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Review

Modification of polysaccharides: Pharmaceutical and tissue engineering applications with commercial utility (patents)

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ABSTRACT

Polymer modifications open new era for the development of polymers with requisite properties. Use of modified polymers is practically boundless. Different studies focus on biomedical applications of chemically modified polysaccharides. Development and utilization of modified polysaccharides get attention to be used as carrier for pharmaceutical drug delivery as well as tissue engineering scaffolds. Grafted polymer shows better cellular regeneration, signal transmission, diagnostic and imaging material than putative form. This review article aims to discuss various approaches to modify naturally derived polymer and their applications as pharmaceutical drug carrier and as a material for wound dressing and artificial cartilage due to better biophysical cues. Manuscript included various patents based on the applications of modified polymers and techniques used to modify polymers.

Contents

1. Introduction

Polymer is made up of two words; polus (means many) and meros (means parts). So polymer by its name shows a structure which is made of repeating units (Fig. 1). Term polymer was coined by Jacob Berzelius in 1883 [1].

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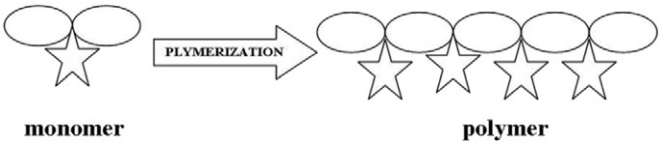

Fig. 1. Schematic diagram of polymerization.

Polysaccharides such as gum and mucilages are abundant, plentiful, cheap and widely used in pharmaceutical confectionary and food industry. Natural polysaccharide (gums and mucilages) have been explored for their uses in food industry, paper and textile, cosmetics and pharmaceutical industry. Increasing demands of polymer for different purposes open the door for the search of new polymers from renewable resources. Contents of any natural polymer depend upon environmental conditions of growth, fermentation process and culture media. Properties of polymer are depends upon their content. Basic properties such as swelling, solubility, mucoadhesion etc. are varying from polymers obtained from plants grown in different conditions [2].

In the formation of gel, linear gums and mucilages occupy more volume of water as compared to branched polysaccharides. That's why linear homogenous polysaccharide show less viscosity than branched polysaccharide for same concentration. Some polymer also shows change in viscosity during storage and viscosity of polymer may be maintained by the modification of polymer [2,3].

As for we know it is the first kind of report deals with various grafting techniques with pharmaceutical and tissue engineering applications together in a single manuscript.

Modified polymers show superior properties to the source crude material in terms of solubility, swellibility, mucoadhesion, sorbency, coagulancy and floccolancy i.e. transformation into customizable material. pH sensitivity of polymer attributed due to presence of free –COOH, –OH,–CH_2OH, —NH_2 etc. groups. Swellibility and solubility of polymer characterized in terms of hydrophilicity, hydrogen binding and ionization. Modifications of these groups entirely changes their properties hence responsiveness towards pH.

Derivatization of natural gums, pectins and mucilages result in development of high performance biological macromolecules. Polymer modification may be required to target drug at required site, to change solubility of polymer, to improve thermal stability of polymer, to make biodegradable polymer, to reduce toxic effect of drug, to make polymer moisture resistant, to make controlled hydration, to make polymer more microbial resistant, to improve transparency of polymer and to improve moisture sensitivity. Modified polymer has been found as stabilizing agent in nano-composite system. Most of the gums are hydrophilic in nature and so soluble in aqueous medium. Due to this reason they become irresponsive in organic solvents. Controlled introduction of small or long hydrocarbon chain on the polymer backbone results in the formation of new derivatives having both hydrophilic and hydrophobic region in their molecular structure. They may act as surfactant and can form micelle in solution. This property of gum may affect sol-gel transition in aqueous solvent.

Characteristics of these polymers can be altered by formation of cacervates and polyelectrolytic complex, grafting of polysaccharide backbone with other synthetic or natural polymers and derivatization of groups by another chemical moieties [3]. In new era of civilization naturally derived polymers are replaced by their modified form. Polymers can be modified by using following three methods:

1. **Blending:** In blending physical mixture of two or more than two polymers are prepared to induce required characters (Fig. 2).
2. **Grafting:** In grafting method different monomers are covalently linked to the polymer and degree of binding and chain length of monomer defined the properties of polymer. Grafted polymer consists of macromolecular chain with one or more monomers attached to the main chain as side chain. Grafting is a way to add desired properties in polymer without significant loss of initial characteristics of polymer (Fig. 3).
3. **Curing:** In this method oligomer mixture is used to adhere over substrate to form a coating. Binding of oligomer mixture is due to physical forces (Fig. 4).

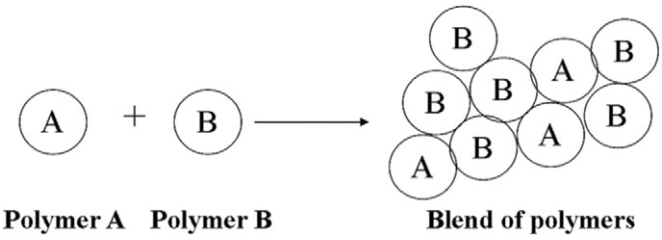

Fig. 2. Schematic diagram of blending.

Natural polysaccharide (gums and mucilages) generally contain –OH groups. In alkaline medium these –OH groups, donates it hydrogen to generate –ve ion on the backbone of gum. This ionic gum can attack carbon atom of epoxy or ester group to form vinyl derivatives of gum. Vinyl derivatives are prepared either by esterification reaction or nucleophilic substitution reaction. Maleic anhydride, acryloyl chloride, acrylic acid, glycidyl methacrylate has been successfully used to form vinyl functionalized gum. Extent of degree of substitution/ modifications also depends upon stearic hindrance caused by –OH group present in gums/mucilages. Free –CH_2OH groups present at side chain and extreme are more susceptible to modification. Schematic diagram of reaction is shown in Fig. 5.

Grafting of another synthetic monomer units over natural polymers alleviate limitations of natural polysaccharides. Grafting lead to comb or brush type graft copolymers. Linear backbone with high grafting density of side chain is the characteristics of brush type graft copolymers while comb type graft copolymers are characterized by a polymer backbone covalently bonded with one or more side chain [4].

Schematic diagram of techniques of grafting are shown in Fig. 6.

In Free radical formation technique an external radical inducing agent is used to produce free radical at main backbone of the polymer. After formation of free radical sites, monomer can get added up through chain reaction and formation of grafted chain takes place. Generally no initiators are used in microwave initiated technique of grafting. In microwave assisted initiators are used to produce free radicals. In both microwave initiated and microwave assisted techniques of grafting microwave energy convert into heat energy due to dipolar relaxation of water (solvent) or localized rotation of polar functional groups of polysaccharides. In plasma radiation induced grafting excited electrons transferred their energy from plasma to polysaccharides and leads to cleavage of bonds, which further produces free radicals. Enzymes are used in reaction mixture, which produces reactive moieties with substrate in enzymatic grafting. These reactive moieties further react to produce *graft*- co polymer. In photochemical grafting; polysaccharides contain chromophore, absorb light and excited electron leads to formation of free radicals. Redox grafting method has less control for monomer distribution over crude biopolymer. Free radical should not rapture the original backbone of parent polymer. Grafting through living polymerization (or living radical polymerization) shows better control over monomer distribution and less influenced by presence of moisture [4].

Fig. 3. Schematic diagram of grafting.