A Review on Formulation and Evaluation of Buccal Patches

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***Abstract*—Drugs that are administered via the buccal mucosa directly go into the systemic circulation, thereby avoiding hepatic first-pass metabolism. As a result, this administration route is useful for improving the bioavailability of drugs that are subject to a broad first-pass effect when delivered orally. For the oral mucosal route of drug administration, different types of dosage forms can be formed. A sublingual tablet can afford rapid drug absorption and an exact pharmacological effect; however, the duration of delivery is short owing to the inevitable loss of a large proportion of the administered dose due to swallowing. To keep away from such losses, a patch can be formulated that is placed on the buccal mucosa of the oral cavity. But this approach is limited by the thicker dimensions of the buccal membrane compared to the others that line the oral cavity and constraints impelled by the delivery system itself (the amount of drug reaching the systemic circulation is limited by the area of the mucosa that the patch covers, which, for patient comfort reasons, is relatively small). A direct estimate of the systemic circulation through the internal jugular vein bypasses drugs from the hepatic first-pass metabolism showing high bioavailability.**

***Index Terms*—buccal mucosa, hepatic first-pass metabolism, patch covers.**

I. INTRODUCTION

Amongst the various routes of drug delivery, oral route is the most preferred to the patient and the clinicians. Based on our present understandings of biochemical and physiological aspects of absorption and metabolism, many drugs cannot be delivered successfully through the conventional oral route because, after administration, the drugs are subjected to extensive pre-systemic clearance, which often leads to a lack of significant membrane permeability, absorption and bioavailability [1].

On the opposite of per oral route, mucosal layer (nasal, rectal, vaginal, ocular and oral cavity) is often considered as promising sites for drug administration and having distinct advantages for systemic drug delivery. These advantages include the hepatic bypass effect and the avoidance of pre-systemic elimination within the GI tract with improved absorption and hence better bioavailability [2]. The nasal cavity has been studied as a site for systemic drug delivery, but the future irritation and the irreversible damage to the ciliary action of the nasal cavity from chronic application of nasal dosage could significantly affect drug absorption from this site [3].

The buccal route has the capacity to maintain a delivery system at a particular position for an extended period of time; therefore, it acts as a great application for both local as well as systemic drug bioavailability. The buccal mucosa is relatively permeable with a rich blood supply, and absorption is efficient; additionally, the route also provides rapid drug transport to the systemic circulation and avoids degradation by gastro-intestinal enzymes and first-pass hepatic metabolism [4].

II. ANATOMY AND PHYSIOLOGICAL FEATURES OF ORAL CAVITY

The oral cavity is the area of the mouth characterized by the lips, cheeks, hard palate, soft palate, and floor of the mouth. The oral cavity consists of two regions:

- Outer oral vestibule, which is enclosed by cheeks, lips, teeth, and gingival (gums).
- Oral cavity proper, which extends from teeth and gums back to the fauces (which lead to the pharynx), with the roof forming the hard and soft palate.

The tongue projects from the floor of the oral cavity.

The protective buccal epithelial membrane is separated into two types:

1. *Keratinized Mucosa*: Which covers the hard palate, gingiva, and dorsal surface of the tongue in the oral cavity.

2. *Flexible Keratinized Mucosa*: Which lines the soft palate, ventral surface of the tongue, sublingual mucosa, floor of the oral cavity, inner lips, buccal pouch [5].

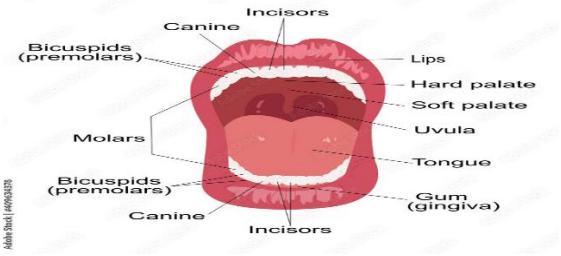

Figure No.1: Structure of Oral Cavity.

III. IDEAL PROPERTIES OF BUCCAL PATCHES

Buccal patches are a fascinating drug delivery system with several ideal properties that make them effective and convenient. Here are some key properties:

- It has the ability to adhere to the buccal mucosa for an extended period, ensuring prolonged drug release [6].
- The buccal patches should be flexible to conform to the contours of the buccal cavity.
- Buccal patches bypass the first-pass metabolism in the liver, leading to higher bioavailability of the drug.
- It is easy to use and simple to apply and remove, making them user-friendly, especially for patients who have difficulty swallowing pills.
- They should be comfortable to wear without causing irritation or pain.
- They should provide a controlled and sustained release of the drug.
- The patches should be stable under various conditions, including temperature and humidity [7].
- The incorporation of permeation enhancers to improve drug absorption through the buccal mucosa.

These properties help buccal patches deliver medication effectively and improve patient compliance [8].

IV. ADVANTAGES

- It bypasses the hepatic portal system and increases bioavailability of orally administered drugs.
- It provides sustained drug delivery.
- It increases ease of drug administration.
- It improves patient compliance by avoiding pain that occurs due to injections and can be given to unconscious patients.
- Rapid onset action.
- Chewing or Swallowing is not necessary [9].

V. FACTORS AFFECTING BUCCAL ABSORPTION

The oral cavity is a complex environment for drug delivery, as there are many factors that reduce the absorbable concentration at the site of absorption. Some of those are:

1. Membrane Factor
2. Environmental factors.

1. Membrane Factor:

This includes degree of keratinization, surface area available for absorption, mucus layer of salivary pellicle, intercellular lipids of epithelium, basement membrane, and lamina propria. As well, the absorptive membrane thickness, blood supply/lymph drainage, cell renewal, and enzyme content will all contribute to reducing the rate and amount of drug entering the systemic circulation [10].

2. Environmental factors:

a. Saliva: The thin film of saliva coats during the liner of buccal mucosa and is known as salivary pellicle or film. The thickness of salivary film is 0.07 to 0.10 mm. The composition and movement of this film affect the rate of buccal absorption.

b. Salivary glands: The minor salivary glands are located in the deep epithelial region of the buccal mucosa. They frequently secrete mucus on the surface of the buccal mucosa. Although mucus helps to keep mucoadhesive dosage forms, it is a potential barrier to drug penetration.

c. Movement of buccal tissues: Buccal region of oral cavity shows fewer active movements. The mucoadhesive polymers are to be combined to keep dosage form in the buccal region for long periods to withstand tissue movements during talking and, if possible, during eating food or swallowing [11].

Some other factors affecting buccal absorption are:

d. Physiochemical properties of drug:

- *Lipophilicity*:

1.Moderate lipophilicity (Log P = 1–3) is ideal for buccal absorption.

2. Highly lipophilic drugs (Log P > 3) poorly dissolve

in saliva, reducing absorption. 3. Highly hydrophilic drugs (Log P < 1) struggle to penetrate the lipophilic buccal membrane.

- *Molecular size:* Smaller molecules (MW < 500 Da) penetrate the buccal mucosa easily, whereas the larger molecules (MW > 500 Da) have reduced permeability and require enhancers.
- *Ionization:* Unionized (lipophilic) drugs penetrate the buccal mucosa easily via passive diffusion, and ionized (hydrophilic) drugs dissolve well in saliva but have poor permeability across the membrane.
- *Solubility:* Balanced solubility (moderate aqueous & lipid solubility) is ideal for buccal absorption. But drugs with high aqueous solubility dissolve in saliva but may struggle to cross the membrane; drugs with high lipid solubility will penetrate the membrane but may have poor dissolution in saliva.
- Ideal log P for buccal absorption: 1–3 (moderate lipophilicity).

e. Enzymatic Activity: Enzymes in saliva or buccal mucosa can metabolize the drug and reduce adsorption.
f. Buccal Mucosa Health: Inflammations, ulcers, and other pathogens affect buccal absorption.
g. Presence of Permeation Enhancers: Permeation enhancers increase drug absorption through the buccal mucosa by modifying membrane properties, loosening tight junctions, or increasing drug solubility.
h. formulation factors:

- pH: The buccal cavity pH (5.5–7.5) affects drug solubility and ionization, influencing absorption. Weakly basic drugs (pKa 6–8) remain mostly unionized, enhancing permeability, while weakly acidic drugs (pKa 3–5) show moderate absorption. Highly ionized drugs have poor permeability and may require enhancers.
- Viscosity: Higher viscosity in buccal formulations (gels, patches) enhances drug retention and prolongs absorption; too high viscosity may slow drug release, reducing absorption.
- Presence of Excipients: Excipients play a crucial role in buccal drug delivery by improving drug solubility, stability, permeability, and retention in the oral cavity.

VI. DESIGN OF BUCCAL PATCHES

Generally, different designs, based on the desired properties, are reviewed for the preparation of the buccal patch. Following Fig. 2 shows several films of mucoadhesive drug delivery with various designs and features of drug delivery.

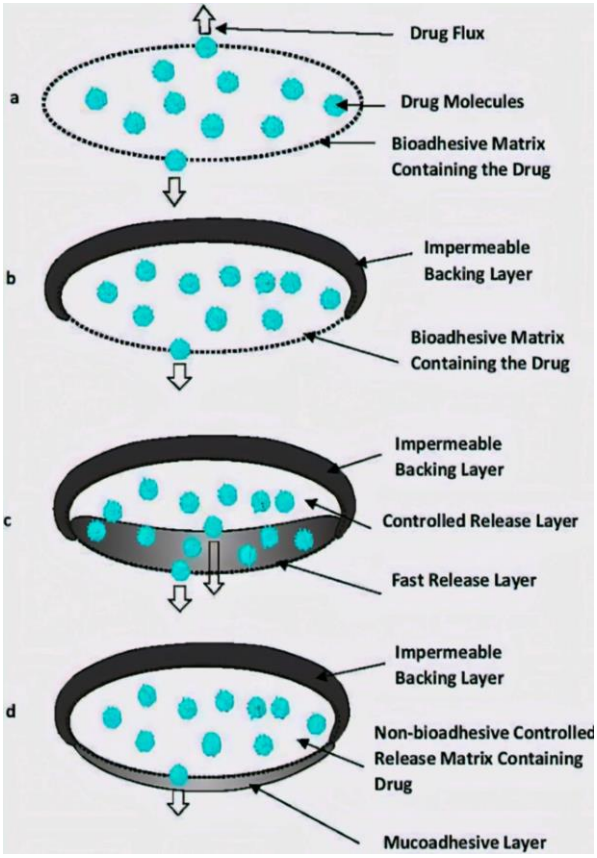

Figure No. 2: Oral Mucoadhesive Patches design.

Types included:
A. Matrix Type
B. Reservoir Type
A. Matrix Type
Drugs and other additives are dissolved uniformly in a hydrophilic or lipophilic polymer matrix in these systems, and their release properties are affected by the penetration of the polymer network. Bi-directional patches release drugs in both the mucosa and mouth sites. So, the most significant negative effects of a bidirectional design are partial absorption and lower drug bioavailability.

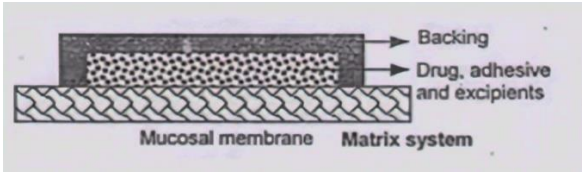

Figure No. 3: Buccal Patch designed for Matrix drug Release

B. Reservoir Type:

The oral patches built as the reservoir or membrane structure, a film or sheet of polymer-containing drugs and additives as well as an impermeable backing layer are used to control the release rate of the drug and to prevent patch deformation and degradation of the drug This style of design is usually used for both local and systemic drug releases [12].

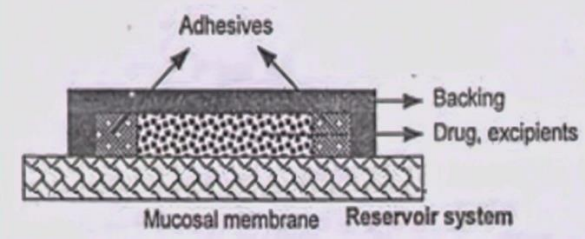

Figure No. 4: Buccal Patch designed for Reservoir type of drug Release

VII. COMPONENTS FOR BUCCAL PATCH PREPARATION

Buccal patches are innovative drug delivery systems designed to administer medication through the mucosal lining of the cheek. This method allows for direct absorption into the bloodstream, providing a quick onset of action and bypassing the digestive system, which can degrade or reduce the effectiveness of certain medications. Those are:

A. Active Pharmaceutical Ingredient
B. Polymers
C. Penetration Enhancers
D. Plasticizers
E. Solvents
F. Backing Layer

A. Active pharmaceutical ingredients: The buccal film technology is possible for delivery of a variety of APIs. Still, the size of the dosage form has limitations; high-dose molecules are difficult to build in buccal film. Generally, 5% w/w to 30% w/w of active pharmaceutical ingredients can be incorporated in the buccal patches [13].

The selection of a suitable drug for the design of a buccal mucoadhesive drug delivery system should be based on the following features [14]:

The conventional single dose of the drug must` be low. The drugs having a biological half-life between 2-8 hours are good candidates for controlled drug delivery. The drug should mask the bad taste and be free from irritancy, allergy and discoloration or erosion of teeth

Drugs Delivered via Buccal Route: Acyclovir, Buprenorphine, Carbamazepine, Nicotine, Nifedipine, Nimodipine [15].

B. Polymer:Polymer hydration and swelling properties likely play the main role. The polymer hydration and, as a result, the mucus dehydration could cause an increase in mucous cohesive properties that promote muco-adhesion. Swelling should favor polymer chain flexibility and inter-penetration between polymer and mucin chains. So, depending on the type of formulation, polymers with different characteristics have to be observed [16].

Characteristics of Ideal Mucoadhesive Polymers: An ideal polymer for a mucoadhesive drug delivery system should have the following details:

- The polymer and its degradation products should be non-toxic and non-absorbable from the GIT.
- It must be non-irritant to the mucus membrane.
- It should ideally form a strong non-covalent bond with the mucin epithelial cell surfaces. It should stick quickly to moist tissue surfaces.
- It should allow easy incorporation of the drug and offer no barrier to its release.
- The polymer must not degrade on storage or during the shelf life of the dosage form.
- The polymer must be easily available in the market and economical [17, 18].

Table No. 1: Mucoadhesive Polymers for Buccal Patches

S. No	CRITERIA	CATEGORY	EXAMPLES
1.	Source	Semi-Natural/Natural Synthetic	Agarose, Chitosan, Gelatine, Hyaluronic acid, Various gums (guar, hakea, xanthan, gellan, carrageenan, pectin and sodium alginate) *Cellulose derivatives* Carboxy Methyl Cellulose (CMC), Thiolated CMC, Sodium CMC, Hydroxy ethyl cellulose (HEC), Hydroxy propyl

			cellulose (HPC), Hydroxy propyl methyl cellulose (HPMC), Methyl Cellulose, and Methyl hydroxyl ethyl cellulose. *Poly (acrylic acid)-based polymers* Poly(methylvinylether-co-methacrylic acid), Poly(2-hydroxyethylmethacrylate), Poly (alkyl cyanoacrylate), Poly(isohexylcyanoacrylate),Poly (isobutylcyanoacrylate), Copolymer of acrylic acid and PEG *Others* Poly (N- 2-hydroxypropylmethacrylamide), Polyxyethylene, Poly vinyl Alcohol (PVA), and Thiolated polymers
2.	Aqueous Solubility	Water soluble Water-insoluble	HEC, HPC (water < 38ºC), HPMC (cold water), polyacrylic acid (PAA), sodium CMC, Sodium alginate, chitosan (soluble in dilute aqueous acids), Ethyl cellulose.
3.	Charge	Cationic Anionic Nonionic	Aminodextran, chitosan, dimethylaminoethyl-dextran, trimethylated chitosan. Chitosan-EDTA, CMC, pectin, PAA, sodium alginate, sodium CMC, xanthan gum
			Hydroxyethyl starch, Hydroxy propyl cellulose, poly (ethylene oxide), PVA, scleroglucan
4.	Potential Bio-adhesive Forces	Covalent Hydrogen Bonding Electrostatic interaction	Cyanoacrylate Acrylates [hydroxylated methacrylate, Poly (methacrylic acid)], PVA Chitosan

C. Penetration Enhancers Substances that make possible the permeation through bucal mucosa is called permeation enhancers. Among the major disadvantages associated with buccal drug delivery is the low flux of drugs across the mucosal epithelium, which results in low drug bioavailability. Several compounds have been looked over for their use as buccal penetration and absorption enhancers to increase the flux of drugs through the mucosa [19].

Mechanisms of Action of Permeation Enhancers:

Mechanisms by which penetration enhancers are to improve mucosal absorption are as follows:

- *Changing mucus rheology:* Mucus forms a viscoelastic layer of varying thickness that affects drug absorption. Additionally, saliva covering the mucus layers also inhibits the absorption. Some permeation enhancers' act by reducing the viscosity of the mucus, and saliva controls this barrier [20].
- *Increasing the fluidity of the lipid bilayer membrane:* The most common mechanism of drug absorption through buccal mucosa is the intracellular route.
- *Acting on the components at tight junctions:* Some enhancers act on desmosomes, a crucial component at the tight junctions, thereby increasing drug absorption.
- *By overcoming the enzymatic barrier:* These act by inhibiting the various peptidases and proteases present within buccal mucosa, in that way overcoming the enzymatic barrier. In addition, changes in membrane fluidity also alter the enzymatic activity indirectly.
- *Increasing the thermodynamic activity of drugs:* Some enhancers increase the solubility of drugs by

changing the partition coefficient. This shows increased thermodynamic activity resulting in better absorption [21, 22].

Table No. 2: Example of Permeation Enhancers

CATEGORY	EXAMPLES
Surfactants	Ionic Sodium lauryl sulfate, Sodium laurate, Polyoxyethylene-20-cetyl ether, Laureth-9, Sodium dodecyl sulfate (SDS) Non-ionic Polyoxyethylene-9-lauryl ether, Tween 80, Nonylphenoxypolyoxyethylene, Polysorbates, Sodium glycolate
Bile Salts and Derivatives	Sodium deoxycholate, Sodium taurocholate, Sodium taurodihydrofusidate, Sodium glycodihydrofusidate, Sodium glycocholate, Sodium deoxycholate.
Fatty acids and derivatives	Oleic acid, Caprylic acid, Mono(di)glycerides, Lauric acid, Linoleic acid, Acylcholines, Acylcarnitine, Sodium caprate.
Chelating Agents	EDTA, Citric acid, Salicylates
Sulfoxides	Dimethyl sulfoxide (DMSO), Decylmethyl sulfoxide
Polyols	Propylene glycol, Polyethylene glycol, Glycerol, Propanediol
Monohydric Alcohols	Ethanol, Isopropanol.
Others	Urea and derivatives, Unsaturated cyclic urea, Azone (1-dodecylazacycloheptan-2-one), Cyclodextrin, Enamine derivatives, Terpenes, Liposomes, Acyl carnitines and cholines.

D. Plasticizers: These are the materials used to attain the softness and flexibility of thin films of polymers or blends of polymers. Examples of some plasticizers used are glycerol, propylene glycol, PEG 200, PEG 400, castor oil, etc. These plasticizers help in the release of the drug substance from the polymer base as well as acting as penetration enhancers. The preference of the plasticizer depends upon the potential of the plasticizer material to solvate the polymer and alters the polymer-polymer interactions. When used in accurate proportion to the polymer, these materials impart flexibility by relieving the molecular rigidity [23].

E. Solvents: Buccal patches often use solvents in their formulation process to dissolve the active pharmaceutical ingredients and polymers. Common solvents include:

Water is often used as a primary solvent due to its safety and compatibility with many polymers. And ethanol is frequently used for its ability to dissolve a wide range of substances and its rapid evaporation rate. When it comes to propylene glycol, it acts as both a solvent and a plasticizer, enhancing the flexibility and adhesiveness of the patch.

These solvents help in creating a uniform and effective buccal patch.

F. Backing Layer: The backing membrane plays a vital role in the attachment of bioadhesive devices to the mucus membrane. The materials utilized in the backing membrane must be inert and impermeable to the drug and penetration enhancer.

The commonly used materials in backing membranes include carbopol, magnesium separate, HPMC, HPC, CMC, polycarbophil etc. [24].

Other additives like:

G. Sweetening agents: Sucralose, aspartame, mannitol, etc.

H. Flavouring agents: menthol, vanillin, clove oil, peppermint oil, cinnamon oil, spearmint oil, and the oil of nutmeg are examples of flavor oils, while vanilla, cocoa, coffee, chocolate, etc. These are added to mask the taste. Mostly used for medication for children.

VIII. METHOD OF PREPARATION OF BUCCAL PATCH

There are various methods for the preparation of mucoadhesive buccal patches branched mainly as traditional and novel methods; traditional includes solvent casting, direct milling, hot-melt extrusion, solid dispersion extrusion, semisolid casting, and rolling process. While solvent casting is considered the most approved method of preparation among others due to its simplicity and cost effectiveness. Recently, electrospinning, electrospraying, and 3D printing methods have been used as novel techniques for the preparation of buccal patches. These methods are more

systemic and do not have the problems related to the solvent casting [25].

1. Solvent Casting Method.
2. Direct Milling Method.
3. Hot Melt Extrusion Method.
4. Semi-solid Casting Method.
5. Rolling Method.
6. Electron Spinning Method and Electron Spraying Method.

1. Solvent Casting Method: In the method of solvent casting, a mucoadhesive polymer, drug, and other excipients are dissolved under the magnet stirrer in enough solvent to extract trapped air and form a homogeneous solution. The blend is then cast into a clean petri dish and dried in a hot air oven at 4000C [26]. Cast patches are set in a desiccator before future evaluation continues. There are a lot of research studies on mucoadhesive patches fabricated by the method of solvent casting. Dubey et. al used solvent casting technique to make mucoadhesive oral patches of hydrochlorothiazide (HCZ) and atenolol (ATN) using different concentrations of sodium alginate, hydroxyl propyl methyl cellulose, Carbopol 934P, sodium carboxy methyl cellulose polymer and polyvinyl alcohol as a backing layer to achieve sustained release and enhanced bioavailability 15 besides having short and simple method, it has some limitations, such as

• Polymers need to be dissolved in a volatile solvent. In addition, a few amounts of solvent may remain in the final film.
• Drug loading capacity in solvent-cast films is low.
• The combined film does not have an appropriate uniformity [27].

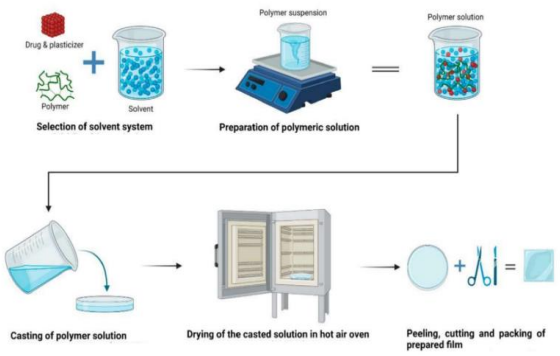

Figure No.5: Schematic representations of Solvent casting method.

2. Direct milling method: Patches formed in this method without the use of solvents. Without the presence of any liquefied solutions, indirect milling or kneading methods are utilized for motorized mixing of drugs and excipients. The wanted thickness is attained by rolling the resulting material. Then the backing material is laminated. The solvent-free process is chosen because residual solvents and health concerns caused by solvents are not likely [28].

3. Hot melt extrusion method: In the hot melt extrusion process, a blend of pharmaceutical ingredients is molten by the extruder, having a heater, and different shapes are supplied via die by forcing the molten mixture through an orifice. Hot melt extrusion has been used for the production of controlled-release matrix tablets, pellets, granules, and oral disintegrating film dosage forms [29]. Here are defined benefits, such as molten polymers during the extrusion process can function as thermal binders and act as drug depots and/or drug release retardants upon cooling and solidification. Considering it is an anhydrous process; the number of processing and time-consuming drying steps has decreased.

Independent of compression properties, a matrix may be massed into a larger unit. De-aggregation of suspended particles in the molten polymer is caused by the extreme mixing and agitation forced by the spinning screw, resulting in a more uniform dispersion, and the process is continuous and efficient. When solubilized or distributed at the molecular level in HME dosage types, the bioavailability of the drug substance may be increased. Pharmaceutical hot-melt extrusion processes can be classified as either ram extrusion or screw extrusion [30].

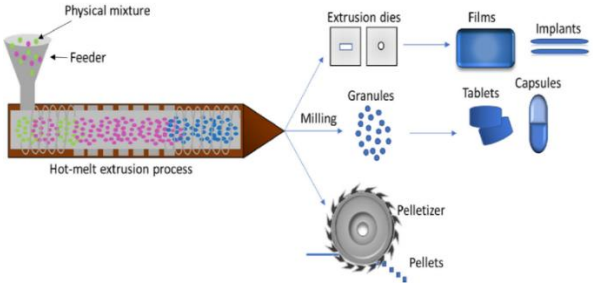

Figure No. 6: Schematic representations of a single-screw hot melt extruder.

4. Semi-solid casting method: Initial, a solution of water-soluble film-forming polymer is produced in the semisolid casting process. The resulting solution is applied to a solution of polymer insoluble in acid (cellulose acetate phthalate, cellulose acetate butyrate) prepared in ammonium or sodium hydroxide. A

sufficient amount of plasticizer is then applied so that a gel mass is obtained. Utilizing heat-controlled drums, the gel mass is eventually cast into films or ribbons. The film's thickness is about 0.015-0.05 inches. The acid-insoluble informing polymer should have a ratio of 1:4 [31].

5. Rolling method: The solution or suspension containing the substance is rolled into a carrier in this rolling method. In actuality, the solvent is water and a combination of water and alcohol [32]. The rolling method for preparing buccal patches involves mixing the drug and polymer in a solvent, spreading the mixture on a flat surface using a rolling pin, drying it to form a thin film, and then cutting the film into patches. This method is cost-effective and produces uniform patches suitable for drug delivery through the buccal mucosa.

7. Electrospinning and Electrospraying**:** Both electrospinning and electrospray techniques are used along at the same time. Simultaneous electrospinning of polymer solution and electrospray of colloidal suspension is carried out in this process from two separate capillary nozzles. A non-woven nanocomposite fabric can be prepared from a polymer material with nanoparticles deposited on a fiber surface using this method [33]. Electrospray can be viewed as an ideal method for producing multi-layer membrane mucoadhesive patch containing droplets made by electrospray method that can be imbedded into the electrospun mats according to the mentioned advantages. It first improves the efficiency of the drug loading and facilitates the production process of a multilayer reservoir system in a single step [34].

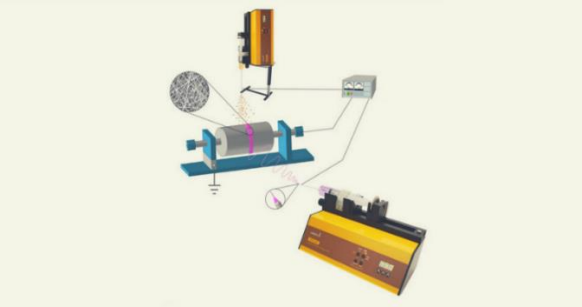

Figure No. 7: Schematic representations of electrospin- electrospraying

IX. EVALUATION OF BUCCAL PATCHES

The following tests are conducted to evaluate the formulated buccal patches:

1. Weight variation: Three films of each formulation are randomly chosen for film weight assessment, and individual weights of each patch are taken based on digital imbalance. The test was taken out to check the uniformity of weight and batch-to-batch variation. The average weight was concluded.

2. Thickness: Utilizing Vernier calipers with a least count of 0.001 mm, the thickness of the patch was evaluated. The thickness uniformity was calculated at five different points, and the average reading was taken.

3. Surface pH study: A combined glass electrode or pH paper may be used for this purpose. Every patch was let to swell for 2 hours at room temperature by placing it in contact with 1 ml of distilled water (pH 6.5 ± 0.05), and the pH was noted by bringing the electrode or pH paper into contact with the surface of the patch and allowing it to balance for 1 minute. A mean reading of three is described.

The standard surface pH value for buccal patches is typically in the range of 5.5–7.0.

4.Folding endurance: For the patch, the folding endurance was measured by folding the patch continuously at the same position before it splits. For this test, randomly, three patches were chosen from the formulation. It was considered satisfactory to reveal good patch properties. The number of times the patch might be folded at the same place without breaking gave the value of folding endurance.

5. Swelling Index: Buccal patches are weighed individually (W1) and placed separately in petri dishes containing phosphate buffer pH 6.8. The patches are removed from the petri dishes, and excess surface water is removed using filter paper. The patches are reweighed (W2), and swelling index (SI) is calculated as follows:

$$SI = (W2-W1)/W1$$

6. Moisture content and moisture absorption: The buccal patches are weighed accurately and kept in a desiccator containing anhydrous calcium chloride. After 3 days, the patches are taken out and weighed. The moisture content is determined by calculating moisture loss using the formula:

Moisture content (%) = Initial weight - Final weight x 100 / Final weight

The buccal patches are weighed accurately and placed in a desiccator containing 100 ml of saturated solution of aluminum chloride, which maintains 76% and 86% humidity (RH). After 3 days, films are taken out and

weighed. The moisture absorption is calculated using the formula:

Moisture absorption (%) = Final Weight-Initial weightx100 / Initial weight

7. In vitro drug permeation: The in vitro buccal drug permeation study of Drugs through the buccal mucosa (sheep and rabbit) was performed using a Keshary-Chien/Franz type glass diffusion cell at 37°C± 0.2°C. The donor and receptor compartments were separated by newly formed buccal mucosa. The buccal tablet was positioned with compartments clamped together and the core facing the mucosa. The donor compartment was filled with 1 ml of phosphate buffer, pH 6.8. The receptor compartment was filled with phosphate buffer pH 7.4, and the hydrodynamics in the receptor compartment were maintained by stirring with a magnetic bead at 50 rpm. A one-ml sample can be withdrawn at predetermined time intervals and analyzed for drug content at suitable nm using a UV spectrophotometer [35].

8. Stability study in human saliva: The stability study of buccal patches is performed in natural human saliva. The human saliva is collected from humans (age 18–50 years). Buccal patches are placed in separate Petri dishes containing 5 ml of human saliva and placed in a temperature-controlled oven at 37°C ± 0.2°C for 6 hours. At regular time intervals (0, 1, 2, 3, and 6 hours), the patches are examined for change in color, shape, and drug content [36];

X. MARKETED BUCCAL PATCHES

S. No	Drug	Product Name	Company	Uses
1.	Lidocaine	Denti Patch	Noven	Topical Anesthesia
2.	Amlexanox	Oradisc	Access Pharmaceuticals	Aphthous ulcer
3.	Natural ingredients	Snoreeze	PFL healthcare	Eliminate snoring
4.	Vitamins and natural ingredients	Solu leaves	Bio Progress	Cold treatment, Vitamin supplement
5.	Diphenhydramine HCl	Triaminic	Novartis	Antiallergic
6.	Dextromethorphan HBr	Theraflu	Novartis	Antiallergic
7.	Simethicone	Gas-x tongue twisters	Gas-x	Flatulence, Nausea
8.	Diphenhydramine	Benadryl	Pfizer	Antiallergic

XI. DISADVANTAGES

Even though the advantages, buccal delivery has restrictions that interfere with the drug delivery, such as [37]:

- Drugs that are unstable at oral pH cannot be given.
- This route does not administer drugs that have a bitter taste or bad taste or an extremely unpleasant scent or irritate the mucosa [38].
- The drug required with a minimal dose can only be administered.
- Drug dilution occurs due to saliva [39].
- Drugs may be swallowed along with the saliva and fail the advantage of the buccal route.
- Eating and drinking may become restricted.
- Minimum area of the oral cavity available for drug absorption [40].

XII. CONCLUSION

The buccal mucosa provides various advantages for controlled drug delivery for prolonged periods of time. The mucosa is well delivered with both vascular and lymphatic drainage, and first-pass metabolism in the liver and pre-systemic elimination in the gastrointestinal tract are avoided. The area is well appropriate for a retentive device and appears to be acceptable to the patient. With the right dosage form design and formulation, the permeability and the local environment of the mucosa can be controlled in order to accommodate drug permeation. Buccal drug delivery

is a favorable area for continued research with the aim of systemic delivery of orally inefficient drugs as well as a feasible and attractive alternative for non-invasive delivery of significant peptide and protein drug molecules. However, the necessary safe and effective buccal permeation/absorption enhancers are an important component for a prospective future in the area of buccal drug delivery.

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