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Buccal Patches: An Advanced Route of Drug Dosage Delivery -A Review

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ABSTRACT

Buccal Patches are the type of drug formulation that has normally a different course of administration through the buccal mucosa for drug delivery. These patches tend to help drug enter directly the systemic circulation escaping hepatic first pass metabolism. This type of drug delivery method is considered beneficial for elevating the bioavailability of drugs. This review is a thorough study to apprehend the procedures involved in assessment of buccal patches and the modern approach towards this type of drug delivery. This article intends to analyze the overall profile of Buccal Patches and scope of future advances.

INTRODUCTION

One of the most valuable methods of administration for systemic and local drugs actions is 'Buccal administration' of drugs. The natural or synthetic polymer adhesion tissues are titled as bio-adhesion and are integrated among mucus membrane and polymer labeled as mucoadhesion. Goblet cells are present in mucus membrane comprised of glycoprotein mucin for secretion of mucus. Buccal mucosa exhibits a rationallyflat and steady surface for the settlement of Mucoadhesive dosage form. The extent of drug that can be integrated is restricted by the size inadequacy of the buccal dosage form. The appropriate dose for buccal dosage forms suggested for daily necessity is 25 mg or less, considered valuable for patients. Drug with small half-life, needing sustained or organized release demonstrating poor aqueous solubility and may be efficaciouslydistributedthrough the buccal mucosa.[1]

The categories mentioned for distribution of drug moieties in oral mucosa are listed as (i) sublingual (ii) buccal (iii) local .[2]

For overcoming inadequacies likehigh first pass metabolism, and drug degradation in the harsh gastrointestinal environment made buccal delivery of drugs asubstitute to the conventional oral route of drug administration. Maximum valuable results given by buccal drugs because of plentiful blood supplied to oral mucosa.Concentration gradient isaccountable for transference of drugs in saliva. A suitable buccal drug delivery should be flexible and possess good bio-adhessive properties. The drug released in a controlled and predictable manner to elicit the required therapeutic response. The efficiency of mucoadhesive preparation is dependent upon the polymer composition used in preparing buccal patches.[3]The benefits of buccal patches are easyexclusion, low enzymatic activity, unproblematic administration of patch, ability to comprise permeation enhancer or enzyme inhibitor or pH changer.[4]

The complications accompanying with buccal drug delivery are food ingestion, loss of dissolved or suspended drug, swallowing of saliva hazard of choking by involuntarily swallowing of buccal dosage forms.[5]The low penetrability of the buccal membrane and a lesser surface area are drawbacks ofbuccal dosage forms.[6]

Oral Mucosa

The outmost stratum of oral mucosa is comprised of a stratified squamous epithelium. Beneath squamous epithelium exists a basement membrane and a lamina propria. The deepest layer of oral mucosa isthe sub mucosa.The epithelium is similar to stratified squamous epithelia found in the rest of the body. The sublingual epithelium comprises of less cell layers than the buccal mucosa epithelium around(40-50) cell layers dense. The thickness depends on site the buccal mucosa measures at 500-800µm, while the mucosal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and the gingival measure at about 100-200µm.[7]

Environment of Buccal Mucosa

Role of Saliva

(1) Saliva has moisturizes nature for buccal dosage forms

(2) It has protecting fluid forall themuscles of oral cavity

(3) Continuous mineralization is another feature of the saliva.

Role of Mucus

(1) The human mucus composed of carbohydrates and protein. They provide lubricating effect

(2) They responsible for adhesion dosage forms with buccal mucosa.[8]

Permeability of Drugs through Buccal Mucosa

Thepotential routes of drug absorption through the oral mucosa are;

(i)Trans-cellular

(ii)Para-cellular

Ideal Drug Candidates for Buccal Drug Delivery System

(1) The drugs used for buccal drug delivery which are absorbed only by process of passive diffusion

(2) They should have no odor and molecular weight of drugs should be between 200-500 Daltons

(3) The having lipophilic and hydrophilic nature can be suitably incorporated in buccal dosage forms

(4) The tasteless and persistent pH drugs are perfect for buccal drug delivery systems.[9]

Buccal adhesive polymers

Adhesives are materials which are used to attach things.The numerous physiochemical features of bio-adhesive polymers including hydrophilicity, hydrogen bond-forming groups, elasticity for inter permeation with mucus and epithelial muscle, and visco-elasticity.[10]

Perfect Polymer Features for Buccoadhesive Drug Delivery System

(1) It is easy to integrate in different sorts of dosage forms. (2) It should be unaffected by different types of conditions like change in pH and food. (3) It should be inert and harmonious with the environment.(4) It should adhere quickly to moist tissue surface and should possess some site specificity.(5) The polymer and its degradation products should be non-toxic absorbable from the mucous layer.(6) The polymer must not decay on storing or during the shelf life of the dosage form.(7) The polymer should be effortlessly accessible in the market and economical**.**[11]

Table 1: Categories of mucoadhesive polymers used in buccal patches

Natural Polymers	**Synthetic Polymers**
Tragacanth	Cellulose derivatives(MC,EC,HEC etc)
Sodium alginate	Poly (Acrylic acid) polymers (Carbomers, Polycarbophil).
Guar gum	Poly hydroxyl ethyl methylacrylate
Xanthan gum	Polyethylene oxide
Soluble starch	Polyvinylpyrrolidone
Gelatin	Polyvinyl alcohol
Chitosan	

Polymer Selection Criteria for Buccal Patches

(1) It has to companionable with oral mucosal membrane. (2) They have narrow delivery through tissues and polymer should have higher molecular weight.[12,13]

Benefits of Buccal Drug Delivery System

Drug administered by means of buccal mucosa have numerous diverse benefits.

(1)The buccal delivery benefits by more blood supply towards oral cavity. (2)First pass effect avoided because drugs directly absorbed from oral mucosa.(3)The usage of buccal dosage forms is easier than others. They can be discontinued if toxic effects appeared. (4)The side effects decreased and improved patient compliance. (5)The peptide molecules that not suitable for delivering through oral route can easily administered by buccal mucosa. Buccal delivery system have capacity to withstand environmental conditions and sustained delivery of drugs possible.[14,15,16]

Drawbacks

The disadvantages of buccal drug delivery system are:

(1)The dilution of the drug takes places by the uninterrupted excretion of the saliva.(2) Drugs with large potency dosage are problematic to be given by buccal route. (3) The unintentional removal of dosage form happens by incessant swallowing of saliva probable loss of medication.(4) Lesser area of the oral cavity available for drug absorption. (5)Drugs which annoy the mucosa or have an acrimonious flavor not appropriate.(6) Barrier properties of the mucosa.(7) Drugs which are unstable at buccal pH cannot be administered.[17]

Manufacturing Methods of Buccal Patches

Following manufacturing methods are used in constructing mucoadhesive buccal patches/films, namely solvent casting, hot melt extrusion and direct milling,semisolid casting,rolling method.

Solvent casting: In solvent casting method mucoadhesive polymers in required quantity is treated with solvent and polymer swell after vortexing. The measured quantity of plasticizer added in polymer mixture and again vortexed.The quantity of drug that needed liquefied in small volume of solvent system and added to the polymer solution and mixed well. Then

entrapped air is removed and blend is transferred into a cleaned petri plate. The patches developed are stored in a desiccator till the evaluation tests are performed.[18]

Direct milling: In this process, patches are fabricated deprived of the usage of solvents. Direct milling or kneading methods are used for motorized mixing drug and excipients without the existence of any liquefied solution.The desired thickness is accomplished by rolling the consequential material. The backing material is then laminated.The solvent-free process is chosen because there is no probability of residual solvents and health issues produced by solvents.[19]

Hot melt extrusion: In hot melt extrusion method blend of pharmaceutical ingredients is molten and different shapes yielded by forcing mixture through an orifice. Hot melt extrusion has been used for the fabrication of controlled release matrix tablets, pellets, granules, oral disintegrating films dosage forms.Solid dispersion extrusion immiscible components are extruding with drug and then solid dispersions are formulated. Finally, the solid dispersions are shaped into films by means of dies.

Semisolid casting: In the semisolid casting process initially a solution of water soluble film forming polymer is organized.The resulting solution is added to a solution of acid insoluble polymer which was prepared in ammonium or sodium hydroxide. Then appropriate aggregate of plasticizer is added so that a gel mass is acquired. Finally, the gel mass is casted into films or ribbons using heat controlled drums.

Rolling method: In this method 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 rollers and cut into desired shapes and sizes.[20]

Types of Buccal Patches

(1) In matrix type-The matrix type buccal patches fabricated by mixing the hydrophilic or lipophilic polymer matrix consistently with the drug. The therapeutic disc with a defined surface area is formed by medicated polymer moulding.

(2) In reservoir type-The reservoir system comprises a cavity for the drug and additives distinct from the adhesive. The drug loss is prohibited by attaching a water-resistant backing.

The Buccal patches Composition

(1) Active Pharmaceutical Ingredient (API): The buccal patches delivery system distributes diverse variety of active pharmaceutical ingredient. Large size drugs are problematic to be included but it has size limitation for active ingredient to be added in buccal patches.

(2) Polymers (adhesive layer): Polymer hydration and swelling possessions possibly play the main role. These are the polymers used hydroxyethylcellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, carbopol.

(3) Diluents: The diluents used in buccal patches are lactose, microcrystalline starch and starch.

(4) Sweetening agents: For sweeting purpose sucralose, aspartame and mannitol are used.

(5) Flavouring agents: The flavoring agents used in formulations are menthol, vanillin, clove oil, Peppermint oil, cinnamon oil, spearmint oil, vanilla, cocoa, coffee, chocolate.

(6) Backing layer: For backing layer in patches ethyl cellulose, Polyvinyl alcohol is used.[21]

(7) Penetration enhancer: The penetration enhancers such as cyanoacrylate, EDTA, Citric acid, PEG-100, 400, propylene glycol are used.[22](Fizaet al., 2013)

Permeation enhancers:

These are substances added to pharmaceutical formulation in order to improve bioavailability of drugs with normally poor membrane permeation properties without damaging the membrane and causing toxicity. Physiochemical properties of the drug, administration site, nature of the vehicle affects enhancer efficacy.[23]

Mechanism of Penetration Enhancers

The mechanisms of penetration enhancers are as follows:

- **Changing mucus rheology**: Saliva overcomes the problem that is because of permeation enhancers lessening the viscosity of the mucus.

- **Increasing the fluidity of lipid bilayer membrane**: The interaction of lipid or protein components with the lipid packing which normally interrupts penetrationenhancer'sfluidity, eventually increased as a result of it.

- **Action at tight junction's components**: Drug absorption enhanced by penetration enhancers acting on junctions.

- **By overcoming the enzymatic barrier:** Enzymatic activity varied by membrane fluidity variations incidentally. They act by obstructing the various peptidases and there for disabling the enzymatic barrier.

- **By enhancing the thermodynamic action of drugs**: The upsurge in solubility of drugamends the partition coefficient.The subsequent better absorption resultant of the enhanced thermodynamic activity. Chelators interfering with the calcium ions, fatty acids by aggregate fluidity of phospholipids surfactants increases permeability of drugs.[24]

Evaluation Parameters of Buccal Patch:

1. Surface pH: Buccal patches applied for 1 hour time period on the surface of the previously prepared agar media plates and pH was determined by means of employing pH paper on the surface of the swollen patch**.**[25]

2. Thickness measurements: Screw gauge with a least count of 0.01 thickness is used for measurement. Thickness measured at five different places and average value was determined**.**[26]

3. Swelling study: Buccal patch is weighed, placed in a 1.5% agar gel plate and incubated at 37 ± 1ºC. After one hour time intermissions up- to 3 h, the patch is removed from the petri dish and additional surface water is desiccated carefully using the filter paper. The swollen patch is then reweighed and the swelling index is estimated.[27]

4. Folding endurance: The folding endurance is accomplished by number of times patches could be doubled repetitively till it broke contributed the assessment of the folding endurance**.**[28]

5. Thermal analysis study: Thermal analysis is executed using differential scanning calorimeter procedure.

6. Buccal patches morphological characterization: Scanning electron microscope is used for studying morphological characters of patches.

7. Water absorption study: Patches are allowed to swell on the surface of agar plates. The pH adjusted with phosphoric acid to pH 6.7. Sample kept in an incubator sustained at 37°C ± 0.5°C. After specified time intermissions samples are weighed (wet weight) and desiccated for 7 days at room temperature. Final constant weights are noted after drying. Water uptake (%) is evaluated by means of the succeeding equation.

Water uptake (%)= (Ww – Wi)/Wf x 100 Where, Ww is the wet weight and Wf is the final weight.

8. *In-vitro* drug release studies: For *in-vitro* release of patches paddle apparatus used. The phosphate buffer pH 6.8 used as dissolution media and temperature maintained at 37°C ± 0.5°C and paddle rotate at 50 rpm. The adhesive material used to attach patch backing layer. The disk is allocated to the bottom of the dissolution vessel. After predetermined time intermissions, fresh medium changed with earlier taken sample. The samples evaluated for drug content after appropriate dilution.[29]

9. Permeation evaluation of buccal patch: For permeation study the receptor compartment is filled with phosphate buffer pH 6.8, and the hydrodynamics in the receptor compartment is sustained by mixing with a magnetic bead at 50 rpm. Samples are withdrawn at predetermined time intermissions and evaluated for drug content.[30]

10. *Ex-vivo* bioadhesion method

A piece of gingival mucosacuterodedwith phosphate buffer (pH 6.8) and knotted with open mouth glass vial. This glass vial is tightly fitted into beaker filled with phosphate buffer.The temperature of the apparatus maintained at 37ºC ± 1ºC and touching the mucosal surface. Cyanoacrylate adhesive used to fixed patch and balance are well-adjusted with weight that of five gram. The weight which loaded in the left hand side pan fastened with the patch over the mucosa removed. The contact time of patch is 5 minutes. Hundred drops per minute water are added to the right-hand side pan gradually until the patch removed from the mucosal surface. The magnitude of mucoadhesive strength required to separate the patch from the mucosal surfaceconcluded by weight in grams.[31]

11. *In-vivo* techniques for buccal patches:The following approaches are used *in-vivo* determination of buccal patches

(1) Use of radioisotopes. (2) Use of gamma scintigraphy. (3) Use of pharmacoscintigraphy (4) Use of electron paramagnetic resonance (EPR) oximetry. (5) X-ray studies. (6) Isolated loop technique.[32]

CONCLUSION

It was concluded that buccal patches have numerous advantages above the conventional drug delivery system. The mucosa is well supplied with both vascular and lymphatic drainage and evading first-pass metabolism. Buccal drug delivery is an encouraging area for continued research with the purpose of systemic delivery of orally inefficient drugs.The usage of buccal drug delivery is safe in patients because drug usage stopped if adverse effects appear. So in the forthcoming years, it is predictable that buccal patches are one of the vital dosage forms in pharmaceutical and healthcare sector.

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