International Journal of Research in Engineering and Science (IJRES)
ISSN (Online): 2320-9364, ISSN (Print): 2320-9356
www.ijres.org Volume 9 Issue 3 ǁ 2021 ǁ PP. 64-67

A Review on Buccal Drug Delivery System

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Abstract
The buccal region of the oral cavity is an alluring target for administration of the drug of cull, concretely in surmounting deficiencies associated with the latter mode of administration. Quandaries such as high first-pass metabolism and drug degradation in the gastrointestinal environment can be circumvented by administering the drug via the buccal route. Moreover, expeditious onset of action can be achieved relative to the oral route and the formulation can be abstracted if therapy is required to be discontinued. It is withal possible to administer drugs to patients who insensate and less co-operative. Bioadhesion can be defined as a phenomenon of interfacial molecular captivating forces in the midst of the surfaces of biological substrate and the natural or synthetic polymers, which sanctions the polymer to adhere to biological surface for an elongated period the drugs which have local action of stay in GIT.

Keywords: *Introduction, Overview of the Buccal mucosa, Theories of bio adhesion, Manufacturing method, Evaluation and Composition.*

Date of Submission: 27-02-2021 Date of acceptance: 12-03-2021

I. INTRODUCTION

Buccal distribution of drugs is one of the alternatives to the oral route of drug administration, concretely to those drugs that undergo first-pass effect 1 .The buccal route appears to offer a number of advantages, like good accessibility, robustness of the epithelium, utilization of the dosage form in accordance with need, and comparatively less susceptibility to enzymatic activity. Hence, adhesive mucosal dosage forms were yare for oral distribution, in the form of adhesive tablets2,3, adhesive gels 4, 5 and adhesive patches6. Mucoadhesive drug distribution systems are distribution systems, which utilized the property of bioadhesion of certain polymers, which become adhesive on hydration and hence can be utilized for targeting a drug to particular region of the body for elongated period of time7. The faculty to maintain a distribution system at a particular location for an elongated period of time has great appeal for both local as well as systemic drug bioavailability8. The epithelium that lines the buccal mucosa is a main barrier for the absorption of drugs9. In order to ameliorate buccal absorption, several approaches have been introduced. Incremented permeation of the drug through the buccal membrane and obviation of the drug degradation by enzymes was achieved by transmuting the physicochemical properties of the drug10. The incorporation of absorption enhancers to the buccal formulation is one intriguing approach. Substances that facilitate the permeation through buccal mucosa are referred as permeation enhancers11. Mucoadhesive drug distribution systems are distribution systems, which utilized the property of bioadhesion of certain polymers, which become adhesive on hydration. The faculty to maintain a distribution system at a particular location for an elongated period of time has great appeal for both local as well as systemic drug bioavailability13.

Ideal characteristics of Buccal drug distribution system

- Should adhere to the site of annexation for a few hours.
- Should be relinquishing the drug in a controlled fashion.
- Should be facilitating the rate and extent of drug absorption.
- Should to be not causing any exasperation or inconvenience to the patient.
- Should to be not interfering with the mundane functions such as verbalizing and imbibing.

II. OVERVIEW OF THE ORAL MUCOSA

Structure

The oral mucosa is inspecting of an outer layer of stratified squamous epithelium. Below this lies a basement membrane a lamina propria followed by the submucosa as the innermost layer.14-15 The epithelium of the buccal mucosa is about 40- 50 cell layers thick while that of the sublingual epithelium contains remotely fewer. The epithelial cells increase in size and become flatter as they peregrinate from the basal layers to the superficial layers.16 The oral mucosa thickness varies depend on the target site the buccal mucosa and measures

at 500-800μm, while the mucosal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and the gingivae measure at about 100-200μm. The composition of the epithelium withal varies depending on the site in the oral cavity. The mucosae of areas subject to mechanical stress (the gingivae and hard palate) are keratinized akin to the epidermis. The mucosae of the soft palate the sublingual and the buccal regions however are not keratinized.17 they withal contain modicums of neutral but polar lipids mainly cholesterol sulfate and glucosyl ceramides. These epithelia have been found to be considerably more permeable to dihydrogen monoxide than keratinized epithelial.

Role of saliva

- Mainly protective fluid for all tissues of the oral Cavity.
- It is continuously mineralization of the tooth enamel.

Role of mucus

- It made up of proteins and carbohydrates.
- It is playing role cell-cell adhesion.

Permeability

The oral mucosa in general is marginally leaky epithelia intermediate between that of the epidermis and intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times more preponderant than that of the skin. In general the permeability of the oral mucosa decrease in the order of sublingual more preponderant than buccal and buccal more preponderant than palatal. This rank order is predicated on the relative thickness and degree of keratinization of these tissues with the sublingual mucosa being relatively thin and non-keratinized, the buccal thicker and nonkeratinized and the palatal intermediate in thickness but keratinized18.

Structure and design of buccal dosage form

1. **Matrix type:** The buccal patch prepare in a matrix configuration contains drug, adhesive, and additives mixed together.
2. **Reservoir type**: The buccal patch prepare in a reservoir system contains a cavity for the drug and additives separately used from the adhesive. An impermeable backing (patch) is applied to control the direction of drug delivery to decrease patch deformation and disintegration while in the mouth and to prevent drug loss.

Permeability of drug through Buccal mucosa

There are mainly two type route of drug absorption through the squamous stratified epithelium of the oral mucosa:

i. Transcellular (intracellular was passing through the cell).
ii. Paracellular (intercellular was passing around the cell).19

Theories of Bioadhesion

1) Electronic Theory

The electronic theory betokens that there is liable to be electron transfer on contact of the bioadhesive polymer and the glycoprotein work which have different electronic structures, which rotate lead to the formation of a double layer of electrical charge at the bioadhesive interface.

2) Adsorption Theory

According to the adsorption theory bioadhesive systems adhere to tissue because of Vander walls hydrogen bonding and cognate forces21, 22.

3) Wetting Theory

Intimate molecular contact is a pre - requisite for development of vigorous adhesive bond, requiring examination of the wetting equilibrium and dynamic demeanor of the bioadhesive candidate material with the mucus. Some paramount characteristic for liquid bioadhessive materials include:

I. A zero or near zero contact angle.
II. A relatively low viscosity
III. An intimate contact that omit air entrapment

4) Diffusion Theory

Interpenetration of the chains of polymer and mucus may lead to formation of an amply deep layer of chains. The diffusion mechanism is the intimate when contact of two polymers or two pieces of the same polymer. During chain interpenetration the molecules of the polymer and the dangling chains of the glycoprotein network are both in intimate to contact. Due to the concentration gradient the bioadhesive polymer

chains perforate at rates that are dependent on the diffusion coefficient of a macromolecule through a cross-linked network and the chemical potential gradient. In integration good solubility of the bioadhesive medium in the mucus is required in order to achieve bioadhesion. Thus the difference of the solubility parameters of the bioadhesive medium and the glycoprotein should be as proximate to zero as possible23.

5) Fracture Theory

According to Fracture theory of adhesion is cognate to disunion of two surfaces after adhesion. The fracture vigor is identically tantamount to adhesive vigor as given by,

$G = (E\varepsilon. /L)$ ½

Where: E= Young's module of elasticity

ε = Fracture energy

L= Critical crack length when two surfaces are separated.24,25,26.

Manufacturing method of Buccal patches

A. Solvent casting: In this method all patch is excipients including the drug co-dispersed in an organic solvent and coated into a sheet of release liner. After solvent evaporation is a thin layer of the protective backing material is laminated into the sheet of coated release liner to form a laminate. That is die cut to form patches of the desired size and geometry 27.

B. Direct milling: this method are used to patches are manufactured without the use of solvents. Drug and excipients are mechanically mixed by direct milling or by kneading, usually without the presence of no any liquids. After the complete mixing process the resultant material is rolled on a release liner until the desired thickness is achieved. The backing material is then laminated as previously described 28. It is there are only minor or even no differences in patch performance between patches fabricated by the two processes the solvent free process is preferred because there is no possibility of residual solvents and no associated solvent related health issues.29

Evaluation of Buccal patches

1. **Surface $p^{H:}$** Buccal patches are place to swell for 2 hrs on the surface of an agar plate. The surface pH is measured by means of a pH paper placed on the surface of the swollen patch.30
2. **Thickness measurements:** The thickness of each film is measured at five different locations (centre and four corners) using an electronic digital micrometer 31.
3. **Folding endurance:** The folding endurance of patches is determined by repeatedly folding 1 patch at the times without breaking 32.
4. **Thermal analysis study:** Thermal analysis study is performed using differential scanning calorimeter (DSC).
5. **Morphological characterization:** Morphological characters are studied by using scanning electron microscope (SEM) 33.
6. **Permeation study of buccal patch:** The receptor compartment is filled with phosphate buffer pH 6.8, and the hydrodynamics in the receptor compartment is maintained by stirring with a magnetic bead at 50 rpm. Samples are withdrawn at predetermined time intervals and analyzed for drug content34.

Composition of Buccal patch

- **I. Polymers (adhesive layer):** HEC, HPC, polyvinyl pyrrolidone (PVP), polyvinyl alcohol (PVA), carbopol and other mucoadhesive polymers.
- **II. Diluents:** Lactose DC is selected as diluents for its high aqueous solubility, its flavoring characteristics, and its physico-mechanical properties, which make it suitable for direct compression. Other example: microcrystalline starch and starch.
- **III. Sweetening agents:** Sucralose, aspartame, Mannitol, etc.
- **IV. Flavoring agents:** Menthol, vanillin, clove oil, etc.
- **V. Backing layer:** EC etc.
- **VI. Plasticizers:** PEG-100, 400, propylene glycol, etc
- **VII. Active ingredients**35.

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