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Review Article

Review Article On: Buccal Patches

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ABSTRACT

The buccal administration rote is a highly appealing option for delivering drugs systemically. Buccal drug administration enables direct entry into the systemic circulation via the internal jugular vein, bypassing hepatic first-pass metabolism and resulting in enhanced bioavailability. The placement of the product occurs between the upper gingiva (gums) and cheek in order to address both local and systemic conditions. This particular drug delivery approach in deemed advantageous in enhancing the bioavailability of medications. Buccal bioadhesive films offer unique advantages compared to conventional dosage forms in the treatment of various diseases by delivering topical drug at a controlled and gradual place within the oral cavity. This review paper covering various aspects such as the oral mucosa, formulation, mechanism of muchoadhesion, active ingredient delivers through buccal route, factors affecting on buccal patches formulation. Furthermore, it also discusses future prospective of buccal patches in drug delivery system.

INTRODUCTION

Among the diverse avenues of drug administration, the oral route is arguably the most favored by both the patient and the clinician.[1] In the process of orally administering a drug product, the drug molecule is introduced directly into the systemic circulation, thereby bypassing first-pass metabolism and potential degradation within the challenging gastrointestinal environment. These factors are commonly linked to the process of oral administration. [2] Notwithstanding, the oral administration of drugs presents certain drawbacks, including hepatic first pass metabolism and enzymatic degradation within the gastrointestinal tract. These limitations impede the oral administration of specific categories of drugs, particularly peptides and proteins.[3] As a result, alternative absorptive mucous membranes are regarded as potential locations for drug administration.[1] The phenomenon of drug absorption through the mucous membranes of the oral cavity was initially observed in 1847 by

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Sobvero, who made the discovery of nitroglycerin. Subsequently, in 1935, Walton conducted the first comprehensive investigation on the systemic absorption of substances through the oral cavity. [4]The transmucosal routes of drug delivery, which encompass the mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavity, present notable advantages over peroral administration for systemic drug delivery. These advantages comprise the potential bypass of the first-pass effect, the avoidance of presystemic elimination of the gastrointestinal tract, and, depending on the specific drug, a more favorable enzymatic flora for drug absorption.[5] In the exploration of novel drug delivery systems, various routes of administration have been attempted. One such route is localized drug delivery to the tissues of the oral cavity, which has been studied for its potential in treating periodontal disease, bacterial infections, and fungal infections. Over the years, cohesion has gained popularity due to its ability to optimize localized drug delivery. This is achieved by retaining a dosage form at the desired site of action, such as within the gastrointestinal tract, or by maintaining intimate contact between the formulation and the absorption site, such as the buccal cavity. Well-defined bio adhesion refers to the capacity of a material, whether synthetic or biological, to adhere to a biological tissue for an extended period of time.[1] The biological surface may consist of epithelial tissue or the mucus layer that covers the surface of a tissue. In the event that adhesion occurs to the mucous layer, this occurrence is commonly known as cohesion.[6] Cohesion, which is defined as the capacity to adhere to the mucus gel layer, plays a pivotal role in the formulation of these pharmaceutical delivery systems.[7] Buccal administration of drugs is regarded as one of the most valuable methods of administration for systemic and local drug actions.[8] The buccal route possesses the capacity to sustain a delivery system in a specific location for a prolonged duration, rendering it highly attractive for enhancing both local and systemic drug bioavailability. The buccal mucosa exhibits a relatively permeable nature, accompanied by a rich blood supply, thereby facilitating efficient absorption. Furthermore, this route enables swift drug transportation to the systemic circulation, while circumventing degradation by gastro-intestinal enzymes and first pass hepatic metabolism.[9] Mucoadhesion is recognized for its ability to enhance the closeness and longevity of interaction between a polymer containing medication and a mucous membrane.[10] Several mucoadhesive devices, such as tablets, films, patches, disks, strips, ointments, and gels, have been recently developed. However, buccal patch offers greater flexibility and comfort than the other devices.[3] The buccal patch is a non-dissolving, thin matrix modified-release dosage form that consists of one or more polymer films or layers containing the drug and/or other excipients.[5] Buccal patches provide enhanced flexibility and comfort compared to alternative devices. Furthermore, patches can overcome the issue of oral gels having a relatively short duration of action on the mucosa, as the gels are easily removed by saliva. The buccal route of drug delivery allows for direct entry into the systemic circulation via the jugular vein, bypassing initial hepatic metabolism, resulting in a higher bioavailability.[1] Additional benefits include exceptional accessibility, minimal enzymatic activity, appropriateness for drugs or excipients that cause only mild and reversible damage or irritation to the mucosa, painless administration, effortless discontinuation, and the ability to incorporate permeation enhancers, enzyme inhibitors, or pH modifiers into the

formulation. Furthermore, it offers versatility in design as a multidirectional or unidirectional release system for local or systemic action.[3]

Structure of the Oral mucosa:

The oral mucosa is comprised of an outermost layer of stratified squamous epithelium. Below this layer, there is a basement membrane, followed by a lamina propria and the submucosa as the innermost layer. The epithelium in the oral mucosa is similar to the stratified squamous epithelia found in other parts of the body. It consists of a basal cell layer that is actively dividing, progressing through various intermediate layers of differentiation until reaching the superficial layers, where cells are shed from the surface of the epithelium. The buccal mucosa has an epithelium that is approximately 40-50 cell layers thick, while the sublingual epithelium has slightly fewer layers. As the epithelial cells move from the basal layers to the superficial layers, they increase in size and become flatter.

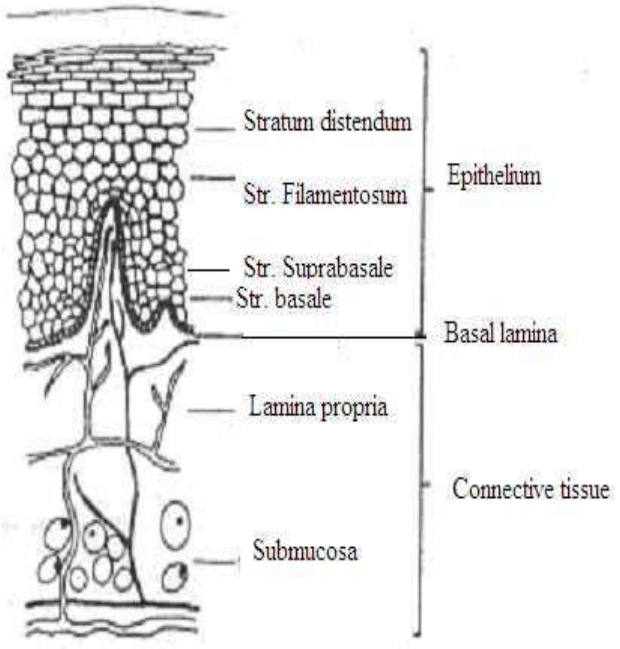

Fig.1: Schematic cross section through the oral mucosa

Oral mucosal sites:

In the oral mucosal cavity, the administration of drugs can be categorized into three distinct groups. [2]

1. Sublingual delivery
2. 2)Buccal delivery
3. 3)Local Delivery

1. Sublingual delivery:

This refers to the methodical administration of medication via the mucosal membrane that lines the lower region of the oral cavity.[2]

OR

The drug is administered through the sublingual mucosa, which refers to the membrane located on the ventral surface of the tongue and the floor of the mouth, in order to achieve systemic circulation.[6]

2. Buccal delivery:

It is administration of drug via the buccal mucosa to the systemic circulation. [6]

3. Local delivery:

It is drug delivery into oral cavity. [2]

Buccal drug delivery systems:

A delivery system has been developed with the purpose of administering drugs either systemically or locally through the buccal mucosa. Buccal delivery pertains to the controlled release of a drug when a dosage form is positioned in the outer vestibule, situated between the buccal mucosa and the gingival tissue.[3]

Novel buccal dosage form:

1. Buccal mucoadhesive tablet
2. buccal patches or film
3. Semisolid preparation (ointment and gels)
4. Powders

1. Buccal Mucoadhesive tablet:

Buccal mucoadhesive tablets are desiccated pharmaceutical preparations that necessitate pre-moistening before being applied to the buccal mucosa. For instance, a dual-layer tablet is

comprised of an adhesive matrix layer consisting of hydroxypropyl cellulose and polyacrylic acid, along with an inner core of cocoa butter that contains insulin and a penetration enhancer, specifically sodium glycocholate.[2]

2. Buccal patches or film:

Buccal patches are composed of two laminates, wherein an aqueous solution of the adhesive polymer is applied onto an impermeable backing sheet. This sheet is subsequently cut into the desired oval shape. A unique mucosal adhesive film known as "Zilactin" is comprised of an alcoholic solution containing hydroxy propyl cellulose and three organic acids. When applied to the oral mucosa, this film can remain securely in place for a minimum of 12 hours, even when exposed to fluids.[3]

3. Semisolid preparation (ointment and gels):

Bio adhesive gels and ointments exhibit lower patient acceptability compared to solid bio adhesive dosage forms. Furthermore, the majority of these dosage forms are exclusively employed for localized drug therapy within the oral cavity. One of the initial oral mucoadhesive delivery systems, known as "Or a base," is composed of finely ground pectin, gelatin, and sodium carboxy methyl cellulose dispersed in a poly (ethylene) and mineral oil gel base. This system is capable of being retained at the site of application for a duration of 15-150 minutes.[2]

4. Powders:

When hydroxypropyl cellulose and beclomethasone are administered in powder form and sprayed onto the oral mucosa of rats, a notable prolongation in the duration of their presence is observed compared to an oral solution. Furthermore, approximately 2.5% of beclomethasone remains on the buccal mucosa for a period exceeding 4 hours.

5. Buccal absorption:

The two primary pathways for transportation in the oral mucosa are paracellular and transcellular. Permeates may utilize both of these routes simultaneously, but the physicochemical properties of diffusion typically favor one pathway over the other. Lipophilic compounds, which have poor solubility due to their hydrophilic properties in intercellular spaces and cytoplasm, face difficulty entering the plasma membrane due to its lipid-loving nature and low partition coefficient. Consequently, intercellular regions pose the greatest barrier to the permeation of lipophilic compounds, while the plasma membrane serves as the main obstacle for water-repelling compounds. Solute permeation may require a combination of both routes, as the oral epithelium is stratified.[7]

Types of Buccal Patches:

1. Matrix type (Bi-directional)
2. Reservoir type (Unidirectional)

1. Matrix tubes (Bi-directional):

The buccal patch, formulated in a matrix configuration, comprises a combination of drug, adhesive, and additives. These patches have the ability to release the drug in both the mucosa and the oral cavity.

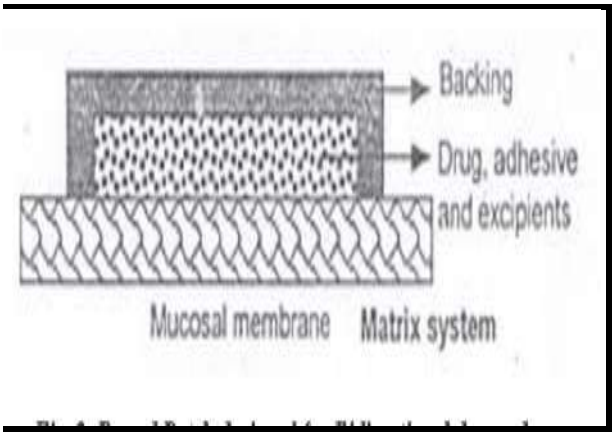

Fig.2: Matrix system

2. Reservoir type (Unidirectional):

The buccal patch, which has been designed with a reservoir system, incorporates a separate cavity for the drug and additives, distinct from the adhesive. An impermeable backing is utilized to regulate the direction of drug administration, minimize patch distortion and disintegration within the oral cavity, and safeguard against drug leakage.

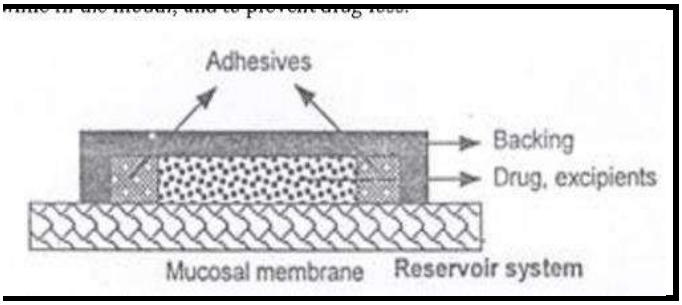

Fig.3: Reservior system

Advantages of buccal patches:

1. The convenience of administration to pediatric, geriatric, immobilized patients, and psychiatric patients who exhibit resistance towards oral ingestion of tablets.[12]
2. The buccal patch is widely recognized for its excellent ability to access the membranes that line the oral cavity, resulting in a painless and comfortable application.[13]
3. This medication effectively circumvents the initial-pass phenomenon, presystolic elimination via the gastrointestinal tract, and untoward drug reactions.
4. Patients have control over the administration time and can halt the treatment in an emergency.[14]
5. It exhibits fewer adverse effects than a pill and increases patient compliance.[15]
6. The oral mucosa is endowed with a copious blood supply. Medications are assimilated from the oral cavity via the oral mucosa and conveyed through the profound lingual or facial vein, internal jugular vein, and brachiocephalic vein into the systemic circulation.[13]
7. The size of the buccal membrane is ample enough to accommodate the placement of a delivery system on various occasions. Furthermore, there are two distinct areas of buccal membranes within the oral cavity, which enables the placement of buccal drug delivery systems on either the left or right buccal membranes as an alternative.[16]
8. The utilization of buccal dosage forms is comparatively more convenient than alternative methods. These forms can be promptly discontinued in the event of any manifestation of toxic effects.[8]
9. Buccal administration allows for direct entry of the drug into the systemic circulation, effectively bypassing the initial metabolic breakdown. This method avoids contact with the digestive fluids of the gastrointestinal tract, which may be detrimental to the stability of certain drugs such as insulin, proteins, peptides, and steroids. Furthermore, the rate of drug absorption remains unaffected by the presence of food or the rate of gastric emptying.[1]
10. Close touch with the mucosa improves the drug's efficacy.[14]
11. The polymer should not be poisonous and should be able to be absorbed through mucosal membranes.
12. The processes of applying, confining, and removing patches are all straightforward procedures.[14]

Disadvantages of buccal patches:

1. The size of the absorptive membrane is comparatively smaller. In the event that the dimensions of a delivery system determine the effective area for absorption, this area subsequently becomes further reduced.[1]
2. Continuous secretion of saliva into the oral cavity leads to the dilution of drugs at the site of absorption, resulting in low drug

concentrations at the surface of the absorbing membrane. The involuntary act of swallowing saliva leads to a significant portion of dissolved or suspended released drug being removed from the site of absorption. Additionally, there is a potential risk that the delivery of the drug may be compromised due to the aforementioned factors.[6]

3. It is not possible to administer drugs that exhibit instability at the buccal ph. [8]
4. consume any food or beverages, as it could interfere with the drug's effectiveness. Additionally, the conventional buccal drug delivery systems often caused discomfort or irritation in the oral cavity. These limitations and drawbacks have prompted the exploration of alternative drug delivery routes.[1
5. The inadvertent elimination of the dosage form occurs due to the continuous ingestion of saliva, which may result in the loss of medication.

Ideal characteristics of buccal patches: [2,9,11]

1. Rapid adhesion to the buccal mucosa and sufficient mechanical robustness.
2. It is imperative to possess a substantial margin of safety, both at the local and systemic levels.
3. It is imperative to ensure the controlled administration of the medication.
4. It is imperative to enhance the speed and magnitude of drug absorption.
5. It must achieve a unidirectional release of the drug towards the mucosa.
6. It must also demonstrate good resistance to the flushing action of saliva
7. The oral drug delivery system must not impede regular activities such as speaking, consuming food and beverages.
8. It must not contribute to the emergence of secondary infections such as dental caries.
9. It is imperative to possess commendable patient compliance.
10. For a limited duration, it is imperative that it remains affixed to the designated point of attachment.

Composition of Buccal Patches:

The components of buccal drug delivery systems (Buccal Patches) are:

1) Active pharmaceutical ingredients
2) Mucoadhesive polymers
3) Backing Membranes
4) Diluents
5) Sweetening agent
6) Flavoring Agents
7) Penetration enhancers
8) Plasticizers

1. Active pharmaceutical ingredients:

In the context of buccal drug delivery, it is imperative to extend and enhance the interaction between the active pharmaceutical ingredient (API) and the mucosal membrane in order to achieve the intended therapeutic outcome. The crucial characteristics of the drug that impact its permeation through the patch and the buccal mucosa encompass its molecular weight, chemical functionality, and melting point.[2]

The crucial characteristics of a drug that impact its diffusion through the patch and buccal

mucosa encompass its molecular weight, partition coefficient, and dissociation constant.[12] The choice of an appropriate medication for the development of a buccal mucoadhesive drug delivery system should be determined by the following criteria:[9]

The conventional dosage of the medication should be minimal.

- Medications with a biological half-life ranging from 2 to 8 hours are ideal candidates for controlled drug delivery

- The absorption of the medication should occur passively when administered orally
- The medication should not possess an unpleasant taste and should be devoid of irritancy, allergenicity, and any potential for discoloration or erosion of teeth.

2. Mucoadhesive polymers (Buccal Adhesive polymer):

Polymer is a highly elongated molecule composed of structural units that are linked by covalent chemical bonds.[12] The term "polymer" originates from the Greek words "polys," meaning many, and "metros," meaning parts. The defining characteristic that sets polymers apart from other molecules is the recurring presence of numerous identical, similar, or complementary molecular subunits within these chains.[17] The subunits, known as monomers, are diminutive molecules with relatively low to moderate molecular weight, and they become interconnected through a chemical process referred to as polymerization.[4] Mucoadhesive refer to both synthetic and natural polymers that engage with the mucus layer enveloping the mucosal epithelial surface, which comprises a significant portion of mucus composition. (9) The initial phase in the advancement of mucoadhesive dosage forms involves the careful selection and thorough characterization of suitable mucoadhesive polymers for incorporation into the formulation. In the case of matrix devices, a polymer is additionally employed to encapsulate the drug within the polymer matrix, thereby controlling the release duration of the drugs.[12]

Characteristics of Mucoadhesive polymers: [8,9]

1. It is facile to incorporate into various types of dosage formulations.
2. The polymer and its degradation products must exhibit non-toxic and non-absorbable properties within the gastrointestinal tract. 3)Additionally, it is imperative that the polymer be non-irritant to the mucus membrane.
3. The substance ought to remain unaffected by various conditions, such as alterations in pH levels and food composition.
4. It should exhibit inertness and compatibility with the surrounding environment.
5. It should promptly adhere to moist tissue surfaces and demonstrate a certain degree of site specificity.
6. It should facilitate the effortless integration of the drug and not impede its release.
7. It is imperative that the polymer does not undergo decomposition during storage or throughout the shelf life of the dosage form.
8. The polymer should be readily accessible in the market and cost-effective.

Mucoadhesive polymers used in Buccal Patches: [7,8,911,,17]

1. On the Basis of Sources:

Natural	Synthetic
Argon	1)Cellulose derivative:
Chiton	Carboxymethyl cellulose, Thiolate CMC, Hydroxyethyl Cellulose, Hydroxypropyl Cellulose, Hydroxypropyl methyl cellulose, Methyl cellulose, Methyl hydroxy ethyl cellulose.
Gelatin	2)Polly (acrylic acid)-based polymer:
Hyaluronic acid, Soluble starch	
Various gums(Guar, hake, xanthan, gellan, carrageenan, pectin and sodium alginate)	

2. On the basis of Aqueous Solubility: [9,18]

Water Soluble	Water Insoluble
Cellulose propionate, Hydroxyethyl cellulose, Hydroxypropyl cellulose Hydroxypropylemthyl cellulose (Cold Water), Sodium CMC.	Sodium alginate, Chiton (Soluble in dilute aqueous acid), Ethyl Cellulose, Polycarbonate.

3. On the basis on Charge:

Cationic	Amino dextran, Chiton, Dimethyl aminoethyl dextran, Trimethylated chitson.
Anion	Chitosan- EDTA, CP,CMC, Pectin, PAA, PC, Sodium alginate, Sodium CMC, Xanthan gum.
non-Anionic	Hydroxyethyl starch, HPC, Poly (ethylene oxide), PVA, PVP, Scleroglucan.

4. On the Basis on Potential Bio adhesive forces:

Covalent	Cyanoacrylate
Hydrogen bonding	Acrylates (hydroxylated methacrylate, Poly (methacrylic acid), CP, PC, PVA.
Electrostatics interaction	Chiton

3. Baking membrane:

The backing membrane assumes a significant role in facilitating the attachment of bio adhesive devices to the mucous membrane. It is imperative that the material used for the backing membrane is inert and impermeable to both the drug and penetration enhancer.[8] The materials frequently employed in the backing membrane are Carbopol, magnesium stearate, hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), carboxymethyl cellulose (CMC), polycarbophil, and others.[9]

4. Diluents:

Lactose DC has been chosen as a diluent due to its notable attributes such as its elevated solubility in water, its favorable flavoring characteristics, and its commendable physico-mechanical properties, rendering it highly suitable for direct compression. Another example of such diluents includes microcrystalline starch and starch [3]

5. Sweetening agent:

Sucralose, Aspartame, Mannitol, etc. [6]

6. Flavoring agents:

Menthol, Vanillin, Clove oil, etc.

7. Penetration enhancers:

Penetration enhancers refer to chemical compounds that effectively augment the permeability of the stratum corneum, thereby facilitating the achievement of elevated therapeutic concentrations of the drug candidate.[4] The permeability of the membrane presents a significant constraint for numerous pharmaceuticals during the advancement of buccal adhesive delivery systems. The epithelial layer that coats the buccal mucosa acts as a highly efficient obstacle against drug absorption. Substances that aid in enhancing the permeability through the buccal mucosa are commonly referred to as permeation enhancers.[1] One of the primary drawbacks linked to buccal drug delivery is the diminished flow of drugs across the mucosal epithelium, leading to reduced drug bioavailability. Numerous compounds have been examined for their potential as buccal penetration and absorption enhancers, aiming to augment the flow of drugs through the mucosa.[9] The compounds that would primarily derive advantages from the incorporation of penetration enhancers are proteins, peptides, and hydrophilic, low-molecular-weight actives.[19] Understanding the relationship between enhancer structure and the effect caused in the membrane, as well as the mechanism of action, makes it possible to create penetration enhancers with higher efficacy and lower toxicity profile. The drug's physicochemical characteristics, site of administration, type of

vehicle, and other excipients all affect the choice of enhancer and its effectiveness.[18]

List of penetration enhancers: [9,18]

Category	Examples
Surfactant	**1) Anionic:** Sodium lauryl sulfate, Sodium dodecameter, sodium laureate, polyoxyethylene-20-ethyl ether, Laurath-9, Sodium dodecyl sulfate (SDS), Dioctyl sodium sulfosuccinate. **2) Non-ionic:** Polyoxyethylene-9-lauryl ether, Tween 80, Nonyl phenoxy polyoxymethylene, Polysorbates, Sodium glycolate, Macrogel esters (myrjs), Macrogel ether (Brijs), Sorbitan fatty acids ester (span).
Bile salt and Derivatives	Sodium deoxycholate,Sodium taurocholate, Sodium taurodihydrofrusidate, Sodium glycodihyrofrusidate, Sodium glycocholate, Sodium deoxycholate.
Fatty acid and their Derivatives	Capric acid, Caprylic acid, Lauric acid, Linoleic acid, Oleic acid, 2-octyldodecyl myristate, 1-[(N,N-dimethylamino)propane-2-yl]dodecanate], Sodium carpate, Acylcholines, Acyles carnitine.
Chelating agent	EDTA, Citric acid, Salicylates, Polyacrylate.
Polymers	Cationic = Chitson, trimethyl chitson, poly-L-arginine, L-lysine.
Sulfoxide	Dimethyl Sulfoxide (DMSO), Decylmethyl Sulfoxide.
Cyclodexdrins	Methylated Cyclodexdrins
Polyols	Dimethylglycol, Polyethylene glyco, Glycerol, Propanediol
Monohydric Alcohol	Ethanol, Isopropanol.
Others	**Urea derivatives:** Unsaturated cyclic urea, Azone(1-dodecylazocycloheptane-2-one), Cyclodextrins, Enamine derivatives, Terpenes, Liposomes, Acyl carnitines and Cholines.

Plasticizers:

These are the components used to make thin films of polymer or a polymer blend flexible and soft.[20] The plasticizer must exhibit compatibility with both the polymer and solvent. The incorporation of plasticizer into the polymer matrix results in improved flow characteristics and enhanced strength. These materials are utilized to achieve the desired smoothness and elasticity of thin films composed of either a single polymer or a mixture of polymers. Additionally, the plasticizer serves a dual purpose by facilitating drug release from the polymer base and acting as a penetration enhancer.[12] The plasticizers commonly utilized include glycerol, propylene glycol, PEG 200, PEG 400, and castor oil, among others. [2]

Methods of Preparation of Buccal Patches:

1. Solvent casting
2. Direct Milling
3. Hot Melt Extrusion
4. Semisolid Casting
5. Rolling Method

1. Solvent casting:

In this method, all ingredients are accurately weighed and mixed using a pestle and mortar. Subsequently, the mixture is gradually added to a magnetically stirred solvent system, which includes the plasticizer. The stirring process is continued until a clear solution is achieved. The resulting solution is then transferred quantitatively to a petri dish. To facilitate solvent evaporation, the petri dish is covered with inverted funnels. These funnels are maintained at a temperature of 20-25ºC for a period of 24 to 48 hours, depending

on the specific solvent system employed. Once the solvents have evaporated, a thin layer of protective backing material is laminated onto the sheet of coated release liner. This lamination process creates a laminate that is subsequently die-cut into patches of the desired size and geometry.[9] The solvent casting method is characterized by its simplicity; however, it is accompanied by several drawbacks, such as prolonged processing time, elevated expenses, and environmental concerns arising from the utilization of solvents. These limitations can be effectively addressed through the implementation of the hot-melt extrusion method.[2]

2. Direct Milling:

Patches are produced in a solvent-free manner, without the utilization of solvents. The drug and excipients are mechanically blended through direct milling or kneading, typically without the inclusion of any liquids. Following the blending procedure, the resulting material is rolled onto a release liner until the desired thickness is attained. Additionally, an impermeable backing membrane may be employed to regulate the drug release direction, prevent drug loss, and reduce deformation and disintegration of the device throughout the application period.[4]

API and excipients are combined through the process of direct milling.

↓

The resulting blend is rolled using rollers.

↓

The backing material is laminated onto the blend.

↓

Finally, the film is collected.[2]

Although there may be minimal or even negligible disparities in the performance of patches produced through both processes, the solvent-free method is favored due to the absence of residual solvents and the elimination of any potential health concerns associated with solvents.[6]

3. Hot Melt Extrusion:

The drug and polymers are combined in a sigma blade mixer for a duration of 10 minutes, during which the plasticizer is gradually introduced. The mixture is then granulated in the presence of an antisticking agent. The resulting granules are stored overnight at a specific temperature and subsequently passed through a 250µm sieve to remove any excess powder and ensure uniform particle size. The dry granular material is then fed into the extruder. Finally, at the conclusion of the preparation processes, the films are cut to the desired dimensions.[12]

4. Semisolid Casting:

In the semisolid casting process, a solution of water-soluble film-forming polymer is initially prepared. This resulting solution is then combined with a solution of acid-insoluble polymer, which has been prepared in either ammonium or sodium hydroxide. Subsequently, an appropriate amount of plasticizer is added to form a gel mass. Finally, the gel mass is cast into films or ribbons using drums with controlled heat.[8]

5. Rolling Method:

A carrier is coated with a solution or suspension of the drug, which may contain water or a mixture of water and alcohol as the solvent. The resulting film is then dried on the rollers to achieve the desired size.[12]

Evaluation of Buccal Patches:

1. Surface PH
2. Thickness measurements
3. Weight Uniformity
4. Folding Endurance
5. Swelling study
6. Moisture content
7. Percentage of moisture loss
8. Drug Content uniformity

9. Morphological character
10. Water absorption capacity test
11. Ex-vivo bioadhesion
12. Ex-vivo Mucoadhesive time
13. In-vitro drug release
14. Permeation study
15. Viscosity
16. Ageing
17. Measurements of mechanical properties
18. Stability studies in Human saliva

1. Surface PH:

The buccal patches are allowed to undergo a swelling process for a duration of 2 hours on the surface of an agar plate. The measurement of the surface pH is conducted using pH paper that is positioned on the surface of the swollen patch.[1]

2. Thickness measurements:

The thickness of each film is assessed at five distinct positions, including the center and four corners, utilizing an electronic digital micrometer.[3]

3. Weight Uniformity:

Five patches are randomly selected from each batch and their weights are measured. The weight variation is then calculated.[9]

4. Folding Endurance:

The folding endurance of patches is ascertained by iteratively folding a single patch at a consistent location until it reaches its breaking point or is successfully folded up to a maximum of 200 times without any breakage occurring.[6]

5. Swelling study:

The individual weighing of Buccal patches, denoted as W1, is followed by their separate placement in 2% agar gel plates. These plates are then incubated at a temperature of 37°C ± 1°C and monitored for any physical alterations. At hourly intervals up to 3 hours, the patches are extracted from the gel plates and meticulously dried of any excess surface water using filter paper. The swollen patches are subsequently reweighed (W2), and the swelling index (SI) is determined using the ensuing formula.[3]

Swelling Index = [{(w2–w1)/w1}100].

6. Moisture content:

The films that have been prepared must be individually weighed and stored in a desiccator that contains calcium chloride at room temperature for a period of 24 hours. Subsequently, the films must be weighed again at specified intervals until a constant weight is achieved. The percentage of moisture content can be determined by utilizing the following formula: [13]

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

7. Percentage of moisture loss:

The assessment of patch integrity under dry conditions was conducted through the measurement of percentage moisture loss. Three patches with a diameter of 1cm were precisely cut and weighed, and subsequently placed in desiccators containing fused anhydrous calcium chloride. After a period of 72 hours, the films were removed and weighed again. The average percentage moisture loss of the three patches was determined using a mathematical expression, which is as follows:[17]

Percentage moisture loss = [(Initial weight - Final weight) / Initial weight]×100

8. Drug Content uniformity:

Three film units, each with a diameter of 20 mm, must be placed individually in separate 100 mL volumetric flasks. Subsequently, 100 mL of solvent should be added to each flask and continuously stirred for a duration of 24 hours. The resulting solutions must then be filtered, appropriately diluted, and analyzed at specified nanometers using a UV spectrophotometer. The final reading for the drug content should be

determined by calculating the average of the three film units.[13]

9. Morphological character:

Morphological characters are examined through the utilization of a scanning electron microscope (SEM).[7]

10. Water absorption capacity test:

Circular patches, with a surface area of 2.3 cm2, are permitted to undergo swelling on the surface of agar plates that have been prepared in simulated saliva. The simulated saliva is composed of 2.38 g Na2HPO4, 0.19 g KH2PO4, and 8 g NaCl per liter of distilled water, which has been adjusted with phosphoric acid to pH 6.7. The agar plates are maintained in an incubator at a temperature of 37°C ± 0.5°C. At various time intervals (0.25, 0.5, 1, 2, 3, and 4 hours), samples are weighed (wet weight) and subsequently left to dry for 7 days in a desiccator over anhydrous calcium chloride at room temperature. The final constant weights are then recorded. The percentage of water uptake is calculated using the following equation:

Water uptake %=[(Ww-Wf) /Wf]×100

where Ww represents the wet weight and Wf represents the final weight. The swelling of each film is measured.[3]

11. Ex-vivo bioadhesion:

A modified balance method was employed to determine the ex vivo mucoadhesive strength, as depicted in Figure 4. Fresh buccal mucosa samples from sheep and rabbits were obtained and used within 2 hours of slaughter. The underlying fat and loose tissues were removed to separate the mucosal membrane. The membrane was then washed with distilled water followed by phosphate buffer at pH 6.8 and maintained at a temperature of 37°C. The buccal mucosa was cut into pieces and further washed with phosphate buffer at pH 6.8. One piece of buccal mucosa was securely fastened to a glass vial, which was filled with phosphate buffer. Prior to the study, the two sides of the balance were made equal by placing a 5-g weight on the right-hand pan. A weight of 5 g was subsequently removed from the right-hand pan, causing the pan to descend along with the tablet over the mucosa. The balance was maintained in this position for a contact time of 5 minutes. Water, equivalent to the weight, was gradually added to the right-hand pan using an infusion set at a rate of 100 drops per minute until the tablet detached from the mucosal surface. This detachment force provided the mucoadhesive strength of the buccal tablet in grams. The glass vial was securely positioned within a glass beaker filled with phosphate buffer at pH 6.8 and maintained at a temperature of 37°C ± 1°C, ensuring that it made direct contact with the mucosal surface. The buccal tablet was affixed to the lower side of a rubber stopper using cyanoacrylate adhesive.[5]

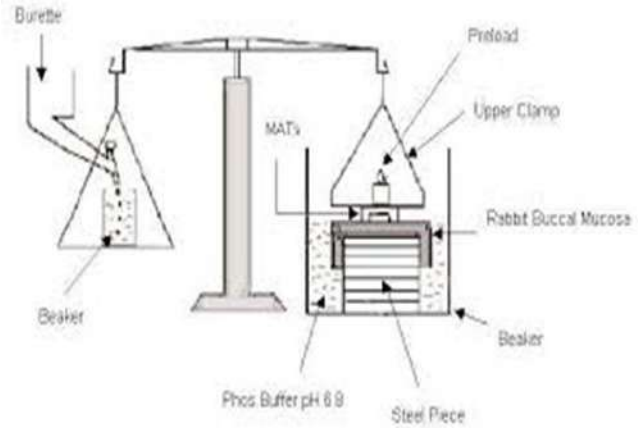

Fig.4 : Measurements of Mucoadhesive strength

12. Ex-vivo Mucoadhesive time:

The ex-vivo mucoadhesion time was conducted subsequent to the application of the buccal patch on freshly excised buccal mucosa from sheep and rabbits. The fresh buccal mucosa was affixed to a glass slide and a mucoadhesive patch was moistened with a single drop of phosphate buffer pH 6.8 and gently pressed onto the buccal mucosa using a fingertip for a duration of 30 seconds. The

glass slide was then placed in a beaker containing 200 ml of phosphate buffer pH 6.8 and maintained at a temperature of 37°C ± 1°C. After a period of 2 minutes, a stirring rate of 50 rpm was applied to simulate the buccal cavity environment, and the adhesion of the patch was monitored for a duration of 12 hours. Any changes in color, shape, collapse of the patch, and drug content were recorded.[1]

13. In-vitro drug release:

The drug release from the bilayered and multilayered patches is studied using the United States Pharmacopeia (USP) XXIII-B rotating paddle method. The dissolution medium utilized is a phosphate buffer with a pH of 6.8. The release process is conducted at a temperature of 37°C ± 0.5°C, with a rotation speed of 50 revolutions per minute. The buccal patch's backing layer is affixed to a glass disk using instant adhesive material. This disk is placed at the bottom of the dissolution vessel. At predetermined time intervals, samples of 5 ml are withdrawn and replaced with fresh medium. These samples are then filtered through wattman filter paper and subsequently analyzed for drug content after appropriate dilution.[9]

14. Permeation study:

The receptor compartment is filled with phosphate buffer at pH 6.8, and the hydrodynamics within the receptor compartment are sustained through stirring with a magnetic bead at a speed of 50 revolutions per minute. Samples are extracted at predetermined time intervals and subjected to drug content analysis.[3]

15. Viscosity:

Aqueous solutions were prepared using identical concentrations of plasticizer and polymer as those found in the patches. The viscosity measurements were conducted using a Brookfield model LVDV-II viscometer, with spindle number four of a helipath being attached. The viscosity was determined at a rotational speed of 20 rpm and at room temperature. The reported values represent the average of three separate determinations.[14]

16. Ageing:

Bioadhesive patches were placed in a petri dish that was lined with aluminum foil and kept at a temperature of 37.5 °C and a relative humidity of 75% for a duration of six months. The patches that were stored were subsequently tested after one, two, three, four, five, and six months to assess any alterations in release behavior, residence time, appearance, and drug content. The data presented represents the average of three determinations. Following the six-month storage period, the scanning electron microscope was utilized to compare the new and old medicated patches.[14]

17. Measurements of mechanical properties:

The mechanical properties of the films, or patches, are evaluated through the assessment of their tensile strength and elongation at break, utilizing a specialized tensile tester. A film strip measuring 60 x 10 mm and devoid of any visible defects is carefully cut and positioned between two clamps, which are separated by a distance of 3 cm. These clamps are designed to secure the patch without causing any damage during the testing process. The lower clamp remains stationary while the upper clamp moves at a rate of 2 mm/sec, pulling the strips apart until the strip breaks. At the point of breakage, the force and elongation of the film are recorded. The values for tensile strength and elongation at break are then calculated using the following formula:[16]

Tensile strength (kg/mm2) = Force at break (kg) / Initial cross-sectional area of the specimen (mm2)

Where:

M = Mass in grams

g = Acceleration due to gravity (980 cm/sec2)

B = Breadth of the specimen in centimeters

T = Thickness of the specimen in centimeters.

18. Stability studies in human saliva:

The stability analysis of buccal patches is conducted using natural human saliva as the medium. The human saliva is obtained from individuals within the age range of 18 to 50 years. The buccal patches are individually placed in Petri dishes, each containing 5 ml of human saliva. These dishes are then positioned in a temperature-controlled oven set at 37°C ± 0.2°C for a duration of 6 hours. At specified time intervals (0, 1, 2, 3, and 6 hours), the patches are meticulously inspected for alterations in color, shape, and drug content.[9]

Future aspects:[10]

- In the development of mucoadhesive placebo buccal patches, potent drugs that meet the criteria for buccal patch drug delivery systems can be utilized.
- The dissolution of medicated mucoadhesive buccal patches can be conducted to study drug release profiles.
- In-vivo studies can be conducted to further evaluate the prepared mucoadhesive buccal patches.
- Stability tests can be performed on the prepared mucoadhesive buccal patches.

CONCLUSION

There is a need for improvement in the current treatment regarding safety and efficacy. The buccal drug delivery system offers several advantages such as bypassing the gastrointestinal tract hepatic portal system, increasing the bioavailability of the drug, and improving patient compliance. Patches have gained significance in the field of pharmaceutical due to their novel, patient-friendly, and convenient nature. There small size and thickness contribute to improved patient compliance compared to tablet. By releasing the drug towards the buccal mucosa, the patch avoids the first-pass effect by directing absorption through the venous system that drains from the cheek. The buccal patch is thin, non-dissolving matrix modified release dosage form composed of one or more polymer patches or layers containing the drug and other excipient. The patch may include a mucoadhesive polymer layer that bonds to the oral mucosa.

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