Novel Approaches in Drug Designing & Development
ISSN: 2575-8942

Juniper PUBLISHERS key to the Researchers

Mini Review
Volume 3 Issue 1 – November 2017

Nov Appro Drug Des Dev

Role of Natural Polymers in Drug Delivery Systems as Challenging Ailments

Lakshmana Prabu S[1]* and Suriyaprakash TNK[2]

[1]*Department of Pharmaceutical Technology, University College of Engineering, Anna University, India*

[2]*Department of Pharmaceutics, Al Shifa College of Pharmacy, India*

Submission: October 10, 2017; **Published:** November 13, 2017

***Corresponding author:** Lakshmana PS, Department of Pharmaceutical Technology, University College of Engineering, Anna University, India, Tel: +91-9750550965; Email: slaxmanvel@gmail.com

Abstract

Recently, polymer based drug delivery systems represents frontier areas in science which attracts numerous research interests from both academia and industry. Nanoparticle system has become important role in science and technology which have found its own role in everyday human life. Over the past decades there has been considerable interest in using polymers from various resources as a carrier in nanoparticle drug delivery systems due to their multifaceted therapeutic benefits. Such polymers have been used in various clinical applications due to their versatile characters like biocompatibility, biodegradability, ready availability and low immunogenicity. These polymers can effectively delivery the drug into the target site which provides better therapeutic effect leads to lesser side effects. Polymer based nanoparticle system widely investigated for its various therapeutic applications, such as sustained and targeted drug release, vaccine and gene delivery.

Polymeric Nanoparticle can have more advantages viz., more amount of drug encapsulation, enhanced circulation in the body, reduce off-target effects, improves drug kinetics and stability. Nature of polymer, its source and physiochemical properties are having important role in drug release and target specificity. Other parameters like particle size, surface charge, morphology of the surface and release rate of the loaded molecules are the important parameters in the nanoparticle delivery system. In this article it is intended to discuss various natural biopolymers used in nanoparticle drug delivery system.

Keywords: Nanoparticle; Polymers; Drug delivery system; Drug release

Introduction

Polymers are large molecule made up of recurring structural units each of which can be regarded as derived from a specific compound called a monomer. Generally polymer consisting of (at least five) repeated chemical units (“mers”) joined together, like beads on a string. Polymers usually contain more than five monomers and some polymer may contain hundreds or thousands of monomers in each chain and characterized based on its different molecular weight. The molecular weight range is sometimes quite narrow, but more often it is very broad [1-2].

Polymeric nanoparticle are defined as submicron (size<1µm) colloidal carriers. It is necessary to ensure that the nanoparticle are carefully delivered only to the infected region of the body without affecting the surrounding healthy tissues. Nanoparticle can escape from the bloodstream at continuous vascular endothelium via paracellular pathway, intracellular process or trans cellular pathway. It is different; the gaps between the fenestration sites on the endothelium are much larger (100nm to 2µm) than in healthy tissues (2-6nm). Therefore, nanoparticle can go through fenestrations thus enhancing drug penetration in tissues and accumulating the drugs in tumor site to provide better therapeutic effect which is called “enhanced permeation and retention effect (EPR effect)”.

In recent years, a number of polymeric materials have been developed as drug delivery carriers. Quantity, type of polymers, particle size, solubility, biodegradability and surface properties have important role in release of bioactive drugs. Generally biopolymers are produced from natural resources and crude oil. 4Four categories of biopolymers are recognized. They are

I. Extracted directly from natural raw materials, such as polysaccharides. Example starch and cellulose proteins like gelatin, casein and silk and marine prokaryotes.

II. Produced by chemical synthesis from bio-derived monomers. Example: poly-lactic acid (PLA) and poly lactic-co-glycolic acid (PLGA), etc.,

III. Produced by microorganisms. Example: polyhydroxyalkanoates (PHA), polyhydroxybutyrate (PHB), hydroxyl-valerate (PHV), bacterial, cellulose, xanthan and pullan.

IV. Produced from crude oil. Example: aliphatic and aromatic polyesters, polyvinyl alcohol and modified polyolefins [3].

Polymers are selected and utilized in the nanoparticle formulation, depends upon the design, requirement and application. Various factors need to be considered while choosing the polymer in nanoparticle drug delivery system, they are:

i. Size of the desired nanoparticle.

ii. Properties of the drug (aqueous solubility, stability, etc.) to be encapsulated in the polymer.

iii. Surface characteristics and functionality.

iv. Degree of biodegradability and biocompatibility.

v. Drug release profile of the final product.

To utilize the polymers in nanoparticle drug delivery system following properties are essential for polymers, they are

i. Nontoxic

ii. Non-thrombogenic

iii. Non-immunogenic

iv. Non-inflammatory

v. Non activation of neutrophils

vi. No platelet aggregation

vii. Biodegradable

viii. Inexpensive

ix. Avoidance of the reticuloendothelial system

x. Prolonged circulation time

xi. Applicable to various molecules, such as small molecules, proteins, peptides, or nucleic acids (platform technology)

xii. Scalable and inexpensive manufacturing process.

Most commonly used polymers for the preparation of biodegradable nanoparticles are poly-lactic acid (PLA); poly-D-L-glycolide (PLG); poly-D-L-lactide-co-glycolide (PLGA) and poly-cyanoacrylate (PCA), polyethylene glycol, gelatin, chitosan, alginate, dextran and variety of proteins such as silk, collagen, casein, zein and albumin etc., [4-5].

Natural Polymers

Gelatin

Gelatin is a translucent, colorless, brittle (when dry), flavorless foodstuff, derived from collagen obtained from various animal by-products. Gelatin is an irreversibly hydrolyzed form of collagen. Gelatin is a mixture of peptides and proteins obtained from collagen by acid and alkaline hydrolysis. It is extracted from the skin, bones and connective tissues of animals such as domesticated cattle, chicken, pigs and fish consisting of glycine, proline and 4-hydroxyproline residues with typical structure of -Ala-Gly-Pro-Arg-Gly-Glu-4Hyp-Gly-Pro. During hydrolysis, the bonds between individual collagen strands are broken down into a form that rearranges more easily. Moreover, their high number of functional groups on polymer backbone can be used for chemical modification such as cross linking and addition of ligands [6,7].

Chitosan

Chitosan is a polysaccharide copolymer composed of randomly distributed β-(1-4)-linked d-glucosamines and N-acetyl-d-glucosamines, obtained by partial alkaline deacetylation of chitin, with different molecular weights (50-200kDa), degrees of deacetylation (40%-98%) and viscosities. Chitosan is a natural polymer with linear polyamine, having reactive amino and hydroxyl groups, biodegradable to normal body constituents, safe and non-toxic, binds to mammalian and microbial cells. The main commercial sources of chitosan are the crustacean shell wastes of crabs, shrimps and lobsters. Chitosan is soluble in aqueous solutions of some acids and some selective N-alkylidination.

Its solubility, biodegradability, reactivity and adsorption of many substrates depend on the amount of protonation of the NH_2 function on the C-2 position of the D-glucosamine unit, whereby the polysaccharide is converted to a polyelectrolyte in acidic media. Chitosan is considered one of the most valuable polymer for biomedical and pharmaceutical applications due to its biodegradability, biocompatibility, antimicrobial, non-toxicity and anti-tumor properties. Various conjugated like thiolation, glycolation and folate chitosan are available. Chitosan is biodegradable, biocompatible, low immunogenicity and nontoxic at low molecular weights (10-50kDa). It has been suggested that the toxicity of chitosan is perhaps due to impurities in the chitosan polymers [8-17]. Structure of chitosan is shown in Figure 1.

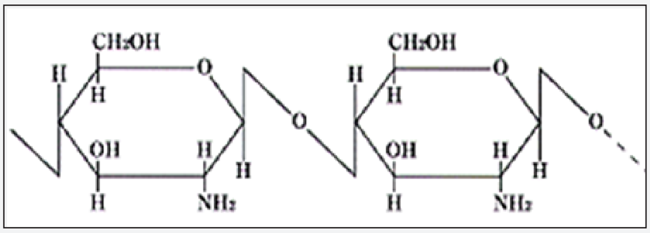

Figure 1: Structure of Chitosan.

Starch

Starch or amylum is a carbohydrate consisting of a large number of glucose units joined together through glycosidic bonds. Pure starch is a white, tasteless and odorless powder that is insoluble in cold water or alcohol. It consists of two types of molecules; the linear and helical amylose and the branched amylopectin. Starch is the second most abundant biomass

How to cite this article: Lakshmana Prabu S, Suriyaprakash TNK. Role of Natural Polymers in Drug Delivery Systems as Challenging Ailments. Nov Appro Drug Des Dev. 2017; 3(1) : 555605

material in nature, found in plant roots, stalks and crop seeds. Depending on the plant, starch generally contains 20 to 25% amylose and 75 to 80% amylopectin by weight [18,19].

Alginate

Alginates are hydrocolloids, water soluble biopolymer, extracted from brown seaweed, composed of α-L-gluuronic acid β-D-mannuornic residues. Both units are linked together through β-1-4 links. The glycosidic linkage can be broken by both acid, alkaline degradation mechanism and by oxidation. When alginate undergoes partial hydrolysis alginate separates into 3 fractions; whereas the two fractions containing almost homopolymeric molecules of G and M respectively, whereas the third fraction consist of equal proportion of both monomers and large number of MG dimer residue. Alginate forms gel with most divalent and trivalent salts [20,21].

Dextran

Dextran is a complex, branched glucan (polysaccharide made of any glucose molecules) composed of chains of varying lengths (from 3 to 2000 kilodaltons). The straight chain consists of α-1,6 glycosidic linkages between glucose molecules, while branches begin from α-1,3 linkages. Dextran is freely soluble in water, methyl sulphoxide, formamide, ethylene glycol, glycerol, 4-methylmorpholine-4-oxide, and hexa methyl phosphoramide (a carcinogenic). Dextran can be synthesized from sucrose by certain lactic acid bacteria [22,23].

Zein

Zein is a class of prolamine protein found in maize (corn). Pure zein is clear, odorless, tasteless, hard, water-insoluble, edible and it has a variety of industrial and food uses. Zeins are renewable, biodegradable, biocompatible and nontoxic. They have more hydrophobic than hydrophilic amino acids in their structure, making them insoluble in water, which is a requirement for the preparation of water-based formulations [24-27].

Silk

Silk is a natural protein fiber which is composed mainly of fibroin and produced by certain insect larvae to form cocoons. Major source are mulberry silkworm Bombyx mori, Tasar silkworm Antheraea mylitta, Oak tasar silkworm Antheraea proyeli, Eri silkworm Philosamia ricini and Muga silkworm Antheraea assamensis. Silk proteins are promising materials as biomaterials due to their slow biodegradability, biocompatibility, self-assembling property, excellent mechanical property (tensile strength and Young's modulus), controllable structure and morphology [28-30].

Collagen

Collagen is the main structural protein in connective tissues and most abundantly present in all animals, making up from 25% to 35% of the whole-body protein content. Collagen is an abundant structural protein in all animals. In humans, collagen comprises one third of the total protein, accounts for three-quarters of the dry weight of skin and is the most prevalent component of the extracellular matrix (ECM). Twenty-eight different types of collagen composed of at least 46 distinct polypeptide chains. The collagen molecule consists of three parallel polypeptide strands in a left-handed, polyproline II-type (PPII) helical conformation coil about each other with a one-residue stagger to form a right-handed triple helix. Collagen is having very good biocompatibility, low antigenicity and biodegradability [31,32].

Cellulose

Cellulose is an organic compound, a polysaccharide consisting of a linear chain of several hundred to many thousands of β(1→4) linked D-glucose units. Cellulose is an important structural component of the primary cell wall of green plants, many forms of algae and the oomycetes. Cellulose is the most abundant organic polymer on Earth. Various cellulose derivates such as carboxymethyl cellulose, hydroxypropyl and hydroxymethyl celluloses, HPMC etc., are used as biodegradable polymer in drug delivery [33,34].

Albumin

Human Serum albumin (HSA) is an abundant multifunctional non-glycosylated, negatively charged plasma protein, with ascribed ligand-binding and transport properties having antioxidant and enzymatic activities. It is synthesized primarily in the liver as preproalbumin which has an N-terminal peptide. Albumin is a globular, water-soluble, un-glycosylated serum protein of approximate molecular weight of 65,000 Daltons. Human serum alubum is nontoxic, non-immunogenic, biocompatible and biodegradable. Specialized nanotechnological techniques like desolvation, emulsification, thermal gelation and recently nano-spray drying, nab-technology and self-assembly that have been investigated for fabrication of albumin nanoparticles [35-37].

Conclusion

Nanotechnology is a science, which is blended in human life specifically for the treatment of various diseases. Polymers from various sources have gained an important role in the nanoparticle drug delivery system. In nanoparticle drug delivery system, drug is entrapped within the polymer, which protect the drug from the various degradation process in the human body leads to achieve long circulation time and improves the therapeutic benefit for that particular disease. In polymeric nanoparticle drug delivery system particle size and distribution of particles are critical parameters in targeting the drug towards the specific organs and tissues. By selecting an appropriate polymer with an optimistic procedure for the preparation of nanoparticle can achieve the organ/tissue specific target delivery, low immunogenicity, good biocompatibility and desired therapeutic effect.

How to cite this article: Lakshmana Prabu S, Suriyaprakash TNK. Role of Natural Polymers in Drug Delivery Systems as Challenging Ailments. Nov Appro Drug Des Dev. 2017; 3(1) : 555605

References

1. Mandelkern L (1972) An introduction to Macromolecules. Springer-Verlag, New York, USA.
2. Treloar RG (1970) Introduction to Polymer Science. Springer-Verlag, New York, USA.
3. Jamshidian M, Tehrany EA, Imran M, Jacquot M, Desobry S (2010) Poly-Lactic Acid: Production, Applications, Nanocomposites and Release Studies. Comprehensive Reviewsin Food Science and Food Safety 9: 552-571.
4. Mahapatro A, Singh DK (2011) Biodegradable nanoparticles are excellent vehicle for site directed in-vivo delivery of drugs and vaccines. J Nanobiotechnology 9: 55.
5. Nitta SK, Numata K (2013) Biopolymer-Based Nanoparticles for Drug/Gene Delivery and Tissue Engineering. Int J Mol Sci 14(1): 1629-1654.
6. Ward AG, Courts A (1977) The Science and Technology of Gelatin. New York, USA.
7. Gelatin information, news, history and more. Gelatin Manufacturers Institute of America. Retrieved 2008-09-26.
8. Synowiecki J, Al-Khateeb NA (2003) Production, properties, and some new applications of chitin and its derivatives. Crit Rev Food Sci Nutr 43(2): 145-171.
9. Hggard MK, Tubulekas I, Guan H, Edwards K, Nilsson M, et al. (2001) Chitosan as a nonviral gene delivery system. Structure property relationships and characteristics compared with polyethylenimine in vitro and after lung administration in vivo. Gene Ther 8(14): 1108-1121.
10. Lee M, Nah JW, Kwon Y, Koh JJ, Ko KS, et al. (2001) Water-soluble and low molecular weight chitosan-based plasmid DNA delivery. Pharm Res 18(4): 427-431.
11. Lee D, Zhang W, Shirley SA, Kong X, Hellermann GR, et al. (2007) Thiolated chitosan/DNA nanocomplexes exhibit enhanced and sustained gene delivery. Pharm Res 24(1): 157-167.
12. Hudson SM, Jenkins DW (2003) Chitin and chitosan. In: Mark HF (Eds.), Encyclopedia of polymer science and technology. New York, USA, pp. 569-580.
13. Kato Y, Onishi H, Machida Y (2003) Application of chitin and chitosan derivatives in the pharmaceutical field. Curr Pharm Biotechnol 4(5): 303-309.
14. Rinaudo M (2006) Chitin and chitosan: Properties and applications. Prog Polym Sci 31: 603-632.
15. Alvarenga ES (2011) Characterization and Properties of Chitosan. In: Elnashar M (Eds.), Biotechnology of Biopolymers. In Tech Publication, Croatia, pp. 91-108.
16. Tungtong S, Okonogi S, Chowwanapoonpohn S, Phutdhawong W, Yotsawimonwat S (2012) Solubility, viscosity and rheological properties of water-soluble chitosan derivatives. Maejo Int J Sci Technol 6(2): 315-322.
17. Pillai CKS, Paul W, Sharma CP (2009) Chitin and chitosan polymers: Chemistry, solubility and fiber formation. Prog Polym Sci 34: 641-678.
18. Rodrigues A, Emeje M (2012) Recent applications of starch derivatives in nanodrug delivery. Carbohydr Polym 87: 987-994.
19. Le Corre DB, Bras J, Dufresne A (2010) Starch Nanoparticles: A Review. Biomacromolecules 11: 1139-1153.
20. https://application.wiley-vch.de/books/sample/3527326251_c01.pdf
21. Lee KY, Mooney DJ (2012) Alginate: Properties and biomedical applications. Progress in Poly Sci 37(1): 106-126.
22. http://tdbcons.com/images/pdf/18116612_AA_p13.pdf
23. Staat RH, Gawronski TH, Schachtele CF (1973) Detection and preliminary studies on dextranase-producing microorganisms from human dental plaque. Infect Immun 8(6): 1009-1016.
24. Frank AM, David JS, John CL, Gordon WS, Sharon AHH, et al. (2006) Structural Characterization of A-Zein. J Agric Food Chem 54(2): 543-547.
25. John WL (2002) Zein: A History of Processing and Use. American Association of Cereal Chemists 79(1):1-18.
26. Reddy N, Yang Y (2011) Potential of plant proteins for medical applications. Trends Biotechnol 29(10): 490-498.
27. Lai LF, Guo HX (2011) Preparation of new 5-fluorouracil-loaded zein nanoparticles for liver targeting. Int J of Pharm 404(1-2): 317-323.
28. Lee S, Alwahab NS, Moazzam ZM (2013) Zein-based oral drug delivery system targeting activated macrophages. Int J Pharm 454(1): 388-393.
29. Nagal A, Singla AK (2013) Applications of Silk in Drug Delivery: Advancement in Pharmaceutical Dosage Forms. Indo Global J Pharma Sci 3(3): 204-211.
30. Numata K, Kaplan DL (2010) Silk-based delivery systems of bioactive molecules. Adv Drug Deliv Rev 62(15): 1497-1508.
31. Elzoghby AO, Samy WM, Elgindy NA (2012) Protein-based nanocarriers as promising drug and gene delivery systems. J Control Release 161(1): 38-49.
32. Shoulders MD, Raines RT (2009) Collagen Structure and stability. Annu Rev Biochem 78: 929-958.
33. Gloria AD, Shawn MS, Jarmo K, Leena AK, James DSA (2002) Mapping the Ligand-binding Sites and Disease-associated Mutations on the Most Abundant Protein in the Human, Type I Collagen. J Biol Chem 277(6): 4223-4231.
34. Yoshiharu N, Paul L, Henri C (2002) Crystal Structure and Hydrogen-Bonding System in Cellulose I β from Synchrotron X-ray and Neutron Fiber Diffraction. J Am Chem Soc 124(31): 9074-9082.
35. Cellulose (2008) In Encyclopædia Britannica. Encyclopaedia Britannica Online.
36. Quinlan GJ, Martin GS, Evans TW (2005) Albumin: Biochemical Properties and Therapeutic Potential. Hepatology 41(6): 1211-1219.
37. Sebak S, Mirzaei M, Malhotra M, Kulamarva A, Prakash S (2010) Human serum albumin nanoparticles as an efficient noscapine drug delivery system for potential use in breast cancer: preparation and in vitro analysis. Int J Nanomedicine 5: 525-532.
38. Elzoghby AO, Samy WM, Elgindy NA (2012) Albumin-based nanoparticles as potential controlled release drug delivery systems. J Control Release 157(2): 168-182.

How to cite this article: Lakshmana Prabu S, Suriyaprakash TNK. Role of Natural Polymers in Drug Delivery Systems as Challenging Ailments. Nov Appro Drug Des Dev. 2017; 3(1) : 555605

How to cite this article: Lakshmana Prabu S, Suriyaprakash TNK. Role of Natural Polymers in Drug Delivery Systems as Challenging Ailments. Nov Appro Drug Des Dev. 2017; 3(1) : 555605