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AN OVERVIEW ON MUCOADHESIVE BUCCAL FILM

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Abstract: *Amongst the diverse routes of drug delivery, oral route is the most desirable to patient and clinician. Peroral administration of drugs has various disadvantages such as first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucosa are considered as potential sites for drug administration. Transmucosal routes of drug delivery offer distinct advantages over peroral administration for systemic drug delivery.*

Key words: *Buccal drug delivery, Oral mucosa, Mucoadhesion, Bioadhesive, Mucoadhesive.*

In recent years, significant interest has been shown in the development of controlled drug delivery to, or via mucous membranes by the use of bioadhesive polymers.[1] Oral route is most preferred route of drug administration but solubility and first pass metabolism sensitivity of drug are important characteristic to be accepted by this route.[2] Buccal region act as a route for many drugs to be delivered into the system. Though less permeable in comparison to the sublingual area, the buccal mucosa is well vascularized and drugs can be rapidly absorbed into the systemic circulation underneath the oral mucosa.[3] The mucosa of the buccal area has a large, smooth and relatively immobile surface, which provides a larger contact surface. The large contact surface of the buccal mucosa contributes to rapid and extensive drug absorption.[4] Buccal drug delivery is well accepted by patients as the buccal cavity is easily accessible for self-medication. In addition, buccal dosage forms allow drug absorption to be rapidly terminated in case of an adverse reaction. Formulations of buccal dosage forms include adhesive tablets, gels, and patches of which patches are preferable in terms of flexibility and comfort [5-11].

Mucoadhesive drug delivery system through *Buccal*, sublingual, rectal and nasal mucosa can be faster and systemic mode of non-invasive drug administration to bypass first pass metabolism. Faster delivery and enhanced bio availability of drugs is observed through mucoadhesive administration.[12] Mucoadhesion is a state in which 2 materials, one of which is mucus or a mucous membrane, is held together for an extended period of time.[13] Various mucoadhesive polymers have been investigated and identified are generally hydrophilic macromolecules that contain numerous hydrogen bond forming groups, and will hydrate and swell when placed in contact with an aqueous solution.[14]

Mechanism of mucoadhesion:

Contact between a pressure - sensitive adhesive material and a surface is called as adhesion, which can be defined as the state in which two surfaces are attached together due to valence interfacial forces or interlocking action or both. [15-17]

Bio adhesion is an adhesion of a synthetic or natural material to biological surface while mucoadhesion is adhesion of material to mucus and/ or an epithelial surface. Mucoadhesion occurs in two stages (Figure 1) depending on nature of dosage form and its delivery:

Stage-I (Contact Stage): wetting, spreading and swelling of the bio adhesive surface creates close contact between a bio adhesive and a membrane. Sometimes additional forces like mechanical system in vaginal delivery, aero dynamics in nasal delivery and peristaltic motions in intestinal delivery of dosage form.[18]

Stage II (Consolidation Stage): moisture breaks molecules and inter penetration or dominant attractive interaction between two surfaces starts due to Vander walls forces, electrostatic attractions, hydrogen bonding and hydrophobic interactions. For complete Bio adhesion attractive forces must overcome repulsive forces. Consolidation step is explained by two theories[19]

Diffusion theory: mucus glycol proteins interact with the mucoadhesive molecules by interpenetrating their chains and forming secondary bonds. This is a chemical as well as mechanical interaction.

Dehydration theory: after contact with mucus, material undergoes dehydration until osmotic pressure balance and jelly mixture of mucus with material is obtained. Solid or hydrated formulation does not work by this theory.[20]

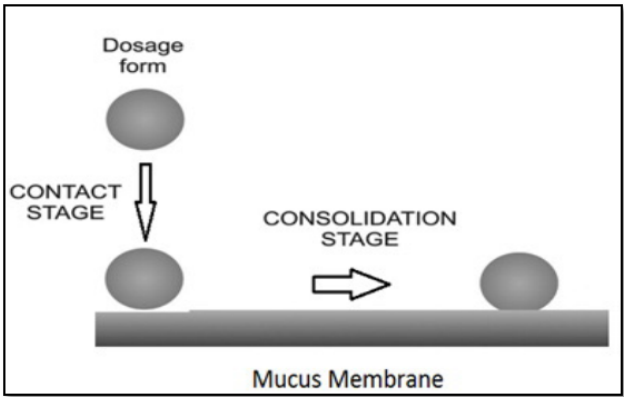

Figure 1: Two steps of Muco-adhesion processes.

Buccal Drug Delivery:

The lip, tongue, cheek, soft palate, hard palate, and floor of mouth comprises oral cavity. Oral mucosal layer consist of three layers: outer epithelium, middle basement and inner connective tissues. 100cm total area of the oral cavity consists of about one third of *Buccal* surface of 0.5mm thickness epithelium.[21]

About 0.5 to 2 litre of saliva runs into oral mucosal surface. PH of salvia varies "between" 5.5 to 7 depending on its flow rate. A neutral lipid like ceramides consisting epithelium is keratinized epithelium while polar lipids like cholesterol sulphate and glucosylceramidesis non-keratinized epithelium.[22]

Non-keratinized region of *Buccal* is most suitable region for drug administration especially proteins/peptides than nasal, rectal and vaginal drug delivery. Drug enters into systemic circulation through jugular ducts via network of blood vessels.[23]

Buccal mucosa, lining of cheek and area between the gums and upper and lower lips is most considerable area for drug delivery. It is estimated that the permeability of the *Buccal* mucosa is 4-4000 times greater than that of the skin.

The order of permeability's of the oral mucosa are sublingual >*Buccal*> palatal which depends on relative thickness and degree of keratinization.[24] Outermost 200 µm of the superficial layer consist of barrier of 'membrane coating granules' (MCG) which varies in keratinized and non-keratinized epithelia.

Intercellular spaces and cytoplasm of oral mucosa being hydrophilic acts as a barrier for lipophilic compounds while cell membrane being lipophilic acts as a barrier for hydrophilic compounds.[25]

To overcome this problem of penetration of high molecular weight compounds, absorption efficieny can be enhanced by few chemicals like fatty acids, bile salts and surfactants such as sodium dodecyl sulfate which are called as absorption enhancers.[26]

Advantages of buccoadhesive drug delivery:[27]

Drug administration via the buccoadhesive drug delivery offers several advantages such as:

1. Drug is easily administered and extinction of therapy in emergency can be facilitated.
2. Drug release for prolonged period of time.
3. In unconscious and trauma patient's drug can be administered.
4. Drugs bypass first pass metabolism so increases bioavailability.
5. Some drugs that are unstable in acidic environment of stomach can be administered by buccal delivery.
6. Drug absorption by the passive diffusion.
7. Flexibility in physical state, shape, size and surface.
8. Maximized absorption rate due to close contact with the absorbing membrane.
9. Rapid onset of action.

Limitations of buccoadhesive drug delivery: [28]

There are some limitations of buccal drug delivery system such as:

1. Drugs which are unstable at buccal pH cannot be administered.
2. Drugs which have a bitter taste or unpleasant taste or an obnoxious odor or irritate the mucosa cannot be administered by this route.
3. Drug required with small dose can only be administered.
4. Those drugs which are absorbed by passive diffusion can only be administered by this route.
5. Eating and drinking may become restricted.

Characteristics of an Ideal Buccoadhesive System: [29-31]

1. Safe and nontoxic.
2. Sufficient patient compliance without hampering normal functions such as talking, eating and drinking.
3. Good mechanical strength.
4. Immediate adherence to the *Buccal* mucosa.
5. Controlled drug release.
6. Optimum drug absorption.

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