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Review

Oral strip technology: Overview and future potential

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ABSTRACT

Over the recent past, many of the research groups are focusing their research on this technology. Amongst the plethora of avenues explored for rapid drug releasing products, Oral Strip Technology (OST) is gaining much attention. The advantages of OST are the administration to pediatric and geriatric patient population where the difficulty of swallowing larger oral dosage forms is eliminated. This technology has been used for local action, rapid release products and for buccoadhesive systems that are retained for longer period in the oral cavity to release drug in controlled fashion. OST offers an alternate platform for molecules that undergo first pass metabolism and for delivery of peptides. The review article is an overview of OST encompassing materials used in OST, critical manufacturing aspects, applications, commercial technologies and future business prospects of this technology.

Contents

1. Introduction

Among the delivery routes, the oral route is the most acceptable from patient compliance aspects. Many pharmaceutical firms have directed their research activity in reformulating existing drugs into

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new dosage forms. One such relatively new dosage form is the oral strip, a thin film that is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity.

The surface of buccal cavity comprises of stratified squamous epithelium which is essentially separated from the underlying tissue of lamina propria and submucosa by an undulating basement membrane [1]. It is interesting to note that the permeability of buccal mucosa is greater than that of the skin, but less than that of the intestine [2–4]. It is also reported that the permeability of the buccal mucosa is approximately 4–4000 times greater than that of the skin [5]. Hence the buccal delivery serves as an excellent platform for absorption of molecules that have poor dermal penetration. However, the primary barrier to permeability in the oral mucosa is the result of intercellular material derived from the so-called 'membrane coating granules' present at the uppermost 200 micron layer [6,7].

The epithelia of oral cavity are also composed of an intercellular ground substance called as mucus which basically consists of proteins and carbohydrates. It maintains hydrated condition of the oral cavity, provides adequate lubrication, concentrate protective molecules such as secretory immunoglobulins, and reduces the attachment of microorganisms. The negatively charged mucin contains sulfhydryl groups and sialic acid residues that are responsible for mucoadhesion phenomena [8]. The saliva and salivary mucin contribute to the barrier properties of oral mucosa [9]. While the major salivary glands consist of lobules of cells that secrete saliva; parotids through salivary ducts near the upper teeth, submandibular (tongue regions), and the sublingual ducts, the minor salivary glands are located in the lips, buccal mucosa, and in linings of the mouth and throat [10]. Total turnover rate of the total whole saliva (output from the major and minor salivary glands) at normal physiological conditions has a flow rate of 1–2 ml/min [11]. Drug absorption through the buccal cavity can take place either by the transcellular route (or intracellular route, crossing across the cell membrane and entering the cell) or paracellular pathway (passing between the cells). The mucosa in sublingual region is relatively more permeable leading to rapid absorption with improved bioavailability [12].

In view of the systemic transmucosal drug delivery, the buccal mucosa is the preferred region as compared to the sublingual mucosa. One of the reasons is that the buccal mucosa is less permeable and is thus not able to elicit a rapid onset of absorption and hence better suited for formulations that are intended for sustained release action. Further, the buccal mucosa being relatively immobile mucosa and readily accessible, it makes it more advantageous for retentive systems used for oral transmucosal drug delivery. The primary disadvantage associated with buccal delivery route is the low flux that in turn results in low drug bioavailability. To overcome this hurdle, various buccal penetration enhancers have been studied which improve the absorption pattern of the molecules (this has been discussed in details in future sections of this article). The constant salivary secretion within the oral cavity makes it quite difficult for dosage forms to be retained for long periods of time. Accidental swallowing of dosage forms and salivary scavenging is another limitation in buccal delivery systems. It is documented that the maximum duration of buccal delivery is 4–6 h [13].

An ideal buccoadhesive system is the one that adhere to the site of attachment for a few hours, releases the drug in a controlled fashion, facilitates the rate and extent of drug absorption, does not cause any irritation or inconvenience to the patient, does not interfere with the normal functions such as talking, drinking etc. and that provides unidirectional drug release toward the mucosa.

In spite of these challenges the buccal route is still the preferred route for delivery of active pharmaceutical ingredients (API) that are prone to high level of degradation in the gastrointestinal tract. Different buccal delivery products have been marketed or are proposed for certain diseases like trigeminal neuralgia, Meniere's disease, diabetes, addiction etc. [14–21]. The buccal cavity can be a platform for mucoadhesive (buccoadhesive) systems, gingival dosage forms, local delivery into the oral cavity and buccal delivery systems.

Developing formulations for children has been a challenging task. Amongst other factors, palatability of formulations of pediatric oral medications is one of the most significant factors influencing compliance to therapeutic regimens [22,23]. Although solid dosage forms are widely accepted by elders and adolescents, younger children tend to prefer liquid formulations that are easier to swallow [24]. Keeping the ease of administration and swallowing in mind, pharmaceutical research has led to the development of Oral Disintegrating Tablets (ODTs). ODTs have been defined as "A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". United States Food and Drug Administration further defines ODTs as solid oral preparations that disintegrate rapidly in the oral cavity, with an in-vitro disintegration time of approximately 30 s or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative [25].

Research and development in the oral drug delivery segment has led to transition of dosage forms from simple conventional tablets/capsules to modified release tablets/capsules to oral disintegrating tablet (ODT) to wafer to the recent development of oral strip (OS). Basically the OS can be considered as an ultra-thin strip of postage stamp size with an active agent or active pharmaceutical ingredient and other excipients. The advantages of convenience of dosing and portability of OS have led to wider acceptability of this dosage form by pediatric as well as geriatric population equally.

The introduction of ODT in market was accompanied by educating the mass about the proper way to administer the product like giving instructions "do not swallow" or "do not chew". The process of manipulating the ODT in oral or buccal cavity was also important. However since the OST derived products were readily popular in the market in the form of breath-freshening strips, no further efforts were needed to re-instruct the populace about the technique of administration of this dosage form. OST was already popular amongst the people in the early 2000 year with the introduction and widespread use of Listerine pocket strips, a new launch in the mouthwash range.

Technology Catalysts forecasts the market for drug products in oral thin film formulations to be valued at $500 million in 2007 and could reach $2 billion by 2010 [26]. However only a few products consisting bitter molecules have been able to be commercialized because of the complexity associated with the OST.

This dosage form enjoys some distinct advantages over other oral formulations such as-

1. Availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity.
2. The disadvantage of most ODT is that they are fragile and brittle which warrants special package for protection during storage and transportation. Since the films are flexible they are not as fragile as most of the ODTs. Hence, there is ease of transportation and during consumer handling and storage.
3. As compared to drops or syrup formulations, precision in the administered dose is ensured from each of the strips.
4. The advantage of ease of swallowing and no need of water has led to better acceptability amongst the dysphagic patients. The difficulty encountered in swallowing tablets or capsules is circumvented. The large surface area available in the strip dosage form allows rapid wetting in the moist buccal environment. The dosage form can be consumed at anyplace and anytime as per convenience of the individual.
5. The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first pass effect [27].
6. Since the first pass effect can be avoided, there can be reduction in the dose which can lead to reduction in side effects associated with the molecule.