AN OVERVIEW ON RECENT ADVANCES AND CURRENT TRENDS IN ORAL MUCOADHESIVE DRUG DELIVERY SYSTEM

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ABSTRACT

Buccal administration of drugs provides a convenient route of administration for both systemic and local drug actions. The major hindrance for the absorption of a drug taken orally is extensive first pass metabolism or stability problems within the GI environment like instability in gastric pH and complexation with mucosal membrane. In both the stimulation of these types of buccal drugs start info, mucoadhesion of system is a key component. Mucoadhesive polymers make been used beneath lots additional dosage variety beneath work to achieve systemic start on medication on both the buccal mucosa. It is also possible to administer drugs to the patients of subconscious and bless co-operative. In order to prevent accidental swallowing on drugs epoxy mucosal dosage variety were meant for oral start, which included epoxy tablets, movies, greases, other dosage variety with various mixtures of polymers, absorption enhancers. Several methodologies have been considered so far, to design and manipulate the release properties towards the invention of buccal mucosal delivery systems.

Key Words: Buccal drug delivery, mucoadhesion, polymers.

INTRODUCTION

Buccal route of drug delivery is a good alternative, amongst the various routes of drug delivery. Oral route is perhaps the most preffered for the patients. Transmucosal ways of drugs delivery which contain the mucosal coatings of nasal, rectal, vaginal, ocular, and dental and oral cavity offer excellent opportunities and potential advantages over pre oral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of presystemic elimination within the GI tract and depending on the particular drug, a better enzymatic flora for drug absorption. Mucoadhesive formulations are usually prepared with mucoadhesive polymers. First generation mucoadhesive polymers are hydrophilic in nature, having limited solubility in other solvents, forming high viscous liquid in water and pH sensitive. Mucoadhesive polymers have been used to formulate tablets, patches, or microparticles, with the adhesive polymer forming the matrix into which the drug is dispersed, or the barrier through which the drug must diffuse. Hydrophilic high molecular weight therapeutic agents such as proteins and peptides are readily available for therapeutic use. However, when administered by the oral route, these agents suffer from problems such as degradation and poor absorption. To overcome these obstacles and for successful delivery of proteins and peptides, the buccal route of drug delivery has acquired significant attention. The concept of use of bioadhesive polymers to prolong the contact time has gained remarkable attention in buccal drug delivery. Mucoadhesion is known to increase the intimacy and duration of contact between drug-containing polymer and a mucous surface. The bioavailability of the drug is improved because of the combined effects of the direct drug absorption and the decrease in excretion rate. Increased residence time and adhesion may lead to lower API concentrations and lower
administration frequency to achieve the desired therapeutic outcome. [5]

CHARACTERISTICS OF BUCCOADHESIVE SYSTEM

An ideal buccal adhesive system should possess the following characteristics:
1. Drug release in a controlled fashion.
2. Good patient compliance.
3. Quick adherence to the buccal mucosa and sufficient mechanical strength.
4. The rate and extent of drug absorption.
5. Should not hinder normal functions such as talking, eating and drinking.
6. Should accomplish unidirectional release of drug towards the mucosa.
7. Should not aid in development of secondary infections such as dental caries.
8. Possess a wide margin of safety both locally and systemically.
9. Should have good resistance to the flushing. [6-9]

ADVANTAGES [10,20,21]

1. Bypass of gastrointestinal tract and hepatic portal computer, increasing the bioavailability of orally administered medication that otherwise passes through hepatic first-pass metabolism prolongs the residence period on the dosage mode at the site of absorption.
2. Specific usage of the systemic blood circulation via the inner jugular vein bypasses drugs through the hepatic first spend body leading to heavy bioavailability.
3. Low enzymatic activity.
4. Drugs are protected by degradation in the acidic environment in the gut. Excellent access.
5. Painless administration.
6. To ease the drugs administration.
7. Vomiting is generally greatly avoided.
8. Described in condition on unconscious and also less cooperative patients. The presence on saliva ensures relatively heavy sum of drinking water for drug dissolution different in case on rectal or transdermal ways.
9. Increased preventing period combined with managed API arrival may end in lower administration rate of recurrence.
10. Drugs, that screen poor bioavailability through the oral route, are administered conveniently. Ex; Medication, which are unsound in the acidic environment of stomach or are commonly destroyed enzymatic and alkaline society of the intestine.

DISADVANTAGES [4,12]

1. The continuous secretion of saliva (0.5-2 l/day) leads to following dilution of the drugs. The hazard on choking by involuntarily swallowing the delivery computer is really a condition. Just the medication which is absorbed through passive diffusion can be utilized through this path.
2. Drugs which are unsound at buccal pH cannot remain administered through which route.
3. Consuming of saliva can also eventually lead to losing melted or displayed drugs absence of permeability of buccal membrane, specifically differentiate to the sublingual layer.

OVERVIEW OF BUCCAL MUCOSA [32,22]

Structure: The oral mucosa is anatomically divided into,
1. Epithelium
2. Basement membrane and connective tissue

Epithelium: The epithelium consists of approximately 40-50 layers of stratified squamous epithelial cells having thickness 500-800μm. [32,22] The epithelium, as a protective layer for the tissues beneath, is divided into (a) non-keratinized surface in the mucosal lining of the soft palate, the ventral surface of the tongue, the floor of the mouth, alveolar mucosa, vestibule, lips, and cheeks, and (b) keratinized epithelium which is found in the hard palate and non-flexible regions of the dental cavity. The epithelial cells, beginning from the basal muscle, older, change its own shape, and radiate while shifting the surface. Non keratinized paper penetrated through tall and conical-shaped connective structures. These tissues, are also known as the lamina propria, consist of collagen particles, a supporting coating of connective tissues, blood, and sleek muscles. [26]

Drugs permeability through buccal mucosa: There're two possible ways of drugs intake through the squamous stratified epithelium of the oral mucosa. Transcellular (intracellular, spending through the panel) and Paracellular (intercellular, spending online cell). Permeation all over buccal mucosa has been considered mainly every paracellular path through paracellular path via the intercellular lipids developed through membrane granules. However passive diffusion is the key mechanism on drugs absorption, custom convey mechanisms make been reported to exist beneath additional oral mucosa (which of the language) for one little drugs and also nutrition; glucose and cefadroxil remained shown to be melted in which way. [32,27]
Membrane coating granules: Membrane Coating Granules (MCG) are spherical or oval organelles (100–300 nm in diameter). MCGs discharge their contents into the intercellular space and thus form the permeability barrier. Major MCG lipid components are cholesterol esters, cholesterol, and glycosphingolipid. Cells increase in size and become flattened as they progressively mature and migrate from the basal layer towards the epithelial surface, showing increasing levels of protein tonofilaments and declining levels of some cytoplasmic organelles.

Basement membrane: The basement membrane (BM) is a continuous layer of extracellular materials and forms a boundary between the basal layer of epithelium and the connective tissues. It provides the required adherence between the epithelium and the underlying connective tissues, and functions as a mechanical support for the epithelium. The underlying connective tissues provide many of the mechanical properties of oral mucosa. The connective tissue, along with the basement membrane, is not considered to influence the diffusion of most compounds of pharmacological interest although these two regions may limit the movement of some macromolecules and complexes.

Mucus: The epithelial muscle on buccal mucosa are encompassed by the intercellular ground material called mucus whose width varies from 40 µm to 300 µm. It acts as an valuable start vehicle through behaving as a lubricant giving cells to step relative to friends and it is thought to play one major role beneath adhesion of mucoadhesive drugs start systems. On buccal pH, mucus will form one strongly cohesive gel mode. Mucus is composed particularly of mucins and its inorganic preservatives suspended beneath water. Mucins are one family on heavy, glycosylated protein composed of glycosidic bonds, specifically a-amylose (pauses 1-4 glycosidic bonds), lysozyme (safety, digests bacterial cell wall) and lingual lipase (destroy the fats). Mucus acts various important features:

1) It moistens the mouth, introduce digestion and protects the teeth from die.
2) It also controls bacterial flowers of the dental cavity.
3) As saliva is heavy in calcium and phosphate, this plays a role beneath mineralization of teenage oral repair and precarious enamel lesions.
4) It cover the oral through forming “safety pellicle”. This signifies one saliva protein coat on the oral, which contains antibacterial compounds.

Factors affecting drug delivery via buccal route

The rate on absorption of hydrophilic ingredient is one cause for the molecular height. Smaller molecules (75100 Da) generally screen rapid transport on mucosa, with permeability limiting when molecular size grows. For hydrophilic macromolecules such as peptides, intake enhancers make remained used to effectively deviate the permeability of the buccal epithelium, giving which route as more suitable the start of big molecules. The partition coefficient is generlly one useful device to study the intake potential of a drugs. in general, increasing adrug’s polarity through ionization or thcarboxyl, and amino circles, wil solubility of any private drug and create a decrease in the lipid-water partition coefficient. Conversely, limiting the polarity of a drugs (e.g. adding methyl or methylene circles) results in greater partition coefficient and also decreased drinking water solubility. Both the partition coefficient is and agonize from pH at the website of drug intake. With developing pH, the partition coefficient. The ionization of drugs is instantly related to both thses pKa and pH across the mucosal floor. Only the nonionized form of many empty acids and also empty bases screen appreciable lipid solubility hence the ability to pass lipoidal membranes. As a result, highest absorption on these types of compounds offers been shown to occur at the pH wherever they are unionized, to absorbability shrinking as ionization increases.
MECHANISM OF MUCCOADHESION

The mechanism of mucoadhesion is generally divided in two steps:

1) The contact stage, and
2) The consolidation stage

The first stage or the contact stage is characterized by the contact between the mucoadhesive and the mucous membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer. In the consolidation, the mucoadhesive materials are activated by the presence of moisture. Moisture plasticizes the system, allowing the mucoadhesive molecules to break free and to link up by weak van der Waals and hydrogen bonds. [13]

THEORIES OF BIOADHESION [13-15]

The theories of polymer-polymer adhesion can be adapted to polymer-tissue adhesion or bioadhesion by recognizing that bioadhesion is different only because of the differing properties of the tissue as opposed to those of the polymer.

Electronic theory: According to this theory, electron transfer occurs upon contact of an adhesive polymer with a mucus glycoprotein network because of differences in their electronic structures. This results in the formation of an electrical double layer at the interface.

Absorption theory: According to this theory, after an initial contact between two surfaces, the material adheres because of surface forces acting between the atoms in the two surfaces. There are two types of chemical bonds resulting from these forces. Primary chemical bonds are of covalent nature, which are undesirable in bioadhesion because their strength may result in permanent bonds. Secondary chemical bonds are having many different forces of attraction, including electrostatic forces, Vander Waal forces and hydrogen bonds.

Wetting theory: It is predominantly applicable to liquid bioadhesive systems and analyses adhesive and contact behavior in terms of the ability of a liquid or a paste to spread over a biological system.

Diffusion theory: According to this theory, the polymer chains and the mucus mix to one sufficient depth to reach a semi permanent epoxy bond. The true depth of the polymer chains penetrate the mucus depends on the diffusion coefficient and also the time on meet.

The concept efforts to speak the difficulty apart of both areas after addition:

G= (Eε/L) ½
Where E is the Young’s 
ε is the fracture energy
L is the critical crack length.

BASIC COMPONENTS OF BUCCAL DRUG DELIVERY SYSTEM

The basic components of buccal drug delivery systems are
1) Drug substance
2) Bioadhesive polymers
3) Backing membrane
4) Permeation enhancers

Drug substance: The selection of suitable drug for the design of buccoadhesive drug delivery systems should be based on pharmacokinetic properties. The drug should have following characteristics.
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.
➢ Tmax of the drug shows wider-fluctuations or higher values when given orally.
➢ Through oral route drug may exhibit first pass effect or presystemic drug elimination.
➢ The drug absorption should be passive when given orally. [24]

Bioadhesive polymers: Polymers are also used in matrix devices in which the drug is embedded in the polymer matrix, which controls the duration of release of drugs. The drug is released into the mucous membrane by means of rate controlling layer or core layer. Bioadhesive polymers which adhere to the mucin epithelial surface are effective and lead to significant improvement in the oral drug delivery. The specialist can have these additional features as swelling in order to promote the disintegration on in meet for the saliva. [26,27] An ideal polymer with account to buccoadhesive drugs delivery resources should have subsequent Characteristics. Polymer need one high molecular stress upto 100.00 or more it is necessary to promote the adhesiveness between the polymer and mucus. This should be inert and compatible with the society. It would make high viscosity. The polymer and its degradation products are usually non-toxic absorbable from the mucous layer. This should adhere instantly to the moist paper surface and would possess such website specificity. Concentration of polymer- a best optimum nurturing is required to promote mucoadhesive strength. [26,27] EX: HPC, CP, HPMC, SodiumCMC, Chitosan, PVP, Xanthumgum etc. [28]
**Backing membrane**: Backing membrane plays a major role in the attachment of bioadhesive devices to the mucus membrane. The materials used as backing membrane be inert, and impermeable to the drug and penetration enhancer. Such impermeable membrane on buccal bioadhesive patches prevents the drug loss and offers better patient compliance. The commonly used materials in backing membrane include carboxopol, magnesium stearate, HPMC, HPC, CMC, polycarbophil etc. [28]

**Permeation enhancer**: [29] Substances that facilitate the permeation through buccal mucosa are referred as permeation enhancers. Selection of enhancer and its efficacy depends on the properties of the drug, site of administration, nature of the vehicle and other excipients.

Mechanisms of action of permeation:
1) Changing mucus rheology:
By reducing the viscosity of the mucus and saliva overcomes this barrier.
2) Increasing the fluidity of lipid bilayer membrane:
Disturb the intracellular lipid packing by interaction with either lipid packing by interaction with either lipid or protein components.
3) Acting on the components at tight junctions:
By inhibiting the various peptidases and proteases within buccal mucosa, thereby overcoming the enzymatic barrier.
In addition, changes in membrane fluidity also alter the enzymatic activity indirectly.
4) Increasing the thermodynamic activity of drugs:
Some enhancers increase the solubility of drug there by alters the partition coefficient.
EX: Sodium glycodeoxycholate, oleicacid, azone etc.

**BUCCAL FORMULATIONS** [16]
The size of the delivery system varies with the type of formulation, i.e., a buccal tablet may be approximately 5–8mm in diameter, whereas a flexible buccal patch may be as large as 10–15cm2 in area. Mucoadhesive buccal patches with a surface area of 1–3 cm2 are most acceptable. It has been estimated that the total amount of drug that can be delivered across the buccal mucosa from a 2-cm² system in 1 day is approximately 10–20 mg. The shape of the delivery system may also, although for buccal drug, an ellipsoid shape appears to be most acceptable. The thickness of the delivery device is usually restricted to only a few millimeters. The location of the delivery device also needs to be considered The maximal duration of buccal drug retention and absorption is approximately 4–6 h because food and/or liquid intake may require removal of the delivery device.

1) Buccal Tablets
2) Buccal Patches and Films
3) Buccal Semisolids(ointments and gels)
4) Buccal Powders

**BUCCAL TABLETS FORMULATION**
A buccal tablet may be approximately 5–8mm in diameter.
- Buccoadhesive tablet may be monolithic or bilaminated system.
- Monolithic is multidirectional release.
- Bilayered containing core layer & backing layer.
- Backing layer may be of water insoluble material like Ethyl cellulose or hydrogenated caster oil or may be polymeric coating layer
- Backing layer avoids sticking of the tablet to the finger during application.

1. **Buccal tablets**: [12,31] Monolithic, two-layered and three layered matrix tablets have been designed for buccal delivery of drugs. Monolithic tablets consist of a mixture of drug with a swelling bioadhesive/sustained release polymer with a bidirectional release. They can be coated on the outer or on all sides but one face with water impermeable hydrophobic substances to allow a unidirectional drug release for systemic delivery. Bioadhesive tablets are usually prepared by direct compression, but wet granulation techniques can also be used. If necessary, the drug may be formulated in certain physical states, such as microspheres, prior to direct compression in order to achieve some desirable properties, e.g. enhanced activity and prolonged drug release. The matrix of the tablet is solidified while the drug is in solution. After melting, the drug is automatically in solution and available for absorption, thus eliminating dissolution as a rate-limiting step in the absorption of poorly soluble compounds. Two layered tablets comprise an inner layer based on a bioadhesive polymer and an outer non-bioadhesive layer containing the drug for a bi-directional release but mainly a local action. In the case of systemic action, the drug is loaded into the inner bioadhesive layer whereas the outer layer is inert and acts as a protective layer. Alternatively, the drug is loaded into a controlled release layer and diffuses towards the absorbing mucosa through the bioadhesive layer, whereas a water impermeable layer assures the monodirectional release. Different drugs have been loaded in matrix tablets, such as propanolol, timolol, metronidazole, metoclopramide, morphine sulphate, nitroglycerin and codein. Peptides, such as insulin, calcitonin and glucagon-like peptide were also loaded in buccal mucoadhesive tablets.
THREE LAYERED BUCCAL COMPACT:
Multilayered matrix tablet are proving to be more potential among the various formulations in the development of oral controlled release dosage form containing highly water-soluble drug to prevent the faster release and dose dumping. The backing layer contains EC and Mg stearate. EC was selected because of its hydrophobic nature and has low water permeability, moderate flexibility, thus preventing drug loss by backward diffusion. Mg stearate was included as anti-adherent MT, sodium alginate and HPMC K4M comprises the core layer. HPMC K4M is a water swellable polymer which controls the release of drug from the core layer by forming a matrix or gel layer. Peripheral layer which adhere to the mucosa should possess good bioadhesive strength and also control the release. Hence, carbopol 934P a potential mucoadhesive polymer along with HPMC K4M was included in peripheral layer.

2. Buccal patches and films: Buccal patches consists of two ply laminates or multilayered thin film round or oval as consisting of basically of bioadhesive polymeric layer and impermeable backing layer to provide unidirectional of drug across buccal mucosa. Buccal bioadhesive films are formulated by incorporating the drug in alcohol solution of bioadhesive polymer. Example: Isosorbid dinitrade in the form of unidirectional erodible buccal film are developed and characterised for improving bioavailability. Buccal film of salbutamol sulphate and terbutaline sulphate for the treatment of asthma Buccoadhesive film of clindamycin used for pyorrhoea treatment.

3. Buccal semisolid dosage forms: A buccal semisolid dosage form consists of finally powdered natural or synthetic polymer dispersed in a polyethylene or in aqueous solution. Example: Gels, Ointments, orabase.

1. Gels are usually clear, transparent, semisolids containing solubilized active substances.
2. Forming hydrophilic polymers is typically used for lipid-freesemisolid dosageforms, e.g. Methylcellulose, carbopol, hydroxyl ethylcellulose etc.
3. Vehicles containing therapeutic agents are especially useful for application to mucus membranes and ulcerated or burned tissues, because their high water content reduces irritancy.
4. Due to plastic rheological behaviour they can remain to the surface of application for a reasonable duration before they are washed off.

5. In comparison to solutions, gels can significantly prolong residence time and hence improve bioavailability. Eg. Glibenclamide.
6. One of the original oral mucosal-adhesive delivery systems- orabase” consists of finely ground pectin, gelatin and sodium carboxy methyl cellulose dispersed in a poly (ethylene) and a mineral oil gel base, which can be maintained at its site of application for 15-150 minutes.

4. Buccal powder dosage forms: Buccal bioadhesive powder dosage forms are a mixture of bioadhesive polymers and the drug and are sprayed onto the buccal mucosa. Yama moto et al., have described a hydroxypropylcellulose and beclomethasone containing powder that was sprayed on the oral mucosa of rats. A significant increase in the residence time relative to an oral solution was seen, and 2.5% of beclomethasone was retained on buccal mucosa for over 4 hours.

METHODS TO INCREASE DRUG DELIVERY VIA BUCCAL ROUTE [30]

Absorption enhancers: Absorption enhancers demonstrated its own performance to send high molecular weight ingredient, such as peptides, which probably exhibit shortage of buccal absorption rates. These may act through a differently machine, such as developing the fluidity of the panel membrane, getting away of inters/intracellular lipids, moving cellular protein or altering floor mucin. The most common intake enhancers are generally azone, fatty chemicals, bile salts and surfactants such as sodium dodecyl sulfate. Solutions greases of chitosan remained and found to show both the transport on mannitol and fluorescent-labelled dextrans across one tissue society kind of the buccal epithelium and Glyceryl monooleates were reported to enhance peptide intake through a co-transport mechanism.

Prodrugs: Hussain et al delivered opioid agonists and antagonists in bitterless prodrug variety and found that the drug used with lack of bioavailability as prodrug. Nalbuphine and naloxone bitter drugs when utilized to animals through the buccal mucosa, the triggered excess salivation and consuming. As a result, the drugs exhibited lack of bioavailability. Administration of nalbuphine and naloxone in prodrug form caused no adverse effects, with bioavailability ranging from 35-50% showing marked improvement over the oral bioavailability of these compounds, which is generally 5% or less.

pH: Shojai et al evaluated permeability on acyclovir at pH lines on 3.3 to 8.8, and the efforts of the
absorption enhancement, sodium glycocholate. The
beneath vitro permeability on acyclovir was access to
be pH dependent and to increase beneath flux and
also permeability coefficient at either pH acute (pH
3.3 and 8.8), compared to the mid-range values (pH
4.1, 5.8, and 7.0).

METHODES OF EVALUATION: [19]

- Hardness test
- Friability test
- Thickness test
- Methods determining shearstress
- Methods determining tensile strength
- Invitro swelling studies
- Invitro permeation studies
- Invitro surface pH studies
- Invitro mucocoahesion strength
- Invitro drug release studies
- Invivio release studies

Measurement of bioadhesive strength of buccal
dosage forms: [17,18]

Modified physical balance test:
Bioadhesive strength of the tablet was measured on
the modified physical balance. The design used for
measuring the bioadhesive strength was shown in
Fig. The apparatus consist of a modified double beam
physical balance in which the right pan has been
replaced by a glass slide with copper wire and
additional weight, to make the right side weight equal
with left side pan. A teflon block of 3.8 cm diameter
and 2 cm height was fabricated with an upward
portion of 2 cm height and 1.5 cm diameter on one
side. This was kept in beaker filled with phosphate
buffer pH 6.8, which was then placed below right
side of the balance. Goat buccal mucosa was used as
a model membrane and phosphate buffer pH 6.8 was
used as moistening fluid. The underlying mucous
membrane was separated using surgical blade and
wash thoroughly with phosphate buffer pH 6.8. It
was then tied over the protrusion in the Teflon block
using a thread.

The block was then kept in glass beaker. The beaker
was filled with phosphate buffer pH 6.8 up to the
upper surface of the goat buccal mucosa to maintain
buccal mucosa viability during the experiments. The
one side of the tablet was attached to the glass slide
of the right arm of the balance and then the beaker
was raised slowly until contact between sheep
mucosa and buccoadhesive dosage form was
established. A preload of 10 mg was placed on the
slide of tablet and goat buccal mucosa for 5 min
(preload time) to establish adhesion bonding
between buccoadhesive and the buffer media. The
preload and preload time were kept constant for all
formulations. After the completion of preload time,
 preload was removed from the glass slide and water
was then added in the plastic bottle in left side arm by
peristaltic pump at a constant rate of 100 drops per
min. The addition of water was stopped when
buccoadhesive tablet was detached from the goat
buccal mucosa. The weight of water required to
detach buccoadhesive tablet from buccal mucosa was
noted as bioadhesive strength in grams. From the
bioadhesive strength following parameter was
calculated.

Force of adhesion (N) = Bioadhesive strength (g)
\times 9.81/1000 Bond strength (Nm-2) = Force of
adhesion/Disk.

RECENT INNOVATIONS

1. Biobadhesive Spray: Buccoadhesive sprays are
gaining popularity over other dosage forms because
of flexibility, comfort, high surface area and
availability of drug in solution form. The fentanyl
Oralet ™ is the first FDA-approved (1996)
formulation developed to take advantage of oral
transmucosal absorption for the painless
administration of an opioid in a formulation
acceptable to children. In 2002, the FDA approved
Subutex (buprenorphine) for initiating treatment of
opioid dependence (addiction to opioid drugs,
including heroin and opioid analgesics) and
Suboxone (buprenorphine and naloxone) for
buccal spray was approved for commercial marketing
and sales in Ecuador.

2. Gel Forming Liquids:

This type of a formulation is liquid upon instillation
and undergoes a phase transition to form a
viscoelastic gel in response to stimulus such as
temperature, ionic strength or pH. Carbomers become
more viscous upon increased pH. Poloxamers and
smart hydrogel®( Advanced medical solution) gel at
approximately body temperature. Gellan gum and
alginate both form gel in response to stimulus such as
increase in ionic strength (particularly with Ca2+ ions). Gel forming
formulations are currently used for sustained ocular
delivery. Recent work has examined the oesophageal
retention of smart Hydrogel®, a liquid that gel in
response to both high force and temperature, with its
gelling temperature at about 32°C.

CONCLUSION:

Buccal route is becoming more and more popular
because it does have significant advantages like
avoidance of first pass metabolism in the liver and pre-systemic elimination in the gastrointestinal tract. Buccal drug delivery holds a great promise for systemic delivery of orally inefficient drugs as well as a feasible and attractive alternative for non-invasive delivery of potent peptide and protein drug molecules. However, the need for safe and effective buccal permeation/absorption enhancers is a crucial component for a prospective future in the area of buccal drug delivery.

**Fig 1:** Cross-section of buccal mucosa

**Fig 2:** Different release geometry for buccal dosage form

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