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Review Article

**A Review on Basics Behind Development of
Muco Adhesive Buccal Drug Delivery Systems**

**KV. Shijith^{1*}, Sarath Chandran C², KV. Vipin² and Ann Rose Augusty² and
K. Premaletha²**

¹Department of Pharmaceutics, Academy of Pharmaceutical Sciences, Pariyaram Medical College,
Pariyaram, Kannur District, Kerala, India.

²Department of Pharmaceutics, Academy of Pharmaceutical Sciences Pariyaram, Kerala, PIN:
670503, India.

ABSTRACT

Oral route is the most convenient route of drug delivery because of several advantages. But due to some reasons such as high first pass metabolism, drug degradation in the GIT etc, certain drugs are not an ideal candidate for conventional route. So in order to retain the patient compliance and also to achieve controlled release, muco adhesive system may be a better choice. The property and existence of such system mainly depends on the polymeric platform, and its interaction with the drug. Several other excipients such as permeation enhancers, plasticizer, etc are also used in order to modify the release pattern and to improving the stability of the formulation. This article briefly describes the basis, requirement, and the standards of an ideal muco adhesive buccal drug delivery.

Keywords: buccal patches, muco adhesion, muco adhesive polymers, permeation enhancers.

INTRODUCTION

Controlled drug delivery systems have become the one of the finest delivery tools developed by the formulation developers. Availability of wide choice of natural and synthetic polymers has made controlled delivery research highly interesting as well as result oriented. In conventional as well as in controlled drug delivery system, oral route is considered as the primary choice, because of its convenience and several other advantages. But in some cases, for example-if the drugs is highly susceptible to the acidic condition of the stomach or possess high first pass metabolism, oral route may not be an efficient way for the drug delivery. To overcome such problems, various mucoadhesive systems has been developed to release drugs through various routes other than the oral (Eg:- buccal, nasal, vaginal etc). The mucosal lining of buccal cavity is an attractive drug delivery site since it is one of the most convenient ways to achieve controlled drug delivery. For achieving a controlled delivery of drug through mucosal lining, the drug or delivery system should stay with the mucosal layer for sufficiently longer period of time for which the bio adhesive mechanism was found

to be a better choice. When a drug delivery system comes in contact with the mucosal layer by utilizing the bio adhesion mechanism it is called as "muco adhesive drug delivery system"^{1,2}. These developed muco adhesive systems mainly utilizes certain properties of selected polymer, which becomes bio adhesive on hydration.

Mucoadhesive buccal drug delivery system should have following ideal characteristics which enables them to deliver the drug through the polymer across the membrane in a most efficient and controlled rate.

- Quick adherence to the buccal mucosa and sufficient mechanical strength.
- Drug release in a controlled manner.
- Improves the rate and extend of drug absorption
- Should have good patient compliance.
- Should not hinder normal functions such as talking, eating and drinking.
- Should accomplish unidirectional release of drug towards the mucosa.
- Should not aid in the development of secondary infections such as dental carriers

- Provide wide margin of safety both locally and systemically.
- Should have good resistance to the flushing action of saliva.^{3,4,5}

Based on these ideal characteristics, following are the advantages and disadvantages of the mucoadhesive buccal systems.

Advantages of mucoadhesive buccal systems,

- Ease of drug administration and termination of drug action can be easily accomplished.
- Permit localization or retention of the drug to the specified area of oral cavity for extended period of time.
- Bypass hepatic first pass metabolism.
- Drug with poor bio availability due to high first pass metabolism can be administered conveniently
- No energy required as the mode of absorption is passive.
- Ease of drug administration to unconscious patient.
- Water content of saliva is being capable to ensure drug dissolution.
- Drugs can be suitably delivered which are proved to be degraded in acidic condition.
- These systems allow local modification of tissue permeability, inhibition of protease activity and reduction in immunogenic response and hence can selectively be used for peptidase, proteins, and ionized species delivery.¹

Disadvantages of mucoadhesive buccal systems

- Drug with large dose are difficult to administer
- Eating and drinking may be restricted.
- Possibility of the patient to swallow the formulation.
- This route cannot administer drug, which are unstable at buccal pH.
- This route cannot administer drug, which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odour.^{1,2}

Apart from the listed advantages, the mucoadhesive buccal systems are able to improve the bioavailability of drugs by localizing the delivery of drugs in a particular region alone. The strong interaction between polymer and mucosal lining of the tissue allows increased contact time, modification of tissue-membrane permeability and localization of drug delivery which results in this improved bioavailability of drugs through mucoadhesive buccal delivery systems. It is also possible to inhibit the metabolizing enzyme in the localized region of mucoadhesion.

Muco adhesive drug delivery system in oral cavity may be divided in to three, they are

1. Sublingual – involve administration of drug via the sublingual mucosa to the systemic circulation.
2. Buccal delivery – involve administration of drug through the buccal mucosa to the systemic circulation
3. Local delivery – involve the administration of bio adhesive system either the palate, gingiva, or the cheek².

Overview of buccal mucosa

A. Structure

The oral mucosa is anatomically divided into

- 1) Epithelium
- 2) Basement membrane and Connective tissues.

1) Epithelium

The epithelium consists of approximately 40–50 layers of stratified squamous epithelial cells having thickness 500-800µm. The epithelium of the oral mucosa serves as a protective covering for the tissues and a barrier to the entry of foreign materials. These functions are reflected in the organization of the epithelium in which individual epithelial cells are closely opposed and stratified so there are a number of layers that show a sequence of differentiation. The uppermost layers form a surface that is resistant to physical insult and to penetration by foreign substances. 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 glycosphingolipids. 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.¹

2) Basement Membrane and Connective Tissue

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. This basal complex anchors the epithelium to the connective tissue and supplements the barrier function of the superficial layers of the epithelium to prevent some large molecules from passing the oral mucosa. The bulk of connective tissue consists of a collagen fiber network, the organization of which determines mechanical stability, resistance to deformation and extendibility of the tissue. Most likely, 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.

B. Environment

The oral cavity is marked by the presence of saliva produced by the salivary glands and mucus which is secreted by the major and minor salivary glands as part of saliva.

Role of Saliva

- Protective fluid for all tissues of the oral cavity.
- Continuous mineralization / demineralization of the tooth enamel.
- To hydrate oral mucosal dosage forms.

Role of Mucus

- Made up of proteins and carbohydrates.
- Cell-cell adhesion
- Lubrication
- Bioadhesion of mucoadhesive drug delivery system¹.

Biochemistry of oral mucosa

All the layer of the oral mucosal membranes contain a large amount of protein in the form of tonofilaments, consisting at least seven protein called “keratins” with molecular size of 40-70 KDa. Both keratinized and non-keratinized tissue of varying thickness and composition are found in oral cavity. Keratinized and non-keratinized tissue occupies about 50% and 30% respectively of the total surface area of the mouth. The difference between keratinized and non-keratinized epithelia is merely the difference in the molecular size of existing keratins. Cells of non-keratinized epithelia contain lower molecular weight protein while those in keratinized epithelia contain mainly higher molecular weight keratin. The lipid content of the cells varies between tissues.

Development in muco adhesive formulations

The history of muco adhesive drug delivery system was marked with the use of muco adhesive polymers in the development of novel pharmaceutical formulations. In 1947 a drug delivery system with penicillin was prepared by using tragacanth and dental adhesive powders to deliver bio-active agents to oral mucosa. Such successful attempts lead to the development of an important formulation by using CMC and petroleum. A muco adhesive delivery vehicle was developed, consisting of finely grounded sodium CMC, pectin and gelatin, which was later marketed as Orahesive^{R,5}. Subsequent study lead to the development of a system consisting of poly ethylene sheet which was laminated with a blend of sodium CMC and poly (isobutylene). The advantage of such system was, the poly ethylene backing membrane act as a protective barrier of the system from the external environment. During the period of 1980's many polymers such as poly

acrylic acid, hydroxyl propyl cellulose, sodium alginate, guar gum, kary gum, methyl cellulose, etc were proved with good muco adhesive property.

Even though many polymers were proved with their ability to become mucoadhesive, but the actual reason behind this adhesive property was not identified. Finally after plenty of in-depth investigations in this area have helped the scientists to come up with following reasons which may be behind the mucoadhesiveness of the polymers.

- Polymer should form tight intermolecular hydrogen bonding with the mucosal layer.
- Polymer should penetrate in to the mucous network or tissue cervices.
- Polymer should easily wet the mucus layer and should have high molecular weight.

But during the development stage of an ideal mucoadhesive drug delivery system, the formulators focused on some ideal characteristics on the polymer, which include,

- Polymer matrix should rapidly adhere to the mucosal layer.
- Polymer should not change the physical of the delivery matrix.
- Should release the active agent with no or minimum interference.
- Polymer should be degradable without producing any toxic byproduct.
- Should provide a positive environment for the penetration of active agent.^{5,6}

Due to low permeability and absorption most of the therapeutic agents, peptides and proteins are administered by parenteral route which has several known draw backs. Where as in oral cavity, which contains several protease and salivary enzymes, reduces the stability of many drugs. Hence mucoadhesive formulations, having the ability to overcome such undesirable conditions, may be considered as the better delivery route for such drugs.⁷

When administered as mucoadhesive systems, the permeability of drug through epithelium of oral mucosa is mainly through following two mechanisms,

1. Trans cellular (intracellular, passing through the cell).
2. Para cellular (inter cellular, passing around the cell).

Out of these two, permeation across the buccal mucosa mainly takes place through para cellular route.⁸

Mechanism of bio adhesion

Bio adhesion can be defined as the phenomenon of interfacial molecular attractive forces between the biological membrane and the natural or synthetic polymer, which allows the polymer to adhere the biological surface for an extended period of time⁸. During the bio adhesion process, both the

attractive and repulsive forces were insisted at the site, but the attractive forces should have sufficient capacity to overcome the repulsive forces.

The mechanism of mucoadhesion involves two stages,

1. Contact stage

During this stage an intimate contact between the bio adhesion system and membrane has established. When the bio adhesive system approaches the mucous membrane, they come in contact with the repulsive forces (osmotic pressure, electrostatic repulsion etc) and the attractive forces (Vander Waals forces and electrostatic attraction). There for in order to make a good contact, the system must overcome the repulsive barrier by the attractive forces.

2. Consolidation stage

After forming a good contact between the two surfaces, the bio adhesive material penetrate in to the tissue surfaces and a chemical bond or bridge is formed because of the interaction between the chains of the bio adhesive of the mucus membrane¹.

THEORIES OF MUCO ADHESION⁹

The theories of muco adhesion is mainly due to the formation of two types of bond between bio adhesive system and mucus membrane and they are

- a) Chemical bond: This may be due to
 - i. Strong primary bond – that is covalent bond
 - ii. Weak secondary bond – such as ionic bond, Vander- Waals bond, and hydrogen bond
- b) Mechanical bond: This bond arises from the physical connection between two surfaces, similar to the interlocking system.

Both type of bond formation have been exploited in developing different bio adhesive systems. Based on the formation of either type of above bonds, there are following five theories postulated,

- A. Electronic theory.
- B. Adsorption theory.
- C. Wetting theory⁹.
- D. Diffusion interlocking theory.
- E. Fracture theory.

A. Electronic theory^{9,10}

As per this theory, there is difference in the electronic structure of mucin surfaces and bio adhesive system and due to this difference, an electron transfer occurs between the two surfaces when they come in contact with each other. This electron transfer results in the formation of an electronic bi-layer at the interface. This bi-layer exerts an attractive force across the double layer, which may result in an effective muco adhesion^{9,10}.

B. Adsorption theory^{9,10}

This theory describes the involvement of both type of chemical bond, that is, primary and secondary bond in the bio adhesion mechanism. Both the surface that is mucin and drug delivery system has their own surface energy. When they come in contact, the adhesion occurs due to the surface energy and results in the formation of two types of chemical bond. Primary chemical bond such as covalent bond, which is strong in nature, thus produces a permanent bonding, whereas secondary chemical bond involves Vander-Waals forces, hydrophobic interaction and hydrogen bonding, which are weak in nature, thus produces a semi-permanent bond^{9,10}.

C. Wetting theory¹⁰

This theory mainly applicable to liquids or low viscous muco adhesive system. This theory gives idea about the spreadability of the drug delivery system across the biological layer. According to this theory, the active components penetrate in to the surface irregularities and gets harden itself¹⁰.

D. Diffusion inter locking theory¹⁰

This theory describes the involvement of a mechanical bond between the polymeric chain of drug delivery system and polymeric chain of mucus membrane, that is, glycol proteins. When two surfaces are in intimate contact, the polymeric chain of drug delivery system penetrates in to the glycoprotein network. Here the bio adhesion primarily depends on the diffusion coefficient of both polymers. The other factors that may influence the inter movement of polymeric chain are molecular weight, cross linking density, chain flexibility, and temperature in order to achieve a good bio adhesion, the bio adhesive medium should have a similar solubility with glycoprotein resulting in effective muco adhesion¹⁰.

E. Fracture theory¹⁰

This theory based on the fact that, the force required to detach the polymeric chain from the mucin layer is the strength of their adhesive forces. The fracture strength can be determine by using the formula

$$G = (E \cdot e/L)^{1/2}$$

G- Fracture strength,

E- Young's modules of electricity,

e- Fracture energy,

L- Critical crack length.

Factors affecting muco adhesion in the oral cavity

The oral muco adhesivity of a drug delivery system may depend on the bio adhesive polymer, as well as the surrounding medium, in which the polymer

will reside. These factors are broadly divided in to two

- A. Polymer related factors
- B. Environmental factors

A. Polymer related factors

1. Molecular weight

For a linear polymer, the bio adhesive property is directly proportional to the molecular weight. For example- PEG having different molecular weights. PEG having molecular weight of 20,000 has little adhesive character, whereas PEG having molecular weight of 2,00,000 has enhanced adhesive property, and PEG having molecular weight 4,00,000 has superior adhesive property.

But in case of nonlinear polymer, the bio adhesiveness may or may not depend on molecular weight. This is mainly because the helical or coiled structures of such polymer may shield some of the adhesive group, which are mainly responsible for the adhesive property. Eg: The adhesive property of dextran having a molecular weight of 19,50,000 is similar to that of PEG having a molecular weight of 2,00,000, due to helical structures of Dextran, that may shield many of adhesive groups⁵.

2. Flexibility and mobility of polymer chain

For an effective bio adhesion, the polymer chain should effectively diffuse in to the mucus layer. For achieving such diffusion, the polymer chain should have sufficient flexibility which depends on the viscosity and diffusion coefficient. Higher flexibility of polymer causes greater diffusion in to mucus network⁸.

3. Concentration of active polymer

At low concentration, only small number of polymeric chain is available for interaction with the mucus, therefor interaction is unstable. At higher concentration, the polymer become coiled, and coiled molecule become separated from the medium, therefore chain available for the penetration gets reduced. Therefore there should be an optimum concentration for each bio adhesive polymer, which results in a better and stable adhesion for a longer period^{5,8}.

4. Hydrogen bonding capacity

For an effective muco adhesion, the polymer should have functional group to form hydrogen bonding⁸.

5. Cross linking density

The cross linking density indicates the number of average molecular weight of the cross linked polymer, which determines the average pore size. When the cross linking density is higher, then the pore size becomes small, so that diffusion of water in to the polymer network occurs at a lower rate, thus there is only an insufficient swelling of

polymer resulting in decreased penetration of polymer in to the mucin⁸.

6. Charge

The bio adhesive property of ionic polymer always higher than that of non-ionic polymer. In neutral or slightly alkaline medium, the cationic polymer shows superior muco adhesive property. It has been proven that, cationic high molecular weight polymer such as chitosan possess good bio adhesive property⁸.

7. Hydration or swelling

Proper hydration to muco adhesive polymer is essential to create macromolecular mesh of sufficient pore size and also induces mobility, which are necessary for enhancing the interpenetration⁸.

B. Environmental factors

Environmental factors, indicating the surround media and physiological condition with which the polymeric bio adhesive drug delivery system will reside should be a concern before designing the bio adhesive system⁸.

1. Saliva

Saliva as the dissolution medium, affect the behavior of the polymer and should affect the bio adhesion property of the polymer. The salivary flow rate and pH of the saliva should be essential. Moving of buccal tissue during eating, drinking and talking may interfere the bio adhesion property of the polymer. During the designing of such drug delivery systems care should be given to minimize the detachment of drug delivery system due to such interference⁸.

2. Applied strength

While placing a buccal muco adhesive drug delivery system, sufficient strength should be applied in order to provide a good bio adhesive property. Even though there is no attractive forces between polymer and mucus, then application of high pressure for sufficient long time make the polymer become bio adhesive with mucus⁵.

3. pH

pH of the medium is important for the hydration of bio adhesive property. Usually pH between 6.5-7.5 is ideal for muco adhesive property. The muco adhesive property reduces as the alkalinity or ionic strength reduces⁵.

4. Initial contact time

There should have a sufficient initial contact between polymer and mucus in order to ensure the swelling and interpenetration of polymeric chain⁵.

5. Mucin turn over

High mucin turn over is not beneficial for the muco adhesive property because of following reasons;

- a) The high mucin turn over limit the residence time of bio adhesive polymer as it detaches from the mucin layer, even though it has a good bio adhesive property.
- b) High mucin turn over may produce soluble mucin molecule, thus molecule interact with the polymer, before they interact with mucin layer. Hence there will not be sufficient muco adhesion⁵.

6. Disease state

The physic chemical property of mucus may alter during some disease state, such as common cold, gastric ulcers, ulcerative colitis, bacterial and fungal infections etc. Thus alteration in the physiological state may affect the bio adhesive property⁵.

Factors Affecting Drug Absorption From The Oral Mucosa

The major factor influencing the drug absorption from the oral mucosa may be broadly divided in to following groups

1. Physico chemical property of the drug.
2. Physiological factors or membrane factors.
3. Miscellaneous.

1. Physico chemical properties of drug

1. Molecular weight

As compared to ions, the molecules penetrate rapidly, through oral mucosa. The molecular weight and size is important in the penetration through the oral mucosa, especially in case of hydrophilic molecule having a molecular weight of below 100 Dalton can cross the oral mucosa very rapidly. As the molecular weight increases, the penetration diminishes⁹.

2. Degree of ionization

Degree of ionization and pKa value plays a role in the absorption. For acidic drug, pKa greater than 2 shows adequate absorption through oral mucosa and for basic drug, pKa less than 10 shows good absorption⁹.

3. Lipid solubility

O/W partition coefficient shows the lipid solubility of the drug. For optimal drug absorption, partition coefficient between 40-2000 is necessary. In addition to high lipid solubility, the drug should be soluble in aqueous buccal fluid for absorption⁹.

B. Physiological factors affecting drug absorption

1. Oral mucosa

Oral mucosa is a highly vascular tissue and always shows higher permeability as that of skin. Based on the relative thickness and degree of keratinization,

difference in permeability. In general sub lingual region shows higher permeability than buccal region. Buccal region has higher permeability than palate⁴. For most of the drugs, the superficial layer of oral mucosa is the penetration barrier. But for some endo toxins, the basement membrane of non keratinized oral mucosa act as penetration barrier. The surfactant present in the oral cavity, due to the usage of tooth paste, mouth washes etc may also affect the absorption of drug through oral mucosa¹¹.

2. Saliva and salivary gland

A thin film of saliva always present throughout the buccal mucosa. The thickness, composition and movement of saliva affect the buccal absorption. The salivary pH also affect the buccal absorption. Un ionized drug shows maximum absorption in salivary pH⁹. Salivary gland consistently secrete mucus on surface of buccal mucosa. Even though the mucus helps to retain the muco adhesive property of dosage form, it act as a potential barrier to drug penetration¹¹.

3. Blood supply

As the oral cavity is highly vascular, the drug molecule, which crosses the oral epithelium are readily absorbed in to the systemic circulation².

C. Miscellaneous

Some drug may bind to oral mucosa, and systemic availability of such drug is very poor. Some drug may stay in the storage compartment of buccal mucosa, resulting in a poor absorption⁹.

Different types of novel muco adhesive buccal drug delivery systems

Even though the muco adhesive buccal drug delivery offers some distinct advantages, the ideal candidate for designing such formulations is always limited due to several factors. One of the important factor is size limitation. For an effective and comfortable buccal drug delivery system, the quantity of drug moiety enclosed should be reasonably small, ideally 25 mg or less is more appropriate for buccal drug delivery². The drugs having a short biological half life can be formulated as buccal drug delivery, and thus offering a sustained, prolonged and controlled delivery of drug from the designed dosage form.

The different type of buccal drug delivery system includes, adhesive tablets, adhesive gels, adhesive patches, adhesive ointments, adhesive powders and buccal chewing gums etc.

Adhesive Tablet⁹

These are similar to conventional tablets, but they have the property of muco adhesion, and instead of swallowing, they held in between cheeks and gums. These tablets are sufficiently dissolved by the

medium, provided from locations where they are placed. But the dissolution of tablet should be slow in order to ensure a sustained and controlled release. A care should be given to ensure the controlled dissolution of such dosage forms. Hence the adhesive tablets does not contain any disintegrants. The usage of flavoring agent and sweeteners will be minimum, in order to control the flow rate of saliva. The higher flow rate of saliva should not be beneficial for an adhesive tablet because of two reasons

1. Higher salivary production may cause higher dissolution of adhesive tablet. As a result higher amount of drug may detaches from the stomach results in the decreased amount of drug to cross the buccal mucosal membrane.
2. Higher salivary production may force the patient to swallow or spitting of saliva that may contain drug.

Buccal adhesive tablets are prepared either by procedure used for granulation or by direct compression. During the formulation, care should be given to ensure that all ingredients should be finely grinded form. This is because the buccal adhesive tablet should stay in the mouth for a longer period and if it is not grounded well, then there will be a chance of irritation. The buccal bio adhesive tablet may be monolithic or bilaminated form. The main disadvantage with monolithic form is the multidirectional release, so that the chances of swallowing of drug will be more.

In order to avoid such disadvantages, bi layered muco adhesive tablets were formulated. This tablet has two layers – drug containing core layer and a backing layer. Usually water insoluble polymer like ethyl cellulose is used for the constriction of backing layer. The other advantages of bilayered system includes, avoiding sticking of the tablet to the finger during the application in the oral cavity.

Buccal adhesive patches or filims¹²

The muco adhesive buccal patches can be of two types,

a) Matrix type

Drug, adhesive and additives mixed together and this mixture is then designed in the form of patches.

b) Reservoir type

Drug and additives should be separated from the additives.

Depending on the presence or absence of a backing membrane, the release from the patch is unidirectional or bi-directional. The presence of backing membrane offers a unidirectional drug release, which reduces patch deformation and disintegration and ultimately prevent drug loss and offers a sustained and controlled release. The unidirectional patches release the drugs only to the

mucous layer. On the other hand patches without backing membrane offers a bi-directional release of drug. Thus drug releases in to both mucosa and mouth, hence offering a rapid dissolution of drug. These patches are mainly used for designing of drug for rapid onset of action.

The adhesive part of the buccal patches may be used as a drug carrier or help in the retention of the drug in the non adhesive layer. It also helps to increase the residence time of the patches in the desired site.

Adhesive semisolid preparation (gel and ointment)^{9,11}

These types of drug delivery systems are mainly used for local effect and have less patient acceptability than solid bio adhesive dosage form. But compared to solutions, they can prolong the residence time and shows higher bio availability. Usually hydrophilic gel forming polymers are used for the formulation of adhesive semisolid preparations (eg: methyl cellulose, carbopol, hydroxyl ethyl cellulose etc). These are usually used to treat buccal ulcers and burned buccal tissues. The major advantage with these systems is that they shows a plastic rheological behavior, and thus offer a prolonged residence time with the surface application.

Buccal chewing gum¹²

Medicated chewing gum is particularly used in the treatment of oral cavity and in nicotin replacement therapy. The major drawback of such formulation is that, it is very difficult to regulate the administered dose.

One of the best example for such formulation is Nicotin chewing gum (Nicorette^R and Nicotinell^R), It is found to increase the acceptability of such formulation for cessation of smoking. Such formulations slowly generate a steady state plasma concentration, rather than the rapid sharp peak which occurs during the smoking. The major drawback with nicotin chewing gum is the considerable loss of nicotin due to swallowing which leads to first pass metabolism and gastric discomfort, thus reducing the effectiveness of such preparation.

Buccal patches are preferred as best mucoadhesive buccal drug delivery system because of its flexibility and patient comfort¹³.

CONCLUSION

As the technologies in pharmaceutical field is developing in a faster rate, the researchers are focusing to replace the conventional delivery system with the novel system, in order to getting the advantages of novel system such as low toxicity, more patient compliance etc. Muco adhesive system was found to be a better alternative to the conventional oral route. This

review concludes that, the muco adhesive system reduces the toxicity, help to overcome the first pass metabolism, suitable for the drug which may reduce in the acidic pH of the stomach, shows a controlled release of drug, ease of application, and the formulation and evaluation of such systems does not have any complication. So we can expect that the muco adhesive system may be one of the important dosage form in the future pharmaceutical and health care sector.

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