expanded to determine whether the PEI-treated viruses are killed. After five hours of use under typical breathing conditions, an air diffusion analysis demonstrated that the PEI incorporated filter layer remained intact [131,148] Thus, there has been instances where masks incorporating these antimicrobial polymers with active moieties like QACs, N-halamine compounds, PEI etc. had been proved to be superior to conventional face masks. The current COVID-19 pandemic has definitely resulted in an impetus to the research related to the use of antimicrobial polymers in masks and personal protective equipments. However, a detailed analysis related to the benefits and drawbacks of their use and disposal should be carried out. Further, establishing standardised methodology and protocols for testing and comparing antimicrobial activities is also vital before the widespread use of antimicrobial masks and protective clothing.

8. Limitations of Current Systems and Need for Adoption of New Methods

Novel non-toxic macromolecular disinfectants with broad antimicrobial activity against a variety of bacteria, including Mycobacterium tuberculosis are still needed to be developed. They should be effective in all kinds of conditions such as alkaline or ionic solutions and aid in the prevention of microbial contamination in public places. Recent years have seen the synthesis of moderately hydrophobic polymer structures connected to primary secondary or tertiary protonated amine groups with relatively high antimicrobial activity, as well as the development of macromolecular systems that are functionalized or quaternized with biologically active groups. These structures exhibit relatively high antimicrobial activity. It is worth noting that several of these polymers' quaternary equivalents exhibit no or very little antibacterial action. Unlike quaternary active polymers, the new polymers' antibacterial activity appears to be attributable to the presence of hydrophilic protonated amine groups in combination with a sufficiently hydrophobic linked structure. Notably, in non-quaternary polymers, shifting the balance between hydrophobicity and hydrophilicity in favour of hydrophilicity dramatically reduces toxicity and enhances selectivity. These properties make non-quaternary bioactive polymers particularly attractive for medical applications requiring biocompatibility. Numerous polymers operate as active membrane agents. Data has been collected using polymer-induced leakage from model liposomes that support the mechanism of membrane disruption caused by the antimicrobial activity of certain non-quaternary amine-group and quaternary biocidal polymers.

A better understanding of the biological characteristics of mammalian cells and pathogens is critical and extremely useful, such as redox state, pH and cell membrane compositions, in order to facilitate the development of highly efficient and safe antimicrobial polymers. Meanwhile, the aim remains to discover novel antimicrobial microbes based on current knowledge. To investigate the differential distribution of antimicrobial units such as peptides, amines and other active species on pathogen and human CM, it would be advantageous to synthesise polymers with an optimal spatial distribution of antimicrobial units. While it has been suggested that the surface charge density of polymers exceeds a critical value and is an important factor in determining its antimicrobial power, careful matching of positive loaded polymer units to negative loaded polymer units on pathogenic CMs is expected to significantly enhance the efficacy of antimicrobial polymers. Nonetheless, the vast pool of known gene delivery polymers, the most of which are polyamines, might be explored for antibacterial applications.

Despite significant scientific progress in recent years, much work remains to be done to address critical challenges such as increasing the long-term stability of antimicrobial polymers, expanding the range of microbes that each material can successfully eliminate and increasing antimicrobial activity. The majority of research on natural polymers has focused on modifying chitosan. It will be of paramount importance to understand the action mechanisms of the polymers that arise from the selective modification of this natural polymer. However, the limits of this method are significant due to the lack of control over the polymer backbone topologies present in all natural polymers. Synthetic polymers may be an appropriate substitute or option in this case.

Another interesting topic is the use of compounds that imitate natural peptides as antimicrobial peptide substitutes. The discovery of novel antimicrobial peptide-like structures will pave the way for additional significant advances in their use as functionalization residues. One more technique involves the use of biocide-containing compounds that are capable of being liberated from the polymer matrix but the limits connected with the resistance development caused when antibiotic compounds release nanoparticles may restrict the future potential of these techniques. Recently, antimicrobial photodynamic inactivation emerged as a potentially viable technique due to its great efficacy, minimal chance of developing resistance, and ability to destroy a broad range of pathogens. One should anticipate tremendous advancements in this strategy, fuelled by the inherent advantages over alternative tactics. It will be critical to increase the systems' efficiency by the development of new photosynthesizers with increased performance at a reasonable cost.

9. Conclusion and Future Aspects

Each year, around 100,000 people die from microbial infections. Antibiotics given incorrectly in viral illnesses, inadequate treatment procedures, systems and the widespread use of antibiotics in animal feedstuff, makes the crisis likely to increase in the near future. Widespread infection will inevitably return to becoming the primary cause of early mortality. This global initiative to produce viable medical therapies is critically dependent on antimicrobial polymers. Since a variety of modified composite polymers have been produced to fulfil the surface requirements, they have increased the adaptability of these polymers, allowing them to be used in a variety of fields. On the other hand, they have also created vast prospects for future study. However, it is critical to develop an innocuous substance that is non-toxic, environmentally friendly, has a broad spectrum of antimicrobial activity, a long duration of action, and is even reusable to continue process.

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