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Review Article

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# APPLICATIONS OF BIOPOLYMERS IN PHARMACEUTICAL PREPARATIONS: A REVIEW

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#### **ABSTRACT**

Biopolymers are first dainty of research as excipient because of its stability, biodegradability, and non- carcinogenic, non-thrombogenic and renewable in nature. This review tells about the biopolymers in drug delivery as in last 2-3 decades, in the field of research in pharmaceutical drug delivery, the excipient development come into the lime light. Because it effects the formulation development and drug delivery process in many ways. Our review canvass, some of the most familiar used biopolymers as excipient in pharmaceutical drug delivery systems.

**KEYWORDS:** Biopolymers, Biodegradable, Drug delivery, Polysaccharides.

#### INTRODUCTION

Polymers of natural occurring termed as biopolymer therefore they are also named as natural polymers. In the plant kingdom, the most wide- ranging organic compound are polysaccharides. They are complex carbohydrates biopolymers composed of monosaccharide units connected together through glycosidic bonds into linear and branched chains of different lengths. They are classified on the basis of their main building units, i.e. are as follows.

- A. Types of linkages,
- B. The anomeric configuration of glycosidic linkages,
- C. Monosaccharide components.

In the life processes of all plants, polysaccharides play pivotal role. They occurs in nature according to their functions that are reserve polysaccharide, structural polysaccharide and protective polysaccharide. Further polysaccharides play vital roles in many biochemical and physiochemical processes when they form glycoconjugates with lipids and proteins resulting in biological macromolecules in the cell wall and cell wall membranes. Starch is one of the most important polysaccharides from an industrial point of view. It is desirable as a raw material owing to its affordability, simple chemical modification and biodegradability. Starch and its derivatives are used in the pharmaceutical, medicinal, and food industry etc.

The natural occurring polymers are formed during the life cycles of green flora, bacteria, animals or polymer matrix composites. These comprise the polysaccharide that is starch, cellulose, the carbohydrate made by fungi and bacteria and animal protein based biopolymers like gelatine, wool and silk.

Biopolymers, predominantly the carbohydrate source, have been set up very favourable industrial use in different forms. The polysaccharide classified below gives short information on its pharmaceutical application, biological source etc.<sup>[1]</sup>

#### Starch

Starch stored and synthesized by plants as an energy reserve. It is mainly deposited in the shape of small granules. The approximately world manufacture of starch amounts to 58 million tonnes, produce from maize (46 million tonnes), potatoes (3.5 million tonnes), and remaining coming from wheat and rice.

It is the richest carbohydrate accessible from plant kingdom and act as reserve food supply for period of growth, dormancy and germination. As, it is a biodegradable polymer with appreciable chemical properties, it act as a flexible renewable resource for various material demand in food and non-food fields. Starch's properties depend on their plant source.

Starch is a heterogeneous polymer of amylose, linear chains of  $\alpha$ - 1, 4 glycosidic bonds and amylopectin having branches which are created in amylose chains by  $\alpha$ - 1,6 glycosidic bonds to another amylose chains.<sup>[2]</sup> In pharmaceuticals products, starch is used enormously as an excipient<sup>[3]</sup> either after partial hydrolysis or unmodified.<sup>[2]</sup>

The characteristics of starch for drug delivery, has been altered in an extent of ways<sup>[4]</sup> like hydrophobic modification,<sup>[5]</sup> hydrophilic modification<sup>[6]</sup> and cross linking.<sup>[3]</sup>

Hydrophobic modification attaches and stabilizes hydrophobic drugs. This biopolymer is used in drugs such as Flufenamic acid, testosterone and caffeine. [2,5]

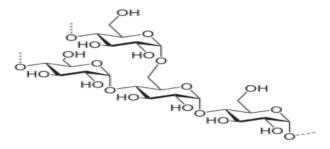


Fig.1: Structure of starch.

#### Chitosan

It is a polysaccharide takes out from the shells of crustaceans such as crab, shrimp, and other sea crustaceans as well as in cell wall of fungi. It is used as a 'medium' for drugs and other therapeutic materials and as regenerative medicine in reconstructive surgery.<sup>[7]</sup> Chitosan have vital applications in different areas like in pharmaceuticals and medicals.

As in pharmaceuticals, it is used as absorbable material with release control of active ingredients, formation of microcapsules gels with anionic polymers, excipient, drug delivery systems and encapsulation of drug.

Chitosan's drug delivery system is polyelectrolyte hydrogel. In this,

- Charge tuned to attach drugs,
- Stabilization of labile drugs in gastric conditions,
- Ammonium groups encourage transmucosal transport ionic cross linking.

It is used in drugs like doxorubicin which is anti-cancer drug.<sup>[8]</sup>

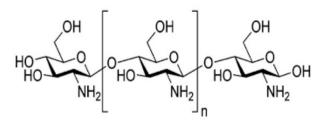


Fig. 2: Structure of chitosan.

#### **Dextran**

This is class of microbial polysaccharides that are polymerised outside the cell by enzymes known as dextran sucrase. Dextrans are collected as fuel in yeasts and bacteria. These polymers have a various uses in medical. It have been used in surgical sutures, as blood volume expanders, to improve blood flow in capillaries in the diagnosis of vascular occlusion and in the treatment of deficiency of vitamin A in both humans and animals.<sup>[9-11]</sup>

The drug which contains Dextrans are Curcumin, doxorubicin, therapeutic peptides and proteins.<sup>[12-14]</sup>

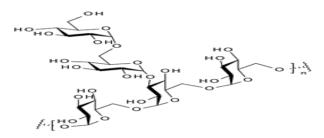


Fig. 3: Structure of dextran.

#### **Cellulose**

Cellulose is a crucial structural part of various plants made up of a linear chain of D-glucopyranosyl units connected through  $\beta$  -1, 4 glycosidic bonds. This is an ample biopolymer on earth. [15]

In its natural form, it has restricted use in pharmaceuticals products because it requires exotic solvents for easy solubility. Instead this biopolymer altered to rearrange its crystallinity, like in hydroxypropyl cellulose, which is miscible in water, harmless, and biodegradable and sanctioned for use in medicines by the food and drug administration.<sup>[16]</sup>

Also in comparison to cellulose, the cellulose esters like cellulose acetate have good solubility in organic solvents<sup>[15]</sup> and become usual components in drug delivery systems.<sup>[17]</sup> Doxorubicin drug contains this biopolymer.

Fig. 4: Structure of cellulose.

#### Hemicellulose

Hemicellulose is highly abundant and renewable resource and present accompanied with cellulose in plant cell walls and in specific woods and grasses.<sup>[18]</sup> It is different from cellulose in being chemically heterogeneous and having particular forms of Hemicellulose involve:

- **A. Glucomannan:** It is a random linear copolymer of mannose and glucose connected by 1, 4 glycosidic bonds with a little amount of branching by 1, 6 glycosidic linkages.<sup>[19]</sup> This hemicellulose has been changes to a carboxy methyl version to allow carboxylate groups for drug delivery application.<sup>[20]</sup>
- **B.** Galactoglucomannan: It is a glucomannan chain in which the mannose residues are partially substituted with galactose groups through 1, 6 glycosidic linkages and acetyl groups at C2 and C3 hydroxyl groups of the mannose.

This biopolymer is used in model protein.<sup>[20]</sup>

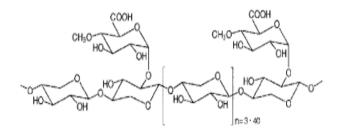


Fig. 5: Structure of hemicellulose.

#### **Pullulan**

This polysaccharide is a harmless, has low immunogenicity and high water solubility, all valuable characteristics for drug delivery. It is transform from starch through a fungus to make a linear polysaccharide comprising maltotriose units linked by  $\alpha$ - 1, 6 glycosidic linkages.<sup>[21]</sup>

For the use of Pullulan in drug delivery, the derivatization of Pullulan through its hydroxyl groups to impart the desired physicochemical properties.<sup>[22]</sup> This involve hydrophobic modification for drug delivery particle formation using amphiphilic self- assembly<sup>[23]</sup> and polyethyleneimine modification for DNA binding and protection.<sup>[24]</sup> Pullulan is used in drugs like model protein, IR dye 800 and siRNA.<sup>[25]</sup>

Fig. 6: Structure of pullulan.

#### **Alginates**

These polysaccharides are linear, unbranched found in brown seaweed and marine algae such as *Laminaria hyperborea* and *Ascophyllum nodosum*.

Alginates consists of two differ monomers in varying proportions, namely  $\alpha$ -L-gulcuronic acid and  $\beta$ -D-mannuronic acid connected  $\alpha$  or  $\beta$ -1,4 glycosidic bonds. They have extreme molecular weight of 20 to 600KDa. These polymers have been used and considered stabilizes in suspending agents, tablets binders and tablet disintegrants. This biopolymer used in drugs such as isoniazid, rifampicin. [28, 29]

Fig. 7: Structure of alginate.

#### REFERENCES

- 1. Singh A Biopolymers in drug delivery: A review. Pharmacol online, 2011; 674: 666-674.
- 2. Robyt, J. F. Starch: Structure, properties, chemistry, and enzymology. In B. Fraser-Reid, K. Tatsuta, & J. Thiem (Eds.). Glycoscience Berlin: Springer-Verlag, 2008; 1437–1472.
- 3. Zhang, A., Zhang, Z., Shi, F., Ding, J., Xiao, C., Zhuang, X., et al. Disulfide crosslinked pegylated starch micelles as efficient intracellular drug delivery platforms. Soft Matter, 2013; 9(7): 2224–2233.
- 4. Masina, N., Choonara, Y. E., Kumar, P., du Toit, L. C., Govender, M., Indermun, S., et al. A review of the chemical modification techniques of starch. Carbohydrate Polymers, 2017; 157: 1226–1236.

- Santander-Ortega, M. J., Stauner, T., Loretz, B., Ortega-Vinuesa, J. L., Bastos-González, D., Wenz, G., et al. Nanoparticles made from novel starch derivatives for transdermal drug delivery. Journal of Controlled Release, 2010; 141(1): 85–92.
- Quadrado, R. F. N., & Fajardo, A. R. Microparticles based on carboxymethyl starch/chitosan polyelectrolyte complex as vehicles for drug delivery systems. Arabian Journal of Chemistry, 2018.
- 7. Crini G. Chitine et chitosane: du biopolymère à l'application. Presses Univ. Franche-Comté, 2009.
- 8. Boddohi, S., Moore, N., Johnson, P. A., & Kipper, M. J. Polysaccharide-based polyelectrolyte complex nanoparticles from chitosan, heparin, and hyaluronan. Biomacromolecules, 2009; 10(6): 1402–1409.
- 9. R. M. Alsop, Prog. Ind. Microbiol. Amsterdam: Elsevier., 1983; 1: 101.
- 10. C. Larsen, Adv. Drug Delivery Rev., 2008; 3(1): 103.
- 11. L. Peng, S. Bihua, Y. Caixia, G. Guanhui, L. Ping, Y. Huqiang, L. Mingxing and B. Wang, Polym. Chem., 2013; 1: 284.
- 12. Chen, Y., Mohanraj, V. J., & Parkin, J. E. Chitosan-dextran sulfate nanoparticles for delivery of an anti-angiogenesis peptide. Letters in Peptide Science, 2003; 10(5–6): 621–629.
- 13. Ramasamy, T., Tran, T. H., Cho, H. J., Kim, J. H., Kim, Y. I., Jeon, J. Y., et al. Chitosan-based polyelectrolyte complexes as potential nanoparticulate carriers: Physicochemical and biological characterization. Pharmaceutical Research, 2013; 31(5): 1302–1314.
- 14. Sarmento, B., Martins, S., Ribeiro, A., Veiga, F., Neufeld, R., & Ferreira, D. Development and comparison of different nanoparticulate polyelectrolyte complexes as insulin carriers. International Journal of Peptide Research and Therapeutics, 2006; 12(2): 131–138.
- Senna, A. M., Novack, K. M., & Botaro, V. R. Synthesis and characterization of hydrogels from cellulose acetate by esterification crosslinking with EDTA dianhydride. Carbohydrate Polymers, 2014; 114: 260–268.
- 16. Tan, J., Kang, H., Liu, R., Wang, D., Jin, X., Li, Q., et al. Dual-stimuli sensitive nanogels fabricated by self-association of thiolated hydroxypropyl cellulose. Polymer Chemistry, 2011; 2(3): 672–678.
- 17. Oliveira, V. A., Veloso, T. C., Leao, V. A., dos Santos, C. G., & Botaro, V. RHydrogels of cellulose acetate crosslinked with pyromellitic dianhydride Part I: Synthesis and swelling kinetics. Quimica Nova, 2013; 36(1): 102–106.

- Voepel, J., Edlund, U., & Albertsson, A.-C. Alkenyl-functionalized precursors for renewable hydrogels design. Journal of Polymer Science A: Polymer Chemistry, 2009; 47(14): 3595–3606.
- 19. Katsuraya, K., Okuyama, K., Hatanaka, K., Oshima, R., Sato, T., & Matsuzaki, K. Constitution of konjac glucomannan: Chemical analysis and 13C NMR spectroscopy. Carbohydrate Polymers, 2003; 53(2): 183–189.
- 20. Du, J., Sun, R., Zhang, S., Govender, T., Zhang, L.-F., Xiong, C.-D., et al. Novel polyelectrolyte carboxymethyl konjac glucomannan–chitosan nanoparticles for drug delivery. Macromolecular Rapid Communications, 2004; 25(9): 954–958.
- 21. Kaneo, Y., Tanaka, T., Nakano, T., & Yamaguchi, Y. Evidence for receptormediated hepatic uptake of pullulan in rats. Journal of Controlled Release, 2001; 70(3): 365–373.
- 22. Singh, R. S., Kaur, N., Rana, V., & Kennedy, J. F. Pullulan: A novel molecule for biomedical applications. Carbohydrate Polymers, 2017; 171: 102–121.
- 23. Morimoto, N., Hirano, S., Takahashi, H., Loethen, S., Thompson, D. H., & Akiyoshi, K. Self-assembled ph-sensitive cholesteryl pullulan nanogel as a protein delivery vehicle. Biomacromolecules, 2013; 14(1): 56–63.
- 24. Kang, J. H., Tachibana, Y., Kamata, W., Mahara, A., Harada-Shiba, M., & Yamaoka, T. Liver-targeted siRNA delivery by polyethylenimine (PEI)-pullulan carrier. Bioorganic & Medicinal Chemistry, 2010; 18(11): 3946–3950.
- 25. Akiyoshi, K., Yamaguchi, S., & Sunamoto, J. Self-aggregates of hydrophobic polysaccharide derivatives. Chemistry Letters, 1991; 1263–1266.
- 26. Aquilera, JM, Stanley DW. Microstructural principles of food processing and engineering. Springer: Aspen, Germany, 1999; 99-103.
- 27. Liew CV, Chan LW, Ching AL, Heng PWS. Evaluation of sodium alginate as drug release modifier in matrix tablets. Int J Pharm, 2006; 309: 25-37.
- 28. Li, T., Shi, X.-W., Du, Y.-M., & Tang, Y.-F. Quaternized chitosan/alginate nanoparticles for protein delivery. Journal of Biomedical Materials Research, 2007; 83(2): 383–390.
- 29. Zahoor, A., Sharma, S., & Khuller, G. K. Inhalable alginate nanoparticles as antitubercular drug carriers against experimental tuberculosis. International Journal of Antimicrobial Agents, 2005; 26(4): 298–303.