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A REVIEW ON BUCCAL PATCHES

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Abstract:

Buccal drug delivery by passes the hepatic first pass metabolism and provides direct access to the systemic circulation through the internal jugular vein, resulting in high bioavailability. For systemic drug delivery, the buccal route is a desirable route of administration. Buccal bioadhesive films offer distinct advantages over conventional dosage forms for the treatment of many diseases because they release topical medications in the oral cavity at a slow and controlled rate. This article reviews recent advancements in buccal adhesive drug delivery systems with the goal of educating young scientists on fundamental concepts that can be used to get around formulation design challenges.

Keywords: Buccal drug delivery system, Mucoadhesive drug delivery system, Mucoadhesion, mucoadhesive polymers, Permeation enhancers, Bioadhesive polymers.

Introduction:

Localized drug delivery to oral cavity tissues has been studied for the treatment of periodontal disease, bacterial infection, and fungal infection among the various routes of administration tried so far in the novel drug delivery systems. Mucoadhesion has gained popularity over the years due to its potential to improve localized drug delivery by keeping a dosage form at the site of action (e. G. By keeping the formulation in close contact with the absorption site (e.G., within the gastrointestinal tract), the formulation can be administered systemically. G. Cavity in the mouth. A well-defined definition of bioadhesion is a substance's propensity to stick for an extended period of time to biological tissues, whether it be synthetic or biological. The biological surface can be a mucous layer covering a tissue's surface or it can be epithelial tissue. Mucoadhesion is the term used to describe a phenomenon where adhesion is to a mucous coat. There are more applications for mucoadhesive polymers in buccal drug delivery. There are many mucoadhesive products that have recently been developed, including tablets, films, patches, disks, strips, ointments, and gels. But compared to other devices, buccal patches offer more comfort and flexibility. Additionally, since oral gels are quickly washed away by saliva, a

patch can get around the issue of the oral gels' relatively brief residence time on mucosa. Buccal drug delivery bypasses the first pass hepatic metabolism and provides direct access to the systemic circulation through the jugular vein, resulting in high bioavailability. Other benefits include excellent accessibility, low enzymatic activity, suitability for drugs or excipients that mildly and temporarily harm or irritate the mucosa, painless administration, simple withdrawal, the ability to incorporate a permeation enhancer, enzyme inhibitor, or pH modifier in the formulation, and flexibility in designing as a multidirectional or unidirectional release system for local or systemic action.

❖ **Advantages:**

i. The buccal mucosa is widely vascularized, making it possible to quickly swallow medications.
ii. Prevents the drugs from entering the gastrointestinal fluids and gets around the first pass effect.
iii. Applying, confining, and removing patches are all simple processes.
iv. The performance of the drug is enhanced by close contact with the mucosa.
v. Increased compliance from the patient when compared to other administration methods.
vi. The confinement of the drug at the disease site can reduce dose-related side effects.
vii. Patients who are unconscious can receive it with ease.
viii. In case of emergencies, patients have control over the administration time and can stop the treatment.

❖ **Limitations:**

i. The buccal route cannot be used to administer mucosa-bothering or strongly-flavored medications.
ii. Small dose medications can only be given.
iii. Saliva production is constant, causing drugs to be quickly eliminated.
iv. Little area for absorption.
v. Involuntary salivation gulping causes a sizable portion of the delivered drug to disintegrate or suspend and be removed from the site of retention. The delivery system itself could also be swallowed, which is another risk.

❖ **<u>Composition Of Buccal Patches:</u>**

a) Active ingredient.
b) Polymers (adhesive layer): HEC, HPC, polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA),carbopol and other mucoadhesive polymers.
c) Diluents: Lactose DC is selected as diluents for its high aqueous solubility, its flavoring characteristics, and its physicomechanical properties, which make it suitable for direct compression. Another example: microcrystalline starch and starch.
d) Sweetening agents: Sucralose, aspartame,Mannitol, etc.
e) Flavouring agents: Menthol, vanillin, clove oil,etc.
f) Backing layer: EC etc.
g) Penetration enhancer: Cyano acrylate, etc

h) Plasticizers: PEG-100, 400, propylene glycol, etc

- **Method Of Preparation:**

- **Solvent casting**

It involves dispersing all of the patch excipients, including the medication, in an organic solvent before coating the mixture on a sheet of release liner. The coated release liner sheet is laminated with a thin layer of protective backing material after the solvent has evaporated. This laminate is then die-cut into patches with the desired size and geometry. A boiling tube was filled with weighed-out HPMC E15. This was then mixed with 20 ml of the solvent solution (1:1 dichloromethane:methanol). An adequate amount of care was taken to avoid lump formation. To give the polymer time to swell, the boiling tube was left idle for six hours. Propylene glycol was added in a precise amount after swelling, and the mixture was vortexed. The final CPH amount was weighed out, and 5 ml of the solvent mixture was used to dissolve it. It was then added to the polymer solution and thoroughly mixed. It was transferred into an anumbra petriplate that had already been cleaned after being set aside for a while to let any trapped air escape. These patches were dried in an oven that was positioned over a flat surface for 8 hours. With no plasticizer added, the process is repeated for HPC EF.

- **Direct milling (solventfree)**

In this process, patches are made without the use of solvents. Direct milling or kneading, typically without the use of any liquids, is used to mechanically combine the drug and excipients. The final product of the mixing process is rolled on a release liner until the desired thickness is reached. Following that, the backing material is laminated as before.

Buccal Films' Potential Benefits.

I. As a result of the large surface area that buccal films offer, the active pharmaceutical ingredient quickly disintegrates and dissolves in the oral cavity, promoting systemic absorption.
II. There is no need to swallow or chew.
III. No chance of choking.
IV. Because the hepatic first pass metabolism is not affected, the film increases the drugs' systemic bioavailability.
V. By GI enzymes and the acidic environment, drugs can be shielded from degradation.
VI. Efficacy with a quick onset and few side effects.
VII. It is possible to administer oneself.
VIII. Precise dosing in contrast to liquid dosage forms.
IX. It's possible to disguise flavors.
X. Increases the bioavailability of the dosage form by extending its time in residence at the absorption site.

XI. Administering the medication should be simple for young children, elderly people, and patients who are mentally ill, physically impaired, or uncooperative.

XII. Satisfactory stability and mouth feel.

Method Of Measuring Buccaladhesive Strength.

The strength of the bioadhesive bond, surface analysis, compatibility, physical and mechanical stability, shear stress strength, buccal adhesive strength, falling sphere method, and detaching force measurement were all tested. These tests included swelling, viscosity, temperature effect on viscosity, shear stress strength, buccal adhesive strength, and detaching force measurement. Each of these will give details regarding the polymers that were used in the formulation. Contact stage: The bioadhesive and mucus membrane come into close contact (wetting) either from a good wetting of the bioadhesive and membrane or from the swelling of the bioadhesive. Consolidation phase: A number of physicochemical interactions, including hydrogen bonding, hydrophobic interactions, and dispersion forces, take place to consolidate and strengthen the adhesive joint, resulting in protracted adhesion.

Ideal Characteristics Of Buccal Adhasive Drug Delivery System:

i. It should speed up drug absorption.

ii. Should not bother or irritate the patient in any way.

iii. For a few hours, it must remain attached to the attachment site.

iv. Ought to administer the medication in a controlled manner.

v. The mucosa should be the only direction in which the medication is released.

Classification Of Buccal Bioadhesive Dosage Forms:

i. Tablets for the buccal mucosa that are buccal bioadhesive are dry dosage forms that must be moistened before use. Currently, double and multilayered tablets are made using bioadhesive polymers and additives. The type of additives contained in the dosage form will determine whether the tablets, which are solid dosage forms created by direct compression of powder, can be placed in contact with the oral mucosa and allowed to adhere or dissolve. This dosage form has multiple routes for delivering medication to the oral cavity or mucosal surface.

ii. Buccal Bioadhesive Semisolid Dosage Forms: These dosage forms are semisolid and contain natural or synthetic polymers in powdered form that is dispersed in polyethylene or water. Arabase is one illustration.

iii. Buccal Bioadhesive Patches and Films: These films or patches include multilayered thin film or two poly laminates that are oval or round in shape, containing primarily of bioadhesive polymeric layer and impermeable backing layer to allow unidirectional flow of drug across buccal mucosa. To create these films, bioadhesive polymers are dissolved in alcohol before being mixed with the medication.

iv. The decrease in diastolic blood pressure following the administration of buccal film and buccal tablets of Nifedipine. Buccal Bioadhesive Powder Dosage Forms: This dosage forms are a mixture of the drug and bioadhesive polymers and are sprayed onto the buccal mucosa.

Basic Components Of Buccal Drug Delivery System Are:

i. Drug Substance

To decide whether the intended action is for a local or systemic effect and for a rapid or prolonged release, mucoadhesive drug delivery systems must first be developed. Drugs' pharmacokinetic characteristics play a crucial role in the formulation of buccoadhesive drug delivery systems. The drug ought to possess the qualities listed below. The drug's standard single dose should be extremely small. For controlled drug delivery, drugs with biological half-lives between 2 and 8 hours make good candidates. When a drug is taken orally, its Tmax undergoes numerous changes or increases in values. First pass effect or presystemic drug elimination may be present in drugs administered orally. When given orally, a drug should be passively absorbed.

ii. Bioadhesive Polymer

The first step in the creation of buccoadhesive dosage forms is the characterization and selection of suitable bioadhesive polymers. In buccoadhesive drug delivery systems, bioadhesive polymers are essential. In order to control the length of the drug release, matrix devices, which enclose the drug in a polymer matrix, also use polymers.The most varied class of polymers is the bioadhesive polymers, which have numerous uses in the treatment and care of patients. The core layer, also known as the rate-controlling layer, is how the drug enters the mucous membrane. Bioadhesive polymers are efficient and significantly enhance the oral drug delivery system by adhering to the mucin or epithelial surface.

iii. Backing Membrane:

In order for bioadhesive devices to adhere to the mucous membrane, the backing membrane is essential. The materials used to make the backing membrane should be inert to the penetration enhancer and medication. The buccal bioadhesive patches' impermeable membrane guards against drug loss and ensures patient compliance. Backing membranes are made of a variety of materials, including magnesium stearate, HPC, polycarbophil, HPMC, CMC, and carbopol.

iv. Permeation Enhancer

Agents that facilitate permeation through the buccal mucosa are known as permeation enhancers. The choice of permeation enhancer and its effectiveness are influenced by the physicochemical characteristics of the drug, the type of vehicle, the site of administration, and other additives.

Evaluation Of Buccal Drug Delivery Systems:

a. Drug-excipients interaction studies

The development of solid dosage forms requires studies of the interactions between drugs and excipients. Differential scanning calorimeters (DSCs), X-ray diffraction (XRDs), Fourier Transform Infrared Spectrum (FTIRs), and thin layer chromatography are all possible methods to assess potential drug excipient interaction studies. Because they display changes in melting endotherms and exotherms, changes in appearance, and variations in the corresponding reaction enthalpies, differential scanning calorimeters are used for quick evaluation of potential incompatibilities.

b. Physical evaluation

It is made up of three parts: content uniformity, weight uniformity, and thickness uniformity. By contrasting the average weight of ten patches from each batch that were chosen at random with the weight of a single patch, weight variation was evaluated. The film's thickness should be measured five times (at the center and in each of the four corners), and the mean thickness should be computed. Samples that have air bubbles, nicks, tears, or a mean thickness variation of more than 5% are disqualified from analysis. Each formulation's three 20 mm-diameter patches were placed separately in 100 ml volumetric flasks with 100 ml of pH 6 point 8 phosphate buffer solution, which was then continuously stirred for 24 hours. Filtered, properly diluted, and then examined with a UV spectrophotometer, the solutions were. As a final reading, the average of three patches was used.

c. Surface pH

In order to look into the possibility of any in-vivo side effects, the buccal patch's surface pH was measured. It is essential to maintain the surface pH as close to neutral as possible because an acidic or basic pH can irritate the buccal mucosa.For this, a combined glass electrode was employed. The buccal patches were kept in contact with 1 ml of distilled water (pH 6.5 0.05) and allowed to swell for two hours at room temperature. The pH was recorded by placing the electrode in contact with the patch's surface and letting it acclimate for one minute.

d. Swelling increases the weight of patch:

A 1x1 cm2 drug-loaded patch was kept, weighed on a pre-weighed cover slip, and 50 ml of phosphate buffer (pH 6 point 6) was then added. Every five minutes, the cover slip was taken off, and it weighed for a total of 30 minutes. Due to water absorption and patch swelling, the weight difference causes weight gain.

e. Ex vivo mucoadhesive strength

For determining ex vivo mucoadhesive strength a modified balance method is used. Fresh buccal mucosa of rabbit or sheep obtained and used within 2 hours of slaughter. The mucosal membrane separated by separating

underlying fat and loose tissues. The mucosal membrane were washed with distilled water and then with phosphate buffer (pH 6.8) at 370 C. The buccal mucosa cut into small pieces and again washed with phosphate buffer (pH 6.8). A piece of buccal mucosa was tied to the glass vial, which was filled with phosphate buffer. The two side of the modified balance was made equal before the study, by putting a 5 g weight on the right-hand side of pan. A weight of 5 g was removed from the right-hand side of pan, which lowered the pan along with the tablet over the mucosa. The balance was kept for 5 minutes contact time in this position. Equivalent to weight, the water was added at a slow rate with an infusion set of 100 drops per minute to the right-hand side of pan until the tablet detached from the mucosal surface. This detachment force gave the knowledge of mucoadhesive strength of the buccal tablet in grams. The glass vial was tightly fitted into a glass beaker filled with phosphate buffer (pH 6.8) at 37 °C ± 1 °C due to which it only touch the mucosal surface. The buccal tablet was stuck to the lower side of a rubber stopper with cyanoacrylate adhesive.

f. Ex- vivo mucoadhesive time

The period of time that passed after the ex vivo mucoadhesion test was conducted on sheep or rabbit buccal mucosa that had just been surgically removed. Fresh buccal mucosa was tied to a glass slide, and each tablet's mucoadhesive core side was moistened with a drop of phosphate buffer (pH 6 point 8), then pasted to the sheep buccal mucosa for 30 seconds with light pressure. The glass slide was then placed in the beaker, which was filled with 200 ml of the phosphate buffer with a pH of 6 point 8, and maintained at 37 °C 1 °C. Tablet adhesion was monitored for 12 hours while a 50 rpm stirring rate was used to simulate the buccal cavity environment after two minutes. The mucoadhesion time, which was measured as the amount of time it took the tablet to separate from the buccal mucosa, was recorded.

g. In vitro drug release

To examine the drug release rate from the bilayered and multilayered tablets, the United States Pharmacopoeia (USP) XXIII rotating paddle method was used. Phosphate buffer with a pH of 6–8 is the dissolution medium. At 37°0°5°C and 50 rpm, the study was conducted. Instant adhesive (cyanoacrylate adhesive) was used to attach the buccal tablet's backing layer membrane to the glass disk. The dissolution vessel's bottom was given to the disc. 5 ml samples were taken out and fresh medium was added at regular intervals. After the appropriate dilution, the samples were filtered through Whatman filter paper and subjected to UV spectrophotometry analysis.

h. In vitro drug permeation

The in vitro buccal drug permeation study of Drugs through the buccal mucosa of sheep or rabbit is carried out at 37°C 0.2°C using Keshary-Chien or Franz type glass diffusion cells. It contains the donor and receptor compartments, both of which were tied with brand-new buccal mucosa. With its compartments clamped together, the buccal tablet's core side was facing the mucosa. The donor compartment is filled with one ml of

phosphate buffer (pH 6 point 8), and the receptor compartment is filled with one ml of phosphate buffer (pH 7 point 4) By agitating the receptor compartment at 50 rpm with a magnetic bead, the hydrodynamics condition was kept. A UV spectrophotometer may be used to extract a one-ml sample at a predetermined time interval and test it for drug content at a suitable nm.

i. Stability study in Human saliva

According to ICH guidelines, a stability study of fast-dissolving films is performed on every batch. After a predetermined amount of time, the films were examined for disintegration speed, drug content, and physical appearance. At 40°C, 37°C, and 75°RH for three months, the stability study of the improved mucoadhesive patch formulation was conducted. After three months, all parameter values remained constant, with the exception of small but significant changes in the parameters for volume entrapment efficiency, percent elongation, and percent drug release after eight hours.

j. Folding endurance

The amount of folds a patch could withstand was tested by manually folding it 300 times, which was deemed sufficient to reveal good patch properties, or folding it repeatedly until it broke. The value of folding endurance is determined by how many times a patch can be folded in the same location without breaking. Five patches are used in this test.

k. Viscosity

Aqueous solutions made with the same concentration of plasticizer and polymer as the patches. The viscometer is a Brookfield model LVDV-II attached to spindle number four of a helipath. 20 rpm and room temperature were used to determine the viscosity. The values listed are the average of three determinations.

l. Ageing

Bioadhesive patches were placed in a petri dish lined with aluminum foil and kept there for six months at a temperature of 37 0point 5 °C and a relative humidity of 75 %. The stored patches were tested after 1, 2, 3, 4, 5, and 6 months for changes in release behavior, residence time, appearance, and drug content. The mean of three determinations was shown by the data. After six months of storage, the scanning electron microscope was used to compare new and old medicated patches.

Conclusion:

Drugs are simply and consistently delivered through the buccal mucosa's extensive vascular and lymphatic system. Furthermore, patches prevent pre-systemic end in the gastrointestinal tract and liver's first-pass digestion. Furthermore, patches are a safe and convenient way to administer medications in the buccal space

because buccal medication can be stopped at any time in cases of toxicity. Therefore, buccal drug delivery has become an attractive alternative for the delivery of powerful peptide and protein drug molecules as well as a promising area for on going research with the goal of systemic delivery.

Reference:

i. Parmar HarshadG et al;" Buccal Patches : A Technical Note"; 2012; 029.

ii. M.M.Veillard et al., "Preliminary Studies of Oral Mucosal Delivery of Peptide Drugs," J. Controlled Release , 1987;1(2):123131 .

iii. Y. Kurosaki et al., "Effects of Surfactants on the Absorption of Salicylic Acid from Hamster Cheek Pouch as a Model of Keratinized Oral Mucosa," Int. J. Pharm. 1988;4(7):13-19

iv. Mohd S. Pendelkar et al ;" Formulation and evaluation of bioadhesive patch for buccal delivery of tizanidine, Acta Pharmaceutica Sinica B"; 2012;2(3):318–324

v. Shinde Pramod et al ;" Buccal Film : An innovative Dosage from Designed to Improve Patient Complaince, international journal of pharmaceutical and chemical sciences. 2012;1 (4):12

vi. Shojaei Amir H., Buccal Mucosa As A Route For Systemic Drug Delivery: A Review, J Pharm PharmaceutSci, 1998;1 (1):15-30

vii. deVries M.E, Ph.D. Thesis, University of Leiden, Leiden, The Netherlands, 1991

viii. P.K. Khobrgade et al ;" Literature studies on preparation and evaluation of buccal patches";2014;25(2):73

ix. Vishnu MP, Bhupendra GP, Madhabhai MP. Design and in vitro characterization of eudragit containing mucoadhesive buccal patches. Int J PharmTech Res2009; 1(3):783-9.

x. Ching HS. Bioadhesive polymers as platforms for oral controlled drug delivery II: Synthesis and evaluation of some swelling, water- insoluble bioadhesive polymers. J Pharm Sci 1985; 74(4):399–405.

xi. Coutel EA, Maitani Y, Veillard M, Machida Y, Nagai T. Combined effects of pH, cosolvent and penetration enhancers on the in vitro buccal absorption of propranolol through excised hamster cheek pouch. Int J Pharm, 1992; 84:117-28.

xii. Patel R, Shardul N, Patel J, Baria A. overview on buccal mucoadhesive films. Arch Pharm Sci & Res 2009; 1(2):212-7.

xiii. Khairnar A, Jain P, Baviskar D, Jain D. Development of mucoadhesive buccal patch containing aceclofenac: in vitro evaluations. Int J PharmTech Res. 2009 Oct;1(4):978-81.

xiv. Apoorva M, Neha C, Geeta A. Formulation and characterization of fast dissolving buccal films: A review. Der Pharmacia Lettre 2011; 3(1):152-65.

xv. Siegel IA, Gordon HP. Surfactant-induced increase of permeability of rat oral mucosa to non electolytes in vivo. Arch Oral Biol.1985;30:43-7.

xvi. Leung SS, Robinson JR. Polymer structure features contributing to mucoadhesion: II. J ContrRel 1990; 12:187–94.

xvii. Bottenberg P, Cleymaet R, Muynek CD, Remon JP, Coomans D, Slop D. Development and testing of bioadhesive, floride- containing slow-release tablets for oral use. J PharmPharmacol 1991; 43:457-64.

xviii. Chandra SK, Ramesh G, Vamshi VY, KishanV, Madhsudanrao Y. Development of mucoadhesive patches for buccal administration of prochlorperazine: Evaluation of in vitro release and mechanical properties: Int J Pharma Sci and Nanotech ;1(1): 64-70.

xix. Peppas NA, Buri PA. Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues. J ContrRel 1985; 2:257–75.

xx. Harshad GP, Janak JJ, Tarun KP,Vishnu MP. Buccal patch: A technical note. Int J PhamSci, Rev Res 2010 Sep-Oct; 4(3):178-82.

xxi. Sudhakar Y, Knotsu K, Bandopadhyay AK. Bio adhesive drug delivery – A promising option for orally less efficient drugs. J Control Rel 2006; 114:15-40.