A Review on grafting and applications of Xanthan gum and its derivatives

Sandhyarani Panda¹*, Mrutyunjaya Satpathy²

1. Faculty of Biological and Chemical Sciences, Mats University, City campus, Raipur, Pandri, C.G.
2. Department of Pharmacy, Govt Womens Polytechnic, Byron Bazar, Raipur, C.G.

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1. Introduction

Xanthan gum is a natural high molecular weight polysaccharide produced by a fermentation process. It swells in the intestine, which stimulates the digestive tract to push stool through. It might slow the absorption of sugar from the digestive tract and work like saliva to lubricate and wet the mouth in people who don’t produce enough saliva. Xanthan Gum was discovered by a team of USDA researchers in the 1960’s. In 1968 it was approved for use as a food additive in the US and Europe. The research laboratories of the US Department of Agriculture discovered that the bacterium Xanthomonascampestris found in cabbage plants produces an extracellular polysaccharide with exceptional rheological properties. Since then a number of improvements in polysaccharide manufacture have been taken place. Today, xanthan gum is the most important microbial polysaccharide available commercially¹. Xanthan gum has been widely used in many important preparations, such as cosmetic and pharmaceutical products as suspending agent, and emulsifying agent².

2. Structure

The primary structure of xanthan gum is shown in Fig. 1. Xanthan gum consists of 1, 4-linked β-D-glucose residues, having a trisaccharide side chain attached to alternate D-glucosyl residues ³⁵. The backbone of the polymer is similar to that of cellulose. The side chains are β-D-mannose- 1,4- β- D-glucuronic acid- 1,2-α -D-mannose, where the internal mannose is mostly O- acetylated and the terminal mannose may be substituted by a 4,6-linked pyruvic acid ketal.

Fig:1 Primary structure of xanthan gum
The molecular weight of xanthan gum is approximately 2 x10^6 g/mol, and it can go as high as 13–50 x10^6. The secondary structure of xanthan gum has been seen to consist of a right-handed, five-fold helix with a rise per backbone disaccharide residue of 0.94nm, i.e., a five-fold helix with a pitch of 4.7nm. This justifies that the trisaccharide side chain is aligned with the backbone, and stabilizes the overall conformation by non-covalent interactions, principally hydrogen bonding. The xanthan gum molecule undergoes a thermally induced order-disorder conformational transition. The disordered form is favored by low salt concentrations and high temperatures, whereas salt stabilizes the ordered conformation. In solution the side chains wrap around the backbone, thereby protecting the labile β - (1-4) linkages from attack. It is thought that this protection is responsible for the stability of the gum under adverse conditions. Most publications give evidence that the ordered conformation of xanthan is double-stranded or dimeric.

3. Properties

This gum is soluble in cold and hot water. It needs intensive agitation upon introduction into the aqueous medium in order to avoid the formation of lumps. At high temperature and in low ionic strength, xanthan exists in solution as a disordered coil, but on cooling and/or addition of salt it undergoes a co-operative conformational transition. The disordered form is favored by low salt concentrations and high temperatures, whereas salt stabilizes the ordered conformation. In solution the side chains wrap around the backbone, thereby protecting the labile β - (1-4) linkages from attack. It is thought that this protection is responsible for the stability of the gum under adverse conditions. Most publications give evidence that the ordered conformation of xanthan is double-stranded or dimeric.

4. Conventional chemical modifications of xanthan gum

Chemical modification of xanthan gums not only minimizes these drawbacks but also enables them for use in specific drug delivery systems.

a) Modification with formaldehyde

Xanthan gum when modified with formaldehyde can improve the dissolution rate. The FT-IR spectra and the X-ray diffraction spectra both show that chemical modification reduces intermolecular interactions and crystallinity of the polymer. The changes hasten the process of swelling and dissolution. Viscosity measurements show that the chemically modified gum dissolves more rapidly than natural xanthan gum.

b) Carboxymethylation of xanthan gum

Xanthan gum derivatised to carboxy methyl xanthan gum is briefly described herein. The required amount of xanthan gum was dispersed in ice cold solution of 45% w/v sodium hydroxide. The temperature of the dispersion was maintained at 5-8°C with continuous stirring for 1h. Monochloroacetic acid solution (75% w/v) was added with stirring in the reaction mixture and the temperature was raised slowly to 15-18°C. After 30 min, the temperature was raised to 75°C and maintained for additional 30 min. The reaction mixture was then cooled to room temperature, the lumps of the modified gum prepared was cut into small pieces and dried at 50°C.

Interpenetrating network (IPN) beads of sodium carboxymethyl xanthan (SCMX) and sodium alginate (SAL) were prepared by ionotropic gelatin process using AlCl₃ as a cross-linking agent. The effect of different formulation variables like total polymer concentration, gelation time, concentration of cross-linking agent, and drug load on the extent of release of ibuprofen (IBP), a non steroidal anti-inflammatory drug, was examined. The study indicated that the IPN beads of SCMX and SAL could be a suitable dosage form to minimize the drug release in acidic solution and to control the drug release in phosphate buffer (PB) solution depending upon the need. Carboxymethylation of xanthan gum, guar gum, locust bean gum and cellulose were also reported under various reaction conditions. Carboxymethylated xanthan gum was prepared and degree of substitution (DS) determined by a colorimetric method and spectroscopic method. When compared to traditional wet chemistry methods, the spectroscopic methods developed are relatively simple, fast, without the use of toxic chemicals, requiring smaller sample size, and are ubiquitous for different types of modifications. Xanthan gum was modified to carboxymethyl xanthan gum for controlled drug delivery of bovine serum albumin for prolonged release of diltiazem and protein delivery.

5. Grafting of xanthan gum by free radicals

Grafting is an effective technique to modify the properties of synthetic and natural polymers. It is a method wherein monomers are covalently bonded onto the polymer chain. Graft copolymerization introduces hydrophobicity and stearic bulkiness, which considerably protects the matrix and carbohydrate backbone. Grafting of acrylic acid or its derivatives on gums has been used for modifying the swelling characteristics, film forming properties and drug release characteristics. Modified xanthan gums can be obtained by reacting with an unsaturated organic acid(acrylic acid) or with acid reactive
derivatives (acryloyl chloride, malic anhydride). Unsaturated xanthan derivatives, which can be used for the development of biodegradable three-dimensional networks, also possess hydrogel properties.

Behari et al. reported the graft copolymerization of acrylamide on to xanthan gum initiated by the Fe$^{2+}$/BrO$_3^-$ redox system in aqueous medium under nitrogen atmosphere. An improvement in grafting parameters was observed with increase in ferrous ion concentration, while with increasing bromate ion concentration, these parameters like, grafting ratio, efficiency, conversion and add on were found to decrease. Graft copolymerization of acrylamide(AAm) onto xanthan gum (XG) was carried out by taking two different ratios of XG to AAm (1:5, 1:10) by free radical initiation polymerization using ceric ammonium nitrate (CAN) as initiator. Briefly, 1.0 g of XG was dispersed in 120 ml of water and dissolved overnight under constant stirring in a 250 ml round-bottomed flask. Then, 5 or 10.0 g of AAm was mixed with 30 ml of water, added to XG solution, and stirred for 1 h. A quantity of initiator equivalent to 0.05 mol was dissolved in 30 ml of water and added to the above solution. Polymerization was carried out at 60°C under continuous purging of nitrogen gas for 4 h in a thermostatic water bath under constant stirring. After complete polymerization, the reaction mixture was cooled by running under tap water and poured into excess acetone to induce the precipitation. Structure of synthesized acrylamide-grafted-xanthan gum co-polymer is shown in Fig. 2.

![Structure of synthesized acrylamide-grafted-xanthan gum co-polymer](image)

Polysaccharide based graft copolymer (xanthan gum-g-4-vinyl pyridine) was also synthesized using potassium peroxymonosulfate / ascorbic acid as redox initiator in inert atmosphere. Graft copolymerization of methacrylic acid onto xanthan gum by Fe$^{2+}$/H$_2$O$_2$ redox initiator and graft copolymerization of acrylic acid onto xanthan gum using a potassium monopersulfate/Fe$^{2+}$ redox pair results in improvement of stability of xanthan gum. Graft copolymer of xanthan gum and 2-acrylamidoglycolic acid has been synthesized by free radical polymerization using bromate/thiourea redox pair in an inert atmosphere. The studies on physical properties of 2-acrylamidoglycolic acid graft xanthan gum copolymer revealed an improvement in properties such as flocculation, solubility, thermal stability, binding strength, water retention and resistance to biodegradation. The graft copolymer of xanthan gum with 2-acrylamido-2-methyl-1-propane sulfonic acid (AMPS) was synthesized using potassium bromate/ascorbic acid as a redox initiator in aqueous medium; the results showed increased swelling property and good sorption of metal ions. The synthesis of a novel biopolymer-based super porous hydrogel (SPH) through chemical cross linking by graft copolymerization of 2-hydroxyethyl methacrylate (HEMA) and acrylic acid (AA) on to xanthan gum (XG) via redox initiator system is also reported.

Graft copolymer of xanthan gum (XG) and ethylacrylate (EA) has been synthesized by free radical polymerization using potassium peroxydisulfate (KPS) as an initiator in an air atmosphere. The method used for synthesis of xanthan gum-graft–poly(ethylacrylate) is summarized in Figure: 3. The grafted copolymer shows improvement in the stability, solubility as well as in their sorbing capacity.

### 6. Chemoenzymatic grafting

Chemoenzymatic synthesis of amylose-grafted xanthan gum was reported by Arimura et al. In this method amine functionalized maltooligosaccharide was chemically introduced into the carboxylated xanthan gum by condensation using a condensing agent to produce a maltooligosaccharide-grafted xanthan gum. Then, amylose-grafted xanthan gum was prepared by thermostable phosphorylase-catalyzed enzymatic polymerization of glucose 1-phosphate from the graft chain ends on the xanthan gum derivative.
7. Microwave-assisted grafting

Microwave-assisted synthesis has expanded the competence of synthetic chemist, since it enables faster and cleaner reactions and more pure products. In chemical processing, microwave irradiation is evolving as efficient tool for chemical processing and has been utilized in various fields of chemistry including polymers. Kumar et al. have reported synthesis of xanthan-g-poly (acrylamide) using microwave assisted grafting and ceric-induced grafting. In this study % grafting was found to be higher with microwave-assisted grafting as compared to ceric-induced grafting. The extent of grafting was found to be directly related to the microwave power and exposure time. The graft copolymer was evaluated for modification of release rate using in matrix tablets of diclofenac sodium. The study revealed the faster release of drug from graft copolymer matrix tablets as compared with the ungrafted xanthan gum.

Fig:3 Synthesis of xanthan gum-graft–poly(ethylacrylate)

8. Plasma assisted chemical grafting:

Plasma chemical modifications are dry chemistry processes with high energy efficiency and cost-effectiveness. Cold plasma technology is an efficient tool for the incorporation of appropriate functional groups (e.g., amine, carboxyl, hydroxyl) onto various polysaccharides. The energy distribution among the plasma species are enough to break the bonds involved in most of the organic molecules and can also lead to the formation of new active chemical states of the carbon atoms. Thus, organic derivatives can be easily modified under selected discharge parameters through both the gas phase and surface molecular fragmentation and recombination processes. The plasma species penetrate about 100 Å from the surface and hence plasma treatment is a surface modification technique summarized in Fig: 4.

Fig:4 Plasma treatment
Jampala et al (2005) has been successfully grafted XG with reactive SiHxCl functionalities in DS-cold-plasma (dichlorosilane-cold-plasma) environment. The subsequent site grafting of primary amine groups facilitated cross-linking of XG. By increasing the plasma treatment time, the frequency independence of the XG network improved, indicating that plasma treatment time and polymer concentration may be optimized to obtain a stable gel from otherwise non-gel-forming XG. The cold-plasma modification improves the network strength, as measured by the dynamic storage modulus, \( G' \), of the aqueous solutions of XG. Thus, the cold-plasma process proves to be an efficient nonenzymatic route to modify XG such that a stable gel can be formed.

9. Conclusions

Xanthan gum is microbial exopolysaccharide produced by *Xanthomonas campestris*. Slow dissolution rate and substantial swelling limited its use to the unmodified forms in oil, textile, cosmetic and pharmaceutical industries. Xanthan gum can be modified by conventional chemical methods like carboxymethylation and by reaction with formaldehyde to improve its dissolution rate. Such modified xanthan gum reduces intermolecular interactions, so that gelatinous layer cannot form, or even if it forms, the molecules present onto the surface of particle leave rapidly facilitating the dissolution as compared with unmodified gum. For sustained release and colon targeting drug delivery, carboxymethylated xanthan gum moieties are cross-linked with the oppositely charged anions to make it resistant to dissociation in acidic pH but can be slowly degradable in the intestine. The grafting of vinyl monomers such as vinyl pyridine, methacrylic acid, 2-hydroxyethyl methyl acrylate, ethyl acrylate, acrylamide, 2-acrylamido-2-methyl propane and 2-acrylamidoglycolic acid onto xanthan gum has gained considerable attention in preparing new polymeric materials with special characteristics with enlarged the range of its utilization.

The properties of grafted polymers depend upon characteristics of monomer, its concentration along with grafting conditions. Grafting of xanthan gum with 2-acrylamido-2-methyl-propane sulfonic acid enhances swelling and metal sorption capacity; while 2-acrylamidoglycolic acid improves flocculation, solubility, thermal stability, binding strength, water retention and resistance to biodegradation properties of xanthan gum. The xanthan gum grafted polyethylene acrylate polymer can be of great use in the field of separation and purification of valuable metals.

References:


