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Review Article

# A review on buccal drug delivery system

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**ABSTRACT**

The oral route is most popular route for the administration of therapeutic agents because of low cost, ease of administration and high level of patient compliance. The most popular oral solid dosage forms are tablets and capsules. Many patients find it difficult to swallow tablets and hard gelatin capsules particularly pediatric and geriatric patients and result in non- compliance. Difficulty in swallowing or dysphasia is seen to afflict nearly 35% of the general population. Fast dissolving drug delivery system is used to overcome this problem. When put on the tongue, this film dissolves instantaneously releasing the medication.

**Keywords:** Buccal route; Adhesion; Super Disintegrates; Swallowing; Fast dissolving films

## INTRODUCTION

Buccal route is the most commonly applicable route of drug administration. Various bioadhesive mucosal dosage forms utilize the buccal route i.e adhesive tablets, gels, ointments, patches (Nehal Siddiqui MD et al., 2011). Buccal drug delivery system is an alternative to other conventional method of systemic drug administration. These mouth dissolving films was developed based on the technology of the transdermal drug delivery system. Difficulty in swallowing is common among all age groups especially in elder people. Fast dissolving buccal drug delivery system were first developed in the 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatrics patients who experience difficulties swallowing (Malke M et al., 2007).

Buccal drug delivery system consists of a very thin oral strip. This strip is simply placed on the patient's tongue or any oral mucosal tissue, instantly becomes wet by saliva and rapidly gets hydrated and adheres on to the site of application. The films rapidly disintegrate and release the medications. These solid oral dosage forms do not require sterile condition and there are cost effective. Fast dissolving films also have an established shelf life of 2-3 years and depend upon the API but extremely sensitive to environmental condition (Alpesh R et al., 2011).

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### Special features of rapid dissolving buccal films

- Easy of administration of patients who are mentally ill, disabled and uncooperative
- Rapid release
- Fast disintegration
- Excellent mucoadhesive
- Thin elegant film
- Cost effective
- Palatable

### Ideal characteristics of a drug to be selection

- The drug to be incorporated should be of lower dose.
- The drugs with smaller and moderate molecular weights are preferable.
- The drug should be stable and soluble in water as well as in saliva.
- It should be partially unionized at the pH of oral cavity.
- The drug should have pleasant taste.

### Advantage

- ✓ Safety and efficacy profile.
- ✓ Oral dissolving films can be administered without water, anywhere, any time.
- ✓ Due to the presence of larger surface area, films provide rapid disintegration in the oral cavity.
- ✓ Oral dissolving films are flexible in nature so they provide ease in transportation, during consumer handling and storage.
- ✓ Suitable for geriatric and pediatric patients, mentally ill and the patients who are uncooperative.

- ✓ Beneficial in cases such as motion sickness, acute pain, suicide episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- ✓ Stable for long duration of time.
- ✓ As 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.
- ✓ The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the bioavailability of medicament.
- ✓ Provide new business opportunity like product differentiation, product promotion, and patent extension (Habib W et al., 2000).

**Disadvantages**

- High doses cannot be incorporated.
- Dose uniformity is a technical challenge.
- Eating and drinking may become restricted.

**Mechanism of action**

The delivery system, when simply placed on a patient's tongue or any oromucosal tissue, instantly becomes wets by saliva.

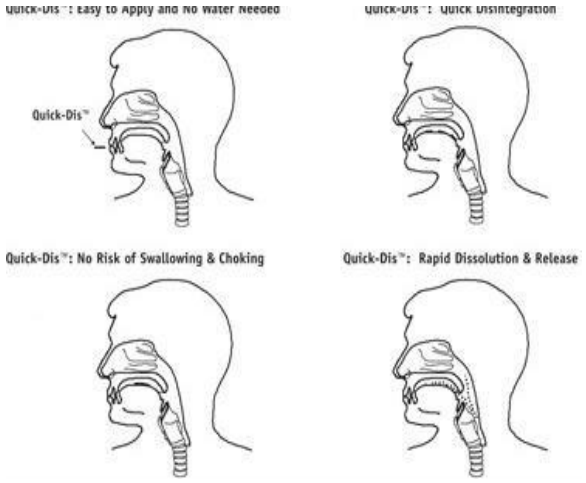


**Figure 1: Mechanism of action of rapidly dissolving drug delivery systems**

Due to presence of hydrophilic polymers and other excipients, the film rapidly hydrates, dissolves and release the medicament (Vollmer U et al., 2006) thus ensuring the absorption of medicament.

**Formulation consideration**

The area of the drug loaded in the fast dissolving films should be between 1-2 $cm^2$. The drug can be loaded up to a single dose of 20 mg. All excipients in the fast dissolving films should be regarded as safe and accessorized for use in oral strips.

**Table 1: Typical composition for fast dissolving films**

| Sl.No | Ingredients | Amounts(w/w) |
|---|---|---|
| 1 | Drug | 1-30% |
| 2 | Film forming polymer | 40-50% |
| 3 | Plasticizer | 0-20% |
| 4 | Saliva stimulating agent | 2-6% |
| 5 | Sweeting agent | 3-6% |
| 6 | Flavouring agent | q.s |
| 7 | Surfactenct | q.s |
| 8 | Colours, Fillers | q.s |

**Active Pharmaceutical ingredients**

Fast dissolving films contain 1-30% of active pharmaceutical ingredients. Several class of drugs can be formulated as mouth dissolving films including anti-ulcer, anti-asthamatic, anti-tussive, NSAIDS, anti-hypertensive drugs (Arunachalam A et al., 2010).

**Film forming polymer**

In this mouth dissolving films water soluble polymers are used. These water soluble polymers (Biradar et al., 2009) achieve rapid disintegration and good mouth feels. As water soluble polymer molecular weight increases disintegration decreases. Examples of the water soluble polymers are HPMC-3, k-3, methylcellulose a-3, a-6, a-15, carboxymethyl cellulose-30, polyvinylpyrilodine-k-90, pectin, gelatin, sodium alginate, hydroxypropilecellulose, polyvinylalcohol, maltodextrins. Polymerizied resins are a novel film forming polymers.

Single or combination polymers are used. Now a days natural polymer is used in film formulation as they are safe and effective.

**Ideal properties of the polymers used in the film formulation**

- ➢ Polymer should be non toxic and non irritant
- ➢ It should be non bitter
- ➢ It should be avoid of leachable impurities
- ➢ It should be cost effective and rapidly available.
- ➢ It should have good wetting and spreadable properties.
- ➢ It should exhibit sufficient shear and tensile strength.
- ➢ It should have sufficient shelf life
- ➢ It should not cause secondary infection in the oral cavity (Dhagla Ram Choudhary et al., 2011).

**Plasticizers**

Plasticizers play an important role in the film formulations. This plasticizer (Sandeep Saini et al., 2011) is used in the 0-20%in the film formulation. It improves the film flexibility and mechanical properties of the film like tensile strength. Plasticizer significantly improves the strip properties by reducing the glass transitions temperature of the polymer. The selection of the polymer depends upon the selection of drug. Film cracking, splitting and peeling takes place by the use of inappropriate plasticizers. Different types of plasticizers

are used in the film formulation such as glycerol, polyethyleneglycol, propyleneglycol, dimethyl, dibutyl, diethylphathlates, tri- butyl, triethyl, acetyl citrate, triacetin and castor oil.

**Sweetening agents**

Sweetening agents are important components in the film formulation i.e 3-6%w/w natural and synthetic sweeteners are generally used. These sweetening agents (Shojaei et al., 1998) are generally used to mask the drugs of bitter taste. These sweetening agents are used alone or in combination. Commonly used sweetening agents are xylose, fructose, glucose, sucrose, maltose, dextrose, liquid glucose, isomaltose. Fructose is more sweetener than sorbitol and mannitol. Artificial sweeteners have gained more popularity in pharmaceutical preparations. Artificial sweeteners used are sodium and calcium saccharides salts, cyclamate salts, polyhydric alcohol such as sorbitol, mannitol and isomalt can be used in combination as they additionally provide good mouth feel and cooling sensation.

**Saliva stimulating agents**

Saliva stimulating agents are used in the film formulation. They are used alone or combination between 2-6% w/w of the strip. The purpose of saliva stimulating agents (Reddy et al., 2002) is to increase the rate of production of saliva. The rate of production of saliva increases the faster disintegration of the oral film. Generally acids are used in the saliva stimulating agents such as citric acid, malic acid, latic acid, ascorbic acid, tartaric acid.

**Flavouring agents**

Flavouring agents impart flavor to any of the formulation. They are selected according to the choice of the individual. Mint, orange, strawberry flavors. These flavouring agents (Divate S et al., 2011) should be compatabile with drug and other exicipients. These flavouring agents are used alone or in the combination.

**Colouring agents**

Colouring agents (Vollmer U et al., 2006) are used to impart colour in the formulation FDA approved colouring agents should be incorporated into the oral films.

**Methods of preparation**

Different methods are used in the preparation of rapid dissolving buccal films.

- Solvent casting method
- Semisolid casting method
- Hot melt extrution method
- Solid dispersion extrution method
- Rolling method

**Solvent casting method**

- In this method (Tejvir Kaur et al., 2011) first water soluble polymers and other exicipients are dissolved in water to form a viscous medium.
- Active pharmaceutical ingredients are dissolved in smaller amount of solution and both solutions are combined using high shear processor.
- Finally the solution is degassed under vacuum to remove the all air bubbles. The solution is moulded into glass and dried at $50^0$c for 24 hr. Finally the film is formed and cut into a desired shape.

**Hot melt extrusion method**

- In this method (Coppens KA et al., 2005) firstly drug is mixed with carrier in solid form. Then the extruder having heaters melts the mixture. Finally the melt is shaped into films by the dies.
- They are certain benefits of hot melt extrusion method
  - Fewer operational units
  - Better content uniformity
  - An anhydrous process
- In this method low molecular weight and low viscosity polymers are used.
- The processing temperature should be 80°C (zone1), 115°C (zone2), 100°C (zone3).

**Semisolid casting method**

- In this method (Aggarwal Jyoti et al., 2011) acid insoluble polymer are used.
- First solution of water soluble polymers is prepared and it is added to a solution of acid insoluble polymers.
- Plasticizer is added in the appropriate amount so that gel mass is formed. This gel mass is casted into the films by using the heat controlled drums.
- Acid insoluble polymers and film forming polymers (Cilruzo F et al., 2008) are used in the ratio of 1:4.

**Evaluation Studies of Oral Films**

There is different type of evaluation tests for oral films.

- Weight variation
- Thickness measurement
- Folding endurance
- Surface pH
- Disintegration time
- Drug content
- In vitro dissolution time
- Dryness test or tack test
- Percent elongation test
- Young's modules test
- Contact angle test
- Swelling test
- Transparency test

- Content uniformity test
- Disintegration time test
- Tear resistance test

**Weight variation test**

Weight variation test can be calculated by weighting 20 films. Average weight can be measured.

**Thickness Test**

Thickness of the film can be measure using micrometer screw gauge or calibrated digital vernier calipers. The film thickness should be measured at five points i.e from the centre and all the four corners and then means thickness is calculated. It is necessary to determine the thickness of the film because it is directly related to accuracy of dose in the film.

**Dryness/Tack Test**

Dryness test (Galfetti P et al., 2006) must be done to measure the solvent or water content present in the film. Tack is the tenacity in which the strip adheres to a piece of paper that has been pressed into contact with the strip. Film drying process have been recognized i.e set-to-touch, dust-free, tack-free, dry-to-touch, dry-hard, dry-through, dry-to-recoat, dry print free.

**Tensile Strength**

It can be measured by applying the maximum stress to a point of film at which the strip means breaks. It can be calculated by applied load at rapture divided by the cross section area of the film as given in the equation.

$$Tensile\ strength = \frac{\text{load at Breakage}}{\text{strip thickness X strip width}} X100$$

**Folding Endurance**

Folding endurance is measured by repeated folding of the film at the same place till the film breaks. The number of times film can be folded without break is computed as the folding endurance value.

**Surface pH Test**

Surface pH of the film can be measured (Gohel MC et al., 2005) by placing the film on the surface of 1.5%w/v agar gel followed by placing pH paper on film; change in the colour of the pH paper was observed.

**Contact Angle**

Contact angle (Cilurzo F et al., 2011) can be determined by using goniometer at room temperature. Collect the dry film and place a drop of distilled water on the surface of the dry film. Images of water droplet were recorded within 10 sec of deposition by means of digital camera, the contact angle was determined on both sides of drop and average is taken.

**Transparency**

The transparency of the films can be measured by using a simple UV-Spectrophotometer. The film is cut in a rectangular shape and placed inside the spectrophotometer cell and this determines the transparency of the film at 600 nm.

The transparency of the film was calculated by following equation

$$\textbf{Transparency} = \textbf{Log } T_{600}\textbf{/b = -€c}$$

Where, $T_{600}$ = transmittance at 600nm
B = film thickness [mm]
C = concentration

**Swelling Test**

The swelling test can be calculated by using stimulated saliva solution. All samples of the film are weighed and pre weighed on a stainless steel wire mesh. 15ml of saliva stimulated solution is added into a plastic container and the mesh containing film sample is submerged into it. Increase in the weight of the film was observed. Swelling test can be calculated using the equation.

$$\alpha = \frac{Wt - Wo}{Wo}$$

Where, Wt =weight of the film at time t
Wo =weight of the film at time o

**Young's Modulus**

Young's modulus (Obermeier P et al., 2006) can be measured to calculate the stiffness of the film. It is represented as the ratio of applied stress over strain in the region of elastic deformation.

$$Young's\ modulus = \frac{Slope}{Film\ thickness\ \ cross\ head\ speed} X100$$

**Disintegration Time**

The disintegration (Cilurzo F et al., 2005) time limit is 90 sec or less. The disintegration test can be carried out by using disintegration test apparatus. Typical disintegration time for oral strip is 5-30 sec.

***In-Vitro* Dissolution Test**

*In-vitro* dissolution test (Apoorva Mahajan et al., 2011) can be measured by using dissolution apparatus i.e standard basket or paddle apparatus described in the USP. The dissolution medium can be selected as per the selective active pharmaceutical ingredient.

**CONCLUSION**

Rapidly dissolving film is a promising approach with a view of obtaining faster action of the drug and would be advantageous in comparison to currently available conventional dosage forms. From the present review it can be concluded that rapidly dissolving film formulations can be a potential novel dosage forms for pediatric, geriatric, and also for general population.

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