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REVIEW

Buccal Delivery Systems

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ABSTRACT

The oral cavity is an attractive site for drug delivery due to ease of administration and avoidance of possible drug degradation in gastrointestinal tract and first-pass metabolism. Buccal drug delivery specifically refers to the delivery of drugs within/through buccal mucosa to affect local/systemic pharmacological actions. This review briefly describes advantages and limitations of buccal drug delivery, anatomical structure of oral mucosa, and methodology in evaluating buccal drug delivery system, focusing on physiology, pharmacology, pathology, and formulation design in line with recent developments in buccal delivery systems.

Key Words: Buccal delivery; Bioadhesion; Penetration enhancer; Enzyme inhibitor; Formulation design.

INTRODUCTION

The oral cavity is an attractive site for drug delivery due to ease of administration and avoidance of possible drug degradation in the gastrointestinal tract and first-pass metabolism. There are four potential regions for drug delivery in the oral cavity, namely buccal, sublingual, palatal, and gingival. Buccal drug delivery specifically refers to the delivery of drugs within/through the buccal mucosa to affect local/systemic pharmacological actions. Buccal-delivered drugs may be used for treatment of diseases in the oral cavity or for systemic use.[1] However, inherent limitations, including short residence time, small absorption area, and barrier property of the buccal mucosa, are challenges to buccal drug delivery.

Oral mucosal and bioadhesive drug delivery systems have been well documented.[1,2] This article will briefly describe advantages and limitations of buccal drug delivery, anatomical structure of oral mucosa, and methodology in evaluating buccal drug delivery systems, focusing on physiology, methodology, and formulation design in line with recent developments in buccal delivery systems.

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ANATOMY AND BIOCHEMISTRY OF ORAL MUCOSA

Oral mucosa is lined with an epithelium supported by a connective tissue termed lamina propria and separated from the epithelium by a basal membrane. The epithelium of oral mucosa is stratified with regional variation in terms of structure and function.[1] Three types of oral mucosa are referred to as masticatory, lining, and specialized mucosa. The epithelium of masticatory mucosa in gingival and hard palate regions is keratinized and further subdivided into four layers, namely, keratinized, granular, prickle-cell, and basal layers. The nonkeratinized epithelium of lining mucosa covers the remaining regions, except the dorsal surface of the tongue and is made up of superficial, intermediate, prickle-cell, and basal layers. Specialized mucosa in the dorsum of the tongue consists of both keratinized and nonkeratinized mucosa. The physiological structure of buccal mucosa is illustrated in Fig. 1. Small vessels and capillaries that open to the internal jugular vein distribute within the lamina propria, thus avoiding the hepatic first-pass clearance of buccal-delivered drugs. Blood flow in the oral mucosa is generally faster and richer than that in the skin.[1,3] The nonkeratinized buccal mucosa was reported to have approximately a thickness of 500–600 μm and surface area of 50.2 cm^2.[1]

Membrane-coating granules are small lipid organelles in the prickle-cell layer.[1] The intercellular lipids discharged from membrane-coating granules are responsible for the epithelial cohesion and formation of the superficial permeability barrier in the epithelium.[3] This main penetration barrier exists in the outermost quarter to one-third of the epithelium. The keratinized epithelia contain more neutral lipids that are associated with the barrier function, while nonkeratinized epithelia contain more polar lipids.[4] The loosely packed intercellular lipids and the presence of large amounts of phospholipids in nonkeratinized, even in keratinized mucosa, account for the overall higher permeability of the oral mucosa than that of the skin stratum corneum.[5] The nonkeratinized mucosa is more permeable than the keratinized mucosa, forming the major administration site in the oral cavity. The oral mucosal membranes do not have tight junctions as seen in intestinal membranes.[1]

The secretion of saliva from salivary glands features regional, individual, and time variations.[1] The buccal region contains minor salivary glands. The mucus layer covers the oral mucosal surface and serves to lubricate and protect as well as to act as a wetting agent. Mucin is a group of glycoproteins composed of oligosaccharide side chains attached to a protein core. Three-quarters of the protein core are heavily glycosylated and impart a gel-like characteristic to mucus. The remaining nonglycosylated groups are involved in cross-linking via disulfide bonds among mucin molecules.[4] Mucus is negatively charged at physiological saliva pH of 5.8–7.4 because of the presence of sialic acids (pKa = 2.6) and ester sulfates at the terminals of some pendant oligosaccharide side chains.[4]

GENERAL CONSIDERATIONS IN FORMULATION DESIGN

Physiological Aspects

The buccal mucosa has a very limited area for application of the buccal delivery system, thus limiting device size and drug load. The actual area for drug absorption depends on the size of the dosage form. Generally, a device with the size of 1–3 cm^2 and a daily dose of 25 mg or less would be preferred for buccal delivery.[4,6] The maximal duration of buccal drug delivery is approximately 4–6 h, as meal

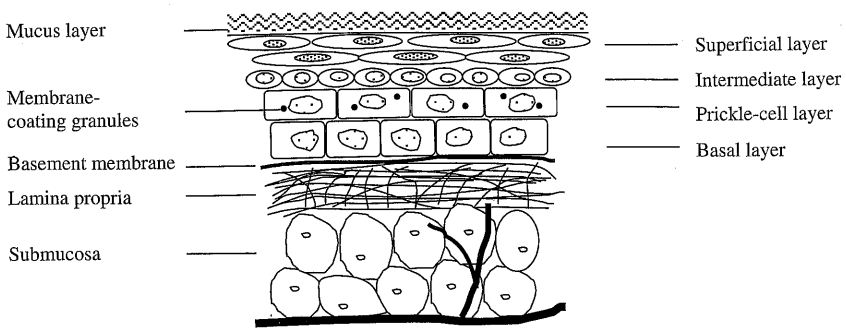

Figure 1. Schematic representation of physiological structure of buccal layer.

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