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The basics and underlying mechanisms of mucoadhesion☆

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Abstract

Mucoadhesion is where two surfaces, one of which is a mucous membrane, adhere to each other. This has been of interest in the pharmaceutical sciences in order to enhance localised drug delivery, or to deliver 'difficult' molecules (proteins and oligonucleotides) into the systemic circulation. Mucoadhesive materials are hydrophilic macromolecules containing numerous hydrogen bond forming groups, the carbomers and chitosans being two well-known examples. The mechanism by which mucoadhesion takes place has been said to have two stages, the contact (wetting) stage followed by the consolidation stage (the establishment of the adhesive interactions). The relative importance of each stage will depend on the individual application. For example, adsorption is a key stage if the dosage form cannot be applied directly to the mucosa of interest, while consolidation is important if the formulation is exposed to significant dislodging stresses. Adhesive joint failure will inevitably occur as a result of overhydration of a dosage form, or as a result of epithelia or mucus turnover. New mucoadhesive materials with optimal adhesive properties are now being developed, and these should enhance the potential applications of this technology.

Keywords: Mucoadhesion; Mucoadhesives; Bioadhesion; Bioadhesives; Mucosal delivery; Carbomers

Contents

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1. 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 periods of time by interfacial forces. In the pharmaceutical sciences, when the adhesive attachment is to mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion [1].

Over the last two decades mucoadhesion has become of interest for its potential to optimise localised drug delivery, by retaining a dosage form at the site of action (e.g. within the gastrointestinal tract) or systemic delivery, by retaining a formulation in intimate contact with the absorption site (e.g. the nasal cavity). The need to deliver 'challenging' molecules such as biopharmaceuticals (proteins and oligonucleotides) has increased interest in this area. Mucoadhesives materials could also be used as therapeutic agents in their own right, to coat and protect damaged tissues (gastric ulcers or lesions of the oral mucosa) or to act as lubricating agents (in the oral cavity, eye and vagina).

This review will consider the basic mechanisms by which mucoadhesives can adhere to a mucous membrane in terms of the nature of the adhering surfaces and the forces that may be generated to secure them together.

2. Mucous membranes

Mucous membranes (mucosae) are the moist surfaces lining the walls of various body cavities such as the gastrointestinal and respiratory tracts. They consist of a connective tissue layer (the lamina propria) above which is an epithelial layer, the surface of which is made moist usually by the presence of a mucus layer. The epithelia may be either single layered (e.g. the stomach, small and large intestine and bronchi) or multilayered/stratified (e.g. in the oesophagus, vagina and cornea). The former contain goblet cells which secrete mucus directly onto the epithelial surfaces, the latter contain, or are adjacent to tissues containing, specialised glands such as salivary glands that secrete mucus onto the epithelial surface. Mucus is present as either a gel layer adherent to the mucosal surface or as a luminal soluble or suspended form. The major components of all mucus gels are mucin glycoproteins, lipids, inorganic salts and water, the latter accounting for more than 95% of its weight, making it a highly hydrated system [2]. The mucin glycoproteins are the most important structure-forming component of the mucus gel, resulting in its characteristic gel-like, cohesive and adhesive properties. The thickness of this mucus layer varies on different mucosal surfaces, from 50 to 450 μm in the stomach [3,4], to less than 1 μm in the oral cavity [5]. The major functions of mucus are that of protection and lubrication (they could be said to act as anti-adherents).

3. Mucoadhesives

3.1. Materials

The most widely investigated group of mucoadhesives are hydrophilic macromolecules containing