# DEVELOPMENT OF MUCOADHESIVE BIOPOLYMERS FOR FOOD FORMULATION

By

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# ABSTRACT

Development of mucoadhesive biopolymer has received great attention in the pharmaceutical application due to its ability to retain the drug dosage at the specific targeted area. This special property could be applied in food formulation for optimum delivery of the active ingredients in the mouth. This research was carried out to study, correlate and review several *in vitro* analytical methods that can be used in development process for characterisation of mucoadhesive polymer. Four well known mucoadhesive biopolymers namely, chitosan, pectin, sodium alginate and sodium carboxymethylcellulose (CMC) were used in this study. A modified rheological characterisation was used to study the interaction between the biopolymers with mucin and the assessment was based on the viscosity synergism. The detachment force characterisation was carried out via pull-off and tensile test using texture analyser and atomic force microscopy (AFM). Kinetic interaction study was done using quartz crystal microbalance with dissipation monitoring (QCMD) and interpretation of data from the modified rheological characterisation. Meanwhile, the removal of biopolymer emulsion after water flushing in a flow cell was observed under a microscope. It was found that mucoadhesion properties of tested biopolymers were affected by the concentration of biopolymer solutions, molecular weight, contact time, ionic strength and pH. Sodium alginate was characterised as the most mucoadhesive material by all the methods while QCMD shows CMC has the highest interaction with mucin layer compared to sodium alginate and pectin.

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## 1.1 General Introduction

Throughout the pharmaceutical industry and more recently, with the introduction of 'functional foods' in the food industry there is a need to deliver active components to consumers especially people with ailments. This is possible by encapsulation technology. This is an advanced technology which is growing in the pharmaceutical, cosmetic, food and printing industry (Heinzen, 2002). Encapsulation can be defined as a technique to coat an active ingredient or a mixture of active materials in a system (Madene et al., 2006). The system or coating material is called shell, wall, material, carrier or encapsulant while the active ingredient that is coated is known as the active material or core material. In food industry, the materials that are normally used as the core material are flavours, colourants, aroma compounds, fats and oils, vitamins and minerals (Shahidi and Han 1993). Enhancement of the quality of food through encapsulation technology has gained increasing importance in the manufacture of health food or functional food. The use of encapsulation technology to achieve a target of flavour release and some other functions encourages researchers to study the mechanisms of flavour release and make enhancement on the existing encapsulation technology. Similar emphasis is given in the pharmaceutical industry where encapsulation of drugs has been explored extensively in order to improve the therapeutic performance of drugs. The reasons for applying encapsulation technology in the industries mentioned are summarised in Table 1.1.

**Table 1.1:** Reason of the encapsulation technology. (Adapted from Finch and Bodmeier, 2005).

| Reason | Description |
|---|---|
| Controlled release | Controlling the release of the active material in a carrier material to have various release profiles. This reason is mainly applied to the food and pharmaceutical industry. |
| Protection of core material against the atmospheric condition | Some of active ingredients are sensitive to the atmospheric condition such as moisture, atmospheric oxygen and temperature. Encapsulation can prevent any active materials from direct contact to the atmospheric condition and thus increase its functionality. |
| Protection of hygroscopic core contents | Flowability and direct compressible nature of hygroscopic core materials such as hygroscopic B group vitamins can be improved with iron phosphate by microencapsulating this core material before compressing it into tablets. |
| Masking of taste and odour | Compounds with unpleasant taste and odour can be masked by microencapsulation in hard gelatine capsules or by incorporating the unpleasant compound in sugar or film-coated tablets. |
| Flavour and aroma release | Encapsulation can control the release profile of |

# Chapter 3:
# Rheological Characterisation

## 3.1 Introduction

Rheological technique that studies the flow and deformation of material due to applied stress and strain is useful in predicting the mucoadhesive properties of polymers or formulations. These techniques have been widely used by previous researchers to study the mucoadhesion properties and mechanisms of interaction of some biopolymers such as pectin, sodium alginate, chitosan and others (Hassan and Gallo, 1990; Mortazavi, 1995; Rossi et al., 2000; Thirawong et al., 2008; Sriamornsak and Wattanakorn, 2008). The interaction between the mucoadhesive polymers with mucin (or mucous) through chain interpenetration, structure conformation and chemical reaction will be reflected by the viscosity and rheology properties (Thirawong et al., 2008). Hence, the reflection of intermolecular friction as characterised by viscosity could be used to describe the mucoadhesion properties. The rheological characterisation for assessing the mucoadhesiveness of polymers *in vitro* was first discovered by Hassan and Gallo (1990). They have tested the interaction of several polymers (e.g. polyethylene glycol, dextran, chitosan, polyacrylic acid and others) with porcine gastric mucin. They introduced the term viscosity synergism and bioadhesion force in order to rank the adhesive strength of the polymers. The viscosity synergism is the increase in viscosity due to bioadhesion between polymers and mucin components in the mixture. The assessment has been considered successful when the results obtained by Hassan and Gallo (1990) were consistent with the results obtained by others.

Several different strategies can be used to study mucoadhesion when using rheology. One of them is the direct method of measuring the viscosity increment or

synergism at different shear rate using shear rheology. Besides the viscosity, the viscoelastic properties of the polymer-mucin mixture can be determined by oscillatory rheology. Rheological enhancement (synergism) is the term used to describe the magnitude of changes in viscoelastic properties of the sample due to mucoadhesion (Sriamornsak and Wattanakorn, 2008). In this technique, the sample is subjected to an oscillatory stress which is enough to excite the sample without breaking its molecular structure. Riley et al. (2001) have successfully investigated and characterised the polyacrylic acid (PAA) as mucoadhesive polymer and its interaction with homogenised pig gastric mucous using the rheological techniques. In their study, concentration and pH of the polymer and mucous were identified as some of the factors affecting the interaction. Another technique is the advanced frequency sweep analysis proposed by Mortazavi (2003). He used lower range frequency (0.0001 - 10 Hz) as compared to ordinary limited frequency sweep study (0.1 - 10 Hz) and reported that the technique could provide a more detailed and accurate data on change in intermolecular structure during the interaction of polymer with mucous layer.

Likewise, the purpose of this investigation is to study the mucoadhesion properties of five well known mucoadhesive biopolymers (chitosan, high DE pectin, low DE pectin, sodium alginate and sodium carboxymethylcellulose) and the factors that affect their interaction with mucin using similar rheological characterisation. However, there was a small modification in the technique used in this research. Instead of using mixtures of biopolymers and mucin as in previous studies, a thin