Review Article

Polymer Based Antimicrobial Coatings as Potential Biomaterial: A Review

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ABSTRACT

Antimicrobial polymers are class of polymers with antimicrobial activity. The control of microbial infection is a very important issue in modern society. Increasing hygiene standards and the threat of infectious disease demand materials with surfaces that inhibit the survival and proliferation of microbes. The antimicrobial polymers are produced by attaching or inserting an active antimicrobial agent onto polymer backbone via an alkyl or acetyl linker. These are the upcoming new class of disinfectants which can be used even as an alternative to antibiotics in some cases. The treatment of microbial infections becomes more and more difficult because the number of resistant microbial strains as well as that of antibiotic-immune patients grows a lot faster than the number of useable antibiotics. The use of antimicrobial polymers offers promise for enhancing the efficacy of some existing antimicrobial agents and minimizing the environmental problems accompanying conventional antimicrobial agents by reducing the residual toxicity of the agents, increasing their selectivity and prolonging the lifetime of the antimicrobial agents. Antimicrobials gain interest from both academic research and industry due to their potential to provide quality and safety benefits to many materials. The present review considers the factors affecting the antimicrobial activity, synthetic methods of preparation and activities of antimicrobial polymers, application of antimicrobial polymers in different fields and future prospects.

Keywords: Polymers, antimicrobial, coatings, micro-organism.

INTRODUCTION

The use of coating with antimicrobial capabilities is an effective strategy for reducing microbial numbers on healthcare surfaces. Antimicrobials agents are materials, capable of killing pathogenic microorganisms[1]. Low molecular weight antimicrobials agents have been widely used for the sterilization of water as antimicrobials drugs (antibiotics), as food preservatives and for soil sterilization[2]. However, these agents have many disadvantages, such as short-term antimicrobials ability and aretoxic to the environment. Therefore, investigation of polymeric antimicrobial agents represents a new and important direction that has developed in the field of antimicrobial agents[3,4]. The ideal antimicrobial polymer should fulfill the following major requirement: a) biocidal to a broad spectrum of pathogenic microorganism. b) Long term (preferably permanently) active. c) Stable (should not decompose to toxic product) d) environment friendly e) easily and inexpensively synthesized f) can be re-generated upon loss of activity g) not soluble in water for many application[5].

Because the polymeric materials which are widely used in food packaging, textiles and medical devices, can be easily colonized by bacteria or other microorganisms capable of causing severe transmitted diseases, the use of synthetic polymers containing biocidal compound has steadily increased. An area of polymer research that presents great current interest, yet has received insufficient attention is that of the development of polymers with antimicrobial activities, generally known as polymeric biocides. Antimicrobials polymers are commonly obtained either by synthesizing monomeric biocide moieties and then polymerizing subsequently or copolymerizing with another monomer[6-8].

The low surface energy chemistry minimizes microbial attachment while antimicrobial additives kill bacteria or inhibit their growth (Figure 1). Moreover, these coating can be engineered to release the active agents over a prolonged time period. Antimicrobial agent can be incorporated into surface coatings by advanced deposition techniques such as vapor deposition, ion implantation, sputtering and electrochemical deposition from solution[9].

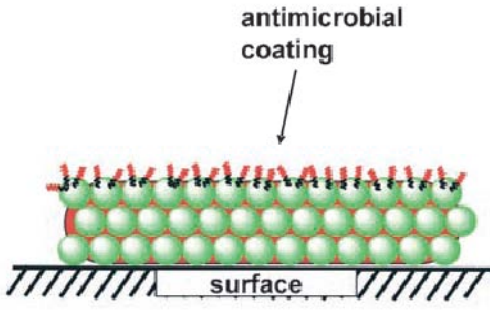

Figure 1: Illustration of antimicrobial coating.

However, the technologies can be costly, not easily applicable to large complex items, may not adhere sufficiently to the substrate without previous surface treatment and may lack transparency after application. Furthermore, the mechanism of action of antimicrobial system is based on either the slow release of toxic

antibacterial agents or contact killing (no release of any active agent)[10,11]. Surface modification that effectively kills microbes on contact without releasing a biocide represents a modern approach towards permanently sterile materials. Contact active surface modification can be achieved through the chemical grafting of antimicrobial polymers such as N-alkylated poly (4-vinylpyridine) quarternizedpolyethylenimine[12] and quaternary derivatives of acrylic acid[13] to numerous common materials such as glass, cellulose and plastics[14]. In these systems, the polymers are not released and are effective against multi-resistant bacteria[15]. It is well known that immobilized quarternary ammonium compound (if they have sufficiently long hydrophobic tails) possess antimicrobial properties by interacting with and disrupting bacterial cell membranes[16-18]. When the bacterial cells are in a contact with such surfaces, long hydrophobic chains presumably penetrate and disrupt the cell membranes. In this review, we describe the recent developments in the field of antimicrobial polymers.

FACTORS AFFECTING THE ANTIMICROBIAL ACTIVITY OF POLYMER

Many factors have been found to affect the antimicrobial efficacy of these materials, efficacy of these materials, such as molecular weight of the polymer, spacer length between active site and the backbone hydrophobic tail length attached to the active site, hydrophilic-hydrophobic balance of the material and nature of counterions[19-20]. Major factors are summarized below:

Effect of molecular weight

The molecular weight is an important factor in the determination of antimicrobial properties. A molecular weight region between $5x10^4$ and $1.2x10^5$ Da was optimal for the required action. When the molecular weight was lower than $5x10^4$ Da, the antimicrobial activity decreased sharply with the increase of the molecular weight of the polymer over $1.2x10^5$ Da. Again the bactericidal properties increase monotonically with molecular weight up to $7.7x10^4$. Polycationic biocides with pendant phosphonium salt have been synthesized by Ikeda & co-workers[21, 22-25]. They concluded that the antimicrobial activity of polymer is increased in the order of increasing molecular weight. Panarin and co-workers[26] reported that the bacteriostatic properties of copolymers of vinylamine, methylacrylate and N-vinyl pyrrolidone with pendent quaternary ammonium groups had no molecular weight dependence. To explain this property, one needs to take into consideration the bacteria structure. Depending upon the cell wall structure, bacteria can be divided into two classes; gram (+)ve (e.g. *S.aureus*) and gram (-)ve (e.g. *E.coli*). Gram (+)ve bacteria tend to have loose cell wall, while gram (-)ve bacteria have an outer membrane structure in the cell wall forming an additional barrier for foreign molecules. It was investigated that molecules with molecular weight up to $5x10^4$ to $9X10^4$ Da creates no problems for diffusing across the cell wall of the gram (+)ve bacterium. Although for gram (+)ve bacteria, the diffusion to the cell membrane is even more complicated due to presence of an outer membrane.

Counterion effect

The antimicrobial activity was found to be affected by the structure of the counter anion. The counter anion, which forms a tight ion-pair with phosphonium ion showed less activity while it was high for those facilitating ionic dissociation to free ions. The antimicrobial properties were in the order of chloride>tetrafluoride >perchlorate>hexafluorophosphate, which could be correlated with the solubility product of the polymers. It is well known that the bacterial cell surface is usually negatively charged. The cytoplasmic membrane is semi-permeable membrane and is composed of a phospholipid bilayer with some functional proteins. The cationic hydrophilic-hydrophobic property of long tailed cationic structure (e.g QACs) provides a good surfactant character resulting in a high binding affinity for bacterial cells[27-28]. The step-by step action of the cationic biocides may be considered as follows[29]: a) adsorption onto the bacterial cell surface b) diffusion through the cell wall c) adsorption onto the cytoplasmic membrane d) disruption of the cytoplasmic membrane e) leakage of the cytoplasmic constituents f) death of the cell. The positive charge results in the stronger polymer-membrane interactions by strengthening the electrostatic attraction between +vely charged QAC and negatively charged bacterial cell membrane. In addition to that the +ve charge has also another very important feature. It was found that the long hydrophobic chains themselves have a capability of penetrating and disrupting the cell membranes of the bacterial cell. However possessing hydrophobic long chain is not enough to exert biocidal activity[17,18,30].

Effect of alkyl chain and spacer length

The spacer length or alkyl chain length refers to the length of the carbon chain that composes the polymer back bone. It is quite reasonable that the antimicrobial activity is dependent on the spacer length due to the change in both conformation and charge density of the polymer which affects the mode of interaction with the cytoplasmic membrane. Ikeda et.al., studied poly(trialkyl vinyl benzyl ammonium chloride) and discovered that the antimicrobial activity was the highest with the longest chain (C_{12})[22]. Results have generally shown that longer alkyl chains resulted in higher activity. There are two primary explanations for this effect. Firstly, longer chains have more active sites available for adsorption with the bacterial cell wall and cytoplasmic membrane. Secondly, longer chains aggregate differently than shorter chain, which again may provide a better means for adsorption.

SYNTHETIC METHODS OF PREPARATION AND ACTIVITIES OF ANTIMICROBIAL POLYMERS

To increase the therapeutic efficiencies of the synthetic or naturally occurring macromolecules should be attach to the bioactive substrate and this lowers their potential

toxicities. There are many theories which can achieve this attachment are discussed as follows:

Synthesis from antimicrobial monomer

This synthetic method involves covalently linking antimicrobial agents that contain functional groups with high antimicrobial activity, such as hydroxyl, carboxyl or amino groups to variety of polymerizable derivatives or monomers before polymerization. Most of the synthesized drug monomers and their polymers are acrylic types of pharmaceutically active compounds. The acrylic-type drug conjugate monomers can be copolymerized to vary the drug concentration and they can be used to prepare different hydrophilic/hydrophobic functionalities in the polymer drug. The antimicrobial activity of the active agent may be either reduced or enhanced by polymerization. This depends on the kind of monomer used and how the agent kills bacteria, either by depleting the bacterial food supply or through bacterial membrane disruption. In this context Ren et.al[31] synthesized the monomer 3-(4'-vinyl benzyl)-5,5-dimethylhydantoin and used it to coat cotton fibers by admicelle polymerization using a cationic surfactant. After chlorination with dilute sodium hypochlorite, the polymeric-coated cotton fabrics effectively inactivated both *Staphylococcus aureus* and *E.coli* in relatively brief contact times. The stability and rechargeability of the coated cotton fabrics were very good as evidenced by standard washing tests.

Two novel organotin monomers (N-tri-n-butyltin) maleimide (N-TBTM) and m-acryloylamino-(tri-n-butyltin benzoate) (m-AATBTB) have been synthesized by Al Diab et.al.[32]. The copolymerization of these two monomers with styrene was carried out at 65°C in sealed tubes under nitrogen atmosphere and used azo, bis, isobutyronitrile as the free radical indicator. The antibacterial activities of the synthesized organotin monomers and copolymers were investigated towards various types of gram (+) ve& gram (-) ve bacteria and contact time was 24hr. The results showed that gram (+) ve bacteria were more sensitive to the above monomer and their styrene copolymers than were the gram (-) ve bacteria. They also reported that copolymerization of monomers with styrene decreased the potency of the monomers (m-AATBTB and N-TBTM) against gram(+)ve and gram(–)ve bacteria. This is expected due to the decrease of active functional groups in the polymer chain by introducing styrene, which has no antimicrobial activity in the chain.

Synthesis and polymerization of trialkyl-3-(and 4-vinyl benzyl) phosphonium chloride by reaction of 3,4-chloromethyl styrene with trialkylphosphine was investigated[33]. The polymerization was carried out in toluene at room temperature under an atmosphere of nitrogen. The results of the antibacterial activity study showed that the polymers were more active than the corresponding model compounds. M. Abdolahifard et.al.[34] investigated the surface modification of poly(ethylene terephthalate) (PET) fabric by graft copolymerization with acrylic acid (AA) and its antibacterial properties. Graft copolymerization of AA onto PET fabrics with the aid of benzoyl peroxide was carried out (Figure 2). The percent grafting was enhanced significantly by increasing benzoyl peroxide concentration up to 3.84g/l and then decreased upon further increase in initiator concentration. The antibiotics treated grafted fabrics showed antibacterial properties towards gram (+) ve and gram (–) ve microorganism.

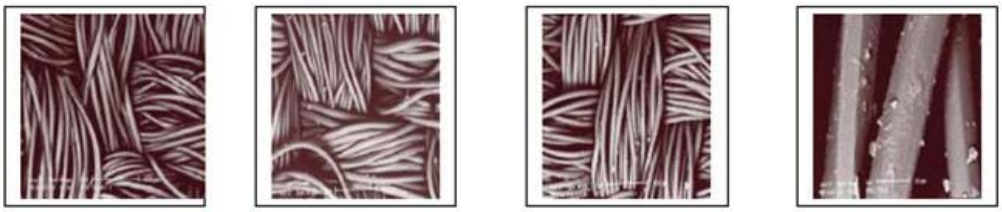

Figure 2: SEM Images of (a) PET fabric (b) 16% grafted PET fabric (c) 18% grafted PET fabric (d) 28% grafted PET fabric

Park. et.al.,[35] synthesized vinyl monomers with phenol and benzoic acid as pendent groups. The polymerization of these monomers was done. The antimicrobial activities of the polymers were explored using the halo zone test after a contact time of 72hr at 28°C. Surprisingly the polymerization of the monomers decreased their antimicrobial activities significantly. The author suggested that even though the antimicrobial activity of the polymers is much lower than that of the corresponding monomers, they could be coated on glassy polymers. Iodine containing quaternary amine methacrylate copolymers have been synthesized by Punyani et.al.[36].The monomers were synthesized via a two-step reaction: the first step was the reaction of ethylene glycol dimethylacrylate (EGDMA) with piperazine in methanol at 35°C for 6hr. The synthesized monomer with 1-iodooctane quaternization was done in second step. The quaternized monomer was copolymerized with 2-hydroxyethyl methacrylate(HEMA) by free radical polymerization using ammonium persulfate and N,N,N',N'-tetramethyl ethylene diamine as redox intiator. Copolymers of quaternized monomer (QAMA) of various ratios were synthesized. The QAMA was further used for antibacterial activities against *E.coli* and *S.aureus*. It was concluded that increasing the QAMA content in the copolymer reduced the contact time required for killing *E.coli*.

Synthesis by adding antimicrobial agents to preformed polymers

This synthetic method involves first synthesizing the polymers, followed by modification with an active species. The monomers are usually used to form the backbone of homo-polymers or copolymers of methylmethacrylate, vinyl alcohol, vinylbenzyl chloride, 2-chloroethyl vinyl ether and maleic anhydride. The polymers are then activated by anchoring antimicrobial species, such as phenol groups, phosphonium salts and ammonium salts via quaternization substitution of chloride or hydrolysis of anhydride. Two poly(ethylene glycol-N-halamine) polymers were synthesized by Eknoian et.al.[37]. Dichlorohydantoins and chloroimidazolidin-4-ones were attached to methoxy-poly-(ethylene glycol)-terminated amine. The resulting water-soluble polymers have inactivated bacteria (*S.aureus*) over a prolonged period of time after 10 min contact time. The polymer containing the hydantoin moiety showed better activity and stability than did the chloroimidazolidin-4-one polymer. Yan Li et.al.[38] demonstrated the effectiveness of a new antimicrobial suture coating. An amphiphilic polymer, poly[(aminoethyl methacrylate)-co-(butyl methacrylate)] (PAMBM), inspired by antimicrobial peptides was bactericidal against *S.aureus* in time-kill experiment. PAMBM was evaluated in a variety of polymer blends using the Japanese Industrial Standard (JIS) method and showed excellent antimicrobial activity at low concentration. Using a similar antimicrobial coating formula to commercial vicryl plus sutures, disk samples of the coating material containing PAMBM effectively killed bacteria (98% reduction at 0.75%). Further Kirby-Bauer assays of these disk samples showed an increasing zone of inhibition with increasing concentration of PAMBM. The PAMBM containing sutures killed bacteria more effectively ($3\log_{10}$ reduction at 2.4 wt %) than vicryl plus sutures ($0.5\log_{10}$ reduction).

Polyacrylamide has been modified by introducing an amino group in the side chain of the polymer by reacting it with ethylenediamine[39]. The amine-modified polymer was reacted with two classes of active compounds. The aromatic aldehydes containing active groups were the first group such as p-hydroxybenzaldehyde, vanillin, p-chlorobenzaldehyde and anisaldehyde. The second group was phenolic ester derivative such as p-hydroxymethylbenzoate, 2,4-dihydroxymethylbenzoate, 2-hydroxy methyl benzoate and 3,4,5-trihydroxypropylbenzoate. The modified polymers showed antimicrobial activity against *Staphylococcus aureus*, *E. coli, B. subtilis, A. flavous, F. oxysporum* and *C. albicans*. The polymer derivative of p-chlorobenzaldehyde was the most effective against bacteria and fungi species. The phenol-modified polymer showed high antimicrobial activities at the same contact time and concentration of 20mg/ml. The mode of action is related to the phenolic moieties. This may be due to the fact that phenols damage cell membranes and cause release of intracellular constituents, leading to cell death or inhibition of cell growth.

S. Jaiswal et.al.[40] has been reported the preparation and rapid analysis of antibacterial silver, copper and zinc doped sol-gel surfaces. The study describes the preparation of metal nitrate (Ag,Cu,Zn) doped methyltriethoxysilane(MTEOS) coating and the rapid assessment of their antibacterial activity using polypropylene microtitre plates. Microtitre plate wells were coated with different volumes of liquid sol-gel and cured under various conditions. The coated wells were challenged with Gram (+)ve and Gram (-)ve bacterial cultures, including biofilm-forming and antibiotic-resistant strains. The antibacterial activities of metal doped sol-gel at equivalent concentrations were found to have the following order: silver >zinc>copper (figure 3). The order is due to several factors including the increased presence of silver nanoparticles at the sol-gel coating surface leading to higher elution rates as measured by inductively coupled plasma atomic emission spectroscopy (ICP-AES). The use of microtitre plates enabled a variety of sol-gel coating to be screened for their antibacterial activity against a wide range of bacteria in a relatively short time. The broad spectrum antibacterial activity of the silver doped sol-gel showed its potential for use as a coating for biomaterials.

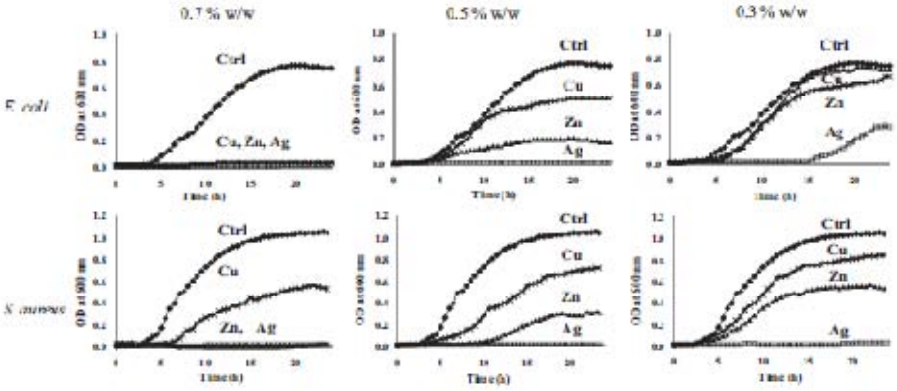

Figure 3: Comparison in the growth curves of Gram negative *E. coli* ATCC25922 and Gram positive *S. aureus* ATCC25923 on the coated sol-gel microtitre well surface containing metal ion (Ag, Zn, Cu) of different concentration (a) 0.7% (w/v) (b) 0.5% (w/v) and (c) 0.3% (w/v) with respect to control (MTEOS coated surface without metal ions) after 24h of incubation.

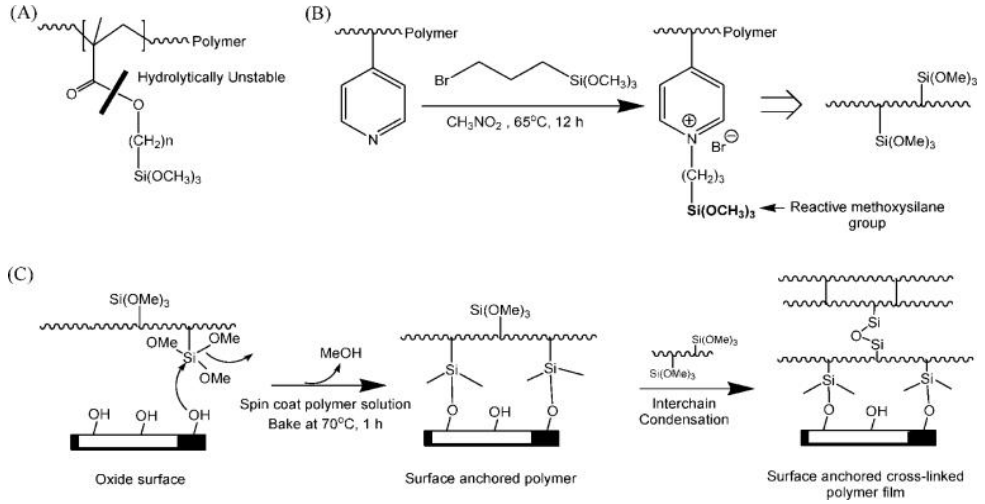

Figure 4: Schematic representation of surface-binding methodology. (A) Incorporating hydrolytically unstable methoxysilane-substituted methacrylate units in a polymer failed to yield detergent resistant coatings. (B) Chemistry for incorporating hydrolytically stable methoxysilane functionalities (N-alkyl methoxysilane pyridinium) in a polymer. (C) Covalent multilayer polymer anchoring on surface.

Quaternary phosphonium salts have been grafted on an insoluble "gel-type" styrene-7% divinyl benzene copolymer by Popa et.al.[41]. The quaternary-phosphonium salts were prepared from chloromethyl styrene-divinylbenzene copolymer and the corresponding phosphine in N,N-dimethylformamide by reacting for 2hr under stirring at room temperature to allow the copolymer beads to swell and then refluxing at 110°C for 72hr. The antibacterial activities of the product were tested against *S. aureus, E. coli* and *P. aeruginosa*. The copolymers were active against the test organism. They may have bacteriostatic properties because the best copolymer showed 40% reduction of the colony units after 18hr of exposure.

Varun et. al.,[42] has reported a versatile methodology combining both covalent surface anchoring and polymer crosslinking that is capable of forming long-lasting coatings on reactive and non-reactive surfaces (Figure 4). Polymers containing reactive methoxysilane groups form strong Si-O-Si links to oxide surfaces, thereby anchoring the polymer chains at multiple points. The interchain cross-linking of methoxysilane groups provides additional durability to the coating and makes the coatings highly resistant to solvents. By tailoring the chemical structure of the polymer, the surface energy can be control to a variety of surfaces over a wide range of water contact angles of 30-140°. The synthesis of covalently linked layer by layer polymeric assemblies from this novel methoxysilane polymer has been reported. Finally, antibacterial agents, such as silver bromide nanoparticles and tri-iodide ions, were introduced into these functional polymers to generate long-lasting and renewable antiseptic coatings on glass, metals and textiles.

Synthesis by adding antimicrobial agents to naturally occurring polymer

Chitin is the second-most abundant biopolymer in nature. It occurs in the shells of crustacean, the cell wall of fungi and the cuticles of insects. The deacetylated product of chitin-chitosan has been found to have antimicrobial activity without toxicity to humans. This synthetic technique involves making chitosan derivatives to obtain better antimicrobial activity. Currently, work has involved the introduction of alkyl groups to amine groups to make quaternized N-alkyl chitosan derivatives, introduction of extra quaternary ammonium grafts to the chitosan and modification with phenolic hydroxyl moieties. Many attempts have been made to use chitosan in several fields such as the food, medical, cosmetics and textiles industries.

Jung et.al.[43] have been reported the grafting of two anionic monomers, viz.mono(2-methacryloyloxy ethyl) acid phosphate (MAP) and vinylsulfonic acid salt(VSS) onto chitosan to obtain copolymers with zwitterionic properties. The antimicrobial studies of the modified chitosan samples have been carried out against *C. albians, T. rubrum and T. violaceum.* Good antibacterial activities were observed at pH 5.75 against *C. albicans*. The antibacterial activities of chitosan-g-MAP and chitosan-g-VSS were 95% and 75% respectively over 48-72hr contact time. When the pH was changed to 6.2, the activities dropped to 10-15%. However, this is expected because it is known that high acidic and high basic media have effect on the microorganisms and the studies showed pH variation upto 6.2 only.Synthesis of chitosan derivatives with quaternary ammonium salts and their antibacterial activity have been investigated by Kim et. al.[44]. N-alkyl chitosan derivatives were prepared by introducing alkyl groups into the amine groups of chitosan via schiffs base intermediate. Quaternization of N-alkyl chitosan derivatives were carried out using methyl iodide to produce water soluble cationic polyelctrolytes, novel chitosan derivatives with quaternary ammonium salt. The antibacterial activities of the chitosan derivatives with quaternary ammonium salt increased with increase in the chain length of the alkyl substituent and this increased

activity could be ascribed to the contribution of the increased hydrophobic properties of derivatives.

Kanaway et.al.[45] introduced biologically active moieties into the amino group of chitosan to given antimicrobial chitosans. Structurally chitosan has an amino group at C-2 & amino groups are nucleophilic and react rapidly with electrophilic reagents. The antimicrobial activities of these modified chitosans were explored against fungi viz. *C.albians* SC5314, *A. flavus* and *F. oxysporium.* They were also tested against bacteria such as *B. subtilis, E. coli* and *S. aureus*. These modified chitosans were found to be highly active towards fungi species in comparison to bacterial species. However, the polymer CTS1 of concentration 20mg/ml was able to kill 100% of *B. subtilis, E.coli*, and *S.aureus*. Again, a lower concentration of 10mg/ml was able to kill 100% of *S.aureus*. The polymer CTS2 showed total kill of 100% for *A. flavus* and *F . oxysporium* at a concentration of 20mg/ml. It was explained that the mode of action could be due to the phenolic hydroxyl group. Superhydrophobic poly(L-lactic acid) (PLLA) surface as potential bacterial colonization substrate have been reported[46]. To evaluate the ability of such material as a substrate for bacterial colonization, this work assessed the capability of different bacteria to colonize a biomimetic rough superhydrophobic (SH) PLLA surface and also a smooth hydrophobic (H) one. The interaction between these surfaces and bacteria with different morphologies and cell walls was studied using the strains of *S.aureus* and *P. aeruginosa*. Results showed that both bacterial strains colonized the surfaces tested, although significantly higher numbers of *S.aureus* cells were found on SH surfaces comparing to H ones.Moreover scanning electron microscopy images showed an extracellular matrix produced by *P. aeruginosa* on SH P1LLA surfaces, indicating that this bacterium is able to form a biofilm on such substratum.Overall, the results showed that SH PLLA surfaces can be used as a substrate for bacterial colonization and have an exceptional potency for biotechnology application.

Harney et.al.[47] investigated the surface self-concentrating amphiphilic quaternary ammonium biocides as coating additives (Figure 5). A variety of amphiphilic quaternary dimethyl ammonium compounds bearing n-alkyl and oxy-ethylene group were designed and synthesized as antimicrobial additives for use in self-decontaminating surfaces. The effectiveness of these additives stems from a unique ability to self-concentrate at the air polymer interface without the incorporation of exotic perfluorinated or polymeric functionalities. X-ray photoelectron spectroscopy analysis revealed surface enrichment as high as 18-fold, providing a 7-log reduction of both *S. aureus* and *E. coli* bacteria. The migration to the surface is a consequence of the hydrophobicity of the additive within the hydrophilic polyurethane resin over which an unprecedented level of control could be exerted by altering the lengths of the n-alkyl and oxyethylene groups. Thus specific surface and bulk coating concentrations could be achieved as desired using a single class of antimicrobial additives (Figure 6).

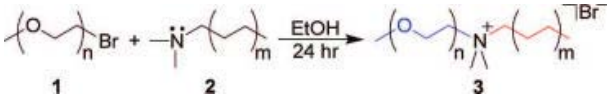

Figure 5: Schematic presentation for the preparation of amphiphilic quaternary ammonium antimicrobials. (1. methoxy-terminated oxyethylene bromides, 2. represent tertiary amines, 3. represents ammonium bromide compounds)

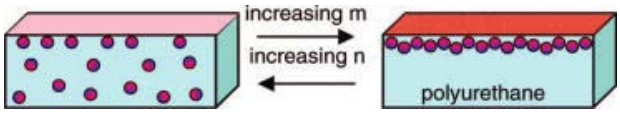

Figure 6: Effect of altering the length of n-alkyl (red) or oxyethylene (blue) groups on the surface concentration.

Synthesis by insertion of antimicrobial agents into polymer backbone

This method involves using chemical reaction to incorporate antimicrobial agents into the polymeric backbone. Polymer with biologically active groups such as polyamides, polyesters and poly urethanes are desirable as they may be hydrolyzed to active drugs and small innocuous molecule. A series of polyketones have been synthesized and studied, which show an inhibitory effect on the growth of *B. subtilis* and *P. fluorescence* and in fungi *A. niger* and *T. viride*.

Han et.al.,[48] reported the influence of electron beam irradiation of antimicrobial coated LDPE/polyamide films on antimicrobial activity and film properties. The antimicrobial polymer effectiveness of several coating of FDA-approved antimicrobial compounds including sorbic acid, carvacrol, trans-cinnamaldehyde, thymol and rosemary oleoresin using selected food pathogen surrogates have been established. The antimicrobial coating were applied to one side of LDPE films and dried. Films were irradiated using a 10MeV linear electron beam accelerator at room temperature. All films showed inhibition zones in an agar diffusion test against *L. innocua* ATCC 33090 and *E. coli* ATCC 884.In the liquid culture test, the antimicrobial significantly ($p \leq 0.05$) reduced the specific growth rate of *L. innocua* by 3.8-8.5% and decreased final cell concentration of both strains by 5.7-14.6% and 7.2-16.8% respectively. All active compounds retained the antimicrobial activity when exposed to 1-3kGy. Neither the presence of active compound nor dose affected the film's tensile strength and toughness. Additionally film became more ductile and had improved moisture barrier functionality. Film's oxygen permeability was not affected by either treatment. Results are an initial step toward the development of self-sterile active packaging materials for use in combination with irradiation treatment of food.

Preparation and in-vitro performance evaluation of novel biocatalytic polymer based antimicrobial coatings as potential ureteral biomaterial have been investigated by

Dave et.al. [49]. Preparation and antibacterial properties of an enzyme-embedded polycaprolactone (PCL)-based coating and co-impregnated with antibiotic gentamicin sulfate (GS) have been developed. The enzyme uses PCL itself as substrate, as a result, the antibiotic get released at a rate controlled by the degradation of the PCL base. In-vitro drug release studies demonstrated sustained release of GS from PCL films throughout its lifetime. In the end, the polymer is completely degraded, delivering the entire load of the antibiotic. The polymer exhibited antibacterial properties against three strains: *E. coli, P. aeruginosa* and *S. aureus.* Foley urinary catheters coated with the modified polymer exhibited sustained in-vitro release of GS over 60 hr periods. The results suggest that the antibiotic-plus-enzyme-loaded polymer can be used as tunable self-degrading antimicrobial biomaterial coating on catheters.

Bithional [2,2'-thiobis (2,4-dichlorophenol)] have been incorporated into the main polymer chain by Donaruma et. al.[50]. Bithional is a known antimicrobial agent and found to react with phosgene to give the bischloroformate and was used for the preparation of altering co-polycarbonates, polyurethanes or co polycarbonates/polyurethanes. The hydrolysis rate of bithional-containing polymers at 57°C in buffer solution at Ph 7.4 has been studied. It releases bithional at about 1% per day. There was no specific antimicrobial study for the prepared polymer reported.

APPLICATIONS OF ANTIMICROBIAL POLYMER

Research concerning microbial polymers represents a great challenge for both the academic world and industry since microbial contamination is a serious issue that involves many areas such as the health and biomedical field, water treatment, food packaging and storage, textile product etc. The low molecular weight antimicrobial agents suffer from many disadvantages, such as toxicity to the environment and short-term antimicrobial ability. To overcome problems associated with the low molecular weight antimicrobial agents, antimicrobial functional groups can be introduced into polymer molecules. The major fields of applications of antimicrobial polymer are.

Food industry

Antimicrobial packaging can be considered an emerging technology that could have a significant impact on shelf life extension and food safety. Use of antimicrobial agents in food packaging can control the microbial population and target specific micro-organisms to provide higher safety and quality products. Many classes of antimicrobial compounds have been evaluated in film structures, synthetic polymer and edible films. Edible coatings and films prepared from polysaccharides. Proteins and lipids have a variety of advantages such as biodegradability, edibility, biocompatibility, appearance and barrier properties. To control food contamination and quality loss, edible coating or biodegradable packaging have been recently introduced in food processing. The packaging can serve as a carrier for antimicrobial and antioxidant compound in order to keep high concentration of preservatives on the food surfaces. Their presence could avoid moisture loss during storage reduce the rate of rancidity causing lipid oxidation and brown coloration, reduce the load of spoilage and pathogen microorganism on the surface of the food and also, restricting the volatile flavor loss. A very interesting review of the need for antimicrobial food packaging has been discussed by Appendini et. al.[51]. The use of appropriate coating can import the choice of an antimicrobial agent is often restricted by the incompatibility of that agent with the packaging material or by its heat instability during extrusion[52, 53].

Polyethylene has been widely employed as the heat-sealing layer in packages; in some cases the copolymer polyethylene-co-methacrylic acid was found to be preferable for this purpose. A simple method for making polyethylene-co-methacrylic acid films with antimicrobial properties has been reported by the incorporation of benzoic or sorbic acids. The results suggest that sodium hydroxide and preservative-treated films antimicrobial effectiveness show dominantly antimicrobial properties for fungal growth due to the higher amount of preservative released from the films than hydrochloric acid and preservative treated films. Antimicrobial agents as organic acids, bacteriocin and spice extracts have been tested for their ability to control meat spoilage[54,55]. Garlic oil is composed of sulfur compounds such as allicin, diallyl disulfide and diallyltrisulfide and possess better antimicrobial activity than the corresponding ground form[56]. Chitosan edible film incorporating garlic oil was compared by Pranoto et.al. with conventional food preservative potassium sorbate and bacteriocinn is in at various concentrations, showing an antimicrobial effect against *S. aureus, E. coli, S. typhimorium, B. cereus* and *Listeria monocytogenes*. However, the application of garlic oil into chitosan films depends on the type of food. The production of a nisin containing cellophane based coating was used in the packaging of chopped meat. The developed bioactive cellophane reduces significantly the growth of the total aerobic bacteria through 12days of storage at 4°C, would result in an extension of the shelf life of chopped meat under refrigeration temperature[57]. New biopolymer containing a chito-oligosaccharide side chain have been synthesized[58]. The chito-oligosaccharide was introduced on polyvinyl acetate by cross-linking with the bifunctional compound N-methylolacryl-amide. It was found that the growth of *S.aureus* was almost completely suppressed by this means. Surface amine groups formed in polymers by electron irradiation were also shown antimicrobial effectiveness.

Various factors involved in the manufacturing of antimicrobial films are: chemical nature of films, process conditions and residual antimicrobial activity; characteristics of antimicrobial substances and food; chemical interaction of additives with film matrix; storage temperature; physical properties of packaging materials

etc. Future work in this field will focus on the use of biologically active derived antimicrobial compounds bound to polymers. The current applications of antimicrobial food packaging are rather limited, although promising. However, more information is required on the chemical, microbiological and physiological effects of these systems on the packaged food especially on the issues of nutritional quality and human safety [59]. It is likely that future research into a combination of naturally-derived antimicrobial agents, biopreservatives and biodegradable packaging materials will highlight a range of antimicrobial packaging in terms of food safety, shelf-life, and environmental friendliness[60, 61].

Medicine and Healthcare Product

The safety of the healthcare environment is of major importance to our society. A significant contributor to patient morbidity and mortality is healthcare-acquired infection. In 2002, it was reported that at least 6% of patients acquired an infection in hospital and that this proportion is rising. The spread of bacteria is a common problem and is the main source of health associated infection. Bacterial exposure during surgical procedures or can be transferred from patient-to-patient from infected hospital surfaces. Antimicrobial polymers are powerful candidates for polymeric drugs with high activities, which can be ascribed to their characteristics nature of carrying the high local charge density of the active groups in the vicinity of the polymer chains. For example, electrospun fibers containing tetracycline hydrochloride based on poly(ethylene-co-vinyl acetate), poly(lactic acid) and blending were prepared to use as an antimicrobial wound dressing[62,63].

Imazato et.al.[64] investigated the synthesis of an antibacterial monomer 12-methacryloyloxydodecyl-pyridinium bromide (MDPB). The monomer MDPB was synthesized by combining quaternary ammonium dodecylpyridinium with a methacryloyl groups, so that the bactericide was immobilized in the resin matrix by copolymerization of MDPB with other monomers. The resin composites incorporating MDPB demonstrated inhibition of dental plaque formation on the surface and no reduction in mechanical properties occurred even after storage for a long period in a wet environment. Catheters and other indwelling devices placed inside human body are prone to bacterial infection, causing serious risk to patients. Infections associated with implants are difficult to resolve, hence the prevention of bacterial colonization of such surface is quite appropriate. Cellulose derivatives are commonly used in cosmetics as skin and hair conditioners, Quaternary ammonium cellulose derivatives are of particular interest as conditioners in hair and skin products. Chitosan and its derivatives have been reportedly used as film formers in hair products, setting agents, hair conditioners and shampoos. Recently hydroxypropyltrimethylammonium chitosan chloride was synthesized for evaluation in a cosmetic application[65].

Efficacy of antimicrobial polymer coating in an animal model of bacterial infection associated with foreign body implant has been investigated by Hart et.al.[66]. In-vitro, the release of levofloxacin from the coated discs occurred at a constant rate and then reached a plateau at different time points, depending on the polymer preparation used. To assess support discs, comprising polyethylene terephthalate (PET) coated with different polymer/levofloxacin combinations for antimicrobial activity in an animal model of infection, in order to explore the use of specific polymer coating incorporating levofloxacin as means of reducing device-related infections. Presently, development of antimicrobial paper presents an opportunity to help reduce the proliferation of bacteria in office environment, hospitals, living rooms with pets, inside vehicles and many other places. Antimicrobial paper includes wallpaper, medical chart paper, paper towel, toilet paper, bank notes etc. Zinc oxide nanoparticles have been coated onto paper, giving an antibacterial surface suitable for use as wall paper in hospitals.

Figure 7: Uses of antibacterial paper

Water treatment

The ideal application of polymeric disinfectants is in surface coated, hand-held water filters and fibrous disinfectants. They can be fabricated by various techniques and can be insoluble in water. Chlorine or water soluble disinfectants have problems with residual toxicity, even if minimal amounts of the substance used. However, soluble disinfectants have the problems of residual toxicity of the agents, even if suitable amounts of the agents are used[67]. The problem of residue cannot be avoided with the use these disinfectants or antimicrobial agents and this bring about more serious consequences. Toxic residues can become concentrated in food, water and in environment. In addition, because free chlorine ions and other related chemicals can react with organic substances in water to yield tri-halomethane analogous that is suspected of being carcinogenic, their use should be avoided. One approach is the use of insoluble contact disinfectants that can inactivate, kill or remove target microorganisms by mere contact without releasing any reactive agents to the bulk phase to be disinfected.

Several workers in the past few decades have attempted to produce insoluble polymeric disinfectants for use in

water treatment Gurangi Ji et.al.,[68] investigated the antibacterial activity of insoluble pyridinium-type polymer with different structures against *E. coli* suspended in sterilized and distilled water. The results show that the antibacterial activity of insoluble pyridinium-type polymers, except for one containing I^-, is characterized by an ability to capture bacterial cells in a living state by adsorption or adhesion, with the process of capturing bacterial cells being at least partially irreversible. This differs from the antibacterial activity of the corresponding soluble polymer, which is characterized by the ability to kill bacterial cells in water. In addition, insoluble pyridinium-type polymers can also capture dead bacterial cells. This implies that insoluble pyridinium-type polymers possess broad prospects for development in new water treatment techniques and whole-cell immobilization techniques.

Alamri et.al.,[69] synthesized benzaldehyde derivatives immobilized onto amine-terminated polyacrylonitrile and investigate their antimicrobial properties for biomedical applications and water treatment. The antimicrobial polymers based on polyacrylonitrile (PAN) were prepared. Functional groups were created onto polyacrylonitrile via amination using different types of diamines such as ethylenediamine (EDA) and hexamethylenediamine (HMDA) to give amine-terminated polymers. Antimicrobial polymers were obtained by immobilization of benzaldehyde and its derivatives. The antimicrobial activity of the prepared polymers against different type of microorganism including Gram (+)ve bacteria (*S. aureus*), Gram (-)ve bacteria (*P. aeruginosa, E.coli & Salmonella typhi*) as well as fungi (*A. flavus, A. niger, C. albicans, C. neoformass*) were explored by viable cell counting methods. Amine-terminated polyacrylonitrile were used as a novel polymeric carrier for benzaldehyde derivatives as antimicrobial agents. It was found that the activity increased with increasing the number phenolic hydroxyl group of the bioactive group.

Chen et.al.,[70] have prepared several cyclic n-halamines that are prepared in the form of highly cross-linked porous beads for water and air disinfection. Functionalization of methylated polystyrene by halogenated hydantoin and imidazolidinone derivatives was reported. Column filter biocidal efficacy tests were conducted for aqueous suspensions of *S.aureus* and *E.coli* for four types of beads. These four types of beads (PHY-Cl, PHY-Br, PMHY-Cl and PI-Cl) were packed with glass column. The suspensions of pathogenic bacteria were pumped through the column. The results showed the efficacies of the bead column for inactivation of *S. aureus* and *E. coli*. The PHY-Cl and PHY-Br polymer beads were able to show complete inactivation of above two species in the contact time interval of 1-2sec. However, the polymer labeled poly 1-Cl complete the same task in less than 1sec. The PMHY-Cl polymer also completely inactivated both species of bacteria in a contact time of less than or equal to 1sec. The last polymer PI-Cl beads inactivated *S.aureus* in a contact time between 2 and 3sec. These polymeric beads will be useful in the disinfection of potable water moist air flowing. Finally it is anticipated that the prepared antimicrobial polymer would be of great help of biomedical applications and biologically water treatment.

Textile product

In recent years antimicrobial textiles have gained interest from both academic research and industry because of their potential to provide high quality life and safety benefits to people. Textile products are proving to host micro-organisms responsible for diseases, unpleasant odor, color degradation and deterioration of textile. Antimicrobial polymer have been used enormously in sportswear, women's wear, undergarments, shoes, furnishing, hospital linens, towel and wipes and aesthetic clothing to impart anti-odor or biostatic properties[71-72] of polymers and fibrous surfaces and changing the porosity, wettability and other characteristic of polymeric substances should produce implants and biomedical devices with greater resistance to microbial adhesion and biofilm formation. Nowadays various advancements are taking place in the field of antimicrobial polymers for textile coating and finishing. Various options are available in the market for obtaining antimicrobial textiles: Insolubilisation of the active substance in the fiber; Treatment of fibers with resins or crosslinking agents; Microencapsulation of antimicrobial agents; Surface coating of the fibres; Chemical modification with covalent bonds; Use of graft polymers, homopolymers or copolymerisation with the fiber (Figure 8).

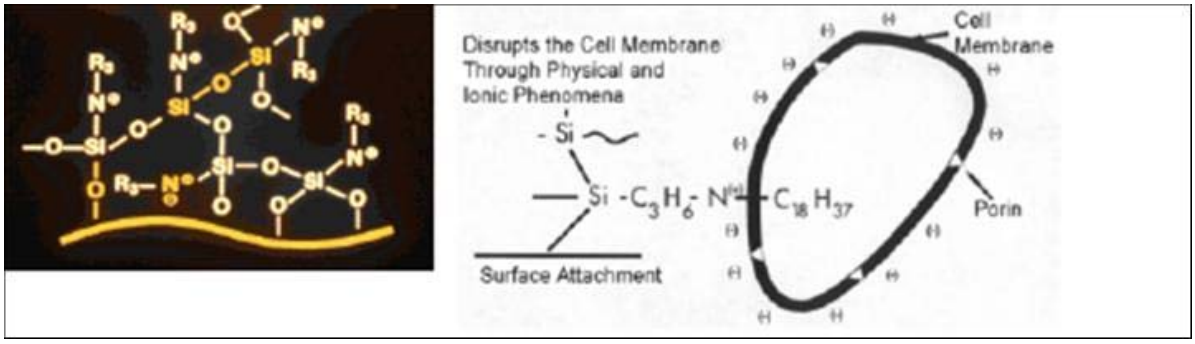

Figure 8: Mechanism for obtaining antimicrobial textile.

Chitosan and its derivatives have been recently proposed as biomaterial for textile industry. In textile field, the application of chitosan is mainly related to its antimicrobial properties. In fact, chitosan is a wide-spectrum biocide with high antimicrobial efficacy against Gram (+)ve & Gram (-)ve bacteria. Carboxymethyl chitosan was applied to cationized cotton[73]. Cationization of cotton was carried out using a commercial cationic agent Quab® (2, 3-epoxypropyl-trimethyl ammonium chloride) by pad-dry cure method. Cationized cotton was then treated with carboxymethyl chitosan. Antimicrobial activity increased by increasing the concentration of Quab® 151 in comparison with the control, as well as the antibacterial activity of carboxymethyl chitosan on cationized fabrics increased by increasing the amount of carboxymethyl chitosan.

Ren et. al.,[74] synthesized 3-(4'-vinylbenzyl)-5,5-dimethyl hydantoin (VBDMH) monomer and polymerized it by admicelle polymerization on cotton fabric at 80°C for 8hrs in water. The coated cotton fabric was immersed in a 10% aqueous sodium hypochlorite solution at pH 11 for 1 hr at room temperature for chlorination. Antibacterial properties were evaluated with *S.aureus* and *E.coli* 0157:H7 using a 'Sandwich test' with contact times of 1.5, 10 and 30 min. The 0.12 wt% Cl^+ coated-cotton fabrics inactivated 99.98% *S. aureus* within 1 min and 100% within 5 min and 99.94% *E. coli* within 5 min and 100% within 10 min of contact time.

Antimicrobial agents are used in the textile sector, principally for hygiene application. There are several commercial agents that can render a textile antimicrobial. The characteristics of an ideal antimicrobial textile are: permanent antimicrobial properties that are not lost during usage or washing, antimicrobial activity on a wide range of microorganism, it should not contain toxic migrating substance and the antimicrobial effect has to be limited on the surface of the textile, do not interfere with skin bacteria.

FUTURE PROSPECTS

This era may come to be remembered as one in which infectious diseases made a dramatic worldwide resurgence, owing to the rise of antibiotic resistance and emergence of new disease. Undoubtedly, the use of polymers in the medical field has reduced the suffering of humans and offered them a better hope for a safer life. At present, the antimicrobial product such as triclosan and silver, suffer from critical limitation, for instance short active duration or high cost. Moreover, low molecular weight antimicrobial agents generally leach out from the fabrics towards the environment and to the skin of the wearers. To overcome this problem, antimicrobial polymers of high molecular weight have been used. Antimicrobial polymers have been increasingly taken into account as a feasible alternative for bactericidal application. The range of application has been extended to include many fields such artificial organs, drugs, health care products, implants, bone replacement, water treatment, food and textile industry etc.

Currently, the majority of antimicrobial polymer materials are produced by either polymer compounding with inorganic or organic biocides or by coating polymer surfaces with biocides including chemical binding. The general problems with the additive approach are poor compatibility, decrease in mechanical and physical properties, loss of antimicrobial activity and health and environment risk.

Synthetic antimicrobial macromolecules which include antimicrobial peptides (AMPs), polymers and peptide-polymer hybrids represent a huge class of molecules which can be in cure effective antimicrobial therapy due to their unique biochemical properties. The use of these antimicrobial macromolecules which target the cytoplasmic membrane of microbes is a promising approach to lower the propensity of pathogen resistant development. Antimicrobial N-halamine polymers and coating have been studied extensively to their numerous qualities such as effectiveness toward a broad spectrum of microorganism, long-term stability, regenerability, safety to human and environment and low cost. It was investigated that these N-halamines have wide application in the water treatment, paints, healthcare equipment and textile industry.

As a result, high demand for intensifying efforts in the R&D of antimicrobial polymers has placed heavy reliance on both academia and industry to find viable solution for producing safer materials in medical & healthcare industry, food packaging, textiles, coating of catheter tubes, necessarily sterile surfaces etc. The greater need for materials that fight infection will give incentive for discovery and use of antimicrobial polymer.

REFERENCES

1. Kenawy ER, Biologically active polymers. IV. Synthesis and antimicrobial activity of polymers containing 8-hydroxyquinoline moiety, J. Appl. Polym. Sci., 82(6), 2001, 1364-1374.
2. Kenawy ER, Abdel-Hay FI, El-Shanshoury AE-R, El- Newehy MH, Biologically active polymers. V. Synthesis and antimicrobial activity of modified poly(glycidyl methacrylate-co-2-hydroxyethyl methacrylate) derivatives with quaternary ammonium and phosphonium salts, J. Polym. Sci.Part A: Polym. Chem., 40, 2002, 2384-2393.
3. Sauvet G, Dupond S, Kazmierski, K, Chojnowaski J, Biocidal polymers active by contact. V. Synthesis of polysiloxanes with biocidal activity, J.Appl.Polm.Sci., 75(8), 2000, 1005-1012.
4. Shin Y, Yoo DI, Min K, Antimicrobial finishing of polypropylene nonwoven fabric by treatment with chitosan oligomer, J.Appl.Polym.Sci, 74(12), 1999, 2911-2916.
5. Kenawy ER, Worley SD, Broughton R, The Chemistry and Applications of Antimicrobial Polymers: A State-of-the-Art Review, Biomacromolecules, 8(5), 2007, 1359-1384.
6. Bankova M, Manolova, N, Markova, N, Radoucheva, T, Dilova, K, Rashkov, I, Hydrolysis and Antibacterial Activity of Polymers Containing 8-Quinolinyl Acrylate J. Bioact. Compat.Polym. 12(4), 1997, 294-307.

7. Oh ST, Han SH, Ha CS, Cho WJ, Synthesis and biocidal activities of polymer. IV. Antibacterial activity and hydrolysis of polymers containing diphenyl ether, J. Appl. Polym. Sci. 59, 1996, 1871-1878.
8. Kanazawa A, Ikeda T, Endo T, Polymeric phosphonium salts as a novel class of cationic biocides. III. Immobilization of phosphonium salts by surface photografting and antibacterial activity of the surface-treated polymer films J. Polym. Sci., Part A: Polym. Chem., 31, 1993,1467-1472.
9. Gray JE, Norton PR, Alnouno R, Marolda CL, Valvano MA, Griffiths K, Biological efficacy of electroless-deposited silver on plasma activated polyurethane Biomaterials. 24(16), 2003, 2759-2765.
10. Tiller JC, Liao CJ, Lewis K, Klibanov AM, Designing surfaces that kill bacteria on contact Proc.Natl. Acad. Sci. USA. 98(11), 2001, 5981-5985.
11. Klibanov AM, Permanently microbicidal materials coatings, J. Mater.Chem. 17, 2007, 2479-2482.
12. Lin J, Qiu S, Lewis K, Klibanov AM, Bactericidal Properties of Flat Surfaces and Nanoparticles Derivatized with Alkylated Polyethylenimines, Biotechnol. Prog. 18 (5), 2002, 1082-1086.
13. Lee SB, Koepsel RR, Morley SW, Matyjaszewski K, Sun Y, Russell AJ, Permanent, Nonleaching Antibacterial Surfaces. 1. Synthesis by Atom Transfer Radical Polymerization Biomacromolecules, 5, 2004, 877-882.
14. Tiller JC, Lee SB, Lewis K, Klibanov AM, Polymer surfaces derivatized with poly(vinyl-N-hexylpyridinium) kill airborne and waterborne bacteria Biotechnol. Bioeng. 79(4), 2002, 465-471.
15. Lin J, Tiller JC, Lee SB, Lewis K, Klibanov AM, Insights into bactericidal action of surface-attached poly(vinyl-N-hexylpyridinium) chains, Biotechnol. Lett. 24(10), 2002, 801-805.
16. Tashiro T, Antibacterial and Bacterium Adsorbing Macromolecules, Macromol. Mater. Eng. 286(2), 2001, 63-87.
17. Davies A, Bentley M, Field BS, Comparison of the action of vantocil, cetrimide and chlorhexidine on Escherichia coli and it is sphereoplasts and the protoplasts of gram-positive bacteria, J.Appl.Bacteriol., 31, 1968, 448-461.
18. Juergensen L, Busnarda J, Caux PY, Kent RA, Fate, behavior, and aquatic toxicity of the fungicide DDAC in the Canadian environment, Environ. Toxicol., 159(3), 2000, 174-200.
19. Ikeda T, Hirayama H, Suzuki K, Yamaguchi H, Tazuke S, Biologically active polycations, 6. Polymeric pyridinium salts with well-defined main chain structure, Makromol.Chem. 187(2), 1986, 333-340.
20. Ikeda T, Tazuke S, Biologically active polycations, 4. Synthesis and antimicrobial activity of poly(trialkylvinylbenzylammonium chloride)s Makromol.Chem. 185(5), 1984, 869-876.
21. Kanazawa A, Ikeda T, Endo T, Antibacterial activity of polymeric sulfonium salts, J. Polym. Sci., Part A: Polym. Chem. 31(11), 1993, 2873-2876.
22. Ikeda T, Yamaguchi H, Tazuke S, New polymeric biocides: synthesis and antibacterial activities of polycations with pendant biguanide groups, Antimicrob. Agents Chemother. 26(2), 1984, 139-144.
23. Kanazawa A, Ikeda T, Endo T, Novel polycationic biocides: Synthesis and antibacterial activity of polymeric phosphonium salts, J. Polym. Sci., Part A: Polym. Chem. 31(2), 1993, 335-343.
24. Dizman B, Elasri MO, Mathias LJ, Synthesis and antimicrobial activities of new water-soluble bis-quaternary ammonium methacrylate polymers J. Appl. Polym. Sci. 94(2), 2004, 635-642.
25. Kanazawa A, Ikeda T, Endo T, Polymeric phosphonium salts as a novel class of cationic biocides. IV. Synthesis and antibacterial activity of polymers with phosphonium salts in the main chain, J. Polym. Sci., Part A: Polym. Chem. 31(12), 1993, 3031-3038.
26. Panarin EF, Solovaskii, MV, Zaikina NA, Afinogenov GE, Biological activity of cationic polyelectrolytes, Makromol. Chem. Suppl., 9, 1985, 25-33.
27. Denyer SP, Stewart GSAB, Mechanisms of action of disinfectants, Intern. Biodeterior. Biodegrad., 41(3-4), 1998, 261-268.
28. Tashiro T, Antibacterial and Bacterium Adsorbing Macromolecules, Macromol. Mater.Eng., 286 (2), 2001, 63-87.
29. Kawabata N, Nishiguchi M, Antibacterial activity of soluble pyridinium-type polymers, Appl. Environ. Microbiol., 54, 1988, 2532-2535.
30. Klibanov AM, Permanently microbicidal materials coatings, J. Mater. Chem., 17, 2007, 2479-2482.
31. Ren X, Kou L, Kocer HB, Zu C, Worley SD, Broughton RM, Huang TS, Antimicrobial coating of an N-halamine biocidal monomer on cotton fiber via admicellar polymerization, Colloids & Surfaces A., 317, 2008, 711-716.
32. Al-Muaikel NS, Al-Diab SS, Salman AA, Zaid AMA, Synthesis and characterization of novel organotin monomers and copolymers and their antibacterial activity, J.Appl.Polym.Sci. 77, 2000, 740-745.
33. Kanazawa A, Ikeda T, Endo T, Polymeric phosphonium salts as a novel class of cationic biocides. V. Synthesis and antibacterial activity of polyesters releasing phosphonium biocides, J. Polym. Sci., Part A: Polym.Chem. 31, 1993, 3003-3011.
34. Abdaalahifard M, HajirBahrami S, Malek RMA, Surface modification of PET fabric by graft copolymerization with acrylic acid aand its antibacterial properties, International Scholarly Research Network, Organic Chemistry, Article ID 265415, 2011, 8 pages, DOI:10.5402/2011/265415.
35. Park ES, Moon WS, Song MJ, Kim MN, Chung KH, Yoon JS, Antimicrobial activity of phenol and benzoic acid derivatives, Int. Biodeterior. Biodegrad., 47(4), 2001, 209-214.
36. Punyani S, Singh H, Preparation of iodine containing quaternary amine methacrylate copolymers and their contact killing antimicrobial properties, J. Appl. Polym. Sc., 102, 2006, 1038-1044.
37. Eknoian MW, Worley SD, Harris JM, New Biocidal N-Halamine-PEG Polymers, J. Bioact. Compat. Polym. 13, 1998, 136-145.
38. Yan L, Kushi NK, Dabbowski JM, Corrigan M, Scott RW, Nusslein K, Tew GN, New Bactericidal Surgical Suture Coating, Langmuir, 28(33), 2012, 12134-12139.
39. Kenawy E-R, Abdel-Hay FI, Abou El-Magd A, Mahmoud Y, Synthesis and antimicrobial activity of some polymers derived from modified amino polyacrylamide by reacting it with benzoate esters and benzaldehyde derivatives, J. Appl. Polym. Sci., 99, 2006, 2428-2437.
40. Jaiswal S, McHale P, Duffy B, Preparation and rapid analysis of antibacterial silver, copper and zinc doped sol-gel surfaces, Colloids and surfaces B. Biointerfaces., 94, 2012, 170-176.
41. Popa A, Davidescu CM, Trif R, Ilia G, Iliescu S, Dehelean G, Study of quaternary 'onium' salts grafted on polymers: antibacterial activity of quaternary phosphonium salts grafted on 'gel-type' styrene–divinylbenzene copolymers, React. Funct.Polym., 55, 2003, 151-158.
42. Sambhy V, Peterson BR, Sen A, Multifunctional silane polymers for persistent surface derivatization and their antimicrobial properties, Langmuir, 24(14), 2008, 7549-7558.
43. Jung BO, Kim CH, Choi KS, Lee YM, Kim JJ, Preparation of amphiphilic chitosan and their antimicrobial activities, J. Appl. Polym. Sci., 72(13), 1999, 1713-1719.
44. Kim CH, Choi JW, Chun HJ, Choi KS, Synthesis of chitosan derivatives with quaternary ammonium salt and their antibacterial activity, Polymer Bulletin, 38(4), 1997, 387-393.

45. Kenawy ER, Abdel-Hay FI, Abou El-Magd A, Mahmoud Y, Biologically Active Polymers: Modification and Anti-microbial Activity of Chitosan Derivatives, J. Bioact. Compact. Polym., 20(1), 2005, 95-111.

46. Sousa C, Rodrigues D, Oliveira R, Song W, Mano JF, Azeredo J, Superhydrophobic poly(L-lactic acid) surface as potential bacterial colonization substrate, AMB Express. 1(34), 2011, 1-9.

47. Harney MB, Pant RR, Fulmer PA, Wynne JH, Surface self-concentrating amphiphilic quaternary ammonium biocides as coating additives, Applied Materials & Interfaces, 1(1), 2009, 39-41.

48. Han J, Castell-Perez, ME, Moreura RG, The influence of electron beam irradiation of antimicrobial coated LDPE/polyamide films on antimicrobial activity and film properties, LWT. 40, 2007, 1545-1554.

49. Dave RN, Joshi HM, Venugopalan VP, Novel biocatalytic polymer-based antimicrobial coatings as potential ureteral biomaterial: Preparation and in vitro performance evaluation, Antimicrobial agents and chemotherapy, 50(2), 2011, 845-853.

50. Albertsson AC, Donaruma LG, Vogl O, Synthetic Polymers as Drugs, Ann. N.Y. Acad. Sci., 446, 1985, 105-115.

51. Appendini P, Hotchkiss JH, Review of antimicrobial food packaging, Innovative Food Sci. Emerging Technol., 3(2), 2002, 113-126.

52. Han JH, Floros JD, Modeling anntimicrobial activity loss of potassium sorbate against Baker's yeast after heat process to develop antimicrobial food packaging materials, Food Sci. Biotechnol. 8(1), 1999, 11-14.

53. Weng YM, Hotchkiss JH, Anhydrides as antimycotic agents added to polyethylene films for food packaging, Packag. Technol Sci., 6(3), 1993, 123-128.

54. Hotchkiss JS, Safety considerations in active packaging, Active Food Packaging, Blackie Academic and Professional.Glassgow, 1995, 238-253,

55. Miller AJ, Call JE, Whiting RC, Comparison of organic acid salts for Clostridium botulinum control in an uncured turkey product, J.Food. Prot., 56, 1993, 958-962.

56. Nychas GJE, Natural antimicrobials from plants. In: New Methods of food preservative, Black Academic and professional, Glassgow, 1995, 59-89.

57. Guerra NP, Macias CL, Agrasar AT, Caatro, LP, Development of a bioactive packaging cellopane using Nisapln as biopreservative agent, Lett. Appl. Microbiol., 40(2), 2005, 106-110.

58. Ozdemir M, Yurteri CU, Sadikoglu H, Physical polymer surface modification methods and applications in food packaging polymers, CRC Crot. Rev.FoodSci.Nut., 39(5), 1999, 457-477.

59. Floros JD, Dock LL, Han JH, Active packaging technologies and applications, Food Cosmet Drug. Packag, 20(1), 1997, 10-17.

60. Nicholson MD, The role of natural antimicrobials in food packaging Biopreservation, J. Plastic Film Sheeting, 14(3), 1998, 234-241.

61. Rodrigus ET, Han JH, Antimicrobial whey protein films against spoilage and pathogenic bacteria, Proceedings of the IFT Annual meeting, Institute of Food Technologists, Chicago, 2001, 191.

62. Kenawy E-R, Bowlin GL, Mansfield K, Layman J, Simpson DG, Sanders EH, Wnek GE, Release of tetracycline hydrochloride from electrospun poly(ethylene-co-vinylacetate), poly(lactic acid), and a blend, J. Controlled Release 81(1-2), 2002, 57-64.

63. Kenawy ER, Abdel-Fattah YR, Antimicrobial properties of modified and electrospun poly(vinyl phenol), Macromol. Biosci 2(6), 2002, 261-266.

64. Imazato S, McCabe JF, Influence of incorporation of antibacterial monomer on curing behavior of a dental composite, J. Dent. Res., 73(10), 1994, 1641-1645.

65. Daly, W. H.; Guerrini, M. M.; Culberson, D.; Macossay J., Preparation and Potential for Application of Cationic Polysaccharides in Cosmetic Formulations, International Frontiers of Polymers and Advanced Materials, 4th, International Frontiers of Polymers and Advanced Materials, Plenum Press: New York, 1998, 493-512.

66. Hart E, Azzopardi K, Taing H, Graichen F, Jeffery J, Mayadunne R, Wickramaratana M., Shea MO', Efficacy of antimicrobial polymer coatings in an animal model of bacterial infection associated with foreign body implants, J. Antimicrob. chemother., 65, 2010, 974-980.

67. Nonaka T, Uemura Y, Ohse K, Jyono K, Kurihara S, Preparation of resins containing phenol derivatives from chloromethylstyrene-tetraethyleneglycol dimethacrylate copolymer beads and antibacterial activity of resins, J. Appl. Polym. Sci., 66(8), 1997, 1621-1630.

68. Gurangji Li, Shen J, A study of pyridinium-type functional polymers. IV. Behavioral features of the antibacterial activity of insoluble pyridinium-type polymers, J. Appl. Polym. Sci., 78(3), 2000, 676-684.

69. Alamri A, Newehy MHEl, Deyab Sal, Biocidal polymers: synthesis and antimicrobial properties of benzaldehyde derivatives immobilized onto amine-terminated polyacrylonitrile, Chemistry Central Journal, 6(1), 2012, 111.

70. Chen Y, Worley SD, Kim J, Wei CI, Chen TY, Santiago JI, Williams JF, Sun G, Biocidal Poly(styrenehydantoin) beads for disinfection of water, Ind. Eng. Chem. Res. 42, 2003, 280-284.

71. Shin Y, Yoo DI, Jang J, Molecular weight effect on antimicrobial activity of chitosan treated cotton fabrics, J. Appl. Polym. Sci., 80, 2001, 2495-2501.

72. Son YA, Sun G, Ionic Interactions with Quaternary Ammonium Salts, J. Appl. Polym. Sci. 90(8), 2003, 2194-2199.

73. Kong M, Chen XG, Xing K, Park HJ, Antimicrobial properties of chitosan &mode of action: A state of art review, Int. J. of Food Microbiology, 144, 2010, 51-63.

74. El-Shafei AM, Fouda MMG, Knittel D, Schollmeyu F, Characterization and solution properties of a partially hydrolyzed graft copolymer of polyacrylamide and dextran, J. of Appl. Poly. Sci. 110(3), 2008, 1289-1296.

75. Ren X, Kou L, Kocer HB, Zhu C, Worley SD, Broughton RM, Huang TS, Antimicrobial coating of an N-halamine biocidal monomer on cotton fibers via admicellar, Colloids & Surfaces A: Physicochemical and Engineering aspect. 317(1), 2008, 711-716.

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