Chapter 10
Engineered Gellan Polysaccharides in the Design of Controlled Drug Delivery Systems

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ABSTRACT

Natural polysaccharides are getting increasing attention in the development of pharmaceutical dosage forms due to their encouraging reports on nontoxicity and biodegradability. Natural gums can also be engineered to have better materials for drug delivery system design. Gellan gum originates from microbial fermentation and has been declared as safe by US FDA for human consumption. It possesses gelling ability in presence of multivalent earth metal cations and thus enabled the design of mutiparticulate drug delivery systems in completely aqueous environment avoiding the use of organic solvents. Due to faster drug release profiles of divalent cation-induced gellan gum particles, nowadays chemically modified forms of gellan polysaccharide are currently being investigated for the controlled release of drugs. This chapter discusses the factors contributing to the varying gelling characteristics of gellan gum and the recent developments in its chemical modification towards the fabrication of novel controlled drug delivery devices.

INTRODUCTION

Polymers are compounds with high molecular masses formed by monomers. The word poly means 'many' and meros mean 'units or parts' in Greek. They consist of different functional groups. Because of their unique properties, polymers are extensively used in pharmaceuticals. The new technology in polymer-based drug release system offer possibilities in the administration of drugs. Pharmaceutically, these polymers are used as a binder in tablets, flow controlling agents in liquids, suspension and emulsions, as film coating agents to mask unpleasant taste of drug, to enhance drug stability, and to modify

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the release characteristics of the drug. The rate of drug release from a matrix product depends on initial drug concentration and relaxation of the polymer chains, which overall displays a sustained release pattern (Uhrich, Cannizzaro, & Langer, 1999).

Natural polysaccharides and their derivatives represent a group of polymers widely used in pharmaceutical dosage forms. Various kinds of natural gums are used in the food industry and are regarded as safe for human consumption. These polysaccharides are obtained usually as plant exudates containing various sugars other than glucose and having significant quantities of oxidized groups in adjunct to their normal polyhydroxy format. In many cases, water-soluble polysaccharides are components of land and marine plants and their seeds. These material results from normal metabolic processes, and many times, they represent the reserve carbohydrate in that system (Bhardwaj, Kanwar, Lal, & Gupta, 2000). Natural gums are often preferred to synthetic materials due to their nontoxic nature, low cost, and free availability. Furthermore, natural gums have been modified to overcome certain drawbacks, like uncontrolled rate of hydration, thickening, drop in viscosity on storage, microbial contamination, and the like (Durso,1980).

Polysaccharides are a diverse class of polymeric materials of natural (animal, plant, microbial) origin formed via glycosidic linkages of monosaccharides (Shukla & Tiwari, 2012). Depending upon the nature of the monosaccharide unit, polysaccharides can have a linear or branched architecture. In addition to structural diversity, polysaccharides have a number of reactive functional groups, including hydroxyl, amino, and carboxylic acid groups, indicating the possibility for chemical modification (Liu, Jiao, Wang, Zhou, & Zhang, 2008). Moreover, polysaccharide molecular weight can vary between hundreds and thousands of Daltons, further increasing diversity (Saravanakumar, Jo, & Park, 2012). Also owing to their native presence within the body, most polysaccharides are subject to enzymatic degradation. Through enzyme catalysis, polysaccharides can be broken down to their monomer or oligomer building blocks and recycled for use as storage, structural support, or even cell signaling applications (Jain, Gupta, & Jain, 2007). For example, glycosidases are common, constituting 1%–3% of the human genome (Rempel & Withers, 2008), and can readily catalyze the hydrolysis of many different glycosidic linkages. In contrast to glycosidase, other enzymes (for example, hyaluronidase is specific for the polysaccharide hyaluronic acid) are more polysaccharide specific. Of note, some polysaccharides are particularly susceptible to degradation by lysosomal enzymes, including esterases, and proteases, following endocytosis pathway (Mehvar, 2003). Thus, enzymatic degradation provides a mechanism of release for therapeutics associated with polysaccharide-based carrier systems.

Mucoadhesion refers to the interaction of a material with a mucosal layer, such as in the gastrointestinal (GI) tract, nasal pathway, or airway. Many polysaccharides possess mucoadhesive property and thus, numerous investigators have explored their use for oral drug delivery. For neutral or negatively charged polysaccharides, hydrogen bonding provides the basis for mucoadhesion (Reddy, Mohan, Satla, & Gaikwad, 2011).

Any pharmaceutical formulation usually contains two types of ingredients one is the active ingredient and other components are excipients. The excipients help in the manufacturing of dosage form and also improve physicochemical parameters of the dosage form. They can influence drug release characteristics and preferably should be compatible, non-toxic, stable, economical etc. They are broadly classified as natural polymers and synthetic polymers. Due to their wide range of applications, the selection of polymer constitutes a vital step in designing any dosage form. Nowadays, due to many problems associated with drug release and side effects, manufacturers are inclined towards using natural polymers (Kulkarni, Butte, & Rathod, 2012).