Abstract

Nature has given us a vast range of resources that may either directly or indirectly be used to enhance and maintain the health of all living things. With the growing interest in using polymers and excipients of natural origin, gums and mucilage are often utilised natural materials for both traditional and new drug delivery methods; the pharmaceutical industry has agreed to employ the majority of them in their formulations. Due to their numerous pharmaceutical applications as diluents, binders, disintegrants in tablets, thickeners in oral liquids, protective colloids in suspension, gelling agents in gels, and bases in suppositories, as well as their use in cosmetics, textiles, paints, and paper making, plant-derived polymers have attracted a lot of attention in recent years. The need for these compounds is always rising, and new sources are often being created. India has historically been a strong source for these items among the Asian nations due to its diverse geography and ecology. To keep up with the rising demand, huge amounts of these items are still being imported from Europe. These naturally available gums can be used without altered form and modified to obtain tailor-made materials for drug delivery systems, giving them an advantage over commercially available synthetic alternatives. Natural polysaccharides possess some advantages such as easy availability, low cost, physical and chemical compatibility with wide range of drugs, biocompatibility, and biodegradability. Being hydrophilic they also allow green manufacturing without use of harsh organic solvents. A significant number of natural polysaccharides such as gum acacia, sodium alginate, gelatin, guar gum, xanthan gum, starch, etc. have been widely used as excipients from very beginning. *Cassia fistula* trees belonging to fabaceae family are native to Indian subcontinent and southeast countries. The endosperm of seeds of this plant is rich in galactomannan polysaccharide which is nonionic in nature and chemically composed of β-(1→4) linked poly-D-mannopyranose backbone with a randomly distributed side chain of α-(1→6) linked D-galactopyranose unit. *Cassia fistula* seed galactomannan (CFSG) has been

reported as film coating agent and its carboxymethylated form has been reported as disintegrating and controlled-release agent. Native form of CFSG has not been reported as tablet binding excipient to date and it is a promising galactomannan like tamarind seed gum and locust bean gum, which might be a potential drug delivery candidate after appropriate tailoring or derivatization. One of the aims of the present investigation was to explore the capability of native CFSG as tablet binder and another one was to chemically functionalize CFSG towards its application as gastro-retentive mucoadhesive sustained release polymer.

In this study one part evaluate the native CFSG as tablet binder polymeric excipient. Water-soluble diclofenac sodium was used as model drug. CFSG was extracted, purified and characterized with polysaccharide content determination, monosaccharide composition analysis, elemental analysis, FTIR, solid-state ^{13}C NMR, molecular weight, zeta potential, DSC, TGA-DTA, XRD, viscosity, pH and surface tension, rheology, SEM and acute oral toxicity study. Prior formulation, the drug-CFSG compatibility was checked by FTIR, DSC and XRD. Diclofenac sodium loaded granules were prepared by wet granulation method and evaluated for various granule properties such as granule-size, bulk density, true density, total porosity, angle of repose, Hausner ratio and Carr's compressibility index. Finally, granules were compressed into tablet and evaluated for apparent density, porosity, packing fraction, percent elastic recovery, weight and content uniformity, hardness, friability, disintegration time and drug dissolution. The binding capacity of CFSG was also compared with standard binder such as gum acacia and polyvinylpyrrolidone (PVP K-30). Second part of this study, investigate the synthesis, characterizations and fabrication of CFSG-g-PSA into aceclofenac loaded gastric-mucosa-adhesive sustained-release tablet. The copolymer was synthesized by microwave-assisted free-radical initiation method using CAN as free-radical initiator and then characterized by elemental analysis, FTIR, NMR, viscosity, DSC, TGA-DTA, PXRD, SEM and biodegradation study. Finally, aceclofenac sustained-release tablets were prepared with

various batches of graft-copolymer by wet granulation method and evaluated for drug-release, mucoadhesion and other parameters. The release-kinetic and mucoadhesive strength were compared to marketed and established polymers such as HPMC and carbopol 974P.