CHAPTER – 3

AIM AND OBJECTIVE
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INTRODUCTION:

Bioadhesion may be defined as “the state in which two materials, at least one of which is biological in nature, are held together for extended period of time by interfacial forces”. When the adhesive attachment occurs to mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion. Therefore, bioadhesive drug delivery systems applied to mucous membrane or mucosal surface are frequently defined as mucoadhesive drug delivery system, but the terms are interchangeable. It is feasible to design a mucoadhesive system in different dosage forms, since the properties of adhesion largely depend on the features of the material used in its preparation.

The potential use for mucoadhesive drug delivery systems (MDDS) as drug carriers lies in its prolongation of the residence time at the absorption site, allowing intensified contact with the epithelial tissue. MDDS consists of the adhesive molecules in a pharmaceutical formulation intended to stay in close contact with the absorption tissue, releasing the drug near to the action site, thereby increasing its bioavailability and promoting local or systemic effects. Thus, by using mucoadhesive molecules, it is possible to retain the preparation at the site of action and to direct the drug to a specific site or tissue. Various administration routes, such as gastrointestinal (oral), ocular, nasal, buccal, gingival, vaginal and rectal, make mucoadhesive drug delivery systems attractive and flexible in dosage form development.

Numerous studies on developing novel mucoadhesive polymers, mechanisms of their interactions with mucins and mucosal membranes, formulating and administering novel active ingredients via transmucosal routes increasingly appear in the literature. The formulation of MDDS depends on the selection of suitable polymer with excellent mucosal adhesion and biocompatibility. In recent years, the researchers are looking
beyond traditional mucoadhesive materials. The focus has been shifted towards the use of biodegradable natural polymers in the mucoadhesive delivery of active substances. Number of studied has been conducted on polysaccharides derived from natural sources; many of them found great applications in mucoadhesive drug delivery systems. The use of natural polysaccharides as mucoadhesive material has witnessed a mammoth growth in last two decades due to their favorable physical, chemical and biological properties.

*Hibiscus esculentus* L (Bhindi) considered to be an Asian or African in origin and is values for its edible pods. It is cultivated as garden plant or home-yard plant through the tropical and subtropical parts of the world. There appears to be a large numbers of different varieties those differs in mucilage content and their chemical composition. The mucilage of bhindi contains proteins, minerals and different neutral and anionic polysaccharide composed of rhamnose, galactose, arabinose, glucose, alactouronic acid.

Literature survey revealed that, ample of the research in the field of pharmaceutical science mostly focused on the crude mucilage of *H. esculentus*. The crude mucilage of *H. esculentus* L showed the presence of impurities, which limits its use as pharmaceutical excipients. Commercial success of the polysaccharide demands extensive studies in its purified form is of substantial importance. Furthermore, according to literature criticism, the crude polysaccharide shown to possess comparatively higher water solubility, lower viscosity and swelling index, which may adversely affect if applicability in novel delivery of active substance specially controlled release and bioadhesive systems. In this regards, cross-linking of the
polysaccharide chain may prove to be a useful tool to improve its effectiveness as novel excipient.

Famotidine, a $H_2$ receptor antagonist, widely prescribed in gastro-esophageal reflux disease (GERD) gastric ulcers, duodenal ulcers, and Zollinger-Ellison syndrome. Following oral administration, famotidine partially absorbs from stomach which results on poor physiological availability of the drug. An extensive survey of available literature pointed out that, among many attempt made to improve the bioavailability of famotidine, gastro-retentive drug delivery systems proved to be useful. Localized delivery also increases the stomach wall receptor site bioavailability and enhances the efficacy of drugs to reduce acid secretion. This principle may be applied for improving systemic as well as local availability of famotidine, which would efficiently reduce gastric acid secretion.

Localization of drug delivery system in a particular location of GI tract by using mucoadhesive polymers has generated enormous interest among the pharmaceutical researchers. Natural polysaccharides and their derivatives due to their favorable molecular and physicochemical properties found wide application in mucoadhesive drug delivery systems.

Considering all these points of view, the objectives of the present investigation are as follows:

1. To isolate and purify the polysaccharide from *Hibiscus esculentus* L. and investigate the physical, chemical and biological properties to assess its functionality as pharmaceutical excipient. Specifically, toxicity profile, solid
state properties, flow characteristics, rheological behavior, elemental composition, thermal properties, *in-vitro* bioadhesiveness will be examined.

2. To cross-link the purified polysaccharide and study the effect of cross-linking on its excipient characteristics.

3. To optimize the oral mucoadhesive tablets of famotidine using purified polysaccharide and its cross-linked derivative employing statistical Design of Experiment (DoE). The optimized formulations will be selected with the desired responses by analyzing the effects of independent variables, using Response Surface Methodology (RSM).

The isolated polysaccharide may provide an alternative to other natural and synthetic polymers and their derivatives to design and formulate suitable novel drug delivery systems. This is also anticipated that, the mucoadhesive drug delivery system of famotidine using purified *Hibiscus esculentus* L. polysaccharide and its cross-linked derivative will provide an effective and economic platform for improvement of its bioadhesivity.