Chapter 1

INTRODUCTION

1.1 INTRODUCTION

Gums are naturally occurring polysaccharides and they find widespread applications because of many advantageous properties they impart to their solutions or dispersions. These properties are mainly manifestations of gums' molecular shape and chemical structure, as interactions take place between the solvent and dissolved or suspended material. It must be borne that the natural gums do not consist of uniform molecules, but contain a distribution of molecular sizes and frequently mixtures of different kinds of molecules. They may be neutral (linear or branched) polysaccharides, polysaccharides with carboxy groups, polysaccharides with strong acid groups or basic groups. Chemical modifications of polysaccharides is useful for alteration of chemical or physical properties to give new applications to these polysaccharides. Possible chemical modifications of gums include introduction of neutral groups, acidic groups or basic groups, graft polymerization and modification by thermal dextrinization, partial hydrolysis and mild oxidation. The ultimate goal is to custom modify low cost polysaccharides to fit new needs and applications.

Guar gum, a galactomannan polysaccharide gum, is obtained from the endosperm of seeds of a legume, *Cyamopsis tetragonolobus*. Structurally comprising of a straight chain of d -mannose with pendant d-galactose side chain on almost every other mannose unit, guar gum has a molecular weight of the order of 2,20,000. It is colorless or pale yellowish-white colored powder, hydrates in either cold or hot water to give high viscosity solutions with pHs of 1 - 10.5. Guar gum finds wide pharmaceutical applications which include its use as suspending agent, thickening agent and disintegrating agent. Guar gum has been modified

chemically as well as physically by many researchers to get products of desired properties. These modifications include acidic, enzymatic or alkaline hydrolysis, periodate oxidation, synthesis of various ethers, hydroxypropylethers, aminoethyl ethers, carboxyalkyl ethers, etc., coprecipitation with other polymers to change hydration characteristics. Interaction properties of guar gum have been studied by varying the galactose-mannose ratio. Grafting of other polymers with guar gum has also been reported. Studies were initiated to investigate the application of guar gum as hydrophilic matrix for oral controlled release drug delivery systems. The work involves modification of guar gum using suitable methods like partial acid hydrolysis, controlled oxidation, partial methylation and carboxymethylation and *in vitro* and *in vivo* evaluation of the modified products for the desired applications.

1.2 RESEARCH ENVISAGED

Cold water swellability, non toxicity, indigenous availability and low cost make guar gum an interesting natural polymer for use in development of hydrophilic matrices for controlled release drug delivery. Guar gum is known to have high intrinsic viscosity but has poor rate of hydration and hence delayed formation of cohesive gel structure. These properties limit its use in development of controlled release matrix tablets at least as an individual hydrogel. For the present investigation, it is assumed that modification of physicochemical nature of the low priced naturally occurring polysaccharide gum, guar gum, may introduce the required qualities in it and thus help to overcome the associated problems in its use as hydrophilic matrix for controlled release tablets. Water soluble drugs, which are known to pose greater challenge to a formulation scientist for producing cost effective and rational controlled release dosage forms, were selected as model drugs for the present

investigations. These include chlorpheniramine maleate, diltiazem hydrochloride and phenylpropanolamine hydrochloride. Any chemical modification which might lead to other such properties that can be exploited in development of pharmaceutical dosage forms, were also investigated.

The proposed plan of work includes-

1. Literature review covering various aspects of guar gum, chemical nature and its possible modifications, controlled release drug delivery systems and mathematical modeling to study release kinetics from different matrices and the drug profile of selected drugs.
2. Development of analytical technique with suitable modifications, wherever necessary, to characterise the modified guar gum products and to evaluate and estimate drugs in the formulations as well as dissolution media and biological fluids.
3. Modification of guar gum chemically by hydrolysis, methylation, controlled oxidation and carboxymethylation; and characterisation of the obtained products through suitable analytical techniques.
4. Formulation and *in vitro* and *in vivo* evaluation of controlled release tablets using modified guar gum as hydrophilic matrix.
5. Investigation of the possible application of modified guar gum as tablet disintegrant.
6. Evaluation of modified guar gum as film former for tablet coating.