Oral Muc
Drug Deli

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Specialized Oral M
Delivery Syste

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I. INTRODUCTION

It is our view that the best illustration of what is invo
mucosal (buccal) patches for the systemic delive
experience. Our work covers the full range from dev
and assessing structure-property relations through st
animals, tests of patch positioning and comfort in hu
studies of delivery efficacy. Recent publications o
incorporated into this review, but much of what is re
published before. Our discussion is prefaced by a sur
transmucosal drug delivery and the problems that mu
a successful product. Many of these issues are revi
earlier chapters of this book.

The oral cavity has a number of features that n
delivery: a rich blood supply that drains directly in
bypassing the liver and sparing the drug from first-pa

of drug delivery even in unconscious patients and those who are permitted nothing by mouth [3]; ready termination of delivery by the healthcare practitioner or the patient; and an abundance of usable sites capable of recovering rapidly from any insult [3]. Therefore, despite its potential drawbacks - the physical and metabolic barriers to drug uptake and the numerous ways a drug or its delivery system can be lost [3] - many efforts have been made to utilize the oral surface clinically. The buccal mucosa was first investigated as a potential site for drug delivery several decades ago [4, 5], as it is an ideal surface for the placement of retentive delivery systems [2].

A. Pertinent Features of the Oral Mucosa

The mucosa of the mouth may be thought of as a multilayer laminate [6]. The outer layer is the saliva, which may take the form of an unstirred fluid layer [7]. Several components of the saliva may affect transmucosal delivery (TMD) systems. For example, the high molecular weight mucin known as MG1 [7] may be important in bioadhesion. Saliva also contains several proteins, including some enzymes, that may bind or inactivate a drug, reducing the concentration available to drive absorption [3, 8]. The pH of saliva is between 6.5 and 7.5 [3].

The next layer, the epithelium, may be either partly keratinized or entirely nonkeratinized, the former type being less permeable to hydrophilic drugs [8]. In the buccal region, the epithelium is nonkeratinized and approximately 500 to 600 μm in thickness [9]. Chronic inflammation and physical damage to the epithelium may reduce its barrier function (increase the permeability) [7]. Underlying the epithelium are a basement membrane (basal lamina) and the lamina propria. The latter is readily permeable to many drugs, whereas the former may limit the rate at which some drugs (e.g., β blockers) are absorbed [6]. The blood flowing through the vessels in the lamina propria acts as a sink for drugs delivered transmucosally [9].

B. Pertinent Features of Drug Uptake from the Oral Mucosa

Drugs applied to the oral mucosa gain access to the circulation principally by passive diffusion according to Fick's law[1] [1, 3]. For the most part, drugs move

[1] Specialized transport systems such as carrier-mediated transport or facilitated diffusion are operative for a small number of drugs; cefadroxil being one example [6].

extracellularly and follow, not the shortest path, bu
[6], which for most agents is through the neutral
separate the cells. The lipid solubility of a cand
important measure of its suitability for a TMD
passive diffusion involves nonionized species, the
important [6, 7].

C. Pertinent Considerations in the Design of a

Successful transmucosal drug delivery requires
bioadhesive to maximize the intimacy of contact
sufficient for optimal drug delivery and to retain th
cavity; (ii) a vehicle to release the drug at an
conditions prevailing in the mouth; and (iii) stra
permeability of the oral mucosa (increase bioavaila

The drug selected for a TMD system n
properties, including size and pKa, that will all
mucosa at a rate sufficient to produce a sustained
the blood [1, 6, 10]. It must either resist or be
metabolic barriers in the form of salivary and tissu
the other materials must not damage the teet
keratinolysis, discoloration, irritation, allergeni
microflora) and they must not produce an objectio

A TMD system may be unidirectional (i.e., r
mucosa) or bidirectional (i.e., release drug into the
must be of a surface area and thickness acceptable
and releasing sufficient drug for therapeutic ne
patches having a surface area of 0.5 to 1 cm^2 are
patches may be tolerated. The shape and conspi
other considerations. Lastly, the TMD system
position.

The principal mechanism for bioadhesion of
be physical entanglement of the adhesive polyme
glycoprotein chains overlying the mucosa [1
secondary (electrostatic, hydrogen, hydrophobic)
be less important mechanisms. The binding prope
affected by its molecular weight, configuration,
and degree of ionization, concentration, and exte
duration of adhesion is affected by the type a
polymer, its viscosity, and the method of patch ma

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