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AN OVERVIEW ON BUCCAL FILMS

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ABSTRACT

Now days, an extensive research is being carried out on the design and development of innovative drug delivery systems to improve the safety, efficacy and patient compliance. One such delivery system is the buccal film technology. Buccal film technology is one such distribution method. This technology has become a cutting-edge replacement for more traditional sorts of drug delivery systems. Through a buccal drug administration device, the film is delivered. It is novel film technology which is fullfills all these requirements. It is administered through buccal drug delivery system. A film is small in size, dose, easily administered so that it is more palatable and acceptable dosage from than other buccal drug delivery system like wafers, lozenges, micro particles, gel, tablets. It is the proven technology for the systemic delivery of active pharmaceutical ingredients [API's]. The buccal mucosa is the best suited site for local, as well as systemic delivery of drugs due to its physiological features. The film is an elegant and effective dosage form with improved bioavailability, when compared to other dosage forms as it bypasses the hepatic first pass metabolism. It is cost effective, biodegradable, fast absorption, elegant, easy to handle, non irritating and no requirement of swallowing of drug henceforth it is more accepted dosage form by geriatric and pediatric patients. It also has the advantages of improved patience compliance because of their reduced size with suitable thickness as compared to certain other delivery system like buccal tablets and lozenges. It favors the delivery of drugs having danger of wastage through first pass effect, having low permeability, enzymatic degradation and can be affected by the variable environment of the gastro intestinal tract.

KEYWORDS: Buccal film, Mucosal membrane, Novel Drug Delivery System, Oral cavity, Patient compliance.

INTRODUCTION

Among various transmucosal routes, buccal mucosa is the most suited for local, as well as systemic delivery of drugs. The unique physiological features make the buccal mucosa as an ideal route for mucoadhesive drug delivery system. It is widely recognised that therapeutic chemicals absorbed from the oral mucosa allow for a direct entry of the medication into the bloodstream, avoiding first-pass hepatic metabolism and gastrointestinal drug degradation, both of which are connected to peroral administration. The most often used route for medication administration is the oral route.[1]

This drug delivery system is suitable for the drugs which passes through high first pass metabolism and is used for enhancing bioavailability with reducing dosing frequency to mouth plasma peak levels, which in turn minimize adverse side effects. Reasons of admiration of oral route are low therapy cost, comfort of administration and self-medication. Above 70% of the marketed drugs are in the form of oral dosage forms due to pain evasion and adaptability. But around 50% of population, generally pediatric and elderly patients avoid taking solid oral preparations such as tablets and capsules due to choking hazard, leading to patient's incompliance.[2]

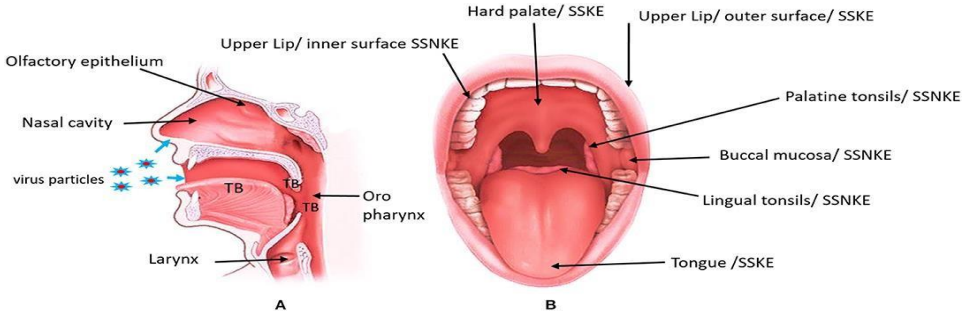

Fig. No. 1: Mucosal region of mouth.

Advantages

- Buccal films provide large surface area that leads to rapid disintegration and dissolution in the oral cavity due to which it promotes the systemic absorption of Active pharmaceutical ingredient.
- No need of chewing and swallowing.
- No risk of chocking.
- The film increases the systemic bioavailability of the drugs, as it bypasses the hepatic first pass metabolism.
- Drug can be protected from degradation by GI enzymes and the acidic environment.
- Rapid onset of action and minimum side effects.
- Self administration is possible.
- Accurate dosing compared to liquid dosage forms.
- Taste masking is possible.
- Prolongs the residence time of the dosage form at the site of absorption, hence increases the bioavailability.
- Ease of administration to pediatric, geriatric patients, and also to the patients who arementally retarded, disabled or non-cooperative.

Disadvantages

- Drug concentration is low when there is buccal film in the mouth cavity because salivating dilutes medications at the site of absorption.
- When a drug is ingested with saliva, the maximum amount of the dissolved or released drug is taken from the site of absorption, increasing the probability that the delivery system will be swallowed as well.
- It's possible that a drug's flavour, tongue irritability, or allergy will manifest.
- There are some unfavourable effects as well, such as tooth erosion or discolouration.
- When using a traditional form of buccal drug delivery system, it is not permitted to eat, drink, or in certain cases, converse at the same time.[3]

Formulation of buccal film

Active pharmaceutical substance can be from any class of pharmaceutically active substances that can be administered orally or through the buccal mucosa. Like antiulcers, antiasthmatics, antitussive, antihistaminic, antiepileptic, expectorants, antianginal etc. For the effective formulation, dose of drug should be in mgs (less than 20 mg/day). Usually 5%w/w to 30%w/w of active pharmaceutical ingredients can be incorporated in buccal film. High dosage of molecules is difficult to incorporate into film.

Ideal characteristics of drug to be selected

- No Bitter Taste.
- Dose lower than 20mg.
- Low molecular weight.
- Good stability in water and saliva.
- Ability to permeate oral mucosal tissue.[4]

Mucoadhesive polymers: Polymers with different characteristics have to be considered depending on the type of formulation. Mucoadhesive polymers are classified into two main groups, such as hydrophilic polymers and hydrogels. The hydrophilic polymers most commonly used in buccal dry or partially hydrated dosage forms include polyvinyl alcohol [PVA], sodium carboxy methylcellulose [NaCMC], hydroxyl propyl methyl cellulose [HPMC], hydroxyl ethyl cellulose and hydroxypropyl cellulose [HPC]. Hydrogels include anionic polymers like carbopol, polyacrylates, cationic polymers like chitosan and non ionic polymers like eudragit analogues.[5]

Table No. 01: Types of polymers.

S. No.	Type	Examples of mucoadhesive polymers
1.	Non- ionic polymers	Hydroxy ethyl cellulose, Hydroxy propyl cellulose, Poly vinyl pyrrolidine, Hydroxy propyl methyl cellulose, Polyvinyl alcohol, Polycarbophil, Polyethylene oxide,Eudragit analogues
2.	Anionic polymers	Sodium alginate, Sodium carboxy methyl cellulose, carbopol, polyacrlylates
3.	Cationic polymer	Chitosan

Plasticizers: It is a component that the oral films must have. The choice of plasticizer is influenced by the polymer's compatibility as well as the type of solvent employed in the casting of the film. It lessens the brittleness of the film and increases its flexibility. They are utilised in concentrations ranging from 1 to 20% by weight of dry polymer. Glycerol, propylene glycol, low molecular weight polyethylene glycols, citrate derivatives such as triacetin and acetyl citrate, phthalate derivatives such as dimethyl and dibutyl derivatives, castor oil, etc. are some examples.[6]

Surfactants: Surfactants are used as solubilising or wetting agent. Film gets dissolved rapidly within seconds by use of surfactant and immediately drug is released. Solubility of poorly soluble drugs in buccal can be improved by using surfactant. For examples are Polaxamer 407, sodium lauryl sulphate, benzalkonium chloride, benzethonium chloride, tweens and spans etc.[7]

- **Penetration enhancers:** Penetration enhancers are also the important excipients to be added in the buccal film formulation. These are required when a drug has to reach the systemic circulation to exert its action. These must be nonirritant and have a reversible effect. The epithelium should recover its barrier properties after the drug has been absorbed. The most common classes of buccal penetration enhancers include fatty acids that act by disrupting intercellular lipid packing, surfactants, bile salts, and alcohols.[8]

- **Stabilizing and thickening agents:** Addition of stabilizing and thickening agents are important to improve the viscosity and consistency of dispersion or solution of the film preparation before casting. Natural gums like xanthan gum, locust bean gum, carragenan and cellulosic derivatives are few examples of stabilizing and thickening agents. They areused in the concentration up to 5%w/w.[9]

- **Saliva stimulating agent:** These agents are used to enhance the production of saliva which assists in the disintegration of the buccal films. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them. These agents are used alone or in combination between 2 to 6% w/w of weight of the film.[10]

- **Flavoring agents:** When it comes to oral dissolving systems, flavouring ingredients are crucial. The initial flavour quality, which is noticed in the first few seconds after the product has been consumed, and the aftertaste of the formulation, which lasts for at least roughly 10 minutes, determine whether a patient would accept the oral disintegrating formulation. Synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers are used for selection of flavoring agent. Depending of flavoring agents strength, need of amount of flavoring agent to m mask taste.

- **Coloring agents:** When some of the formulation ingredients or medications are present in insoluble or suspension form, pigments such titanium dioxide or FD&C approved colouring additives are used (Not exceeding concentration levels of 1%w/w) in buccalfilm formulation.[11]

Manufacturing method of preparation

The buccal film manufacturing process includes the following techniques.

1. Solvent casting technique.
2. Hot melt extrusion technique.
3. Direct milling method.

❖ **Solvent casting method:** The solvent casting method is widely preferred for the manufacture of buccal films. This process involves the following steps:

- Water soluble ingredients (polymers) are dissolved in water to form homogenous viscous solution.
- API and other excipients are dissolved in suitable solvent to form a clear viscoussolution.
- Both the solutions are mixed and the resulting solution is casted as a film and allowed to dry as shown in figure number 2 and 3.

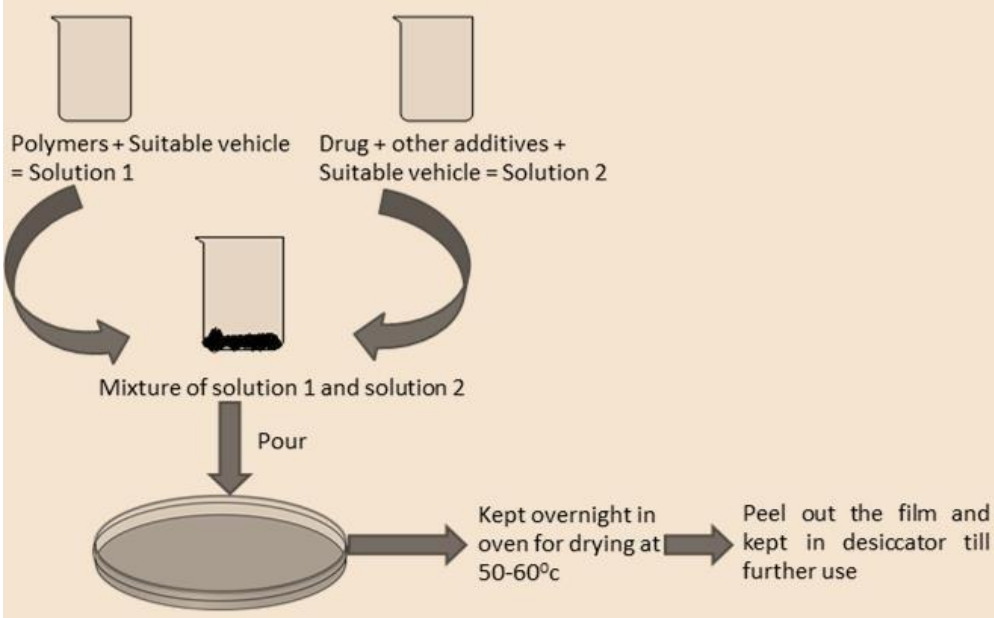

Fig. No. 2: Solvent casting method.

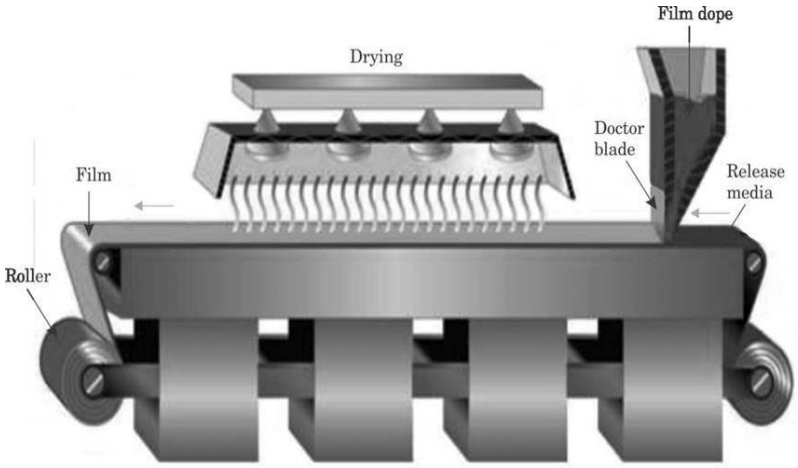

Fig. No. 3: Solvent casting method.

❖ **Hot melt extrusion technique:** This procedure makes use of a hot melt extruder. In this method, a polymer is heated and then shaped into a film. A mixture of dry pharmaceutical materials, including API, is added to the hopper, transported, mixed, and heated before being extruded out in molten form by the extruder. The film is cast using the molten mass that has now solidified. The casting and drying process is a crucial step. Steps involved in Hot Melt Extrusion Method are:

Step 1: First, the medication is combined with solid carriers. Step 2: A heater-equipped extruder melts the mixture.

Step 3: Using dies, the melted substance is finally moulded into films.

Table No. 02: Ingredients used in hot melt extrusion technique.

S. no.	Ingredients	Quantity
1.	API	5-30%(w/w)
2.	Mucoadhesive polymer	45%(w/w)
3.	Plasticizers	0-20%(w/w)
4.	Sweetening agents	3-6%(w/w)
5.	Saliva stimulating agents	2-6%(w/w)
6.	Colors and Flavors	Q.S

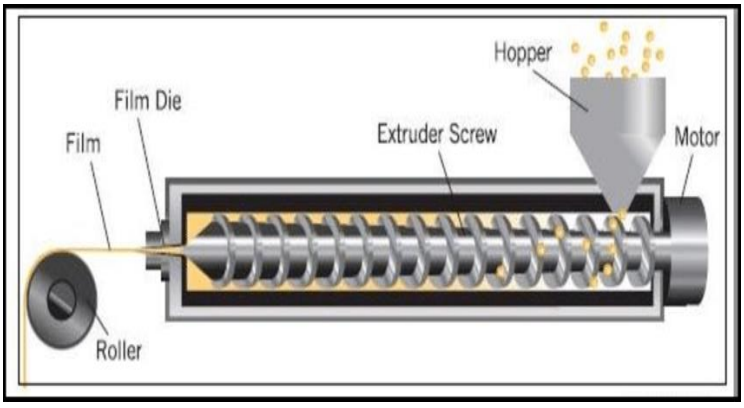

Fig. No. 4: Hot melt extrusion technique.

❖ **Direct milling method:** This technique doesn't use any solvents. Using either direct grinding or kneading, the medicine and excipients are combined in this manner without the use of fluids. The finished product is then rolled till it reaches the desired thickness on a release liner. This approach is typically recommended because there is zero chance of leftover solvent and zero correlation with any health issues associated to solvents.[12]

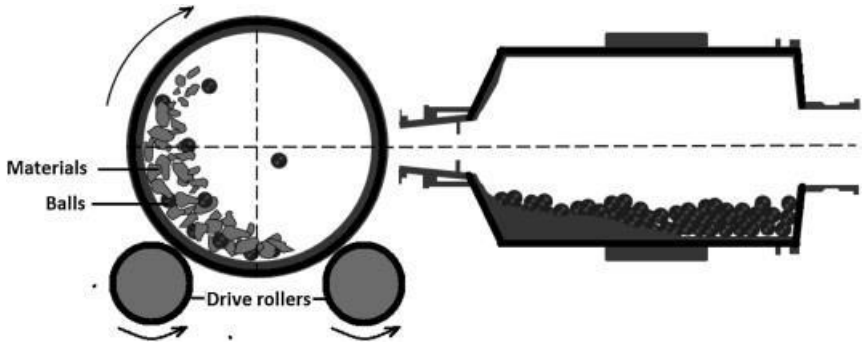

Fig. No. 5: Direct milling method.

Evaluation techniques of buccal films

The buccal films are evaluated by[13]

1. **Weight and thickness of the film:** For evaluation of film weight, three films of every formulation are taken and weighed individually on a digital balance. The average weights are calculated. Similarly, three films of each formulation were taken and the film thickness is to be measured using micrometer screw gauge at three different places, and the mean value is to be calculated.

2. **Surface pH of films:** For determination of surface pH, three films of each formulation are allowed to swell for 2 hours on the surface of an agar plate. The surface pH is to be measured by using a pH paper placed on the surface of the swollen patch. A mean of three readings is to be recorded.

3. **Swelling index:** After determination of the original film weight and diameter, the samples are allowed to swell on the surface of agar plate kept in an incubator maintained at 37 ± 0.2ºC. Weight of the films (n=3) is determined at different time intervals (1-5 h). The percent swelling, % S is to be calculated using the following equation:
   Percent swelling [% S] = [Xt –Xo /Xo] × 100Where, Xt = The weight of the swollen film after time t Xo = The initial film weight at zero time.

4. **Moisture content:** The produced films need to be weighed separately and maintained at room temperature in desiccators with calcium chloride for 24 hours. After a predetermined amount of time, the films must be weighed again until they display a steady weight. The following formula should be used to compute the % moisture content.
   % Moisture content = [Initial weight–Final weight/Final weight] × 100.

5. **Tensile strength:** The tensile strength is the property of the film that requires a load to cause load deformation failure of film. Film strips in special dimension is held between two clamps positioned at a specific distance. Tensile strength is calculated by applying load at rupture and cross sectional area of fractured film from following equation. Tensile strength (N/mm2) = breaking force (N)/ cross sectional area of sample (mm2).

6. **Drug content uniformity:** Buccal film is dissolved in 100 ml of pH 6.8 buffer separately and mixture is suitably diluted. The amount of drug in film is measured absorbance spectrophotometrically at 242 nm. The average drug content is calculated.

7. **In vitro disintegration time:** It is determined visually in a petr iplate containing 2 ml distilled water with swirling every 10 seconds. The time at which film started to break ordisintegrate is recorded as the in vitro disintegration time.

8. **In vitro dissolution study:** An in vitro dissolution study is carried out using USP type II apparatus (Basket type apparatus). pH 6.8 buffer (50 mL) is used as a dissolution medium at 50 rpm speed and 370C temperature. At specific time intervals, 1 ml samples were withdrawn and replaced with the equal quantity of fresh dissolution medium.

   Buccal films are filtered through 0.45 µm Whatman filter paper, and analyzed spectrophotometrically at λmax of active pharmaceutical ingredient.

9. **Organoleptic evaluation:** The prepared buccal film should possess the desired features of sweetness and flavor, which is acceptable to a large mass of population. Controlled human taste panels are used for psychophysical evaluation of the product. In-vitro methods of utilizing taste sensors, specially designed electronic tongue measurement devices can be used for this purpose.

Table No. 03: Approved drugs.

Drug	Year of Approved	Company	Use
Suboxone	31/08/2010	Reckitt Benckiser pharmaceutical Inc	Psychological support and patient counselling
Zuplenz	January 2010	Pharm Film technology	Prevention of nauseaand vomiting beforeand

			after of cancer chemotherapy.
Ondansetron	23/03/2010	APR Applied pharma Research s.a and Labtec	Prevention of nauseaand vomiting before and after cancer chemotherapy and radiotherapy .
Zelapar	October 2005	Valent pharmaceuticals International Inc.	Parkinson's Disease

Applications

- Multilayer drug film construction is possible, which an emerging area for immediate application. Two or more drugs could be combined into one format and the layers may be formulated to have the same or various dissolution rates.
- It is feasible to create multilayer drug films, which is an emerging field with direct application. It is possible to mix two or more medications into one format, with the dissolving rates of the layers being the same or different.[14]
- Films acts as gastro retentive dosage forms, in which the dissolution of the films could be triggered by the pH or enzyme secretions of gastro intestinal tract, and could be potentially used to treat gastro intestinal disorders.
- The films can be formulated in such a way that the dissolution rates of the drugs can range from minutes to hours.
- Good accessibility, robust epithelium, quick and easy removal of the dosage form in case of need, good drug absorption, reduction of the first-pass metabolism, andpatient compliance.[15]

CONCLUSION

The present review concludes that the buccal film is the most accurate and acceptable dosage form, which bypasses the hepatic first pass effect and shows good bioavailability. This is the most innovative and promising technology that benefits people of all ages, especially children and the elderly as well as those who have trouble swallowing. Buccal film is promising area for continued research with the aim of systematic delivery of orally inefficient drugs. It can replace the conventional dosage forms, including fast disintegrating tablets due to its advantages over the conventional dosage forms, and they can be manufactured with low cost. This technology offers a useful tool for maintaining the medicinal and financial worth of pharmaceuticals. It is buccoadhesive drug delivery system which enhances safety, efficacy and stability of active pharmaceutical ingredient. It is novel technology due to its better option to optimize therapeutic efficacy.

In conclusion, buccal films offer a promising avenue for drug delivery, particularly for medications requiring rapid onset of action, improved bioavailability, or targeted delivery. However, further research is needed to optimize formulation techniques, enhance stability, and investigate long-term safety and efficacy profiles. Overall, buccal films hold significant potential to revolutionize the pharmaceutical industry and improve patient outcomes.

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