ISSN: 2349-2678

Contents lists available at www.ijpba.in

International Journal of Pharmaceutical and Biological Science Archive

Volume 5 Issue 1; January-February; 2017; Page No.17-22

Review Article

Excellency of natural polymer in drug delivery system: A Review

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ABSTRACT

The purpose of writing this review on natural polymer based drug delivery system (NPBDDS) was to compile the recent literature with special focus on the principal mechanism involved coating technology based on natural polymer to achieve therapeutic goal for prolongation of drug release to the desire site of action. It is well known that the growth of human society was influenced by the expansion of man-made polymers. The recent developments of novel drug delivery technology using synthetic polymers including the physicochemical properties and formulation variables affecting drug release from its dosage form and for that it is essential approaches to design NPBDDS. The natural polymers are presented from their molecular structure point of view along with main fields of applications through advance in drug delivery system (ADDS). This review also summarizes the *in vitro* techniques, *in vivo* studies to evaluate the performance and application of NPBNDDS and applications of these systems. These systems are useful to several problems encountered during the development of a pharmaceutical dosage form.

Keywords: Natural polymer, NPBDDS, synthetic polymers, ADDS, *in vitro* and *in vivo*

INTRODUCTION

Any drug delivery system utilizing carrier systems prepared with a wide range of synthetic and natural polymers is currently a multibillion dollar industry. The market for drug delivery is expanding enormously as several pharmaceutical and biotech startup companies are engaged seriously in the development of drug delivery systems (NDDS) using carries from natural source[1]. A polymer is a large molecule (macromolecules) composed of many repeated subunits, known as monomers. Natural polymers and their derivatives are commonly used in medicine and pharmacy. Particular attention has recently been paid to natural polymers, because they are biocompatible and biodegradable, so they can be hydrolyzed into removable and non-toxic products. The word "polymer" is derived from the Greek roots "poly" and "mer," which mean "many parts."In our everyday life polymer plays a significant role. However synthetic polymer resources are getting depleted continuously while the demand for the natural polymer is ever increasing for the formulation of novel drug delivery system. According to the literature, by the beginning of the next century the natural polymer will be scarce for the whole world (Singh, 1982). This situation has led to the development of natural polymer[2]. Among the various synthetic materials that have been explored and advocated, natural polymer claims a major share as pharmaceutical excipience. Plastics are used for almost everything from the articles of daily use to the components of complicated engineering structures and heavy industrial applications (Rai & Jai Singh, 1986). Polymers are a broad class of materials which are made from repeating units of smaller molecules called monomers. Polymers can be natural in origin, such as the lignin of tree branches, the starches of homemade bread, or the chitin of lobster shells[3]. Other polymers are called synthetic, because they are made by humans from naturally-occurring materials. A lot of macromolecular prodrugs have been developed using various kinds of polymeric carriers, mainly in the field of cancer chemotherapy and found to be useful to control drug release, modify biodistribution or excretion and achieve drug targeting[4]. Recently, biological data on the toxicity and pharmacokinetic behavior of various macromolecules has been compiled, and consequently very safe macromolecules are utilized as drug carriers without toxicity[5]. Synthetic polymers, such as HPMC and poly-(L-glutamic acid) and natural macromolecules, such as dextran and albumin are often used as a drug carriers for the conjugates of antitumor agents[6]. These

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macromolecules are water-soluble, and their conjugates are also water-soluble; therefore, such conjugates have generally been administered intravenously in a solution dosage form[7]. Any dosage form made up by using natural polymer is an extremely variable process and ability to prolong and control the drug release which is a valuable asset for controlled drug delivery system. Biomaterials are materials intended to interface with biological systems to evaluate, treat, augment, or replace any tissue, organ, or function of the body[8]. The essential prerequisite to qualify a material as a biomaterial is that it should be biocompatible. Biocompatibility is the ability of a material to perform with an appropriate host response in a specific application[9]. The criteria for determining the biocompatibility of a material depend on its endues application. Consequently, a wide range of materials encompassing all the classical materials such as metals, ceramics, glasses, and polymers have been investigated as biomaterials[10]. Among these, polymers form a versatile class of biomaterials that have been extensively investigated for medical and related applications. This can be attributed to the inherent flexibility in synthesizing or modifying polymers matching the physical and mechanical properties of various tissues or organs of the body[11].

Origin of natural polymer

One reason why NP has become of interest is undoubtedly because it can be obtained from natural sources that are abundant and renewable also ease to get. Isolated natural polymer second most abundant in nature after cellulose (Roberts, 1992). Polysaccharides are found in abundance in nature and are readily available from sources such as algae (e.g. alginates), plants (e.g. pectin, guar gum, mannan), microbes (e.g. dextran, xanthan gum) and animals (e.g. chitosan, chondroitin) and they can also be produced by means of recombinant DNA techniques[12]. Monosaccharide polymers have many favourable properties such as high stability, nontoxicity, hydrophilicity, biodegradability, gel forming properties and ease of chemical modification. An enormous variety in plant polysaccharide structural composition exists, which is not only associated with different plants, but also with the part of the plant that they originate from, such as the leaves, seeds, roots and tubers[13]. The complexity and variety of polysaccharides can be explained by two unique structural features: firstly monosaccharides can be linked together in different ways and in an α- or β-configuration) and secondly, due to the presence of branched side-chains[14].

Physicochemical properties of natural polymer

Heterogeneity/Polydispersity: natural polymers such as proteins are rather uniform in size – there is no variation. Such polymers are said to be homogeneous or monodisperse. Most of natural polymers are naturally built by condensation polymerization[15]. Natural polymers tend to be readily biodegradable - they show no adverse effects on the environment or human beings[16].

Advantages of natural polymer

There are several advantages in natural polymer based novel drug delivery system which improve the pharmacokinetics and increase biodistribution of therapeutic agents to target organs, which will result in improved efficacy including a noninvasive method of drug delivery[17]. It has wide molecular weight distribution, variety of visco-elastic properties, biocompatible, phase transition characteristics and acceptable taste[18].

Disadvantages of natural polymer[19-22]

Apart from advantages in natural polymer they are having some disadvantages

a) Microbial contamination during production due to their natural sources.

b) Batch to batch variation – as result to difference of resources and resource regions.

c) Slow Process – as the production rate is depends upon the environment and many other factors, it can't be changed.

d) Potential impurities – may also result in unwanted immune reactions. Heavy metal contamination – that often associated with herbal polymeric excipeints.

Natural degradation of polymers

The American Society for Testing of Materials (ASTM) and the International Standards Organization (ISO) define degradable plastics as those which undergo a significant change in chemical structure under specific environmental conditions[23]. The term 'biodegradation' is limited to the chemical processes that alter either the molecular weight or solubility of the polymer. Natural polymers are biodegradable since they have unstable links in their backbone and structure[24]. They are broken down into biologically acceptable molecules that are metabolized and removed from the body via normal metabolic pathways BIODEGRADATION ENZYMATIC

DEGRADATION COMBINATIONHYDROLYSIS BULK EROSION SURFACE EROSION[25]. Degradation of all polymers follows a sequence in which the polymer is first converted to its monomers, after which the monomers are mineralized. Most polymers are too large to pass through cellular membranes, so they must first be depolymerized to small monomers before they can be absorbed and biodegraded within microbial cells[26-27]. The initial breakdown of a polymer can result from a variety of physical, chemical, and biological forces with chemical hydrolysis probably being the most important[28].

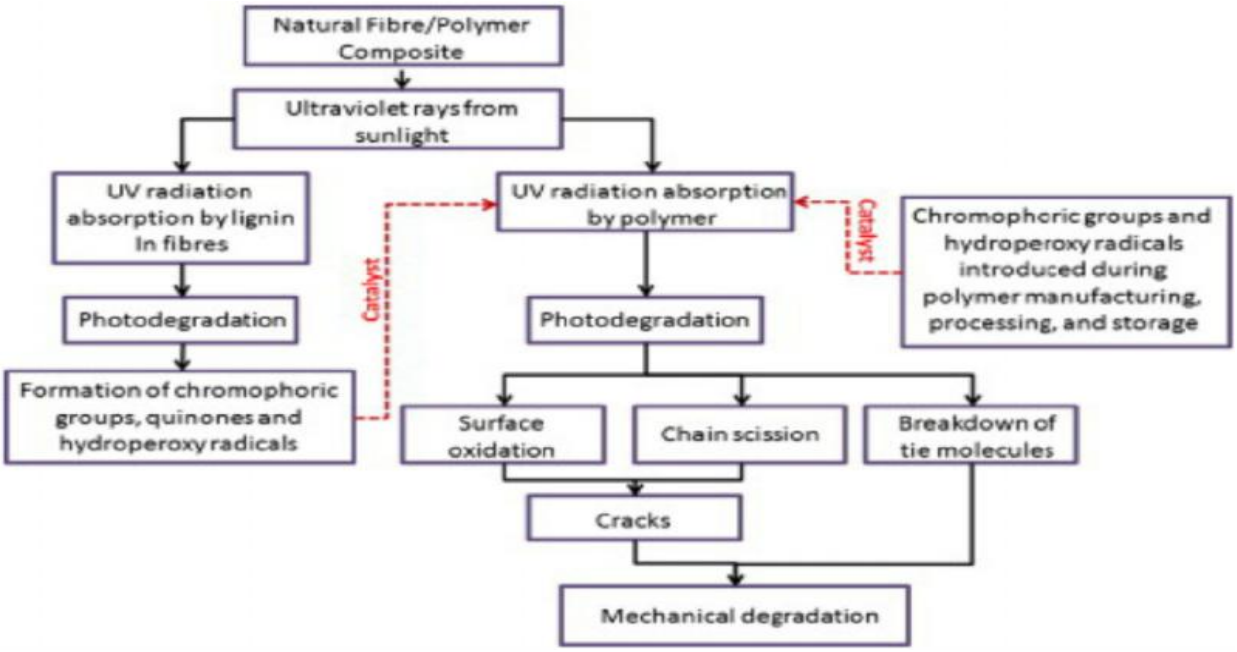

Fig:1 Natural degradation of polymers

Classification of Natural polymers[29-32]

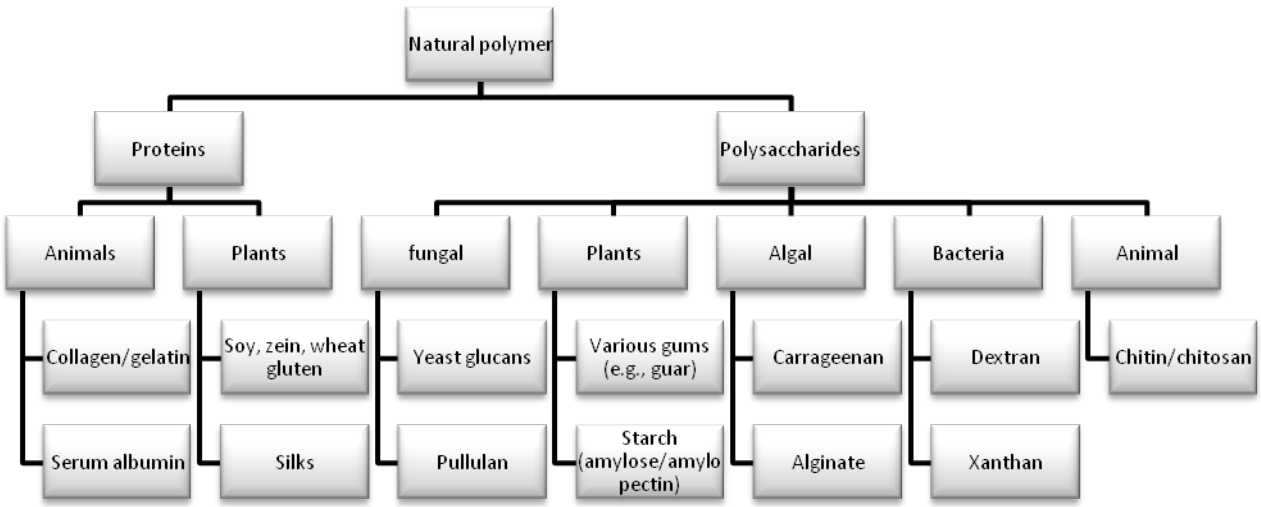

Fig: 2 Classification of Natural Polymers

Application of natural polymer in drug delivery system

Colon delivery: Degraded by microflora present in human colon which supports colon drug delivery. Coating material: Good film forming property and mucoadhesive property. Microspheres for colon delivery developed. Ciofani et al (2008) developed alginate-based drug delivery system for neurological applications, specifically, by considering the target application of neural regeneration and neuroprotection[33].

Topical delivery: Carrageenans are a family of sulfated polysaccharides extracted from red marine algae and that are widely utilized in the industry because they can form reasonably stiff and thermo reversible gels[34-35].

Ocular delivery: Chitosan along with an excellent film capability make chitosan suitable for development of ocular bandage lenses[36-39].

Mucosal delivery: Natural polymer gets protonated in acidic solution, so it binds strongly to negatively charged cell surface making it useful to formulate bioadhesive dosage forms.

Transdermal drug delivery: Studies on propranolol hydrochloride (prop-HCl) delivery systems using various natural polymer with different crosslink densities as drug release controlling membranes and chitosan gel as the drug reservoir have been performed[40-42].

Gene Delivery: Natural polymer typically isolated from the shell of shrimp, has the ability to react with DNA and compact it to produce a nanoparticle. Such nanoparticles are more readily taken up by cells[43].

Conclusion

Natural polymers have received much more attention in the last decades due to their applications in the fields related to environmental protection and the maintenance of physical health. To improve the properties of them, a number of methods have been developed, such as random and block copolymerization or grafting. These improve both the biodegradation rate and the mechanical properties of the final products. To provide added value to biodegradable polymers, some advanced technologies have been applied such as active packaging technology and natural fibre reinforcements. From the discussion, it can be concluded that natural polymers and theirmodified derivatives are very promising candidates for the mucosal, colonic and different targeted protein/peptide, gene/vaccine, and anticancer drug delivery. This review is based on several research reports and their outcomes have been cited here in a concise manner. We hope this article will contribute to the new researchers for further investigations.

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