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Eminent Role of Polymers in Drug Delivery

Madhu Gupta*, Neha Raina and Radha Rani

Department of Pharmaceutics, Delhi Pharmaceutical Sciences and Research University, India

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***Corresponding author:** Madhu Gupta, Department of Pharmaceutics, Delhi Pharmaceutical Sciences and Research University, India

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Abbreviations: NCPs: Cationic Polymers; DEX: Cationic Dextran; PLL: Poly-L-lysine; WHO: World Health Organization; PEG: Polyethylene Glycol; PDMAEMA: Poly(2-N,N-dimethylaminoethylmethacrylate)

Introduction

Polymers are indispensable part of drug delivery system. Polymers are macromolecules, made up of repeated subunits and these macromolecules to a large extent are utilized in sphere of drug delivery (for instance drug and protein conjugates of protein and drugs, micro as well as nanoparticles, nanocapsules, matrices and hydrogels, polymersomes, complexing polymers etc.). Furthermore, there is ample utilization of Polymers, aimed at improving the functioning of other drug delivery systems (such as stealth liposomes). They are used as flow controlling agents in emulsions, suspension, liquids, as viscosity controlling binders in tablets, to improve drug stability, as film coaters headed for concealing medicines unpleasant taste and to improve drug release profile. At the present time polymer or combinations of polymers are employed for releasing accurate amount of the therapeutic agent at right time in exact body compartment without hampering function of other organs. Since thirty years, mounting demand aimed at upgrading properties of polymers has led the progression in polymer mixture composites for surmounting the biologically dwindling performance as well as to augment the rigidness, an innovative class of polymers has been recognized depending on intermingling of polymers emanate or synthetically or from natural sources formulated either alone or in combinations (Figure 1).

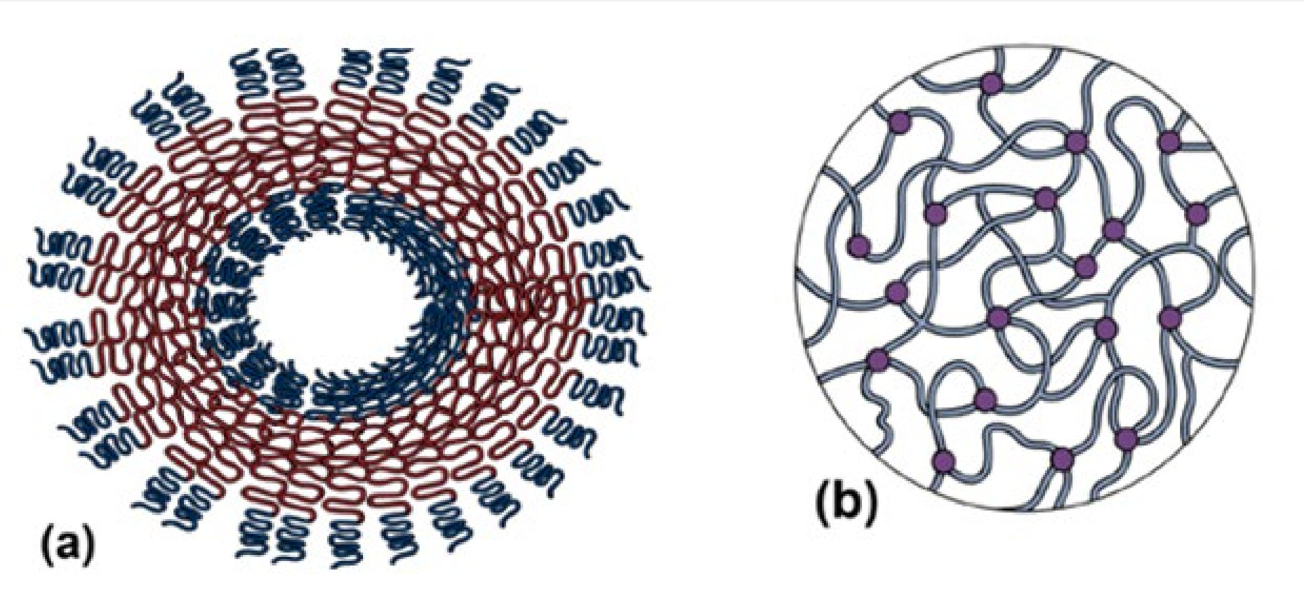

Figure 1: Structure and crosslinking of polymers (a) Structures of polymersomes and (b) Stiff highly cross-linked polymers.

These class of polymers formulated via blending of two polymers is widely known as Interpenetrating polymer network [1]. Polymers have enormous applications in the sphere of artificial organs in addition to medical devices implantation, prosthesis, scaffolds development, bone repair, dentistry, ophthalmology and numerous medical spheres [2]. The rate at which formulations is to be released is governed by means of polymers. Polymers extensive applications are taken into consideration while designing drug delivery system [3]. These new drug delivery systems include modification of drug by carrier-based drug delivery system and by drug incorporation in polymeric pumps or matrices that are positioned in apposite organ. In biomedical sphere biodegradable polymers have been broadly employed on account of their biodegradability besides biocompatibility. Mostly polymers are used as implants because of minimum side effects and more efficiency [4]. various categories of macromolecules/polymers are employed in the drug delivery system for e.g. cationic polymers, and antibacterial polymers. Cationic polymers have been categorized as the macromolecules which exhibit positive charge, which may exist either intrinsically in the polymer side chains and/or its backbone. Cationic polymers (NCPs) that are natural in origin exhibit intrinsic positive charge and also regarded as structures that are biodegradable having least toxicity along with marginal immunogenicity. By means of facile alteration of reactive sites prevailing at the most NCPs, their physicochemical properties can be effortlessly upgraded.

The list of cationic polymers comprises of Cationic gelatin that is a cost-effective, decomposable as well as natural polymer having biocompatibility that emanates from collagen in addition highly employed for therapeutic and biomedical purposes [5]. Cationic chitosan is a, natural in origin cationic copolymer encompassing arbitrarily disseminated D-glucosamine and N-acetyl glucosamine, which differs in molecular chain length, arrangement and composition [6].Cationic cellulose is, a ringed linear chain having b-1,4-D-glucan molecules, as the chief component of the plant cell wall, is the utmost plenteous polymer besides the highest plentiful organic material disseminated out all over the globe. Cellulose possesses numerous beneficial properties for instance biodegradability, biologically compatible, along with antibacterial properties developing as a supreme choice for a variety of medicinal applications [7,8]. Cationic Dextran (DEX) is a homopolysacharide of glucose, that is hydrophilic in nature and as well identified as a natural analogue to PEG [9]. And some polymers synthetic in origin and cationic in nature are Poly(2-N,N-dimethylaminoethylmethacrylate)(PDMAEMA) owns intrinsic cationic charge as a result of its tertiary amine groups present at the polymer surface which eventually convert to partially protonated at the physiological solution by which PDMAEMA is well thought-out as a promising candidate for delivery of gene [10] besides delivery of drug. Poly-L-lysine (PLL)Poly-L-lysine (PLL) was unique and the first cationic polymers inspected for developing polyplexes in conjunction with nucleic acids intended for receptor-mediated gene delivery [11].

Another category of polymers comprises of antibacterial polymers. In the treatment of bacterial infections, the major concern of healthcare system is the resistance of multiple drugs by disease causing bacteria's [12] and as per the statement of WHO (World Health Organization), it becomes the prime cause of mortality in whole world. It as an idea that in coming 30 years it may results in 10 million of death [13]. Because the pathogenic bacteria become resistant to conventional multidrug therapy, some novel agents having activity against pathogens are required to develop [14]. From the past few decades, large number of macromolecules from the class of antimicrobial systems, copolymers, and polymers are developed and functionalized with some groups (bioactive in nature) but in current time, novel and moderate polymers are also synthesized which are hydrophobic in nature. These new hydrophobic polymers comprise of protonated primary/secondary/tertiary amine which exhibits high activity against microbes as compared to others described above [15].

Classification

The antimicrobial polymers classified depending on their mechanism of action are as follows:

Passive Polymers

The layer of passive polymers decreases on bacterial surface and avert the bacterial adhesion, hence without any active interaction they cause effective bacterial repulsion. Depending on the type of bacteria (positive or negative) typical passive polymers comprises of following properties:

i. SLIPS (slippery liquid-infused porous surface) and self-healing for instance poly(dimethyl siloxane);

ii. Uncharged polymer like PEG (polyethylene glycol), poly-poly(n-vinyl-pyrrolidone), polypeptoid and poly(2-methyl-2-oxazoline)

iii. Charged polyampholytes and zwitterionic polymers for example phospholipids, sulfobetaine and phosphobetaine [12,16].

Active Polymers

These polymers actively destroy the pathogens after the functionalization of their surface with the help of active agents such as antibiotics, cationic biocides and anti-microbial peptides.

a) Examples: The cationic quaternary ammonium compounds are the widely used active polymers cause the leakage of cellular components within a cell and consequent mortality of cell by interacting with cell wall and damage of cytoplasm membrane [17]. N-halamine, polyethyleneimine and polyguanidine are other examples of active antimicrobial polymers having different action mechanisms [18].

The antimicrobial activity of polymers can be moderate by affixing active groups on them and depending on this basis these polymers are also categorized as follows:

I. Polymeric Biocides: Polymeric biocides are attached with repeating biologically active units having activity against bac-

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teria with covalent bonds like hydroxyl, carboxyl and amino groups [19,20]. Polymers used as biocides are quaternary ammonium, N-halamine, halogen, benzimidazole and sulfonium salt [21-23].

II. Polymeric Biocidals: the anti-microbial activity of biocidal polymers is comprised due to the complete macromolecule hence not required attachment of biologically active repeating units. Polymers that comprises of biocidal activity are generally cationic biocides for example Guanidinium, tertiary sulfonium, phosphonium and quaternary ammonium compounds [24,25].

Artificial Mimics of Anti-microbial Peptides (SMAPs): Currently, SMAPs gain the major inetrest of researchers because they provide the properties of anti-microbial peptides inside a polymer construct formed synthetically. Different types of synthetically mimicked anti-microbials are as follows:

i. Polyanilines [26]

ii. Polyvinyl pyridines [27]

iii. Polynorbornenes [28]

iv. Polycarbodiimides [29]

v. Polymethacrylates [30]

Conclusion

An antimicrobial polymer comprises potential activity against microbial infections and can play a vital role in elimination of consequences of deaths caused due to these infections globally. With the help of SMAPs possibility of designing and synthesizing macromolecules with precised antibacterial activity is enhanced.

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