Development And Evaluation of Mucoadhesive Buccal Film of Vildagliptin : A Comprehensive Review

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Among the available antidiabetic agents, Vildagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, is widely used for the management of Type 2 diabetes mellitus due to its ability to improve glycemic control by enhancing incretin hormone activity. However, conventional oral administration of Vildagliptin is associated with limitations such as first-pass metabolism, short half-life, and the need for frequent dosing. Mucoadhesive buccal films have emerged as a promising alternative drug delivery system capable of improving bioavailability, prolonging residence time, and enhancing patient compliance.

This review focuses on the development and evaluation of mucoadhesive buccal films of Vildagliptin. It discusses the anatomy and physiology of the buccal mucosa, theories and mechanisms of mucoadhesion, and the advantages of buccal drug delivery systems. Various formulation components including mucoadhesive polymers, plasticizers, penetration enhancers, sweetening agents, flavouring agents, and saliva stimulants are reviewed in detail. The article also highlights different manufacturing methods such as solvent casting, hot melt extrusion, direct milling, and semisolid casting techniques. Furthermore, important evaluation parameters

including film thickness, folding endurance, surface pH, swelling index, drug content uniformity, in-vitro dissolution, ex-vivo permeation, and mucoadhesive strength are summarized.

Overall, mucoadhesive buccal films of Vildagliptin represent a promising and patient-friendly approach for effective diabetes management with improved therapeutic efficacy and enhanced bioavailability.

Key words : Vildagliptin, Mucoadhesive buccal film, Buccal drug delivery system,Diabetes mellitus, Mucoadhesion.

INTRODUCTION

Diabetes mellitus is a long-term medical condition when the body is unable to regulate blood sugar levels. All ages, from young toddlers to the elderly, may be impacted. Type 1 and Type 2 diabetes are the two types of diabetes. Type 1, Type 2, and gestational diabetes are the three basic categories of diabetes. When the immune system kills the pancreatic cells that produce insulin, little or no insulin is produced, leading to type 1 diabetes. For the rest of their lives, these people will need to take insulin from outside sources. Type 1 is characterised by the autoimmune destruction of insulin-producing cells in both children and adults. The most prevalent kind, type 2 diabetes, arises when the body develops resistance to the effects of insulin and eventually the pancreas is unable to produce enough to meet the body's demands. Although genetics also plays a significant part, lifestyle factors like being overweight, eating poorly, and not exercising are strongly associated with it. Adults over 40 are more likely to experience it. When insulin resistance increases due to hormonal changes during pregnancy, gestational diabetes develops. It raises the chance of getting Type 2 diabetes later in life, even though it usually goes away after delivery.[1,2]

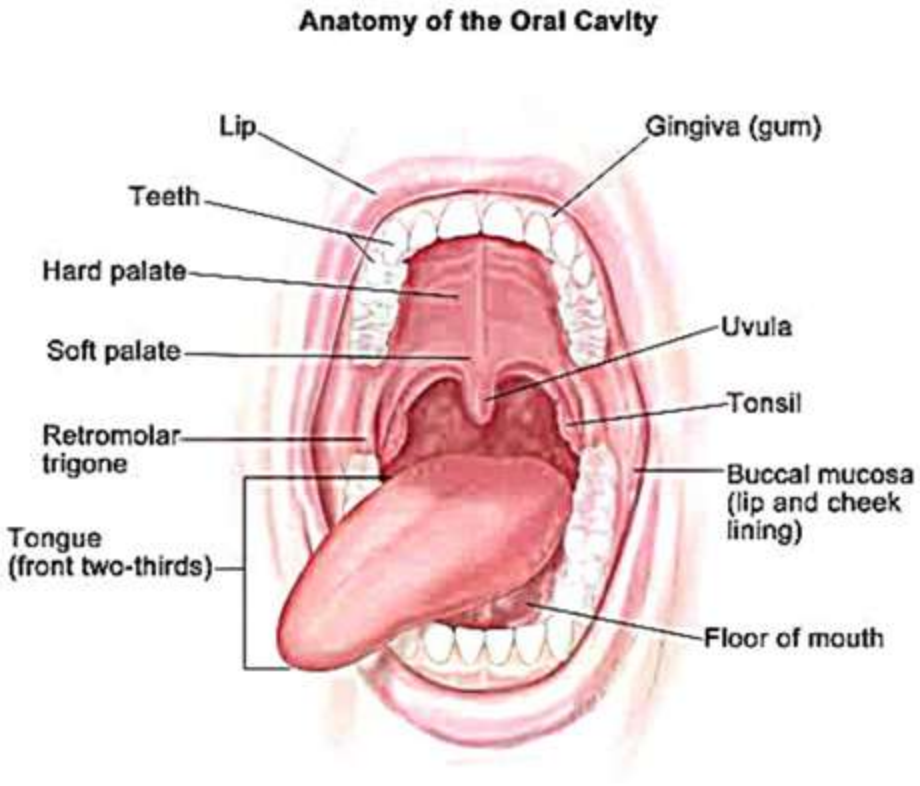
Increased thirst, frequent urination, exhaustion, blurred eyesight, and unexplained weight loss are typical signs of diabetes. A family history of diabetes, being overweight, not exercising, and aging are risk factors for the disease. The World Health Organization estimates that 830 million people worldwide had diabetes by 2022, up from about 200 million in 1990. According to projections, 1.3 billion people worldwide may have diabetes by 2050.[3,4]

In addition to being more prevalent, diabetes has a significant negative impact on society and the economy worldwide. It impacts people's daily lives and increases the cost of medical care. Strong public health plans and coordinated care are necessary because this life-threatening condition also affects families and the healthcare system. This entails educating people about diabetes at an early age, lowering the cost of treatment, and ensuring that various healthcare professionals collaborate to manage and prevent diabetes problems.[3,4]

Effective diabetes management depends on glycemic control. It lowers the chance of consequences like renal difficulties, heart disease, nerve damage, and visual problems. In addition to enhancing quality of life, keeping blood glucose levels within a specific range prevents long-term health problems.[5]

Buccal mucosa route for systemic drug delivery

Concept of oral mucosa



The inner lining of the cheeks is home to the buccal mucosa, a specialized area of the mucous membrane of the oral cavity. It covers the buccal surface and covers an area of around 200 cm^2. It is an essential component of the oral endometrial tissue. This tissue is made up of 40–50 cell layers, the majority of which are stratified squamous epithelial cells that are non-keratinized and serve both absorption and defense.[6,7,8]

The moist, pink mucosal tissue that lines the inside walls of the cheeks in the mouth cavity is known as buccal mucosa, or oral mucosa. Its primary function, especially in mucoadhesive buccal films, is to function as a barrier while permitting selective permeability for the absorption of particular medications. For regular oral

mechanics including mastication, speaking, and swallowing, the tissue steadily maintains hydration, resilience, and flexibility. In addition to having a rich capillary network for drug delivery and nutrient exchange, the cells in this area actively support barrier qualities.[6,7,8]

Anatomical site of oral mucosa

The buccal mucosa extends from the inner aspect of the lips towards the sidewall of the cheeks up to the point where the upper and lower teeth meet. It is anatomically located between the labial mucosa, which lines the lips, and the palatal mucosa, which covers the palate. It covers the region next to the molars and premolars and borders the gingival mucosa and the alveolar ridge. In addition to the cheeks, related areas include the palatal surface (the roof of the mouth) and the sublingual mucosa (behind the tongue), which are identified in schematics for localization and use in delivery studies.The buccal mucosa is roughly 500–800 μm thick, the palatal mucosa is roughly 100–200 μm thick, and the sublingual/tongue ventral surface is likewise relatively thin. These variations have an impact on medication absorption rates, permeability, and the therapeutic utility of targeted treatments. The buccal mucosa is a popular site for research in pharmaceutical formulations, such as buccal films and patches, since it balances penetrability and protective qualities, making it ideal for non-invasive drug administration.[6,7,8]

THEORIES OF MUCOADHESION :

There are five different theories, which explain phenomenon of mucoadhesion :

1. Wetting Theory

This theory states that mucoadhesion occurs when the polymer spreads easily over the mucosal surface. The better the wetting ability and surface contact, the stronger the adhesion. Hydrophilic polymers with good swelling ability support this mechanism.[9]

2. Electronic Theory

According to this theory, mucoadhesion results from electrical charge differences between the mucus surface and the polymer. When opposite charges meet, attractive electrostatic forces form, leading to adhesion.[10]

3. Diffusion Theory

This theory proposes that mucoadhesion happens when polymer chains penetrate into the mucus network and interdiffuse with mucin molecules. The deeper the polymer chain penetration, the stronger the bond. This requires enough contact time and polymer flexibility.[11]

4. Adsorption Theory

Adsorption theory suggests that mucoadhesion occurs due to primary and secondary chemical bonds, such as hydrogen bonds, van der Waals forces, and hydrophobic interactions. Although these bonds are individually weak, collectively they contribute to strong mucoadhesion.[11]

5. Mechanical Interlocking Theory

In this theory, adhesion takes place when polymer chains fill the irregularities and pores of the mucosal surface. The polymer becomes trapped within the surface structure, creating a mechanical lock.[12]

6. Fracture Theory

This theory describes the force required to separate a mucoadhesive system from the mucosa. Stronger adhesion means greater force is needed to break contact between polymer and mucus.[12,13]

MECHANISM OF MUCOADHESION :

Mucoadhesion is the process by which a drug delivery system attaches to the mucus layer or epithelial surface of the oral cavity. This phenomenon allows a formulation such as a buccal film to remain at the site of application for an extended period, improving drug absorption and prolonging therapeutic action.[14]

The mechanism of mucoadhesion generally takes place in two main stages:

1. Stage -1 Contact (Wetting) Stage

In this initial phase, the mucoadhesive polymer comes in contact with the mucus layer on the oral mucosa. Saliva hydrates the polymer, causing it to swell and spread over the mucosal surface. Good wetting and spreading allow the polymer chains to enter mucus pores and start interacting with the mucosal tissues.[15]

2. Stage -2 Consolidation (Adhesion) Stage

In the second stage, polymer chains interlock with mucus glycoproteins through chemical and physical interactions. This results in strong adhesion between the formulation and the mucosal surface.[16]

The adhesion keeps the dosage form at the site long enough for the drug to diffuse through tissues into the systemic circulation. This stage can be explained by two mechanisms:

a) Diffusion Theory

Hydrated polymer chains penetrate into the mucus layer while mucin molecules diffuse into the polymer. The chains interlock and entangle, forming a strong adhesive interface. Greater interpenetration results in stronger mucoadhesion.[17]

b) Dehydration Theory

The polymer absorbs water from mucus, causing it to swell while the mucus becomes more concentrated. This water movement reduces the distance between polymer and mucosa, increasing contact and promoting bonding. Swelling also improves chain mobility, enhancing adhesion strength.[18]

DRUG PROFILE

Vildagliptin is an orally anti-hyperglycemic agent used for the treat non-insulin dependent diabetes mellitus (NIDDM). It improves glycemic control by enhancing incretin hormone activity and is considered a promising candidate for novel drug delivery systems such as mucoadhesive buccal films due to its pharmacokinetic limitations.[19]

Table no. 1

Parameter	**Description**
Drug Name	Vildagliptin
Therapeutic Class	Dipeptidyl Peptidase-4 (DPP-4) inhibitor
Indication	Type 2 Diabetes Mellitus
Molecular Formula	$C_{17}H_{25}N_3O_2$
Molecular Weight	303.4 g/mol
Chemical Structure	Adamantane derivative with nitrile functional group
Solubility	Freely soluble in water
pKa	~9.4

BCS Classification	Class III (High solubility, low permeability)
Mechanism of Action	Inhibits DPP-4 enzyme, increases GLP-1 and GIP levels, enhances insulin secretion
Absorption	Rapid and extensive
Bioavailability	~85%
Tmax	1–2 hours
Half-life (t½)	2–3 hours
Metabolism	Limited hepatic metabolism (non-CYP mediated)
Excretion	Primarily renal (~85%)
Dose	50 mg once or twice daily

Formulation Aspects of Buccal Films: -

1. 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.[20]

2. 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.[20]

Table. no.2

• TYPES OF MUCOADHESIVE POLYMERS:

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

3. 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.[21]

Table.no. 3

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

4. 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.[20,21]

Table.no. 4

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

5. 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.[22]

6. 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.[23]

7. 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.[24]

8. Flavouring agents - 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.[23,24,25]

9. 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. 5

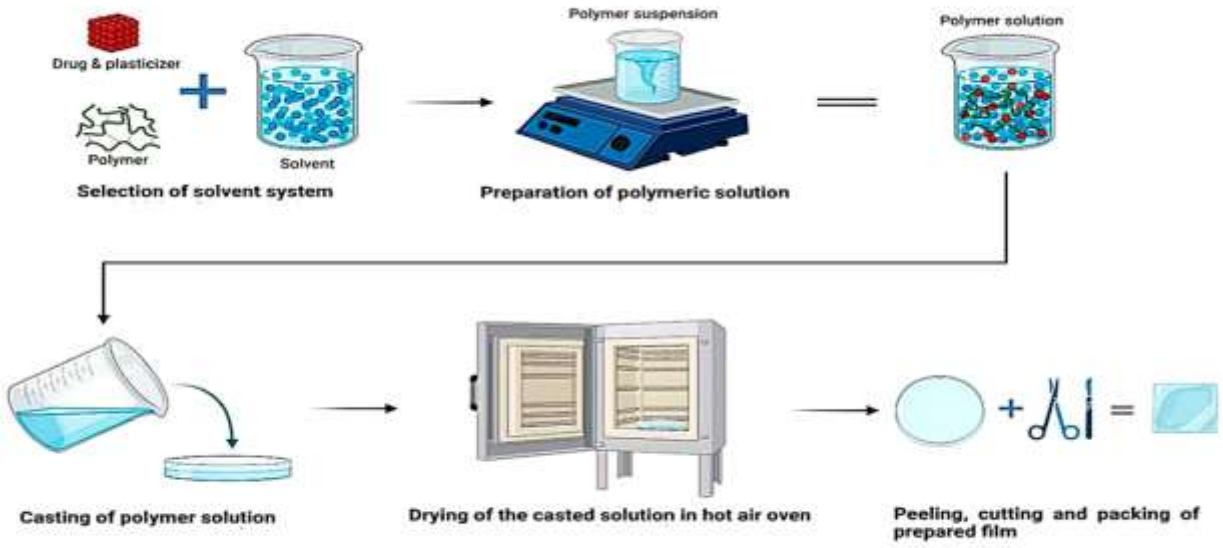
Sr. No	Ingredients	Quantity
1.	API	5- 30 % (w/w)
2.	Mucoadhesive Polymer	45 % (w/w)
3.	Plasticizer	0- 20 % (w/w)
4.	Sweetening agents	3-6 % (w/w)
5.	Saliva stimulating agents	2-6 % (w/w)
6.	Colors and Flavours	Q.S

Manufacturing Methods of Buccal Film: -

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:

• **Preparation of Polymer Solution :** Mucoadhesive polymer (e.g., HPMC, chitosan) is dissolved in a suitable solvent such as water or hydroalcoholic mixture.

• **Addition of Plasticizer :** Plasticizer (e.g., glycerol, PEG 400) is added to improve flexibility and stirred to obtain a uniform solution.

• **Drug Incorporation :** Drug is dissolved or dispersed in the polymer solution with continuous stirring.

• **Addition of Other Excipients :** Permeation enhancers, sweeteners, or flavoring agents are added if required.

• **Casting of Solution :** The prepared solution is poured onto a flat, leveled surface such as a glass plate or petri dish.

• **Drying :** The casted solution is dried at controlled temperature (e.g., 40–50°C) to evaporate the solvent.

• **Film Removal and Cutting :** The dried film is carefully peeled and cut into desired size and shape.[25]

Advantages of solvent casting method: -

• Simple, reproducible, and established process

• Industrial solvent casting offers better control over film thickness & polymer concentrations.[25]

Disadvantages of the solvent casting method: -

• Drug re-crystallisation after production

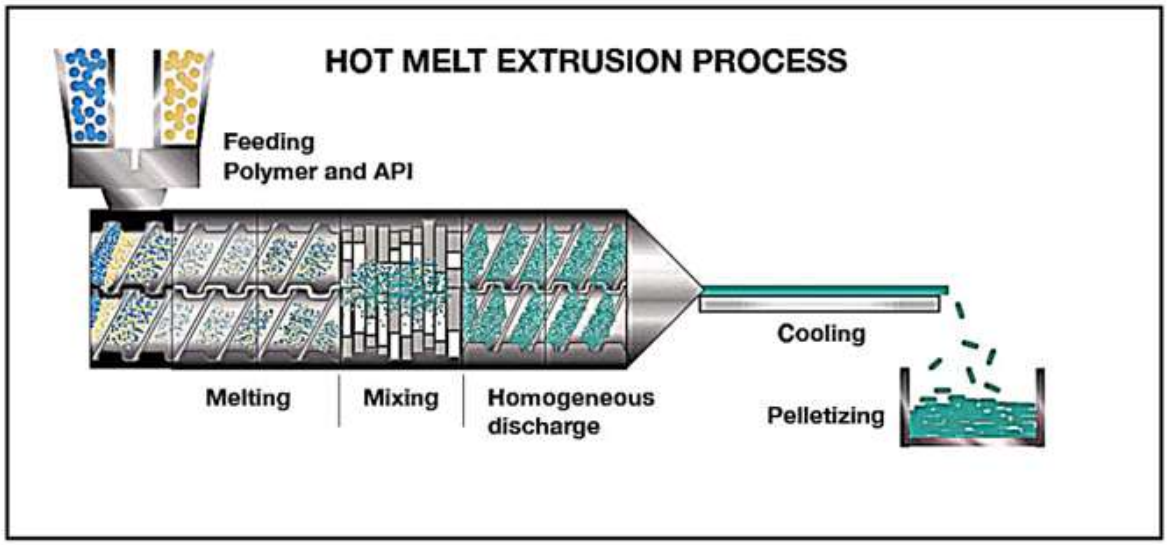
• Changes in film mechanical properties due to plasticising small molecules

• Difficult to achieve dose uniformity

• Potential for entrapped air bubbles

• Lack of control over film thickness and polymer concentration.[23]

❑**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.[26]

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.[26]

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.[25]

❑**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.[22,26]

❑**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.[26]

❑**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, heatcontrolled 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.[27]

❑**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.[26,27]

EVALUATION OF BUCCAL FILM : -

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.[27]

• 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.[28]

• 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.[28]

• 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.[29]

% 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.[29]

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

• 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: [30]

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.

• 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.[31]

• 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.[32]

• 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.[33]

• 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.[34]

• **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.[35]

• **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.[36]

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