Review Article

Natural Polymers and their Applications

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ABSTRACT

Active ingredient and excipients are two main ingredients of any pharmaceutical formulation. Excipients help in the manufacturing of dosage form as well as improve physicochemical parameters of the dosage form. Polymers play a vital role in any dosage form as excipients. The influencing capacity of polymers towards the drug release and should be compatible, non-toxic, and stable and economic etc. They are broadly classified in three categories viz. natural polymers, semi-synthetic and synthetic polymers. Natural polymers are generally used as rate controlling agents, taste masking agents, protective and stabilizing agents in the oral drug delivery system. To provide uniform drug delivery certain polymers are used to reduce the frequency of dosing and to increase effectiveness of the drug by localization at the site of action. Nowadays, due to many problems associated with drug release and side effects of synthetic polymers manufacturers are inclined towards using natural polymers. Natural polymers being polysaccharides are biocompatible and without any side effects. Applications of natural polymers in pharmacy are large in comparison to the synthetic polymers and have wide scope in food and the cosmetic industry.

Keywords: Polymers, agar, cellulose, starch, sustained release, controlling agents.

INTRODUCTION

The word 'polymer' is derived from Greek words, poly which means 'many' and meros means 'parts or units of high molecular mass'. Each molecule consists of a very large number of single structural units joined together in a regular manner by covalent bonds. Polymers are the giant molecules of high molecular weight called macromolecules which are formed by linking together a large number of small molecules, called monomers. The process by which monomers combine to form polymer is known as polymerization[1].

The polymerization is defined as a chemical reaction in which two or more substances combine together with or without evolution of water, heat or any other solvents to form a molecule of high molecular weight. The product obtained is called polymer and the starting material from which the polymers are made is called monomer.

Natural polymers

These polymers are found in nature generally from plants and animals sources.

Examples are proteins, cellulose, starch, resins.

Semi-synthetic polymers

These polymers are obtained from natural polymers by simple chemical treatment to change the physical properties of natural polymers like Starch, silicones.

Synthetic polymers

The fibers which are synthesized in laboratory by polymerization of simple chemical molecules are called synthetic polymers, example: Nylon, polyethene, polystyrene, synthetic rubber, PVC, Teflon etc.

The specific application of natural polymers in pharmaceutical formulations include their use in the manufacture of solid implants, films, beads, microparticles, nanoparticles, inhalable and injectable systems as well as viscous liquid formulations[2-4].

Within these dosage forms, polymeric materials have fulfilled different roles such as binders, matrix formers or drug release modifiers, film coating formers, thickeners or viscosity enhancers, stabilizers, disintegrants, solubilisers, emulsifiers, suspending agents, gelling agents and bioadhesives.[5]

Importance of Herbal Polymers over Synthetic Polymers

Biodegradable

Naturally occurring polymers produced by all living organisms. They show no adverse effects on the environment or human being. In contrary, synthetic polymers, being prepared by the help of chemicals have side effect on atmosphere as well as on the human being.

Biocompatible and non-toxic

Chemically, nearly all of these plant materials are carbohydrates in nature and composed of repeating monosaccharide units. Hence they are non-toxic as compared to synthetic polymers.

Economic

Natural polymers are cheaper and their production cost is less than synthetic material.

Safe and devoid of side effects

They are found in a natural form and hence, safe and having no side effects whereas synthetic polymers being prepared by using chemicals have side effects.

Easy availability

Natural polymers are growing in the form of herbs in many counties being economical than synthetic polymers and having no side effect and keeping in view their huge application in many industries, they are produced in large quantity hence their availability is ensured than synthetic polymers.[6]

Drawbacks of Herbal Polymers

Microbial contamination

During production, they are exposed to external environment hence there are chances of microbial contamination.

Batch to batch variation

Synthetic manufacturing is controlled procedure with fixed quantities of ingredients while production of natural polymers is dependent on environment and various biotic and abiotic factors.

The uncontrolled rate of hydration

Due to differences in the collection of natural materials at different times, as well as differences in region, species, and climate conditions the percentage of chemical constituents present in a given material may vary.[6]

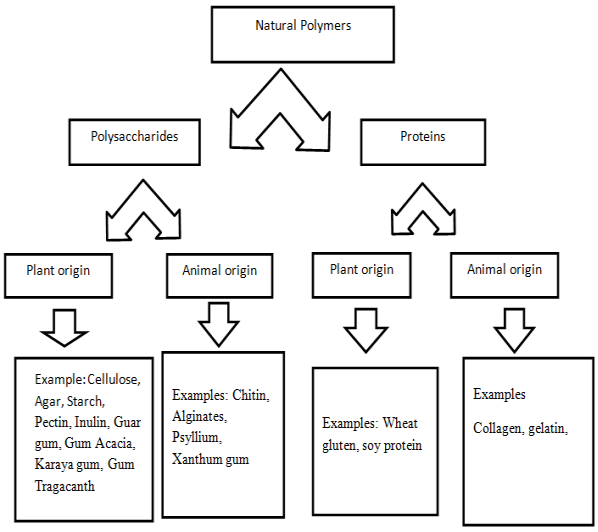
Slow Process

Natural polymers have a slow rate of production as the production rate is depends upon the environment and many other factors.

Heavy metal contamination

There are chances of Heavy metal contamination often associated with herbal excipients.[7]

Classification



Polysaccharides from Plant Origin

Cellulose

Composition

It is an organic polysaccharide consisting of a linear chain of several hundred to over ten thousand β(1→4) linked D-glucose units having the formula $(C_6H_{10}O_5)_n$.[8] The plant cell wall mainly consist of cellulose, hemicelluloses and pectin.[9]

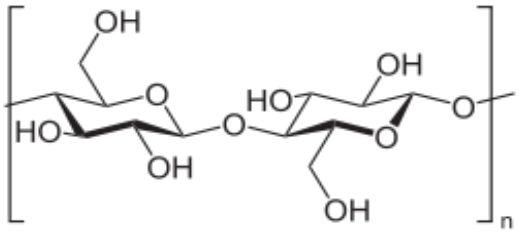


Figure 1: Structure of Cellulose

Applications

- **Microcrystalline cellulose** is mainly used in the pharmaceutical industry as a diluent/binder in tablets for both the granulation and direct compression processes.[10]
- **Carboxylated methyl cellulose** is used in drug formulations, as binder for drugs, film-coating agent for drugs, ointment base etc.[11,12,13]
- **Cellulose acetate fibers** are used in Wound dressings.[14,15]

Agar

Source

Agar or agar-agar consists of dried gelatinous substance obtained from *Gelidium amansii* (Gelidaceae) and it is also obtained from several other species of red algae like, gracilaria (Gracilariaceae) and Pterocladia (Gelidaceae).[16]

Composition

Agar consists of a mixture of agarose and agaropectin. The agarose is a linear polymer which is made up of the repeating monomeric unit of agarobiose. Whereas, Agarobiose is a disaccharide made up of D-galactose and 3,6 - anhydro-L-galactopyranose. Agaropectin is a heterogeneous mixture of smaller acidic molecules that gel poorly.

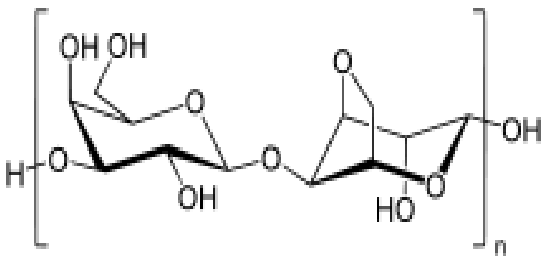


Figure 2: Structure of Agar

Applicatons:

- Agar is used as Suspending agent, emulsifying agent, gelling agent in suppositories, surgical lubricant, tablet disintegrants, medium for bacterial culture, laxative.
- It is also used for the preparation of jellies, confectionary items, tissue culture studies, and in microbiology study.[17]

Starches

Source

Starch is the principal carbohydrate reserved material in green plants and it is mainly present in seeds and underground organs. Starch occurs in the form of granules (starch grains). A number of starches are recognized for pharmaceutical use and these include maize (*Zea mays*), rice (*Oryza sativa*), wheat (*Triticum aestivum*), and potato (*Solanum tuberosum*).[16]

Composition

Starch or amylum is a carbohydrate consisting of a large number of glucose units joined together by glycosidic bonds. It consists of two polymers, namely amylose (a non-branching helical polymer consisting of α-1, 4 linked D-glucose monomers) and amylopectin (a highly branched polymer consisting of both α-1,4 and α-1,6 linked D-glucose monomers).[18]

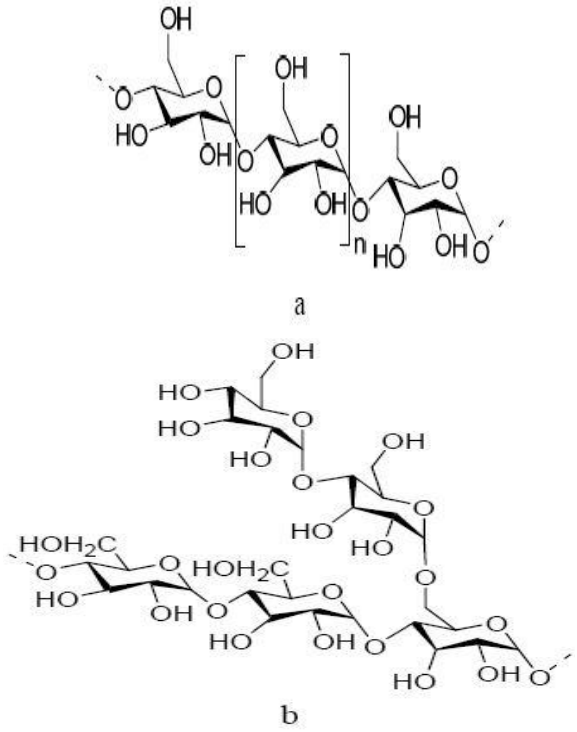


Figure 3: Structure of a) Amylose and b) amylopectin

Applications

Thermoplastic starch is used in packaging, containers, mulch films, textile sizing agents, adhesives[19]

Inulin

Source

It is a polysaccharide obtained from the bulbs of Dehlia, *Inula Helenium* (Compositae), roots of Dendelion, *Taraxacum officinale* (Compositae). Burdock root, *Saussurea lappa* (Compositae) or chicory roots, *Cichonium intybus* (Compositae).[16]

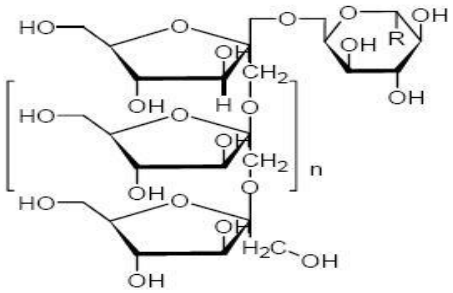


Figure 4: Structure of Inulin

Applications

- Inulin with a high degree of polymerization was used to prepare biodegradable colon-specific films in combination with Eudragit® RS that could withstand break down by the gastric and intestinal fluids.[20]

Guar Gum

Source

Guar gum is also called guaran, clusterbean, Calcutta lucern, Gum cyamposis, and Cyamopsis gum, Guarina, Glucotard and Guyarem[21]. Guar gum is the powder of the endosperm of the seeds of *Cyamopsis tetragonolobus* Linn. (Leguminosae).[16]

Composition

Chemically, guar gum is natural polysaccharide composed of the sugars galactose and mannose It is a galactomannans which is a linear polysaccharide consisting of (1→4)-diequatorially linked β-D- mannose monomers, some of which are linked to single sugar side-chains of α-D-galactose attached.[21] Guar gum has a backbone composed of β-1,4 linked- D-mannopyranoses to which, on average, every alternate mannose an α-D-galactose is linked 1→6.[22]

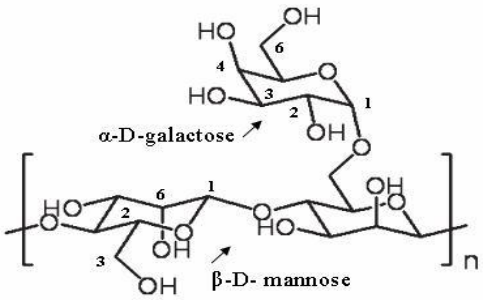


Figure 5: Structure of Guar Gum

Applications

- Several modifications of guar gum is used for drug delivery system[23]
- Carboxymethyl guar film is used for the formulation of transdermal therapeutic system.[24]
- Guar gum is particularly useful for colon delivery because it can be degraded by specific enzymes in this region of the gastrointestinal tract. The gum protects the drug while in the stomach and small intestine environment and delivers the drug to the colon where it undergoes assimilation by specific microorganisms or degraded by the enzymes excreted by these microorganisms.[25]

Polysaccharides from Animal Origin

Chitin

Source

Chitin is the polysaccharide derivative containing amino and acetyl groups and are the most abundant organic constituent in the skeletal material of the invertebrates.

It is mainly found in mollusks, annelids, arthropods. It is also a constituent of the mycelia and spores of many fungi.[16]

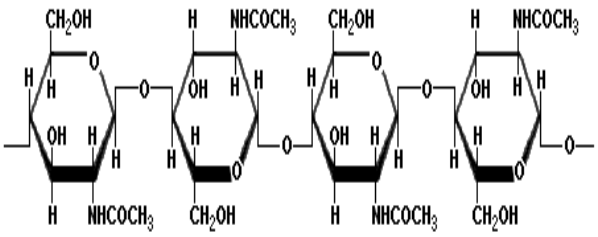


Figure 6: Structure of Chitin

Applications

- Chitosan and their derivatives (*N*-trimethyl chitosan, mono-*N*-carboxymethyl chitosan) are safe and effective absorption enhancers to improve mucosal, nasal, peroral drug delivery of hydrophilic macromolecules such as peptide and protein drugs and heparins.
- Chitosan nanoparticles and microparticles are also suitable for controlled drug release.[26]

Xanthan Gum

Source

Xanthan gum is a high molecular weight extracellular polysaccharide produced by the fermentation of the gram-negative bacterium *Xanthomonas campestris*.

Composition

The primary structure of naturally produced cellulose derivative contains a cellulose backbone (-D-glucose residues) and a trisaccharide side chain of -D-mannose- -D gluronic acid – -D-mannose attached with the main chain of alternate glucose residues.[27]

Applications

- Xanthan gum is widely used in oral and topical formulations, cosmetics, and in food industry as a suspending and stabilizing agent.
- It has also been used to prepare sustained release matrix tablets.[28]

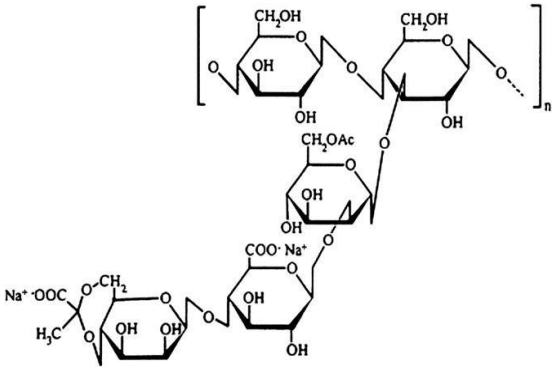


Figure 7: Structure of Xanthan Gum

Alginate

Source

Alginate is a water-soluble linear polysaccharide extracted from brown seaweed.

Composition

It is composed of 1–4 linked -L-glucuronic and -D-mannuronic acid residues.[29,30]

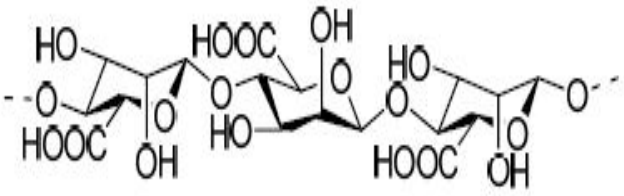


Figure 8: Structure of Alginate

Applications

- Alginate based mesalazine tablets are used for intestinal drug delivery system.[31]
- Alginate is also as encapsulation materials for controlled drug delivery to mucosal tissue.[32]
- It is also used to prepare mucoadhesive drug delivery systems.[33]

Psyllium

Source

Psyllium mucilage is obtained from the seed coat of *Plantago ovata* by milling the outer layer of the seeds.[34]

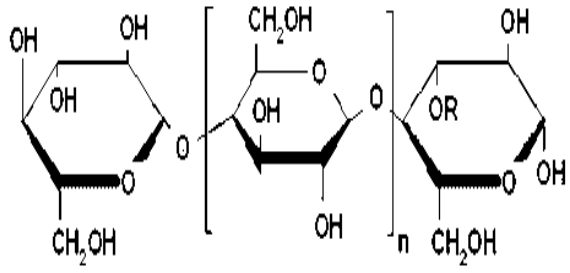


Figure 9: Structure of Psyllium

Applications

- It has tablet binding properties.[34]
- Psyllium husk was used in combination with other excipients such as hydroxypropyl methylcellulose to prepare a novel sustained release, swellable and bioadhesive gastro retentive drug delivery systems for ofloxacin.[35]

Proteins from Animal Sources

Collagen

Source

Collagen is the primary protein component of animal connective tissues[36]. The most abundant sources of collagen are pig skin, bovine hide, and pork and cattle bones.[37]

Composition

27 types of collagen exist and composed of different polypeptides, which contain mostly glycine, proline, hydroxyproline and lysine.[36,37] The flexibility of the collagen chain depends only on the glycine content[36].

Applications

- Collagen films are used in ophthalmology as drug delivery systems for slow release of incorporated drugs.[38]
- It was also used for tissue engineering including skin replacement, bone substitutes, and artificial blood vessels and valves.[39]

Gelatin

By denaturation and/or physical–chemical degradation of collagen, a high molecular weight polypeptide is produced, called gelatin[40]. Gelatin is also a protein and consists of 19 amino acids[41]. It is water soluble. Elastin, albumin and fibrin are other proteins from animal sources.[42]

Applications

These widely include emulsifiers, foaming agents, colloid stabilizers, biodegradable film-forming materials, and microencapsulating agents.[43]

Proteins from Vegetal Sources

Wheat Gluten

Wheat gluten is a protein by-product of the starch fabrication.

Composition

Wheat gluten contains two main groups of proteins, gliadin and glutenin. Gliadins are proteins molecules with disulphide bonds and have low molecular weight and a low level of amino acids with charged side groups. Glutenins are more sophisticated proteins, with a three dimensional structure. Their molecular weight is at least ten times higher than that of gliadins.

Advantages

- Wheat gluten materials have the fastest degradation rates.
- Gluten is fully biodegradable and the products obtained are non-toxic.
- It is readily available in high quantity and at low cost.

Applications

Wheat gluten has been proven to be an excellent film forming agent.[44]

Soy Protein

Source

According to the production method different categories of soy proteins exist: soy protein isolate, soy protein concentrate and textured soy protein.

Composition

Soy protein isolate is the most refined form of soy protein and contains about 90 percent protein. Soy protein concentrate is basically soybean without the water soluble carbohydrates. It contains about 70 percent of protein.

Application

It has been used since 1959 as an ingredient in a variety of foods for its functional properties, which include emulsification and texturizing. Recently the popularity of soy protein has been increasing, mainly because of its health benefits. It has been proven that soy protein can help to prevent heart problems.[45]

CONCLUSION

Polymers play a vital role in the drug delivery system. So, the selection of polymer plays an important role in the manufacturing of drugs. But, selection of polymers has to be taken with care regarding its toxicity, drug compatibility and degradation pattern. Thus, we can say that natural polymers can be good substitute for the synthetic polymers and many of the side effects of the synthetic polymers can be overcome by using natural polymers.

REFERENCES

1. Gowariker V. R., Viswanathan N. V. and Shreedhar J., Polymer Science, New Age International, New Delhi, 2005, 1-15.
2. Pandey R., Khuller G.K., Polymer based drug delivery systems for mycobacterial infections, Curr. Drug Deliv. 1, 2004, 195-201.
3. Chamarthy S.P., Pinal R., Plasticizer concentration and the performance of a diffusion-controlled polymeric drug delivery system, Colloids Surf. A. Physiochem. Eng. Asp. 331, 2008, 25-30.
4. Alonso-Sande M., Teijeiro D., Remuñán-López C., Alonso M.J., Glucomannan a promising polysaccharide for biopharmaceutical purposes, Eur. J. Pharm. Biopharm. 72 Suppl 2**,** 2009, 453-62.
5. Guo J., Skinner G.W., Harcum W.W., Barnum P.E., Pharmaceutical applications of naturally occurring water-soluble polymers, PSTT. 1, 1998, 254-261.x
6. Girish K. Jani, Dhiren P. Shah, Vipul D. Prajapati, Vineet C. Jain, Gums and mucilages: versatile excipients for pharmaceutical formulations Asian J. Pharm. Sci. 4 Suppl 5, 2009, 309-332.
7. Shirwaikar A., Prabu S.L., Kumar G.A., Herbal excipients in novel drug delivery systems, Indian J. Pharm. Sci. 70, 2008, 415-422.
8. Nishiyama, Yoshiharu, Langan, Paul, Chanzy, Henri, Crystal Structure and Hydrogen-Bonding System in Cellulose Iβ from Synchrotron X-ray and Neutron Fiber Diffraction, J. Am. Chem. Soc. 124 Suppl 31, 2002, 9074–9082.
9. Scheller H.V., Jensen J.K., Sørensen S.O., Harholt J., Geshi N., Biosynthesis of pectin, Physiol. Plant. 129, 2007, 283-295.
10. Dumitriu S. Ed. Hon, D.N.-S. Cellulose and its derivatives: Structures, Reactions and Medical Uses, In Polysaccharides in medicinal applications. Marcel Dekker, Inc: New York, NY, USA; 1996, 87-106.
11. Chambin DC, Debray C, Rochat-Gonthier MH, Le MM, Pourcelot M (2004) Effects of different cellulose derivatives on drug release mechanism studied at a pre-formulation stage. J Control Release, 95(1), 2004, 101–108.
12. Obae HI, Imada K (1999) Morphological effect of microcrystalline cellulose particles on tablet tensile strength. Int J Pharm 182, 1999, 155–164.
13. Westermark S, Juppo AM, Kervinen L, Yliruusi J (1999) Microcrystalline cellulose and its microstructure in pharmaceutical processing. Eur J Pharm Biopharm, 48, 1999, 199–206.
14. Orawan S, Uracha R, Pitt S (2008) Electrospun cellulose acetate fiber mats containing asiaticoside or Centella asiatica crude extract and the release characteristics of asiaticoside. Polymer, 49(19), 2008, 4239–4247.
15. Abdelrahman T, Newton H (2011) Wound dressings: principles and practice. Surgery, 29, 2011, 491–495.
16. Kokate C.K., Purohit A.P., Gokhale S.B., Pharmacognosy, 22nd ed. India: Nirali Prakashan; 2003, 133-166.
17. Trease G.E., Evans W.C., Text Book of Pharmacognosy, 15th ed. London: Balliere, Tindall; 2002, 200-201.
18. Te-Wierik G.H., Eissens A.C., Bergsma J., Arends-Scholte A.W., Bolhuis G.K., A new generation starch product as excipient in pharmaceutical tablets, III: Parameters affecting controlled drug release from tablets based on high surface area retrograded pregelatinized potato starch, Int.J. Pharm. 157, 181-187.
19. Zhao 2008; Maurizio 2005; Ozdemir and Floros 2004; Dave 1999; Guo 2005; Kumbar 2001; Li 2011.
20. Vervoort L., Kinget R., *In vitro* degradation by colonic bacteria of inulin HP incorporated in Eudragit RS films, Int. J. Pharm. 129, 1996, 185-190.
21. Doyle J.P., Lyons G., Morris E.R., New proposals on hyperentanglement of galactomannans: Solution viscosity of fenugreek gum under neutral and alkaline conditions, Food Hydrocol. 23, 2008, 1501-1510.
22. Coviello T., Alhaique F., Dorigo A., Matricardi P., Grassi M., Two galactomannans and scleroglucan as matrices for drug delivery: Preparation and release studies, Eur. J. Pharm. Biopharm. 66, 2007, 200-209.
23. Sharma RL. Synthesis and characterization of graft copolymers of N-Vinyl-2-Pyrrolidone onto guar gum for sorption of Fe2+ and Cr6+ions. Carbohydr Polym, 83, 2011, 1929-36.
24. Murthy S, Hiremath S, Paranjothy K. Evaluation of carboxymethyl guar films for the formulation of transdermal therapeutic systems. Int J Pharm, 272, 2004, 11-8.
25. Dürig T., Fassihi R., Guar-based monolithic matrix systems: effect of ionizable and nonionizable substances and excipients on gel dynamics and release kinetics, J. Control Release. 80, 2002, 45-56.
26. Inez M. Van der Lubben, J. Coos Verhoef, Gerrit Borchard, Hans E. Junginger, Chitosan and its derivatives in mucosal drug and vaccine delivery, European Journal of Pharmaceutical Sciences, 14 Suppl 3, 2001, 201-207.
27. Gohel M.C., Amin A.F., Patel K.V., Panchal M.K., Studies in release behavior of diltiazem HCl from matrix tablets containing (hydroxypropyl) methyl cellulose and xanthan gum, Boll. Chim. Farm. 141, 2002, 21-28.
28. Wade A and Weller P J, Hand Book of Pharmaceutical Excipients, 2nd Edn, The Pharmaceutical Press, London, 1994, 186-190, 383, 384, 362-366.
29. Haug A, Larsen B, Smidsrod O. Studies on the sequence of uronic acid residues in alginic acid. ActaChemScand, 21, 1967, 691-704.
30. Haug A, Larsen B. Quantitative determination of the uronic acid composition of alginates. Acta Chem. Scand, 16, 1962, 1908-18.
31. Tug˘cu-Demiro¨z F, cartu¨rk F, Takka S, O¨ znur Konus-Boyunag. Evaluation of alginate based mesalazine tablets for intestinal drug delivery. Euro J Pharm Biopharm, 67, 2007, 491-497.
32. Moebus K, Siepmann J, Bodmeier R. Alginate–poloxamer microparticles for controlled drug delivery to mucosal tissue. Euro J PharmBiopharm, 72, 2009, 42-53.

33. Davidovich-Pinhas M, Harari O, Bianco-Peled H. Evaluating the mucoadhesive properties of drug delivery systems based on hydrated thiolated alginate. J Control Rel, 136, 2009, 38-

34. Kulkarni G.T., Gowthamrajan K., Rao B.G., Suresh B., Evaluation of binding properties of plantago ovata and Trigonella foenum graecum mucilages, Indian Drugs. 38, 2002, 422-468.

35. Chavanpatil M.D., Jain P., Chaudhari S., Shear R., Vavia P.R., Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin, Int. J. Pharm. 316, 2006, 86-92.

36. Gelse K.; Poschi E.; Aigner T. Collagens – structure, function and biosynthesis. *Adv. Drug Deliv. Rev*. 55, 2003, 1531-1546.

37. Gomez-Guille MC, Gimenez B, Lopez CME, Montero MP (2011) Functional bioactive properties of collagen and gelatin from alternative sources: a review. Food Hydrocolloids, 25, 2011, 1813–1827.

38. Rubin AL, Stenzel KH, Miyata T, White MJ, Dune M (1973) Collagen as a vehicle for drug delivery: preliminary report. J of Clinical Pharmacology, 13, 1973, 309–312.

39. Lee HC, Anuj S, Lee Y (2001) Biomedical applications of collagen. International J of Pharmaceutics, 221, 2001, 1–22.

40. Sperling L.H.; Carrher C.E. Gelatin. *Encyclopedia of polymer science and engineering*; Mark H.F., Bikales N.M., Overberger C.G., Menges G., Eds.; J. Wiley and sons: New York, USA, Volume 12, 1988, 672.

41. Gomez-Guillen M.C.; Perez-Mateos M.; Gomez-Estaca J.; Lopez-Caballero E.; Gimenez B.; Montero P. Fish gelatin: A renewable material for developing active biodegradable films. *Trends Food Sci. Technol*. 20, 2009, 3-16.

42. Nair L.S.; Laurencin C.T. Biodegradable polymers as biomaterials. *Progr Polym. Sci*. 32, 2007, 762-798.

43. Draget KI, Skjåk-Braek G, Smidsrød O (1997) Alginate based new materials. Int J Biol Macromol, 21, 1997, 47–55.

44. Attenburrow G.; Barnes D.J.; Davies A.P.; Ingman S.J. Rheological properties of wheat gluten. *J. Cereal. Sci*. 12, 1990, 1-14.

45. Shurtleff W.; Aoyagi A. *Soy Protein Isolates, Concentrates, and Textured Soy Protein Products*; Soyfoods Center: Lafayette, USA, 1989.

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