IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
August 2023 Vol.:28, Issue:1

Mucoadhesive Buccal Films: An Innovational Drug Delivery System

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Submitted: 25 July 2023
Accepted: 18 August 2023
Published: 30 August 2023

Keywords: Mucoadhesive Buccal Films, Innovational Drug Delivery System

ABSTRACT

Nowadays, extensive research is being done on the design and production of a new drug delivery system to improve safety, efficiency and compliance issues. A buccal drug delivery system directly enters systemic circulation. It uses a jugular vein pass to deliver drugs from hepatic first-pass metabolism, which boosts their bioavailability. Buccal films release drugs orally in a slow and predetermined dose that provides well defined benefits in addition to standard dosage forms for the prevention and treatment of certain diseases. Buccal films share certain features like reduced size, volume, and dynamic control, which is why they taste better and more acceptable forms than other buccal drug delivery systems such as gels, pills, lozenge, and micro-particles. It does not require swallowing of the drug, which is most suitable for paediatric as well as geriatric patients. The medications that are used to increase bioavailability and have a high first-pass metabolism are ideal for this drug delivery strategy. Rolling, hot-melt extrusion, solid dispersion, solvent casting, or semi-solid casting can all be used to make mucoadhesive buccal films. The solvent casting method is the most popular of them. Organoleptic evaluation, thickness, transparency, surface pH, moisture content, tensile strength, per cent elongation, folding endurance, swelling assets, drug content, and in vitro dissolution tests are a few of the mechanical assets that are assessed for the mucoadhesive buccal film.

INTRODUCTION: -

The most recent development in buccal administration is muco-adhesive buccal films. They are now more important than ever as patient-friendly, cost-effective, and cutting-edge Active Pharmaceutical Ingredient (API) delivery techniques. Since muco-adhesive buccal films are designed to hold to the muco-adhesive buccal films, they can be made to have both local and systemic activity. The muco-adhesive buccal films may be more flexible and pleasant than buccal pills. Instead of going through the liver's first-pass processing, muco-adhesive buccal films inject API directly into the bloodstream via the internal jugular vein. The mucoadhesive buccal film's large surface area also makes it easier to quickly moisten, which speeds up the API's absorption. The buccal mucosa is an important region for medicine absorption because of its rich blood supply. Its bioavailability is increased by prolonging its residence time at the site of absorption since the dosage form is simple to provide to paediatric and geriatric patients, as well as those who are intellectually challenged, uncooperative, or have physical or mental disabilities. The buccal mucosa is rich with blood supply, which acts as a perfect and fast site for the absorption of a drug. Mucoadhesive buccal films have also been formulated to show the local action to treat fungal infections in the oral cavity.

Potential Benefits of Buccal Films: -

→ Buccal films provide a large surface area that leads to rapid disintegration and dissolution in the oral cavity which it promotes the systemic absorption of Active pharmaceutical ingredient.

→ No need of chewing and swallow.

→ No risk of chocking.

→ The film increases the systemic bioavailability of the drugs, as it bypasses the hepatic first pass metabolism.

→ Drugs 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 increasing the bioavailability.

→ Ease of administration to paediatric, geriatric patients, and to the patients who are mentally retarded, disabled or non-cooperative.

→ Good mouth feels and good stability.

→ Ease of transportation, storage and consumer handling.

→ Requires less excipient.

→ More economical.

Anatomy and Physiology of Oral Mucosa: -

Oro mucosal region is adhesive in nature and acts as a lubricant, allowing the cells to move relative to one another with less friction. Four sites namely the buccal cavity, the lingual area, the palate and the gingival region have been used for drug administration. The most used site for drug administration of the four sites mentioned above is the buccal route. The anatomic site for drug administration between the cheek and gingival is known as the buccal mucosa. The oral mucosa is composed of three layers. The first layer is the stratified squamous epithelium, underneath this layer lays the basement membrane. The basement membrane overlies the lamina propria and submucosa. The constitution of the epithelium within the different sites of the oral cavity shows dissimilarity. The epithelium in the soft palate, buccal and sublingual area is not keratinized, therefore not containing ceramides and acylceramidesm which are associated with providing a barrier function. The mucosa of the buccal and sublingual region has only small amounts of ceramide and is thus more permeable when compared to other regions of the oral cavity. A layer of mucus is present on the surface of the epithelial layer of cells. This plays a major role in cell-to-cell adhesion, oral lubrication, as well as Muc adhesion of mucoadhesive drug delivery systems. The buccal area has an expanse of smooth and relatively immobile surface, which is suitable for placement of a retentive system. For buccal drug delivery, adhesion to the oral mucosa permits not only the intimacy of contact and the possibility of improved drug absorption but also the ability to achieve an optimum residence time at the site of administration. These characteristics make the buccal mucosa as a more appropriate site for prolonged systemic delivery of drugs.

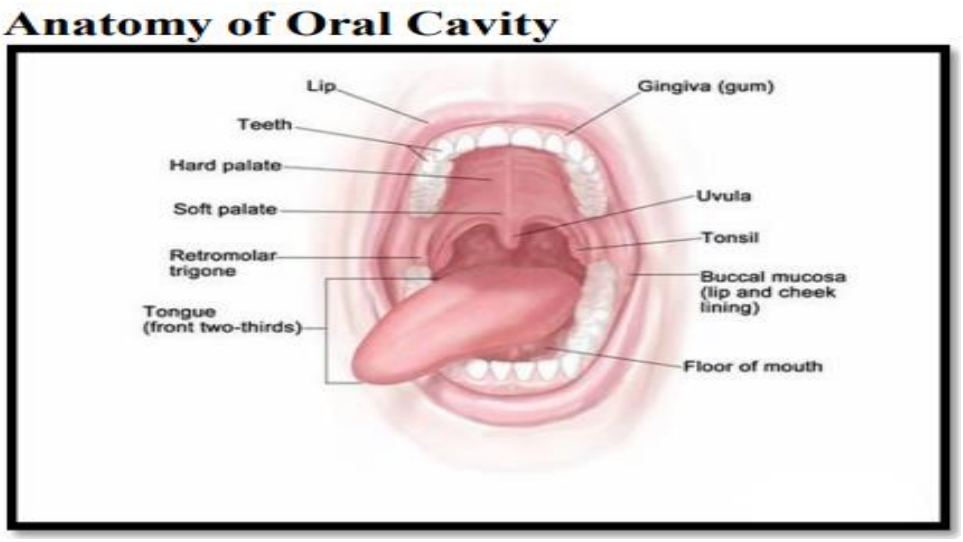

Fig.no. 1

Therapeutic opportunities for mucoadhesive buccal films: -

Due to the wide-ranging applicability of mucoadhesive buccal films, there are many therapeutic and clinical opportunities whereby the mucoadhesive buccal film technology can be utilised to deliver quality, efficacious and safe therapy.

Mucoadhesive buccal films and special patient populations: -

Mucoadhesive buccal films represent a clear therapeutic advantage in special patient populations (paediatric and geriatric age groups), due to the prevalence of dysphagia and instances of swallowing difficulties. In the paediatric population, this has been associated with respiratory disorders, cardiac disorders, gastrointestinal disorders, neurological disorders, congenital abnormalities, maternal and petri-natal issues, iatrogenic complications, and caustic injuries. Swallowing difficulties in this population are also a consequence of the developmental process, resulting in the use of different dosing aids e.g., oral syringes. Ostrom, Meltzer, and Welch demonstrated that a vast majority of children aged between 6 and 11 years old were able to swallow a small oral tablet, while Bracken et al. demonstrated that most children aged 4–8 years successfully swallowed tablets upon attempting to do so. These results, however, are based on individual populations of children and are subject to variability, which makes the definition of an age from which children can definitively swallow tablets problematic. Difficulty in swallowing may be a prominent issue in geriatric patients who are >65 years old, which emphasises the requirement for alternative routes of administration, such as the buccal route. Dysphagia in this population has been referred to as

a distinct geriatric syndrome, due to increased incidences of multi morbidity and poly pharmacy, which may also induce dry mouth. Therefore, the development of buccal delivery systems requires special consideration in this age group. Both the geriatric and paediatric populations are thought of as heterogeneous age groups, where marked differences in the chronological ageing process can be seen amongst people due to their lifestyle, genetic make-up, and overall health. Heterogeneity is more prominent in the older population because of this. This heterogeneity amongst individuals within these age populations suggests there is a need for the personalisation of treatment regimens, which is thought can be achieved through 3D printing technologies. Situational swallowing-related difficulties can occur in the form of hyperactivity and unconsciousness, whereby mucoadhesive buccal films can be deployed to illicit effective therapy in these situations. This is evidenced by the development of rapidly dissolving mucoadhesive buccal films containing diazepam, indicated for the treatment of seizures, currently pending FDA approval. Additionally, it is advantageous with respect to the administration of injectable formulations in instances where seizures occur in environments away from trained healthcare professionals in terms of safety.

Mucoadhesive buccal films and personalised medicine: -

Conventional mass-produced dosage forms, such as tablets and capsules are beginning to be recognised as sub-optimal in terms of their effectiveness in treatment. This is due to the inherent differences between patients, inflexible dose strengths and the problematic nature of adjusting drug doses within oral-solid dosage forms (i.e., tablet splitting). This leaves the present ‘one size fits all’ approach to treatment inefficient.

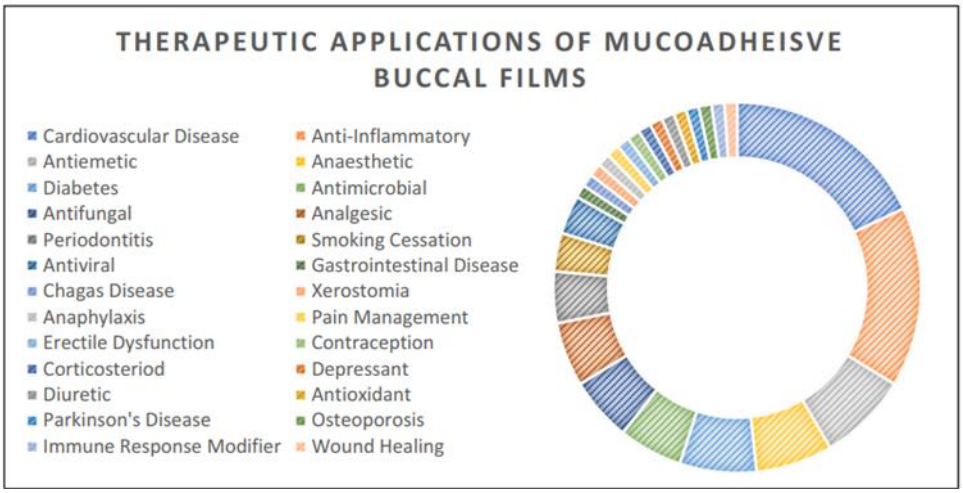

Fig.no. 2

Patient-related factors influencing mucoadhesive film development. The therapeutic needs of patients should be prioritised when developing medicines. Although this is often the case, there are typically more confounding factors that influence the performance of drug products that developers may be aware of or are willing to thoroughly explore during the development process. It is therefore necessary to design effective, quality and safe dosage forms with patient physiology, and the various factors that may influence physiological characteristics in mind. In addition to the effects of concomitant medications and/or drivers of patient acceptability to increase the likelihood of positive therapeutic outcomes.

Permeability: -

It is found that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin. The permeability of the oral mucosae is greater in buccal than sublingual. This is dependent on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa being relatively thin and nonkeratinized, the buccal thicker and nonkeratinized, and the palatal intermediate in thickness but keratinized.

Introduction to buccal film:

Buccal film is a non-dispersible thin type of spreadsheet modified release dosage form made up of one or more polymer matrix or coverings that holds the medicine and/or additional excipients. When relative to other dosage forms, the buccal film is an exquisite and effective dosage form with enhanced bioavailability since it skips hepatic first-pass metabolism. Due to its tiny size, modest dose, and film thickness, it is the most agreeable and appetizing dosage form. Oral mucosa, teeth or gingiva may get adhered due to the presence of mucoadhesive polymers in the film. This enhances the oral cavity getting appropriate medication release leading to produce better therapeutic effects which is defined as unidirectional release, individually in the oral cavity by unidirectional release or the two of them together i.e., bidirectional release. After a set amount of time, the patch is removed from the mouth and discarded.

Buccal Dosage Form Structure and Design:

Buccal Dosage Forms include:

1) Matrix type (Bi-directional): A buccal patch with medication, adhesive, and additives combined in a matrix format.

2. Reservoir type (Unidirectional): A reservoir system buccal patch has a chamber for both medicine and additives but not adhesives. To regulate the direction of medication distribution, decrease patch deformation and disintegration while in the mouth, and avoid drug loss, an impermeable backing is used.

Mechanism of buccal absorption:

A slow dispersion of non-isolated or individual species results in better buccal absorption of drugs. The concentration gradient plays a wide role in the regulation of the entire process through intertwined epithelium spaces. Transmission of non-ionic species throughout the buccal lipid membrane is the primary mode of transport. The buccal mucosa is said to be a lipoidal barrier to drug overdose, as it does in many other mucosal pores and where the drug molecule is lipophilic, it is where it is most easily absorbed. The dynamics of buccal drug absorption can be adequately explained by the first dose procedure. Dearden and Tomlinson (1971) have shown that saliva begins to change buccal absorption kinetics from drug solution by doing significant changes and alterations of the drug overload in the mouth. The correspondence between saliva and time is given as follows:

$$\mathbf{dm/dt = Kc/ViVt}$$

where, M - Mass of drug in the mouth at time t

K - Proportionality constant

C - Concentration of drug in the mouth at time

Vi - The volume of solution in the mouth cavity and

Vt - Salivary secretion rate.

Advantages of Buccal Films:

- Buccal delivery can be used to deliver drugs that are not able to tolerate the stomach's acidic environment.
- Passive diffusion is a method of drug absorption.
- Physical condition, shape, size, and surface flexibility.
- The absorption rate is increased.

- Action takes place quickly.
- If therapy must be stopped, the formulation can be withdrawn.
- The oral cavity's large contact surface aids in quick and thorough medication absorption.
- Because the extent of perfusion is greater, absorption is faster and more effective.
- Nausea and vomiting are reduced to a minimum.
- Stratum corneum is absent in mucosal surfaces, while they are present in TDDS. As a result, with transmucosal routes of administration, the primary barrier layer to transdermal drug transport is not a problem. As a result, transmucosal systems have a faster start and stop time than transdermal patches.

Disadvantages of buccal films:

- When compared to transdermal patches, transmucosal administration is less variable amongst patients, resulting in lower inter-subject variability.
- Smooth muscle and somewhat immobile mucosa are present, making it suited for the administration of retentive dose forms.
- Drugs or excipients present in the film may cause adverse effects by causing irritation to the mucosa hence must be determined first before processing.
- The thinner the film better is the dose accuracy than liquid formulations since each strip is produced to contain a specific amount of medicine, making it more stable, robust, and quick to dissolve.

Formulation Aspects of Buccal Films: -

- **Active pharmaceutical ingredient [APIs] -** Generally 5% w/w to 30% w/w of active pharmaceutical ingredients can be incorporated in the buccal film. Water-soluble APIs are present in the dissolved state in the buccal film or in the solid solution form. The water insoluble drugs are dispersed uniformly in the film. This involves the distribution of water insoluble molecules in water miscible polymer, or the solubility of the drug can be enhanced by complexation with various cyclodextrins. Depending upon the desired release profile, APIs can also be added as milled, micronized, or in the form of nanocrystals or particles. The use of micronized API will improve the texture of the film and also for better dissolution and

uniformity in the buccal film. The buccal films are more advantageous in certain clinical situations where instantaneous release of the medicaments is necessary for prompt relief. Some of such type of clinical situations includes cough, allergy, motion sickness, pain and other local oral manifestations.

- **Mucoadhesive polymers -** Polymers with different characteristics must be considered depending on the type of formulation. Different situations for buccal Muco-adhesion are possible depending on the dosage form. Mucoadhesive polymers are classified into two main groups, such as hydrophilic polymers and hydrogels. The hydrophilic polymers most used in buccal dry or partially hydrated dosage forms include polyvinyl alcohol [PVA], sodium carboxymethylcellulose [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.

Table. no.1

- **TYPES OF MUCOADHESIVE POLYMERS:**

TYPE	**EXAMPLE**
Natural	Tragacanth, Sodium alginate, Guar gum, Xanthan gum, Soluble starch, Gelatin, Lectins (naturally occurring proteins), Antigen K99-fimbriae, an attachment protein derived from E. coli
Synthetic	Polyacrylic acid (PAA), Polyvinyl alcohol (PVA), Hydroxypropyl methylcellulose (HPMC), Hydroxyethyl cellulose (HEC), Hydroxypropyl cellulose (HPC) and Sodium alginate, glyceryl monooleate (GMO), chitosan or deacetylatedgellan gum

- **Plasticizers-** Typically, the plasticizers are used in a concentration of 0-20% w/w of dry polymer. Plasticizer is an important ingredient of the film, which improves the flexibility of the film and reduces the bitterness of the film by reducing the glass transition temperature of

the film. The selection of plasticizer depends upon the compatibility with the polymer and type of solvent employed in the casting of film. Plasticizers should be carefully selected because improper use of the plasticizers affects the mechanical properties of the film. PEG 400, Propylene glycol, Glycerol, and castor oil is the most used plasticizers.

Table.no. 2

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

- **Penetration enhancers -** Penetration enhancers are also important excipients to be added in the buccal film formulation. These are required when a drug must reach the systemic circulation to exert its action. These must be non-irritant 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.

Table.no. 3

No.	Permeation enhancer
1	Aprotinin
2	Azone
3	Benzalkonium chloride
4	Cetylpyridinium chloride
5	Polysorbate 80
6	Sodium EDTA
7	Chitosan

- **Taste masking agents -** Taste masking agents or taste masking methods should be used in the formulation if the APIs have a bitter taste, as the bitter drugs makes the formulation unpalatable, especially for paediatric preparations. Thus, before incorporating the API in the

buccal film, the taste needs to be masked. Various methods can be used to improve the palatability of the formulation, such as complexation technology, salting out technology, etc.

- **Sweetening agents** - Sweeteners have become the important excipients for oral disintegrating drug delivery systems. The sweet taste in formulations is more important in case of paediatric population. Natural sweeteners, as well as artificial sweeteners, are used to improve the palatability of the mouth dissolving formulations. The natural sweeteners include sucrose, dextrose, fructose, glucose, liquid glucose and maltose. The sweetness of fructose is perceived rapidly in the mouth as compared to sucrose and dextrose. Artificial sweeteners should be used if the dosage form is meant for diabetic patients. Saccharin, cyclamate and aspartame are the first generation of artificial sweeteners, followed by acesulfame-K, sucralose, alitame and neotame, which come under the second-generation artificial sweeteners.

- **Saliva stimulating agent** - Generally, acids that are used in the preparation of food can be utilized as salivary stimulants. The purpose of using saliva stimulating agents is to increase the rate of production of saliva which would aid in the faster disintegration of the rapid dissolving film formulations. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are a few examples of salivary stimulants, citric acid being the most preferred among them. These agents are used alone or in combination between 2 to 6% w/w of the weight of the film.

- **Flavouring agents -** the flavouring agents are very important in case of oral dissolving systems. The acceptance of the oral disintegrating formulation by a patient depends on the initial flavour quality, which is observed in the first few seconds after the product has been consumed and the aftertaste of the formulation which lasts for at least about 10 min. Peppermint oil, cinnamon oil, spearmint oil, and oil of nutmeg are examples of flavour oils, while vanilla, cocoa, coffee, chocolate and citrus are fruity Flavors. Apple, raspberry, cherry, pineapple are a few examples of fruit essence type. Flavors can be used alone or in the combination. The amount of flavour needed to mask the taste depends on the flavour type and its strength. Preferably, up to 10% w/w Flavors are added in the buccal film formulations. To improve the flavour strength and enhance the mouth-feel effect of the product, cooling agents like monomethyl succinate can be added.

- **Colouring agents -** To improve the elegant appearance of films, colouring agents are incorporated in the formulation. FD&C-approved colouring agents are used.

Table.no. 4

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.

Manufacturing Methods: -

The buccal film manufacturing process includes the following techniques-

1. Solvent casting technique

2. Hot melt extrusion technique.

3. Direct Milling

4. Solid dispersion extrusion

5. Semisolid casting

❑ **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 a homogenous viscous solution.

- API and other excipients are dissolved in a suitable solvent to form a clear viscous solution.

- Both the solutions are mixed, and the resulting solution is cast as a film and allowed to dry.

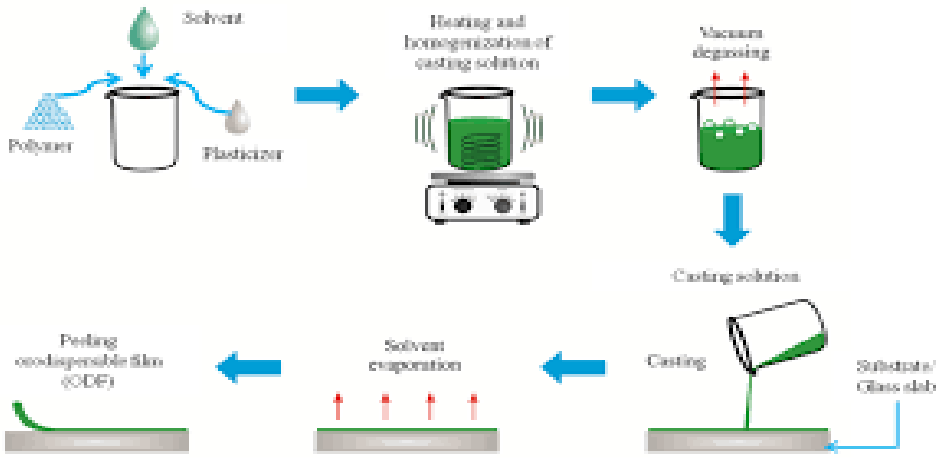

Fig.no 3

Advantages of solvent casting method: -

- Simple, reproducible, and established process
- Industrial solvent casting offers better control over film thickness & polymer concentrations.

Disadvantages of the solvent casting method: -

- Drug re-crystallisation after production
- Changes in film mechanical properties due to plasticising small molecules
- Difficult to achieve dose uniformity
- Potential for entrapped air bubbles
- Lack of control over film thickness and polymer concentration.

❑ **Hot melt extrusion technique: -**

A hot melt extruder is used in this process. This technique involves shaping a polymer into a film via the heating process. A blend of pharmaceutical ingredients including API in the dry state is filled in the hopper, conveyed, mixed and subjected to the heating process, and then extruded out in a molten state melted by the extruder. The molten mass thus formed is used to cast the film. A critical step is the casting and drying process. This technique has many advantages, such as this process involves lower temperature and shorter residence times of

the drug carrier mix, absence of organic solvents, continuous operation possibilities, minimum product wastage, good control of operating parameters and possibilities to scale up.

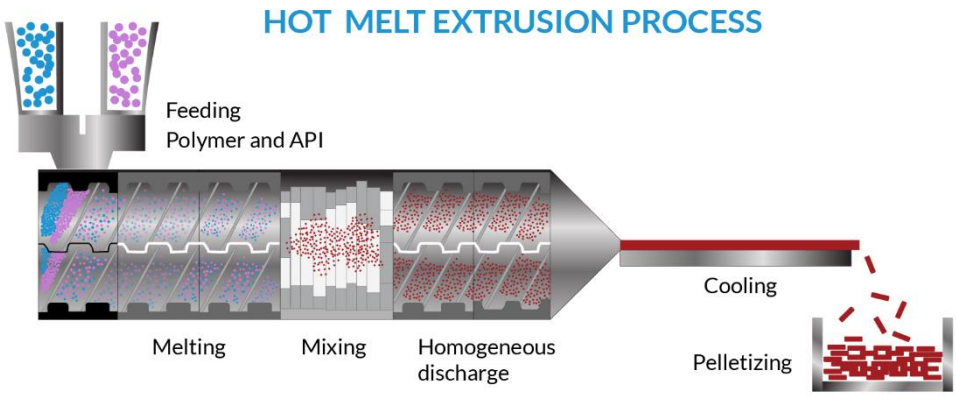

Fig.no. 4

Advantages of the hot melt extrusion method: -

- Solventless, continuous process, with fewer operations and better content uniformity than solvent casting
- Ability to incorporate poorly soluble drugs.

Disadvantages of hot melt extrusion method: -

- Drug re-crystallisation after production
- Swelling of the film after leaving the die
- Limited and specialist excipients required
- Agglomeration of ingredients
- Weight variations due to improper flow
- Problems with chemical stability.

❑ **Direct Milling: -**

Direct milling or kneading is used to mix the medicine and excipients in the absence of liquid. The resulting material is then rolled on a release liner until it reaches the desired thickness, as the thickness of the film plays a major role in proper administration and absorption. If the solvents are not present in this solution, it would not affect much to this

procedure. This procedure is frequently used because there is no risk of leftover solvent and no link between solvent and health problems.

❑ **Solid dispersion extrusion: -**

This process involves extruding immiscible components with the medication. Further based on the above process solid dispersions are prepared. Finally, dies are used to mould the solid dispersions into films.

❑ **Semisolid casting: -**

A solution of water-soluble film-forming polymer is created initially in the semisolid casting procedure to enhance faster absorption of the medication. The resultant solution is allowed to get mixed with an ammonium or sodium hydroxide solution of acid-insoluble polymer (cellulose acetate phthalate, cellulose acetate butyrate) for the formulation of buccal films. The appropriate amount of plasticizer is then added, resulting in a gel mass. Finally, heat-controlled drums are used to diffuse the gel mass and convert it into films or ribbons. The film is around 0.015-0.05 inches thick. The acid insoluble-producing polymer should be used in a 1:4 ratio.

❑ **Rolling Method: -**

A drug-containing solution or suspension is rolled on a carrier in the rolling method. Water and water-alcohol mixtures are the simplest solvents to be used in this method. The film is cut into suitable shapes and sizes after removing moisture by drying on rollers.

Evaluation of Buccal Films: -

The buccal films are evaluated by

- **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 a micrometre screw gauge at three different places, and the mean value is to be calculated.

- **Surface pH of films: -**

For determination of surface pH, three films of each formulation are allowed to swell for 2 h 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.

- **Swelling index: -**

After determination of the original film weight and diameter, the samples are allowed to swell on the surface of the 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] ×100,

Where Xt =The weight of the swollen film after time t, x

Xo =The initial film weight at zero time.

- **Folding endurance: -**

Three films of each formulation of the required size are cut by using sharp blade. Folding endurance is to be determined by repeatedly folding the film at the same place, till it is broken. The number of times, the film could be folded at the same place without breaking gives the value of folding endurance.

- **Moisture content: -**

The prepared films are to be weighed individually and kept in a desiccator containing calcium chloride at room temperature for 24 h. The films are to be weighed again after a specified interval until they show a constant weight. The per cent moisture content is to be calculated by using the following formula.

% Moisture content= [Initial weight–Final weight/Final weight] ×100

- **Moisture uptake: -**

Weighed films are kept in desiccators at room temperature for 24 h. These are then taken out and exposed to 84% relative humidity using a saturated solution of potassium chloride in desiccators until a constant weight is achieved. % moisture uptake is calculated as given below.

% Moisture uptake= [[Final weight–Initial weight/Initial weight] ×100

- **In-vitro residence time: -**

The in vitro residence time is determined using an IP disintegration apparatus using 900 mL of the disintegration medium maintained at 37 ± 2°C. The segments of rat intestinal mucosa, each of 3 cm length, are to be glued to the surface of a glass slab, which is then vertically attached to the apparatus. Three mucoadhesive films of each formulation are hydrated on one surface and the hydrated surface is brought into contact with the mucosal membrane. The glass slab is vertically fixed to the apparatus and allowed to move up and down. The film is completely immersed in the buffer solution at the lowest point and is out at the highest point. The time required for complete erosion or detachment of the film from the mucosal surface is to be recorded.

- **Drug content uniformity: -**

Three film units (each of 20 mm diameter) of each formulation have to be taken in separate 100 mL volumetric flasks, 100 mL of solvent has to be added and continuously stirred for 24 h. The solutions have to be filtered, diluted suitably and analysed at specified nm in UV spectrophotometer. The average of drug contents of the three films has to be taken as final reading.

- **Surface characterization studies: -**

The scanning electron photomicrograph of the film is taken at 6000 X magnification. The prepared film containing the drug is examined for a clear and colourless surface. The photomicrographs of the film with the drug and the blank film are compared and examined whether the drug is distributed uniformly throughout the film in an amorphous form.

- **In-vitro dissolution studies: -**

Dissolution studies are carried out for all the formulations, employing USP dissolution apparatus at 37 ± 0.5ºC, rotated at a constant speed of 50 rpm using 900 mL of dissolution medium. A sample of drug film is used in each test. An aliquot of the sample is periodically withdrawn at suitable time intervals and the volume is replaced with a fresh dissolution medium. The sample is analysed spectrophotometrically at specified nm.

- **Organoleptic evaluation: -**

The prepared buccal film should possess the desired features of sweetness and flavour, which is acceptable to a large mass 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.

- **Packaging: -**

Many options are available for buccal films packing, such as single pouch, blister card with multiple units, multiple-unit dispenser and continuous roller dispenser. Single packaging is mandatory for films. An aluminium pouch is the most used packaging system. There are some patented packaging systems for oral films. Labtec company has patented packaging technology called Rapid Card and Amcor Flexibilities Company has patented Core-peel technology.

- **Ex–vivo Permeation Studies: -**

The modified Franz diffusion cell is used for permeation studies. It consists of two compartments; one is donor compartment, and another is a receptor compartment of 18 mL capacity and having 0.785 cm2 effective diffusion area. The receptor compartment was covered with a water jacket to maintain 37°C.

The porcine or rabbit buccal mucosa can be used for these studies. The buccal mucosa is carefully separated from fat and muscles using a scalpel. The buccal epithelium is isolated from the underlying tissue. The buccal epithelium was used within 2 hrs upon removal. The separated buccal epithelium is mounted between two chambers and receptor chamber is filled with PBS pH 7.4. The buccal epithelium is allowed to stabilize for a period of 1 hr. After stabilization of the buccal epithelium, the film is kept on the buccal epithelium and periodically samples are withdrawn, and some fresh volume is replaced. The aliquots are analysed spectrophotometrically.

- **Flexibility in Formulation of Buccal Films: -**

There is wide range of flexibility in developing the buccal films. The main benefits of buccal film formulation include that many of the eligible Active pharmaceutical ingredients (APIs) can be formulated as buccal films and many of the physical properties can be altered, such as material composition, film dissolution rates and API absorption rates. The formulation of

buccal films includes film-forming polymers and other additives. Formulators can design the films to release the drug immediately in seconds as immediate drug release formulations, or to deliver the dose over a period of hours as controlled release formulations by modifying the combination of film-forming polymers and film thickness. The buccal mucosal area, as it has an expanse of smooth and relatively immobile surface, the area is well suited for placement of a retentive device and appears to be acceptable to the patient. The anatomical features of the buccal mucosa make it as an appropriate site for prolonged systemic delivery of drugs. The buccal mucosa permits not only the intimacy of contact and the possibility of improved drug absorption but also the ability to achieve an optimum residence time at the site of administration. Buccal film formulation is a more feasible drug delivery method even for the systemic delivery of orally inefficient drugs, and it as an attractive alternative for the delivery of protein and peptide drug molecules.

Buccal Film: Future Aspects: -

- Potent drugs that meet the parameters for buccal film as a drug delivery technology can be included in mucoadhesive buccal films.
- For drug release profile investigations, we can assess the dissolution of buccal film.
- In-vivo research can be enhanced for the preparation of buccal film.
- For the buccal film, we can do a stability study.

Applications: -

- Multilayer drug film construction is possible, which is 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.
- The films can be formulated in such a way that the dissolution rates of the drugs can range from minutes to hours.
- Films acts as gastroretentive dosage forms, in which the dissolution of the films could be triggered by the pH or enzyme secretions of the gastrointestinal tract and could be potentially used to treat gastrointestinal disorders.

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