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BUCCAL PATCHES- A REVIEW

Ramteke K.H[*1], Dighe P.A[*1], Kharat A. R[1], Patil S.V[2]

[1]PES's Modern College of Pharmacy (for ladies), Moshi, Pune, India
[2]Ashokrao Mane College of Pharmacy, Peth-Vadgaon, Kolhapur, India

***Corresponding author e-mail:** dr.kuldeepramteke@gmail.com, dighe.priya7@gmail.com

ABSTRACT

Transmucosal drug delivery is an alternative method of systemic delivery of the drug which offers different advantages over existing methods by enhancing the bioavailability of drug due to rich in blood supply in mucosal surface and prolongs residence time at the site of application to permit once or twice daily dosing. Buccal route is an attractive and easy transmucosal route of administration for systemic drug delivery**.** Delivery of the drug via buccal route leads direct access to the systemic circulation through the internal jugular vein bypasses drugs from hepatic first pass metabolism leading to higher bioavailability. Buccal bioadhesive patches, releases topical drugs in the oral cavity at a slow and predetermined rate and provides advantages over traditional dosage forms for treatment of many diseases and disorders. The objective of this article is to review buccal patches by discussing their composition, method of preparation and evaluation.

KEYWORDS: Transmucosal, bioavailability, mucosal surface, residence time, buccal patches.

INTRODUCTION

There are different routes of administration of dosage form of specific drug; among that oral route is most commonly preferred route. But there are several disadvantages of this route like hepatic first pass metabolism and enzymatic degradation in the GI tract, that prohibit oral administration of number of drugs especially peptides and proteins. These problems are overcome by using transmucosal route. This route involves the delivery of the drug through the mucosa hence, also called as "Bioadhesive drug delivery system".

The term bioadhesion is generally used to describe the adhesion between polymer (synthetic or natural) to soft tissue of the body. In the mucus membrane the goblet cells are present for the secretion of mucus, which is composed of glycoprotein mucin.

Buccal delivery of drug provides an easy alternative to the oral route of drug administration. As drug action can be terminated in case of toxicity by removing the dosage from the buccal cavity, buccal delivery offers a safer method of drug delivery. It is also possible to administer drugs to patients who cannot be given drugs orally[1-2].

Buccal route provides the direct access to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to higher bioavailability. Other advantages such as excellent accessibility, low enzymatic activity, suitability for drugs or excipients that damages or irritate the mucosa, administration without pain, easy removal, facility to include permeation enhancer or enzyme inhibitor or pH modifier in the formulation, versatility in designing as multidirectional or unidirectional release system for local or systemic effect[3].

Buccal patch is a non dissolving thin matrix modified release dosage form composed of one or more polymer films or layers containing the drug and/or other excipients. The patch may contain a mucoadhesive polymer layer which bonds to the oral mucosa, gingiva, or teeth for controlled release of the drug into the oral mucosa (unidirectional release), oral cavity (unidirectional release), or both (bidirectional release). The patch is removed from the mouth and disposed of after a specified time[4].

Buccal patches are highly flexible and thus readily tolerated by the patient than tablets or other dosage form. Patches are also ensure more

accurate dosing of the drug as compared to gels and ointments[5].An ideal buccal patch should be flexible, elastic, soft and strong to withstand breakage due to stress because of mouth activities. Moreover, it must also exhibit good mucoadhesive strength so that it can be retained in the mouth for appropriate time. As such, the mechanical, mucoadhesive, and swelling properties of buccal patches are important and essential to be evaluated.

Structure of buccal mucosa[6-7]:-

The oral mucosa is composed of (Fig.1.)[6]

a) Stratified squamous epithelium
b) Lamina propria
c) Submucosa

a) Stratified squamous epithelium:-

The buccal epithelium contains of 40 to 50 layers of non keratinized stratified squamous cells. It is about 500 to 800μm in thickness with varying degrees of maturity. The uppermost superficial layer of cells is made up of flattened compact differentiated cells having 150μm thickness. Oral mucosae are leaky epithelia intermediate between the epidermis and intestinal mucosa. Permeability is 4- 4000 times greater than that of skin.

b) Lamina propria:-

The lamina propria is also called as basement membrane it is a continuous layer of extracellular materials and forms a boundary between the basal layer of epithelium and the connective tissues. The lamina propria comprises collagen fibrils, which is a supporting layer of connective tissue, blood vessels, and smooth muscle. The structure of the lamina propria is not much dense and it is not a barrier to drug permeation.

c) Submucosa:-

The submucosa is a dense connective tissue that contains a few accessory salivary glands, called as *mucus acinus.* Mucus acini are surrounded by myoepithelial cells that help in the secretion of saliva. The oral cavity is marked by the presence of saliva produced by the salivary glands. The mucus is secreted by the major and minor salivary glands as part of saliva.

Mechanism of buccal absorption[8]:-

The absorption of the drug through buccal mucosa follows three steps mechanism.

Step 1:- Wetting and swelling of polymer to permit intimate contact with biological tissue (Fig.2.)[9].

Step 2:- Inter-penetration of bioadhesive polymer (BP) chains and entanglement of polymer and mucin chains (Fig.3.)[9].

Step 3:- Formation of chemical bonds between the entangled chains (Fig.4.)[9].

Routes of buccal absorption [10-11]:-

There are two permeation pathways or routes for passive drug transport across the oral mucosa: paracellular and transcellular routes.

a) Paracellular route:

Drug having low molecular weight and water-soluble compounds may cross the mucosa via the paracellular route i.e. moving between the junctions of the epithelial cells. Tight junctions are rare in oral epithelia. Thus in the majority of cases, drug absorption for small hydrophilic moieties is thought to occur via paracellular penetration. Intercellular space of the epithelial cells contains lipidic material through which lipidic moieties may be able to permeate, hence absorbed via the paracellular route.

b) Transcellular route:-

Drug having low molecular weight and lipophilic drugs may be absorbed transcellularly, by passive diffusion across the cells of the epithelium. Again, movement occurs down a concentration gradient (Fick's Law). The stratified nature of the epithelium means that lipophilic moieties must permeate across several layers of cells to reach the underlying blood capillaries. The drug can be transported by different processes such as passive diffusion, carrier mediated transport or Endocytosis as shown in fig.5[11].

Approaches of buccal dosage form:-

1) Matrix type.
   I. Conventional buccal tablets.
   II. Novel buccal adhesive tablets.
2) Reservoir type.
   I. Buccal patches
3) Buccal films.
4) Buccal mucoadhesive hydrogel.
5) Buccal spray.
6) Fast dissolving buccal tablets.
7) Buccal wafers.
8) Buccal microspheres.

BUCCAL PATCHES

Buccal mucoadhesive patches are modified release dosage form that provides controlled drug delivery from 1 to 24 hrs. They adhere to buccal mucosa for longer period of time.

Buccal patches are of different types

1. Matrix type: The buccal patches in a matrix type contains drug, adhesive, and additives mixed together.

2. Reservoir type: The buccal patch in a reservoir system contains a cavity of the drug and additives separate from the adhesive. An impermeable backing is applied to control the direction of drug delivery; to reduce patch deformation and disintegration while in the mouth; and to prevent drug loss[12].

They consist of solid matrix (non-dissolvable or slowly dissolvable). They may be

- ✓ Unidirectionally.
- ✓ Bidirectionally.
- ✓ Multidirectionally.

Adhesive polymer itself acts as drug carrier or adhesive layer link between drugs loaded layer and mucosa. Size generally 1-16 cm^2 but 1-3 cm^2 used .Large sized patches are placed at central position of buccal mucosa.

Three basic types of buccal patches to achieve targeted drug release.

a. Monolithic matrix(for multidirection release)
b. Multilayer matrix (having semi permeable backing layer)
c. Multilayer matrix (having impermeable layer over back and side of device)

COMPOSITION OF BUCCAL PATCHES:

1. Active ingredient
2. Polymers (adhesive layer)
3. Diluents
5. Sweetening agents
6. Flavoring agents
7. Backing layer
8. Penetration enhancer
9. Plasticizers

1. Active ingredients[13-14]:-

Active drug (s) used in the formulation of buccal patches, should have following characteristics

1. The conventional single dose of the drug should be small.

The drugs having biological half-life between 2-8 hours are good candidates for controlled drug delivery.

2. T_{max} of the drug shows wider-fluctuations or higher values when given orally.

3. The drug absorption should be passive when given orally.

2. Polymers(adhesive layer)[15]:-

The first step in the development of buccoadhesive dosage forms is the selection and characterization of bioadhesive polymers in the formulation. Bioadhesive polymers are most important in buccoadhesive drug delivery systems of drugs. Polymers are also used in matrix devices in which the drug is mixed in the polymer matrix, which controls the time of release of drugs. An ideal polymer for buccoadhesive drug delivery systems should have following characteristics.

1. It should be inert and compatible with the environment

2. The polymer and its degradation products should be non-toxic absorbable from the mucous layer.

3. It should adhere quickly to moist tissue surface and should possess some site Specificity.

4. The polymer must not decompose on storage or during the shelf life of the dosage form.

5. The polymer should be easily available in the market and economical.

Criteria followed in polymer selection

- Non-toxic, non-irritant and free from leachable impurities.
- Should adhere quickly to buccal mucosa and should possess sufficient mechanical strength
- Should possess peel, tensile and shear strengths at the bioadhesive range.
- Good spreadability, wetting, swelling and solubility and biodegradability properties.
- It should form a strong non covalent bond with the mucin or epithelial surface
- It must have high molecular weight and narrow distribution.
- Should show bioadhesive properties in both dry and liquid state.
- It should be compatible with the biological membrane.

The polymers that are commonly used as bioadhesive in pharmaceutical applications are[16]:

1. Natural polymers
   i. Tragacanth
   ii. Sodium alginate
   iii. Guar gum
   iv. Xanthan gum
   v. Soluble starch
   vi. Gelatin
   vii. Chitosan
2. Synthetic and semisynthetic polymers
   i. Cellulose derivatives (Methylcellulose, Ethyl cellulose, HEC, HPC, HPMC, Sod.CMC).
   ii. Poly (Acrylic acid) polymers (Carbomers, Polycarbophil).
   iii. Poly ethylene oxide.
   iv. Poly vinyl alcohol.
   v. Poly hydroxyl ethyl methylacrylate.
   vi. Poly vinyl pyrrolidone.

3. Diluents, Sweeteners and Flavors:-

These are the pharmaceutical excipients used to enhance the morphological properties of the dosage form, such as size, taste, and odor.

As the patches are of buccal use taste and odor are also taken into considerations for that purpose flovours and sweeteners are used. Diluents are used as fillers for the low dose of the drug.

Diluents- eg. Lactose, Microcrystaline starch, starch.

Sweetening agents- eg. Sucralose, aspartame, mannitol
Flavoring agents- eg. Menthol, vanillin, clove oil

4. Backing layer[17]:-

Backing membrane plays important role in the attachment of bioadhesive devices to the mucus membrane. The materials used as backing membrane should be inert, and impermeable to the drug and penetration enhancer to prevent release of it from the patch.
The commonly used materials include carbopol, magnesium separate, HPMC, HPC, CMC, sodium CMC, polycarbophil etc.

5. Penetration enhancer[17-18]:-

Membrane permeation is the major limiting factor for many drugs in the development of buccal adhesive patches. The epithelium which lines the buccal mucosa is a very effective barrier to the absorption of drugs. Materials that facilitate the permeation of drug through buccal mucosa are called as permeation enhancers.
Penetration enhancers are enhances the release of the drug. They are also helps in the systemic drug delivery by allowing the drug to penetrate more readily into the viable tissues.
Mechanism of penetration enhancers are as follows[19]

- Changing mucus rheology
- Increasing the fluidity of lipid bilayer membrane
- Acting on the components at tight junctions
- By overcoming the enzymatic barrier
- Increasing the thermodynamic activity of drugs

Eg.

- Chelators: EDTA, citric acid, sodium salicylate, methoxy salicylates.
- Surfactants: sodium lauryl sulphate, polyoxyethylene,, Benzalkonium chloride, cetylpyridinium chloride, cetyltrimethyl ammonium bromide.
- Bile salts: sodium glycocholate, sodium deoxycholate, sodium taurocholate, sodium glycodeoxycholate, sodium taurodeoxycholate.
- Fatty acids: oleic acid, capric acid, lauric acid, lauric acid/ propylene glycol, methyloleate, phosphatidylcholine.
- Non-surfactants: unsaturated cyclic ureas.
- Inclusion complexes: cyclodextrins.

6. Plasticizers[20]:-

Plasticizers are important factors that affect mechanical properties of films. The mechanical properties like tensile strength and elongation to the films. Variation in the concentration of plasticizers may affect these properties. The commonly used plasticizers are glycerol, di-butylpthallate, and polyethylene glycol etc.

Method of preparation[21]:-

There are six methods of preparation of buccal patches.

1. Solvent casting method
2. Semisolid casting method
3. Solid dispersion extrusion method
4. Rolling Method
5. Direct milling method
6. Hot melt extrusion method

1. Solvent casting method:-

In this method, all patch excipients including the drug co-dispersed in an organic solvent and coated onto a sheet of release liner. After solvent evaporation a thin layer of the protective backing material is laminated onto the sheet of coated release liner to form a laminate that is die- cut to form parches of the desired size and geometry.

2. Semisolid casting method:-

In semisolid casting method firstly a solution of water soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.

3. Solid dispersion extrusion method:-

In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

4. Rolling Method:-

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cut in to desired shapes and sizes. (Fig.7)[22]

5. Direct milling method[21-22]:-

In this, patches are manufactured without the use of solvents. Drug and excipients are mechanically mixed by direct milling or by kneading, usually without the presence of any liquids. After the mixing process, the resultant material is rolled on a release liner until the desired thickness is achieved. The backing material is then laminated as previously described. While there are only minor or even no differences in patch performance between patches fabricated by the two processes, the solvent-free process is preferred because there is no possibility of

residual solvents and no associated solvent-related health issues.

6. Hot melt extrusion method:-

In hot melt extrusion blend of pharmaceutical ingredients is molten and then forced through an orifice to yield a more homogeneous material in shape of films. Hot melt extrusion has been used for the manufacture of controlled release matrix tablets, pellets and granules, as well as oral disintegrating films.

The normal buccal patch is as given in Fig.8[22].

EVALUATION

1. Thickness[23-25]

The thickness of each patch measured by using thickness tester or standard screw gauge or Electronic digital micrometer at different positions of the patch and calculate the average.

2. Weight uniformity[23]

Cut the patch size of 1 x 1 cm^2 or 10 mm. Take the weight of each patch and calculate the weight variation.

3. Surface pH study[26-28]

Buccal patches are swell within 1 hr on the surface of the agar plate, prepared by dissolving 2% (w/v) agar in warmed isotonic phosphate buffer of pH 6.8 under stirring and then poured the solution into the petridish allowed to stand till gelling at room temperature. Measure the surface pH by pH paper placed on the surface of the swollen patch. Calculate the mean of three readings.

4. Morphological characterization

Morphological characters are studied by using scanning electron microscope (SEM).

5. Content uniformity[29-37]

Drug content uniformity was determined by dissolving the buccal patch (10 mm in diameter) from each batch by homogenization in 100 ml of an isotonic phosphate buffer (pH 6.8) for 6 hrs under occasional shaking. The 5 ml of resulting solution was diluted to 20ml with buffer and filtered through a whattman filter paper. The drug content was then determined after proper dilution and measured the absorbance by using a UV-visible spectrophotometer.

6. Folding endurance[38-39]

Folding endurance of the patches determined by repeatedly folding one patch at the same place till it broke or folded upto 200 or 300 times manually, which was considered satisfactory to reveal good patch properties. The number of times of film could be folded at the same place without breaking gave the value of the folding endurance.

7. Swelling % study[40-41]

Buccal patches are weighed individually (W_1), and placed separately in 2% agar gel plates, incubated at 37°C ± 1°C. Plates examined for any physical changes at regular 1 hour time intervals until 3 hours, patches are removed from the gel plates and excess surface water is removed carefully using the filter paper. The swollen patches are then reweighed (W_2) and the swelling index (SI) is calculated using the following formula.

$$SI = \frac{W_2 - W_1}{W_1} \times 100$$

8. Water absorption capacity test[42]

Circular Patches, with a surface area of 2.3 cm^2 are allowed to swell on the surface of agar plates prepared in simulated saliva (2.38 g Na_2HPO_4, 0.19 gKH_2 PO_4, and 8 g NaCl per lit. of distilled water adjusted with phosphoric acid to pH 6.7), and kept in an incubator maintained at 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 then left to dry for 7 days in a desicator over anhydrous calcium chloride at room temperature then the final constant weights are recorded. Water uptake (%) is calculated using the following equation,

$$\text{Water uptake (\%)} = \frac{(W_w - W_i)}{W_f} \times 100$$

Where, W_w is the wet weight, W_i is the initial weight and W_f is the final weight. The swelling of each film is measured.

9. Thermal analysis study

Thermal analysis study is performed using differential scanning calorimeter (DSC).

10. Ex vivo Bioadhesion test[43]

The fresh sheep mouth separated and washed with phosphate buffer (pH 6.8). A piece of gingival mucosa is tied in the open mouth of a glass vial, filled with phosphate buffer (pH 6.8). This glass vial is tightly fitted into a glass beaker filled with phosphate buffer (pH 6.8, 37°C ± 1°C) so it just touched the mucosal surface. The patch is stuck to the lower side of a rubber stopper with cyano acrylate adhesive. Two pans of the balance are balanced with a 5g weight. The 5g weight is removed from the left hand side pan, which loaded the pan attached with the patch over the mucosa. The balance is kept in this position for 5 minutes of contact time. The water is

added slowly at 100 drops/min to the right-hand side pan until the patch detached from the mucosal surface (Fig.9.)[43]. The weight, in grams, required to detach the patch from the mucosal surface provided the measure of mucoadhesive strength.

11. In vitro drug release[44]

The United States Pharmacopeia (USP) XXIII-B rotating paddle apparatus or type I apparatus is used to study the drug release from the patches.
Dissolution medium- phosphate buffer pH 6.8
Temperature- 37°C ± 0.5°C
Rotations- 50 rpm.
The backing layer of buccal patch is attached to the glass disk with instant adhesive material. The disk is allocated to the bottom of the dissolution vessel. Samples (5 ml) are withdrawn at predetermined time intervals and replaced with fresh medium. The samples filtered through whattman filter paper and analyzed for drug content after appropriate dilution.

12. In vitro permeation study of buccal patch[45-46]

The in- vitro buccal permeation through the buccal mucosa (sheep and rabbit) is performed using Keshary-Chien/Franz type glass diffusion cell at 37°C± 0.2°C (Fig.10.). Fresh buccal mucosa is mounted between the donor and receptor compartments. The buccal patch is placed with the core facing the mucosa and the compartments clamped together. The receptor compartment is filled with phosphate buffer pH 6.8, and the hydrodynamics in the receptor compartment is maintained by stirring with a magnetic bead at 50 rpm. Samples are withdrawn at predetermined time intervals and analyzed for drug content.

13. Ex vivo mucoadhesion time[47]

The fresh buccal mucosa is tied on the glass slide, and a mucoadhesive patch is wetted with 1 drop of phosphate buffer pH 6.8 and pasted to the buccal mucosa by applying a light force with a fingertip for 30 seconds. The glass slide is then put in the beaker, which is filled with 200 ml of the phosphate buffer pH 6.8, is kept at 37°C ± 1°C. After 2 minutes, a 50-rpm stirring rate is applied to simulate the buccal cavity environment, and patch adhesion is monitored for 12 hours. The time for changes in colour, shape, collapsing of the patch and drug content is noted.

14. In vivo residence time[48]

The experiment was performed in eight healthy adult male volunteers, aged between 22 and 28 years. The volunteers were asked to record the residence time of the patch on buccal mucosa in the oral cavity, which was taken as the time for the patch to dislodge completely from the buccal mucosa by continual sensation of the patch as well as the backing membrane. In vivo residence time was recorded in each case.

15. Tensile strength[49-50]

Tensile strength of the films (patches) includes evaluated using a tensile tester. Film strip with the dimensions of 60 x 10 mm cut and positioned between two clamps separated by a distance of 3 cm. The lower clamp held stationary and the strips are pulled apart by the upper clamp moving at a rate of 2 mm/sec until the strip break. The force and elongation of the film at the point when the trip break is recorded. The tensile strength and elongation at break values are calculated using the formula,

$$T = \frac{m \times g}{b \times t} \ Kg/mm^2$$

Where,
M-Mass in gm, g – Acceleration due to gravity (980 cm/sec^2), B- Breadth of the specimen in cm
T- Thickness of specimen in cm

16. Stability study in human saliva[51]

The human saliva is collected from humans (age 18-50years). Buccal patches are placed in separate petridishes containing 5ml of human saliva at temp. 37°C ± 0.2°C for 6 hours. At regular time intervals (0, 1, 2, 3, and 6 hours), the sample is collected and absorbance is taken to check stability.

17. Vapor transmission test (VTR)[49,52]

Vapor transmission method was employed for the determination of vapor transmission from the patch. Glass-bottle (length= 5 cm, narrow mouth with internal diameter =0.8 cm) filled with 2 g anhydrous calcium chloride and an adhesive spread across its rim, was used in the study. The patch was fixed over the adhesive and the assembly was placed in a constant humidity chamber, prepared using saturated solution of ammonium chloride and maintained at 37±2 °C. The difference in weight after 24 h, 3rd day and 1 week was calculated. The experiments were carried out in triplicate and vapor transmission rate was obtained as follow:
VTR = (Amount of moisture transmitted) / (Area x Time)

ADVANTAGES[53-58]:-

i. Avoid first pass effect
ii. Painless, easy and comfortable application.
iii. Larger buccal area to allow drug delivery to be placed at different occasion (i.e. left or right cheek).
iv. Drug is protected from degradation due to pH and digestive enzymes of the middle gastrointestinal tract.
v. Easy termination in case of overdose.

vi. Enhances the stability of drug.
vii. Rapid onset of action.
viii. Easy for unconscious and uncapaciated patients.
ix. Improved patient compliance due to the elimination of associated pain with injections.
x. Sustained drug delivery.
xi. In comparison to TDDS, mucosal surfaces do not have a stratum corneum. Thus, the major barrier layer to transdermal drug delivery is not a factor in transmucosal routes of administration. Hence transmucosal systems exhibit a faster initiation and decline of delivery than do transdermal patches.
xii. Though less permeable than the sublingual area, the buccal mucosa is well vascularized, and drugs can be rapidly absorbed into the venous system underneath the oral mucosa.
xiii. Transmucosal delivery occurs fewer variables between patients, resulting in lower intersubject variability as compared to transdermal patches.

LIMITATIONS[59-62]:-

i. Saliva is continuously secreted into the oral cavity diluting drugs at the site of absorption resulting in low drug concentrations at the surface of the absorbing membrane. Involuntary swallowing of saliva results in a major part of dissolved or suspended released drug being removed from the site of absorption. Furthermore, there is risk that the delivery system itself would be swallowed.
ii. Drug characteristics may limit the use of the oral cavity as a site for drug delivery. Taste, irritancy, allergy and adverse properties such as discoloration or erosion of the teeth may limit the drug candidate list for this route. Conventional type of buccal drug delivery systems did not allow the patient to concurrently eat, drink or in some cases, talk.
iii. The area of absorptive membrane is relatively smaller. If the effective area for absorption is dictated by the dimensions of a delivery system, this area then becomes even smaller.
iv. Drugs which are unstable at buccal pH cannot be administered.
v. Drug required with small dose can only be administered.
vi. Those drugs which are absorbed by passive diffusion can only be administered by this route.

Patented and Marketed Preparations[63]

Patented and marketed preparations are given in table no. 1 and 2 respectively.

CONCLUSION

Buccal drug delivery is useful for the drugs that undergo first pass metabolism and GI degradation. In this drug delivery system the formulation keeps in contact with the mucosal surface resulting in better absorption and prolonged resident time. Buccal patches are shows better patient compliance because of decrease in frequency of administration, hence increases bioavailability of the drug. Hence, buccal drug delivery is more advantageous over the other oral dosage forms.

Table 1: Patented preparations

Patent no.	Inventors	Work
2011003541	Myers, Garry L, Hilbert,Samuel D., Boone, Bill J.,Bogue, Sanghvi.	Used the polymers of cellulose for the preparation of buccal patch of buprenorphine.
4900552	Sanvordeker, Dilip R., Leung, Sau-hung S	Development of trilaminate patch showing sustained release of active ingredient in buccal cavity.
594294	Repka, Staci L., McGinity, James W.Michael A.	Prepared a patches using water soluble & swellable polymers like HPC or polyethylene oxide for controlled release of drug depending on size & shape of films.
20070172515	Fuisz, Richard C.	Development of multicomponent system comprises of one or more mucoadhesive films that adhere to mucosal surface.
20100266669	Meyer, Stephan, Slominski, Greg, Fankhauser, Christopher, Edward ouis, Nicole	Development of single layer oral disintgrating films having two different zones which consist of nicotine for buccal absorption.
20100063110	Meyer, Stephan, Slominski, Greg, Fankhauser, Christopher, Edward	Development of mucoadhesive oral disintegrating film that completely disintgrate to mouth within 1-10 min.
200715577	Moormann, Joachim opitz, Klaus, Hoffmann, Hans rainer	Development of films of Deoxypeganin and its derivatives for transmucosal administration.

Table 2: Marketed preparations.

Trade name	Drug	Company	Indication
DentiPatch®	Lidocaine	Noven	Local analgesia
Cydot®	Melatonin	--	Normalizing circadian rhythms.
Onsolis®	Rozatriptan Fentanyl	Merck	--

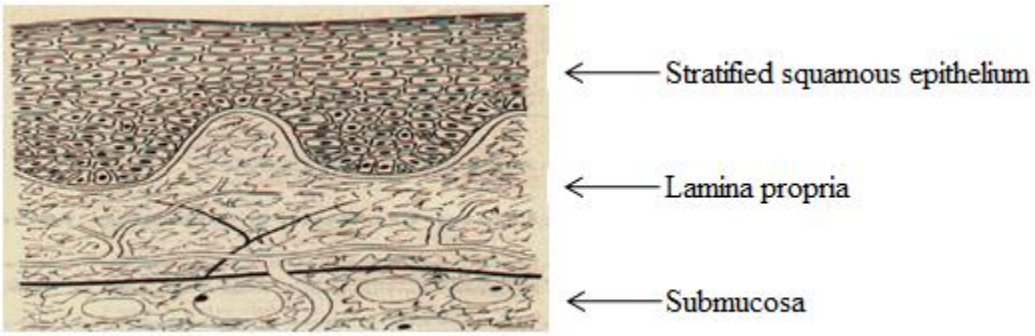

Figure1: Structure of buccal mucosa.

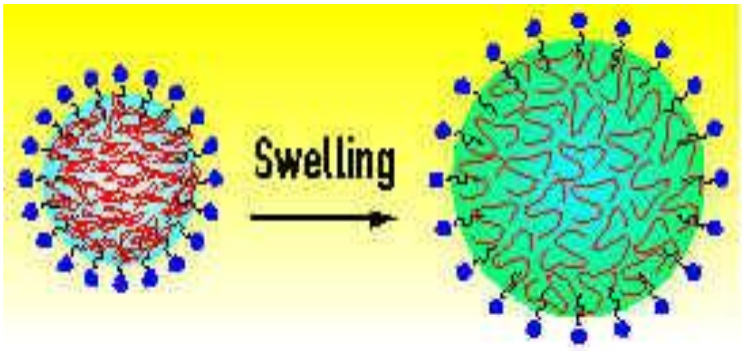

Figure 2: Wetting and swelling of polymer.

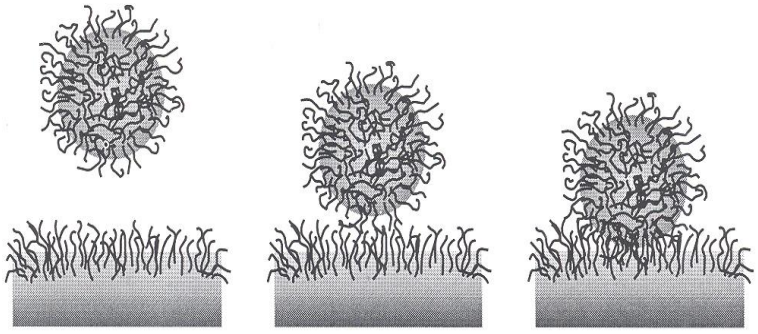

Figure 3: Inter-penetration of two polymer chains.

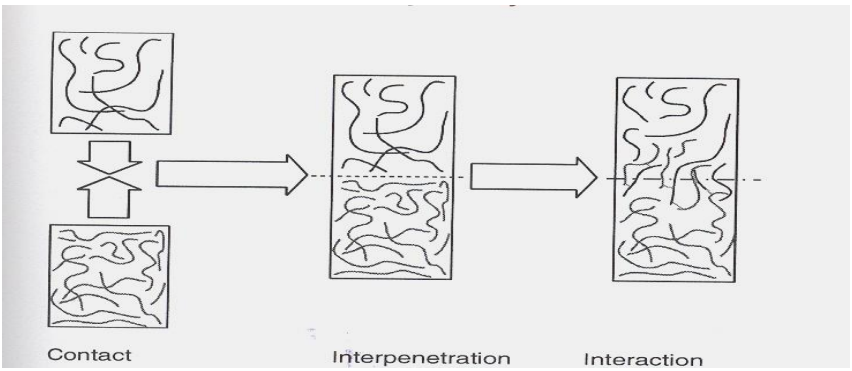

Figure 4: Chemical bond formation.

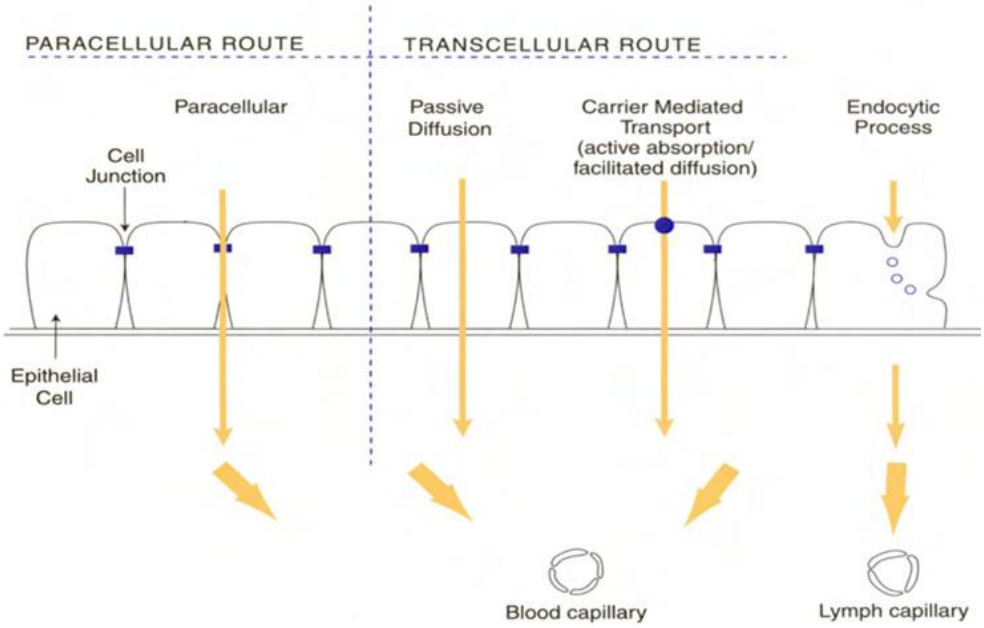

Figure 5: Routes of buccal absorption.

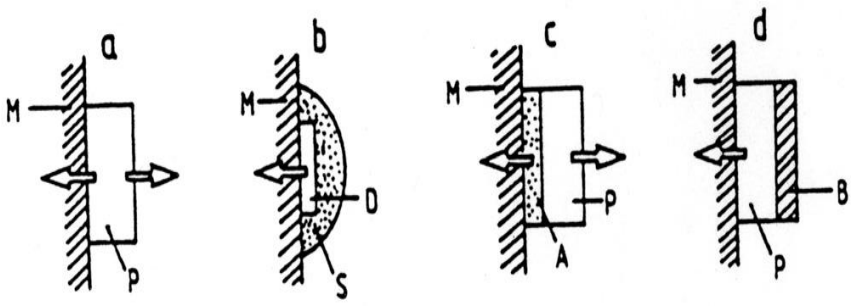

Figure 6: a) Bidirectional release from patch by dissolution or diffusion;
b) Unidirectional release from patch embedded in an adhesive Shield
c) Bidirectional release from a laminated patch;
d) Unidirectional release from a laminated patch.

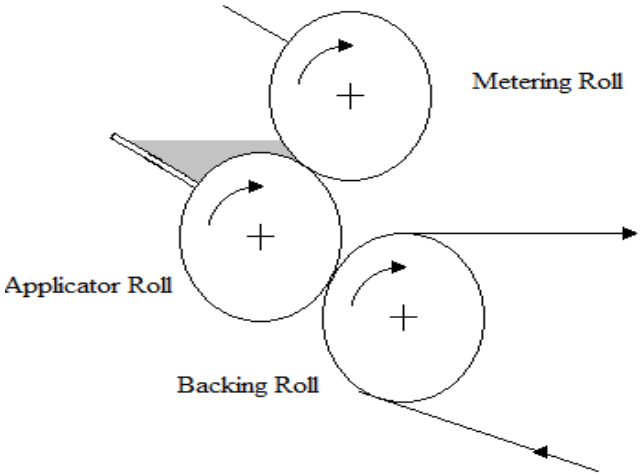

Figure 7: Rolling method.

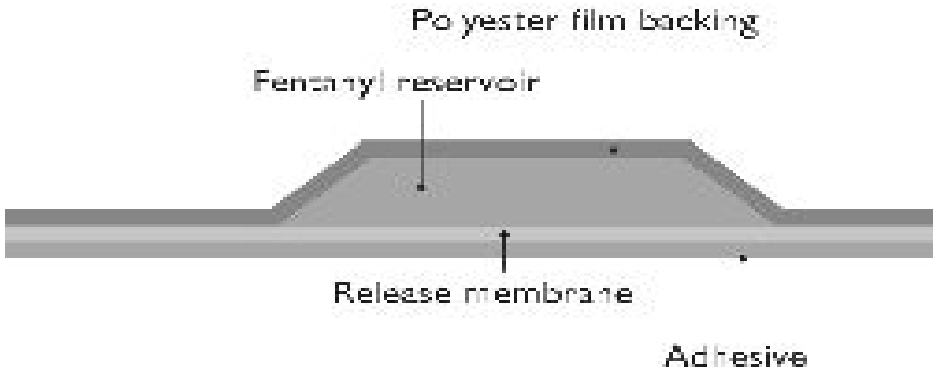

Figure 8: Normal Buccal Patch.

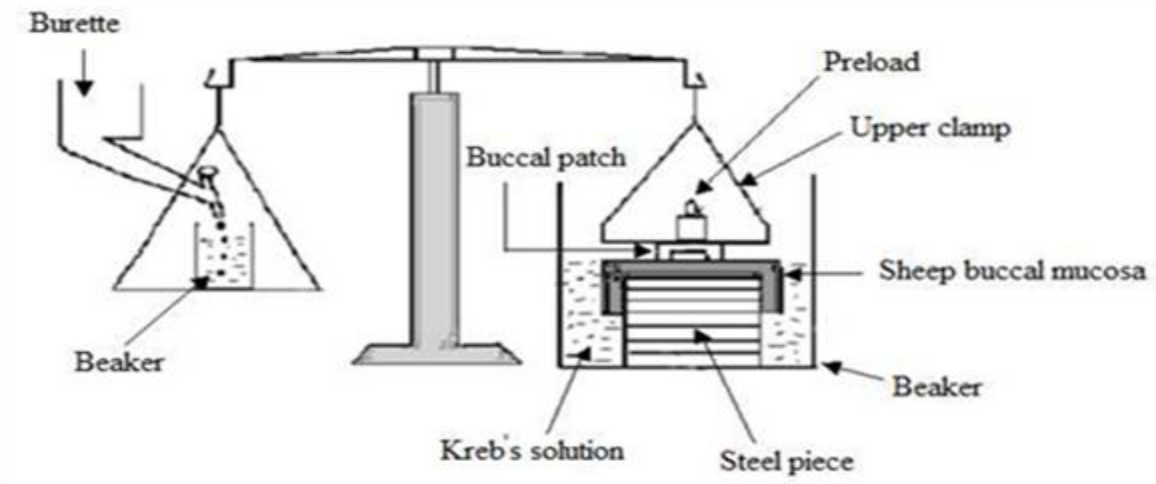

Figure 9: Ex vivo bioadhesion test.

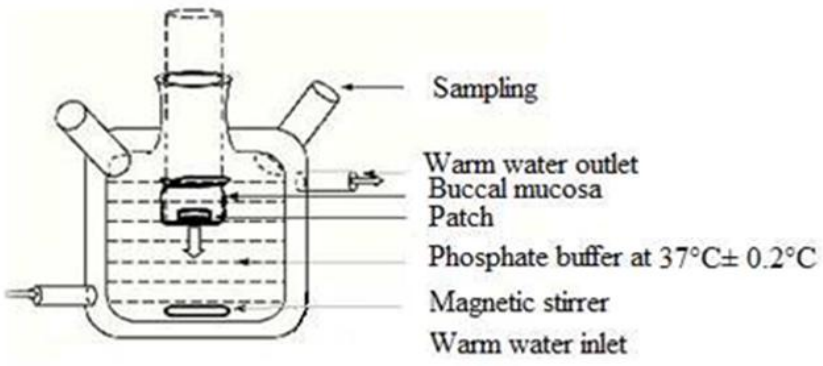

Figure 10: Franz diffusion cell for buccal patch.

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