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A REVIEW ARTICLE ON ORAL FAST RELEASE DRUG DELIVERY SYSTEM

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Abstract : The most cutting-edge oral solid dosage delivery method is fast dissolving oral films. Mouth dissolving film made of an extremely thin oral strip that is only present on the patient's tongue and is moistened by saliva. Fast-dissolving films provide precise, safe dosing in an efficient format that is portable and easy to use. For the quick release of one or more pharmaceutical active components, oral thin films are disintegrated on the tongue of the patient in a matter of seconds. Researchers refer to the rapidly dissolving dosage forms by a variety of names, including mouth dissolve or melt in mouth dosage forms, quick disintegrating, orally disintegrating, and rapidly disintegrating. Fast dissolving drug delivery systems have recently gained popularity and recognition as innovative drug delivery systems that aim to improve patient compliance while increasing safety and efficacy of a therapeutic molecule by formulating in to a convenient dose form for administration. They quickly disintegrate and release the medicine in the salivary secretions of the oral cavity in less than a minute. Almost all oral drug intake involves saliva, and the GIT is where the medicine is absorbed. Researchers refer to the fast-dissolving dosage forms by a variety of names, including mouth-dissolve, melt-in-the-mouth, quickly.

Index Terms - Drug Delivery system, Immediate drug release, Buccal mucosa, Methods.

INTRODUCTION

DRUG DELIVERY SYSTEM

The geriatric and pediatric patients who experienced difficulties in swallowing traditional oral solid-dosage forms are now treated with the fast dissolving drug-delivery systems which was developed in the late 1970s as an alternative to capsules, tablets and syrups. As there are many benefits of the film such as fast, accurate dosing, safe efficacy, convenience, portability, etc. So the fast dissolving oral films are used as practical mutually exclusive to orally transmitted over the counter medicines. Rapid absorption of the drug is potential as the fast dissolving oral film utilise sublingual route, which lastly lead to immediate onset of drug action.

As new drug delivery systems what one aim to increase safety and efficacy of a drug molecule by formulating in to a commodious dosage form for administration and it reach better patient compliance, so lately the fast dissolving drug delivery systems have get rolling capture fame and acceptance. In the salivary fluids of the oral cavity in less than a minute, they undergo rapid disintegration, whither they release the drug. Virtually the drug swallowed orally with saliva and absorption of drug takes place in the GIT. The fast dissolving dosage forms are referred by various names by the researchers like quick disintegrating, orally disintegrating, rapidly disintegrating, mouth dissolve or melt in mouth dosage forms.[1,2]

Fast dissolving oral films are the most advanced form of oral solid doses form. Mouth dissolving film formed of a very lean oral strip, that is just located on the patient tongue an oral mucosal tissue and moist by saliva. Fast dissolving films are accurate safe dosing in efficacious format convenient and portable, without need for water. Oral thin films are disintegrate an patient's tongue in a few seconds for rapid release of one or more pharmaceutical active ingredients. [2,3,4]

IMMEDIATE RELEASE DRUG DELIVERY SYSTEM:

Immediate drug delivery system has major benefit over the conventional dosage form since the drug gets rapidly disintegrated and dissolves in the saliva without use of water. It provide the drug condut in to the systemic circulation thereby avoids the 1st pass effect and relief of administration. This delivery system be made of a lean film is merely takes under the tongue in oral cavity instantaneously moist by saliva, the film speedily dissolves. The medication for systemic absorption release drug of film fastely disintegrate and dissolves. Owing to prominent surface area of the film give primary fast dissolving action, when expose to the moisture from sublingual environment film wetted quickly. The absorption of buccal way is 3-10 time more than oral route , is only stifled aside hypodermic injection & permeability of buccal mucosa is approximately 4 to 4000 time more than of the skin. Hence the buccal delivery gives as excellent platform for absorption of molecules to compare poor dermal penetration. Fast dissolving films are better delivery for drug in case of chronic condition of patient it obtained high therapeutic blood levels and above in comparison to other oral established dosage forms.[3,4]

THE DESTINATION IN PURPOSE OF ORAL FAST DISSOLVING DRUG DELIVERY SYSTEM;-

The greater destination are purpose of oral fast dissolving drug delivery is;

- Rapid onset of action
- Avoid first pass metabolism and increase bioavailability of drug
- Increase absorption rate with in a mint by mucoadhesive membrane
- Improve dosage accuracy
- Reducing dose depend side effect

In this rout drug release going to unidirectional not only for local &site but also systemic circulation. This delivery system consist of a thin film , film placed in to buccal mucosa then it will be wetted by saliva, saliva help to swallow film then it disintegrate rapidly and dissolve to release drug for oral mucosal absorption. Fast dissolving action is firstly due to the large surface area of the film which quickly wet by salivary environment of mouth. Fast dissolving film formulation is semi solid preparation of solid doses form, in this preparation quantity of drug is low but it give 100% therapeutic effect because of it avoid first pass effect metabolism and drug goes to direct systemic circulation via buccal mucosa. The basic goal of this system rapid onset of action in the critical situation of patient and improve doses accuracy .[1,4,7,2]

1.1 Advantages of fast release drug delivery:-

- Administration of tablet at easy to patient who refuse to swallow it, for eg;- pediatric geriatric patient and psychiatric patient.
- In comparison to liquid formulation convenience is drug administration and accurate dosing.
- No requirement of water to swallow the dosage form, account for convenience to travelless and to people who do not have an immediate access to water.
- The change in the basic view of medication as “bitter pill particularly for paedriatric patients.
- Rapid onset of action due to fast dissolution of medicament and its absorption.
- The bioactivity of is increased as a part of the drugs are absorbed from the mouth, esophagus and pharynx as the saliva passes go through in to the stomach. [4,5,6,]

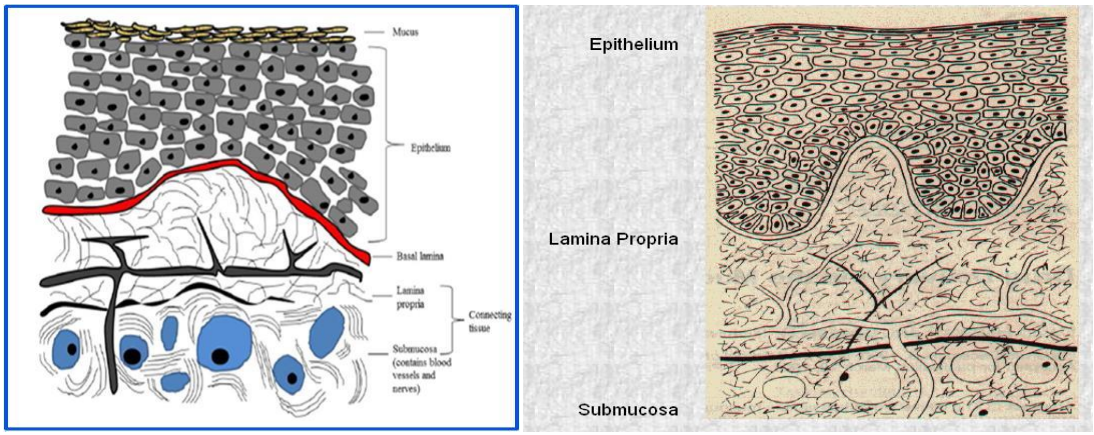
1.2 Disadvantage of fast release drug delivery

- Feeding, drinking and talkie is interfered through sublingual and buccal film administration of drug therefore the route is inapplicable for extended administration.
- Improper to sustained delivery systems.
- An insensible or unco-operative patient cannot be administered with sublingual or buccal medication.
- After smoking induce vasoconstriction of the blood vessels, the patient should not smoke get through picking sublingual or buccal medication. [4,5,6,]

2. Anatomy and Physiology of Buccal Mucosa

The graded squomous epithelium makes the outmost layer of the oral mucosa. This is followed by the layer of cellar membrane, lamina propria that is followed by the sub mucosa as the inner most layer. The epithelium resembles to the stratified squomous epithelium establish is stay of the body that has a mitotically active basal cell layer, that advance through differentiating intervening layers to the outer layers, whither cell slough from the surface of the epithelium. 40-50 cell layers of epithelium get the buccal mucosa, under which the sublingual epithelium comprise few layer relatively. The increase the size and flattening maintain as they move from the basal layers to the superficial layers. Buccal epithelium has an estimated overturn time of 5-6 days, that believably defend the oral mucosa as a overall. The

site determine the thickness of the oral mucosa get through 100-200µm is the estimated thickness of the tough & flabby palates, the base of the mouth, ventral tongue, and the gingivae. The site in the oral cavity is also the measure out of the mixture of the epithelium. Keratinized mucosa is ascertained the area subjected to automatic stress (gingival and hard palate) that ours resemblance to the epidermis. The non keratinized mucosa contain the soft palate, the sublingual & buccal regions. [5,6,7,13]



FigNo 2.1:Structure of buccal mucosa

TISSUE	ATRUCTURE	EPITHELIAL THIKNESS (µ M)	RESIDENCE TIME	BLOOD FLOW (ML/MIN/CM2)
Buccal	Non-keratinize	500-600	+	2.40
Sublingual	Non-keratinize	100-200	--	0.97
Gingival	Keratinize	200	+	1.47
Palatal	Keratinize	250	--	0.89

Table 1: Regional variation in the compound of oral mucosa.

Permeability:

The oral mucosa intervening between the epidermis & intestinal mucosa in general is moderately a leaky epithelia. The permeability of the buccal mucosa is estimated to be 4 to 4000 time more than that of skin. The increase permeability of oral mucosa in general is the rate of palatal littler than buccal and buccal littler than sublingual the comparatively thickness and level of keratinization of the tissues decides the order – the sublingual mucosa is thin and non keratinized, the buccal is thick and non-keratinized & palatal is intermediate but keratinized. It's a common believe which the intercellular substance derived from the so-called 'membrane coating granules' resultant the permeability barrier in the oral mucosa.[7,5,]

Buccal film:-

The high bioactivity is gained by the systemic circulation through the internal jugular vein which by pass drug from the hepatic first pass the buccal drug delivery. This route is desirable for the administration of systemic drug delivery. For the treatment of local and systemic condition these preparation are located in the mouth between the upper gingivae(gum) and the cheek. Excellent accessibility, low enzymatic activity, suitability for drugs or excipients that mildly and reversibly damage or irritate the mucosa, painless administration, easy withdrawal, facility to include permeation enhancer/enzyme inhibitor or pH modifies in the formulation, versatility is designing as multidirectional or unidirectional release system for local or systemic action are amid other reward.[8,11]

Buccal Mucosa:-

Buccal mucosa is the anatomic site for administration between the cheek and gingival. Oral mucosa is a composition of these layers-

1. The stratified squomous epithelium
2. The basement membrane
3. Lamina propria and submucosa

There is a dissimilarity in the formation of the epithelium inside the different sites of the oral cavity.

The non-keratinized area includes the epithelium in soft palate, buccal & sub-lingual, therefore that is no ceramides and acylceramidesm associated to barrier function. The buccal mucosa and sublingual part is higher permeable than other part of the oral cavity as these part have only a low amount of ceramidem.[9,10]

Oral mucosal site :

The delivery of drugs inside the oral mucosal cavity is classified into 3 categories-

- **Sublingual delivery**- The sublingual mucosal administration of drug.
- **Buccal delivery**- The buccal mucosal administration of drug.
- **Local delivery**- Oral cavity treatment, principally ulcers, fungal conditions and periodontal disease.

The anatomy, permeability to an applied drug and their ability to retain a delivery system for a desired length of time is where the difference is observed in the oral mucosal sites.[9,12,]

Structure of buccal cavity - The buccal cavity is the space between skin and lips. The upper part of mouth formed by the tough palate and inside surface of the cheeks conceived sides of the oral cavity. The last part of oral cavity is the level of the mouth, which covered by the tongue.[11,12,]

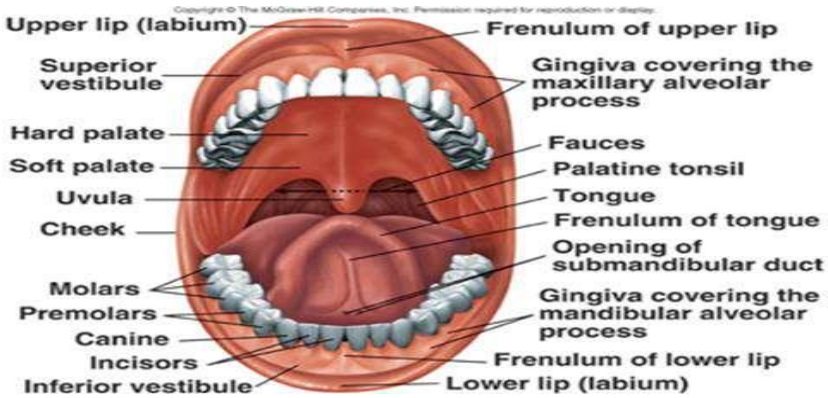


Fig 1.2 : Structure of buccal cavity

Mucus :- The region of the alimentary tract which depending upon the individual mucus lining has a maximum thickness of =300µm and minimum thickness =40-50µm the alimentary track. Most of Mucus is water 95-99%by weight and a class of glycoprotein known as mucins 1-5%. It is large molecules 0.5 over 20MDa molecular mass ranging.[5,10,12]

Function of the mucus layer:-

- Made up of carbohydrate and proteins.
- Adhesion of cell to cell.
- Mucus layer role as a barrier in tissue absorption of the drugs and influence bioavailability.
- Mucus has strong cohesion properties in adhesion. [10,12,]

Salivary secretion:- A film maintenance of saliva on her surface is dependent upon nerve –mediated reflex salivary gland secretion. Saliva secretion in oral cavity depend upon three gland;

1. Parotid gland
2. Sublingual gland
3. Submandibular gland [10,12,]

Saliva: A water containing substance composed of 99.5% water called saliva is located in mouth of human and animal. It is an organic and inorganic material containing complex fluid. [5,10,12]

Function of saliva:

Saliva maintain the digestion of food and lubricate the food for mastication, swallowing and contribute of oral hygiene.

Bioadhesion: Bioadhesion is defined the which substance are capable for the interacting with biological material and being retained on holding together for extended period of time called Bioadhesion . those material are natural polymer which play a role of adhesives. Carbohydrate and protein consist of bioadhesive properties are a variety of substance.

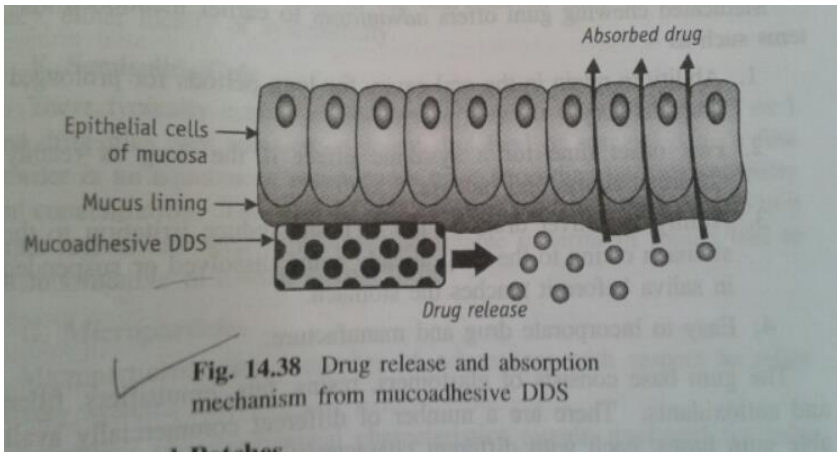


Fig. 14.38 Drug release and absorption mechanism from mucoadhesive DDS

Fig:1.3 : drug release and absorption mechanism from mucoadhesive DDS.

Mechanism of Bioadhesion:

- Wetting and swelling polymer are permit intimate contact with biological tissue.
- Chemical bonds are week form between entangled chain.
- Bioadhesive penetration into the service of the tissue take place.
- Interpenetration of mucin chain and bioadhesive polymer chain and entanglement of polymer.

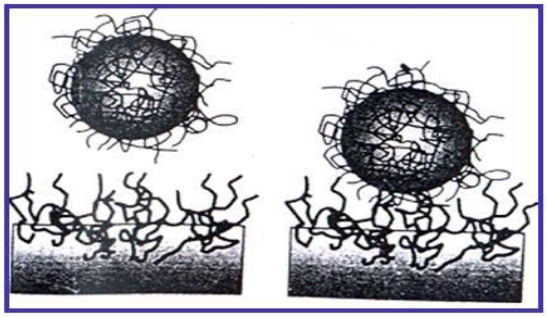


Fig:1.5 Interpenetration of bioadhesive and mucous polymer chains.

3. Theory of Bioadhesion:

Bioadhesion describe of the polymeric material with biological surface in the theoretical form of work for easily extended to polymer-polymer adhesion .The several theories have been explain to the fundamental Bioadhesion mechanism.

3.1 Electronic theory:

Electronic theory indicates that closely to be electron transfer on near of the Bioadhesion polymer. The glycoprotein network which have different structures of electronic and it will turn lead to the double layer of electrical charge formation at Bioadhesive interface.

3.2 Adsorption theory:
In this adsorption theory Bioadhesion initial contact between two surface because of atoms or there surface force action. Vander-waals and hydrogen and hydrophobic bond are involve primary and secondary chemical bond in adsorption process.

4. Wetting theory:
This is principally applicable to liquid bioadhesive system. It analyses adhesive and contact behavior in term of liquid or past to spread over a biological system.

4.1 Fraction theory:
According of this theory adhesion is related to separation on two surface after adhesion. Fracture strength is equivalent to the adhesive strength as given by mathematically;-

G=(Ee/L)1/2

Where: E= youngs module of elasticity
e= fracture energy
L= critical crack length when two surface are separated.

4.2 Diffusion theory:
According to diffusion theory the polymer chains and mucus may lead to formation to a sufficient depth to make a semi–permanent adhesion bond. The correct depth to which the polymer chain penetration depend on diffusion coefficient in contact time of mucus.
The physical entanglement and interpenetration of mucin strand in to the porous structure of the polymer chain describe this diffusion theory, diffusion coefficient depend on the molecular weight between cross links and decreases significantly as also cross linking density decreases.

Mechanism of buccal absorption:

Buccal drug absorption followed passive diffusion of their nonionized species. This process governed firstly by a concentration of radiant through the intercellular spaces of epithelium of mucous membrane. The primary transport mechanism are passive transport of non ionic species across the lipid membrane of buccal cavity. Drug should be passes through lipoidal barrier in buccal mucosa. In the case of other mucosal membrane and more lipophilic drug molecule are more readily absorbed by this barrier.

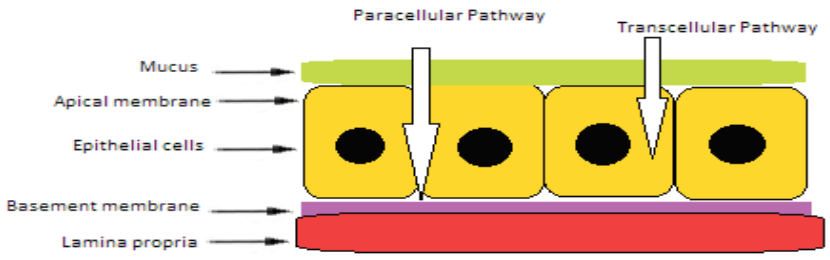


Fig: 1.5 : Mechanism of buccal absorption.

Drug absorption of buccal dynamics could be adequately described by first order rate process. The several potential barriers to buccal drug absorption have been identified. Deaeden and Tomlisom 1971 identify the salivary secretion alters the buccal absorption kinetic from drug solution by altered the by changing the concentration of drug in mouth. The linear relationship between salivary secretion and time is given as :

-dm/dt =kc/ViVt

Where, m = mass of drug in mouth at a time.

k = proportionality constant.

c = concentration of drug in mouth at time.

Vi = the volume of solution put in to mouth cavity

Vt = salivary secretion rate.

Benefits of buccal film: [13,11]

- ❖ Buccal film leads to quick disintegration and dissolution due to large surface area of film, in the oral cavity it promotes the systemic absorption of active pharmaceutical ingredient.
- ❖ Good stability and good mouth feel.
- ❖ Quick onset of action and minimum side effect.
- ❖ Self administration is possible.
- ❖ Easy to given accurate dosing compared to liquid doses form.
- ❖ Taste masking is possible.
- ❖ The doses form prolong the residence time at the site of absorption , hence increases the bioavailability.
- ❖ The film increase the therapeutic index of drug as it bypass hepatic first pass metabolism.
- ❖ GI enzymes and acidic environment drug should be protected from disintegration.
- ❖ No risk of choking
- ❖ No need of swallowing and chewing.
- ❖

5. Different method for preparation of buccal film or patch

The following process can be use to manufacture the mouth dissolving films;

I. Solvent casting method
II. Hot melt extraction
III. Semisolid casting
IV. Solid dispersion extrucsion
V. Rolling method
VI. Direct melting method

5.1 Solvent casting method:

In this method only water soluble polymer are dissolve in water and the drug with other excipients is dissolve in suitable organic solvent then the solution of polymer mixed with drug, excipient solution and stirred and finally placed in to petri dish and dried.

5.2 Hot melt extrusion:

In this method firstly the drug is mixed with carriers in solid form. Then the squeeze out having heater melts the mixture. Finally the melt is shaped films by the dies.

5.3 Semisolid casting method:

In this method firstly the polymer is dissolve in water and prepare a solution. Then the prepared solution is added to a solution of acid insoluble polymer (eg.Cellulose acetate butyrate, cellulose acetate phthalate), which was prepared in ammonium or sodium hydroxide. Then the less amount of plasticizer is added.

5.4 Solid dispersion extrusion:

In this method immiscible components are squeeze out with water and then prepared a solid dispersion. Finally the solid dispersion are shaped the dies.

5.5 Rolling method;

In this method a solution containing drug is involute on a 336earer.The solution is water and admixture of water & alcohol. The film is dehydrated to the roller and cut in to craved shape and size.

5.6 Direct melting method;

In that method film are manufactured without using of solvent. Direct melting method drug and excipient are mixed, liquid are not required for melting on this method. After the mixing the resulting materials rolled on release line until the craved thickness is achieved.

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