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Recent Advances in Oral Drug Delivery System

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ABSTRACT

Evolution of an existing drug molecule from a conventional form to a novel delivery system can significantly improve its performance in terms of patient compliance, safety, and efficacy. Systemic administration of drugs leads to therapeutic concentrations at the site of infection, but for short period of time and in reduced dosage. To minimize drug degradation, harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under development. This review article gives an overview of the recent advances in drug delivery system pertaining to dentistry.

KEYWORDS: Bioavailability, Delivery systems, Buccal mucosa, Transdermal

INTRODUCTION

The method by which a drug is delivered can have significant effect on its efficacy [1]. Any drug delivery system may be defined as a system comprising of drug formulation, medical device or dosage form/technology to carry the drug inside the body, and mechanism for its release. Conventional drug delivery involves the formulation of the drug into a suitable form, such as a compressed tablet for oral administration or a solution for intravenous administration. But these systems have been found to have serious limitations in terms of higher dosage required, lower effectiveness & toxicity.

Certain drug delivery systems have been developed or are being developed to overcome these limitations of the conventional drug delivery systems. Few amongst them being, pulmonary delivery in the form sprays, powders, transdermal drug delivery system, trans-tissue systems in the form of gels, transmucosal system etc. Among the various transepithelial sites available, the oral mucosa allows drug delivery for both local and systemic therapies.

Various indications for local delivery of drugs in oral cavity comprise of periodontal diseases, bacterial and fungal infections, aphthous stomatitis and vesiculo bullous diseases. The therapeutic benefits of these new systems can be increased efficacy of the drug, site specific delivery, decreased toxicity/side effects, better patient compliance, increased convenience, shorter hospitalizations, treatments for previously incurable diseases, potential for prophylactic applications and more over a lower healthcare costs-both in the short and long term courses.

Various New Drug Delivery systems

Despite the tremendous advances in drug delivery, the oral route remains the preferred route for the administration of therapeutic agents due to low cost, ease of administration and high level of

patient compliance. However, significant barriers impose for the peroral administration of drugs, such as hepatic first pass metabolism and drug degradation within the gastrointestinal (GI) tract prohibiting the oral administration of certain classes of drugs. Consequently, other absorptive mucosae are being considered as potential sites for drug administration including the mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavity. These transmucosal routes of drug delivery offer distinct advantages over peroral administration for systemic drug delivery such as possible bypass of the first pass effect and avoidance of presystemic elimination within the GIT[2].

Oral transmucosal system

The oral mucosa includes the buccal, sublingual, gingival, palatal and labial mucosa. The lining mucosa comprises approximately 60%, the masticatory mucosa approximately 25%, and the specialized mucosa approximately 15% of the total surface area of the oral mucosal lining in an adult human[3]. The environment of the oral cavity presents some significant challenges for systemic drug delivery. The drug needs to be released from the formulation to the delivery site (e.g. buccal or sublingual area) and pass through the mucosal layers to enter the systemic circulation. Certain physiological aspects of the oral cavity play significant roles in this process, including pH, fluid volume, enzyme activity and the permeability of oral mucosa. For drug delivery systems designed for extended release in the oral cavity (e.g. mucodhesive systems), the structure and turnover of the mucosal surface is also a determinant of performance[4].

Mucosal retention

The retention of the dosage form at the site of absorption is an important factor which determines the success or failure of buccal drug delivery system. The utilization of mucoadhesive systems is essential to maintain an intimate and prolonged contact of the formulation with the oral mucosa allowing a longer duration for absorption. Some adhesive systems deliver the drug towards the mucosa only with an impermeable product surface exposed to the oral cavity which prevents the drug release into oral cavity[5].

The most widely investigated group of mucoadhesives used in buccal drug delivery systems are hydrophilic macromolecules containing numerous hydrogen bond-forming groups[6]. The presence of hydroxyl, carboxyl or amine groups on the molecules favours adhesion. They are called wet adhesives as they are activated by moistening and will adhere nonspecifically to many surfaces. For dry or partially hydrated dosage intimate contact is formed between the mucoadhesive and mucous membrane after which various physicochemical interactions occur to consolidate and strengthen the adhesive joint, leading to prolonged adhesion[7].

Oral trans mucosal systems for systemic drug delivery are usually designed to deliver the drug for either

i) Rapid drug release for immediate and quick action
ii) Pulsatile release with rapid appearance of drug into systemic circulation and subsequent maintenance of drug concentration within therapeutic profile
iii) Controlled release for extended period of time

Continuous research into the improvement of the oral transmucosal delivery of drugs has resulted in the development of several conventional and novel dosage forms which can be broadly classified into liquid, semi-solid, solid or spray formulations[8]

Liquid dosage forms

Liquid dosage forms include solutions or suspensions made of drug solubilised or suspended into suitable aqueous vehicles. Such types of dosage forms are usually employed to exert local action into the oral cavity like antibacterial mouthwashes and mouth-fresheners. The limitation associated with these liquid[9] dosage forms are that they are not readily retained or targeted to buccal mucosa and can deliver relatively uncontrolled amounts of drug throughout oral cavity. Patel et al [10] found that polymers are adsorbed from solution onto the buccal cells in vivo. From the wide range of polymer solutions screened, chitosan gave the greatest binding, followed by methylcellulose, gelatin, carbopol and polycarbophil.

Semisolid dosage forms

Semisolid dosage forms usually include gels, creams and ointments, which are applied topically into the mucosal surface for either local or systemic effects. These typically contain a polymer, drug and an excipient suspended as a fine powder in an aqueous or non-aqueous base. Hydrogels can also be used in semi-solids for drug delivery to the oral cavity[11]. Semi-solid formulations can be applied using the finger or applicator to a target region and tend to be more acceptable to patients relative to a solid dosage form.

Sprays

An aerosol spray can deliver the drug into the salivary fluid or onto the mucosal surface and thus is readily available for the absorption. As the spray delivers the dose in fine particulates or droplets, the lag time for the drug to be available for the site of the absorption is reduced. Pharmacokinetic study of buccal insulin spray in patient with Type I diabetes revealed no statistical difference in glucose, insulin and C-peptide plasma level compared to insulin administered subcutaneously [12].

Various drug delivery systems which uses the oral mucosa as a drug delivery site such as:

a. Buccoadheshive film and tablets
b. Fast dissolving tablets
c. Orodissolving films
d. Chewing gum

Buccoadhesive films & tablets

Buccal delivery system specifically refers to the delivery of drugs within/through the mucosa lining the inner cheeks. Compared with other mucosal tissues, buccal mucosa is more tolerant to potential allergens and has a lesser tendency to irreversible damage. Additionally, it is a well-vascularized, relatively immobile tissue and has relatively lower enzymatic activity. The buccal mucosa is well suited for retentive device and appears to be acceptable to the patient. With the right dosage form design and formulation, the permeability and the local environment of the mucosa can be controlled and manipulated in order to accommodate drug permeation.

Local delivery to tissues of the oral cavity has a number of applications, including treatment of local conditions such as toothaches13, periodontal disease14, bacterial and fungal infections, aphthous and other nonspecific stomatitis15.

Advantages of buccoadheshive films & tablets16

- Ease of administration and removal from the site of application.
- Permits local and systemic action of the drug to the oral cavity for longer period of time.
- A significant reduction in dose, thereby reducing dose dependent side effects.
- Increased bioavailability hence can be administered to unconscious patients.
- Offers excellent route for systemic delivery of drugs with high first pass metabolism.

Buccal mucosa as a site for drug delivery has limitations as well. One of the major disadvantages associated with buccal drug delivery are the low flux which results in low drug bioavailability& the lack of retention at the site of absorption.

Fast Dissolving Tablet (FDT):

Recently fast dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery system, because they are easy to administer and lead to better patient compliance. Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may be significantly greater than those observed from conventional dosage forms. Over a decade, the demand for development of Fast Dissolving Tablets (FDTs) has enormously increased as it has significant impact on the patient compliance. Fast dissolving tablets offer an advantage for populations who have dysphagia[17] and it is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting and motion sickness complication[18]. FDTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population.

Fast dissolving tablets are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, oral rapid disintegrating tablets, rapid dissolving tablets, porous tablets and rapimelts. However, of all the above terms, United States Pharmacopoeia (USP) approved those dosage forms as Orally Disintegrating Tablets[19] (ODTs).

Fast Dissolving Films:

Mouth dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed based on the technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application[20]. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. The special features of mouth dissolving films being thin elegant film, available in various size and shapes and has excellent mucoadhesion and rapid release.[21]

Chewing gums

The first medicated chewing gum was introduced in the USA in 1924 with the brand name Aspergum® [22]. In recent years chewing gums are considered to be friendly oral mucosal drug delivery systems[23] which has been used to deliver therapeutic agents such as nicotine for smoking cessation therapy. A medicated chewing gum is solid, single-dose preparation that is intended to be chewed for a certain period of time, deliver the drug and which may contain one or more than one active pharmaceutical ingredient[24]. During chewing the drug contained in the gum is released into the saliva which can either be absorbed through the oral mucosa or may reach the stomach for GI absorption.

CONCLUSIONS

Due to the ease of access and avoidance of the hepatic metabolism, oral transmucosal drug delivery offers a promising alternative to overcome the limitations of conventional oral drug delivery and parental administration. The buccal and sublingual routes, in particular, present favourable opportunities and many formulation approaches have been explored for such an application; although the current commercially available formulations are mostly limited to tablets and films. Oral mucoadhesive dosage forms will continue be an exciting research focus for improving drug absorption although, the palatability and irritancy and formulation retention at the site of application need to be considered in the design of such medicines.

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