INTRODUCTION

Oral drug delivery is the most preferable route of drug administration due to ease of administration, patient compliance, flexibility in formulation etc. There is novel drug delivery system like buccal drug delivery system which is painless and without discomfort, precise dosage form and facilitates ease of removal without significant associated pain. Moreover it shows better stability, patient compliance; uniform and sustained drug release and...
above all easy and cheap methods of preparation which can be done with various commonly available biocompatible polymers. Bioadhesive formulations have a wide scope of application for both systemic and local effects of drugs. The mucosa is relatively permeable, well supplied with both vascular and lymphatic drainage. The oral transmucosal drug delivery bypasses liver and avoids presystemic elimination in the gastrointestinal tract and liver\(^1\).

The term bioadhesion refers to any bond formed between two biological surfaces or a bond between a biological and a synthetic surface. In case of bioadhesive drug delivery, the term bioadhesion is used to describe the adhesion between polymers, either synthetic or natural and soft tissues or the gastrointestinal mucosa. In cases where the bond is formed with the mucus the term mucoadhesion may be used synonymously with bioadhesion. Mucoadhesion can be defined as a state in which two components, of which one is of biological origin are held together for extended periods of time by the help of interfacial forces. Generally speaking, bioadhesion is an term which broadly includes adhesive interactions with any biological or biologically derived substance, and mucoadhesion is used when the bond is formed with a mucosal surface.

Mucoadhesive drug delivery systems includes the following\(^1\):
- Buccal delivery system
- Oral delivery system
- Vaginal delivery system
- Rectal delivery system
- Nasal delivery system
- Ocular delivery system

The buccal region offers an attractive route for systemic drug delivery for extended periods of time. Bioadhesive formulations have a wide scope of applications, for both systemic and local effects of drugs. Over the last two decades mucoadhesion becomes of interest for its potential to optimize localized drug delivery, by retaining a dosage form at the site of action (with in gastrointestinal tract) or systemic delivery, by retaining a formulation in intimate contact with absorption site (in the buccal cavity).

Good defined mucoadhesion as the state in which two materials, at least one biological in nature, are held together for an extended period of time by interfacial forces. It is also defined as the ability of a material (synthetic or biological) to adhere to a biological tissue for an extended period of time. In case of mucoadhesion, the biological tissue is the mucous membrane. For mucoadhesion to occur, a succession of phenomena is required. The first stage involves an intimate contact between a mucoadhesive polymer and a membrane, either from good wetting of the mucoadhesive surface or from the swelling of the mucoadhesive. In the second stage, after contact is established, penetration of the mucoadhesive into the crevice of the tissue surface or interpenetration of the chains of the mucoadhesive with those of the mucus takes place. Low chemical bonds can then settle. Mucoadhesive polymers Mucoadhesive polymers are water soluble and water insoluble polymers, which are swellable networks, jointed by cross-linking agents. These polymers possess optimal polarity to make sure that they permit sufficient wetting by the mucus and optimal fluidity that permits the mutual adsorption and interpenetration of polymer and mucus to take place. Mucoadhesive polymers that adhere to the musin epithelial surface can be conveniently divided into three broad classes:

1. Polymers that become sticky when placed in water and owe their mucoadhesion to stickiness.
2. Polymers that adhere through nonspecific, non covalent interactions that is primarily electrostatic in nature (although hydrogen and hydrophobic bonding may be significant).
3. Polymers that bind to specific receptor site on tile self surface. All three polymer types can be used for drug delivery.

**An ideal mucoadhesive polymer has the following characteristics:**

1. The polymer and its degradation products should be nontoxic and should be non absorbable from the gastrointestinal tract.
2. It should be nonirritant to the mucous membrane.
3. It should preferably form a strong non-covalent bond with the mucin-epithelial cell surfaces.
4. It should adhere quickly to most tissue and should possess some site-specificity.
5. It should allow daily incorporation to the drug and offer no hindrance to its release.
6. The polymer must not decompose on storage or during the shelf life of the dosage form.
7. The cost of polymer should not be high so that the prepared dosage form remains competitive.

Molecular Characteristics:

Investigations into polymers with various molecular characteristics conducted by many authors have led to a number of conclusions regarding the molecular characteristics required for mucoadhesion. The properties exhibited by a good mucoadhesive may be summarized as follows:
1. Strong hydrogen bonding groups (-OH, -COOH).
2. Strong anionic charges.
3. Sufficient flexibility to penetrate the mucus network or tissue crevices.
4. Surface tension characteristics suitable for wetting mucus/mucosal tissue surface.
5. High molecular weight.

Although an anionic nature is preferable for a good mucoadhesive, a range of nonionic molecules (e.g., cellulose derivatives) and some cationic (e.g., Chitosan) can be successfully used.

1.1. Factors Important To Mucoadhesion
The bioadhesive power of a polymer or of a series of polymers is affected by the nature of the polymer and also by the nature of the surrounding media.

1.1.1 Polymer-Related Factors
(a) Molecular Weight:
The optimum molecular weight for maximum bioadhesion depends on the type of bioadhesive polymer at issue. It is generally understood that the threshold required for successful bioadhesion is at least 100,000 molecular weight. For example, polyethylene glycol (PEG), with a molecular weight of 20,000, has little adhesive character, whereas PEG with 200,000 molecular weight has improved, and a PEG with 400,000 has superior adhesive properties. The fact that bioadhesiveness improves with increasing molecular weight for linear polymers imply two things:
- Interpretation is more critical for lower molecular weight polymers to be a good bioadhesive.
- Entanglement is important for higher molecular weight polymers.
- Adhesiveness of a nonlinear structure follows a quite different trend. The adhesive strength of dextran, with a very high molecular weight of 19,500,000 is similar to that of PEG, with a molecular weight of 200,000. The reason for this similarity may be that the helical conformation of dextran may shield many of the adhesive groups, which are primarily responsible for adhesion, unlike the conformation of PEG.

(b) Concentration of active polymers:
There is an optimum concentration of a bioadhesive polymer to produce maximum bioadhesion. In highly concentrated systems, beyond the optimum level, however, the adhesive strength drops significantly because the coiled molecules become separated from the medium so that the chains available for interpenetration become limited.

(c) Flexibility of polymer chains:
It is critical for interpenetration and entanglement. As water-soluble polymers become cross linked, mobility of individual polymer chains decrease and thus the effective length of the chain that can penetrate into the mucus layer decreases, which reduces bioadhesive strength.

(d) Spatial conformation:
Besides molecular weight or chain length, spatial conformation of a molecule is also important. Despite a high molecular weight of 19,500,000 for dextran, they have similar adhesive strength to the polyethylene glycol with a molecular weight of 200,000. The helical conformation of dextran may shield many adhesively active groups, primarily responsible for adhesion, unlike PEG polymers which have a linear conformation.

1.1.2. Environment Related Factors
(a) Applied strength:
To place a solid bioadhesive system, it is necessary to apply a defined strength. Whatever the polymer, poly (acrylic acid / vinyl benzene poly (HEMA) or carbopol 934, the adhesion strength increases with the applied strength or with the duration of its application, up to an optimum (Dchene et al., 1988). The pressure initially applied to the mucoadhesive tissue contact site can affect the depth of interpenetration. If high pressure is applied for a sufficiently long period of time, polymers become mucoadhesive even though they do not have attractive interaction with mucin.

(b) pH:
It can influence the formal charge on the surface of mucus as well as certain ionisable bioadhesive polymers. Mucus will have a different charge density depending on pH due to difference in dissociation of functional groups on the carbohydrate moiety and the amino acids of the polypeptide backbone. pH of the medium is important for the degree of hydration of crosslinked polyacrylic acid, showing consistently increased hydration from pH 4 to 7 and then a decrease as alkalinity and ionic strength increases.

(c) Initial Contact Time:
Contact time between the bioadhesive and mucus layer determines the extent of swelling and interpenetration of the bioadhesive polymer chains. Moreover, bioadhesive strength increases as the initial contact time increases.

(d) Swelling:
It depends on the polymer concentration, ionic concentration, as well as the presence of water. Over hydration results in the formation of a slippery mucilage without adhesion.

1.1.3. Physiological Variables
a) Mucin Turnover:
The natural turnover of mucin molecules is important for at least two reasons. First, the mucin turnover is expected to limit the residence time of the mucoadhesive on the mucus layer. No matter, how high the adhesive strength, mucoadhesive are detached from the surface due to mucin turn over. Second, mucin turnover results in substantial amounts of soluble mucin molecules. These molecules interact with the mucoadhesive before they have a chance to interact with the mucus layer. Mucin turnover may depend on other factors such as presence of food.

b) Disease States:
The physiochemical properties of mucus are known to change during disease conditions such as common cold, gastric ulcers, and ulcerative colitis, and cystic fibrosis, bacterial and fungal infections of the female reproductive tract.

1.2. Classification of Polymers
A short list of mucoadhesive polymers is given below

1.2.1. Synthetic polymers:
Cellulose derivatives (methylcellulose, ethylcellulose, hydroxyethylcellulose, Hydroxypropyl cellulose, hydroxypropyl methylcellulose, sodium carboxy methylcellulose, Poly (acrylic acid) polymers (carbomers, polycarbobphil), Poly (hydroxyethyl methylacrylate), Poly (ethylene oxide), Poly (vinyl pyrrolidone), Poly (vinyl alcohol),

1.2.2 Natural polymers:
Tragacanth, Sodiumalginate, Karaya gum, Guar gum, Xanthan gum, Lectin, Soluble starch, Gelatin, Pectin, Chitosan.

1.2.3. Hydrophilic Polymers:
These are the water-soluble polymers that swell indefinitely in contact with water and eventually undergo complete dissolution, e.g. Methyl Cellulose, Hydroxyl Ethyl Cellulose, Hydroxyl Propyl Methyl Cellulose, Sodium Carboxy Methyl Cellulose, Carbomers, Chitosan and Plant gums.

1.2.4. Hydrogels:
These are water swellable materials, usually a cross-link polymer with limited swelling capacity, e.g. poly (acrylic acid co acrylamide) copolymers, carrageenan, sodium alginate, guar gum and modified guar gum, etc.

1.2.5. Thermoplastic Polymers:
These polymers include the non-erodible neutral polystyrene and semi-crystalline bio-erodible polymers, which generate the carboxylic acid groups as they degrade, e.g. polyanhydrides and polyactic acid. Various synthetic polymers used in mucoadhesive formulations include polyvinyl alcohol, polyanhydrides, polyesters, polycarbonates, polyalkylene glycols, polyvinyl ethers, esters and halides, polyethers, polycarboxylic acid, polyethylenimide, Polyethylene Glycol, Hydroxypropyl Methyl Cellulose, Hydroxypropyl Cellulose, and Sodium Carboxymethyl Cellulose. Various biocompatible polymers used in mucoadhesive formulations include cellulose-based polymers, ethylene glycol polymers and its copolymers, polyvinyl alcohol, polyvinyl acetate, polyvinyl acetate, poly (lactic-co-glycolides), polycaprolactones, polyvinyl cyanoacrylates. Polyoxyethylene, polyphosphoesters, polyorthoesters, polyphosphazenes are the recent additions to the polymers.

1.3. Mucoadhesive Dosage Forms:
The primary objective of mucoadhesive dosage forms is to provide intimate contact of the dosage form with the absorbing surface and to increase the residence time of the dosage form at the absorbing surface to prolong drug action. Due to mucoadhesion, certain water-soluble polymers become adhesive on hydration and hence can be used for targeting a drug to a particular region of the body for extended periods of time. The mucosa lines a number of regions of the body including the gastrointestinal tract, the urogenital tract, the airways, the ear, nose, and eye. These represent potential sites for attachment of any mucoadhesive system.

1.4. Mucoadhesive buccal drug delivery system
Drug delivery via the mucosal membranes of the oral cavity can be subdivided into following parts. Sublingual delivery: Drug administration via sublingual mucosa to the systemic circulation. Buccal delivery: Drug administration via buccal mucosa to the systemic circulation. Local delivery: Drug administration via bioadhesive system either to the palate (the gingival) or the cheek.

1.4.1. Advantages of mucoadhesive buccal drug delivery system
Mucoadhesive via buccal route offers following advantages:

i. Ease of drug administration and termination of drug action can be easily accomplished.

ii. Permits localization or retention of the drug to the specified area of oral cavity for extended period of time.

iii. Bypass hepatic first pass metabolism.

iv. Drugs with poor bioavailability owing to the high first pass metabolism can be administered conveniently.

v. No energy is required as the mode of absorption is passive.

vi. Ease of drug administration to unconscious patients.

vii. Water content of saliva is being capable to ensure drug dissolution.

viii. Some drug can be suitably delivered which are prone to degraded in acidic media.

ix. Lack of prominent mucus secreting goblet cells and therefore there is a hindrance of a diffusion limited mucous build up, beneath the applied designed system.

x. These system allow local modification of tissue permeability, inhibition of protease activity and reduction in immunogenic response, and hence can selectively be used for peptides, proteins and ionized species delivery.

1.4.2. Limitations of buccal drug administration
There is certain limitation via drug administered through buccal route

i. Drugs with ample dose are often difficult to be administered.

ii. Possibility of the patient to swallow the tablet being forgotten.

iii. Eating and drinking may be restricted till the end of drug release.

iv. This route is unacceptable for those drugs, which are unstable at pH of buccal environment.

v. This route cannot administer drugs, which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odor.

vi. Limited surface area is available for absorption.
1.5. Overview of the Oral Mucosa:

1.5.1. Buccal mucosa Structure:

The total area of the oral cavity is about 100cm². Out of this about one third is the buccal surface, which is lined with an epithelium of about 0.5mm thickness (Fig. 1). The keratinized and non keratinized regions of the oral epithelium differ from each other in terms of lipid composition of the cells. The keratinized epithelium has predominantly neutral lipids (e.g., ceramides) while the non keratinized epithelium has few but polar lipids, particularly cholesterol sulphate and glucosylceramides. Buccal membrane has numerous elastic fibers in the dermis, which is another barrier for diffusion of drug across the buccal membrane. Drug that penetrates this membrane enters the systemic circulation via network of capillaries and arteries. The lymphatic drainage almost runs parallel to the venous vascularization and ends up in the jugular ducts. The oral mucosal surface is constantly washed by the saliva (daily turn out is about 0.5 to 2 liters). The drug absorption across the oral mucosa occurs in the non-keratinized sections for protein/peptide delivery buccal route offers distinct benefits over other mucosal routes like nasal, vaginal, rectal, etc.

1.5.2. Permeability:

The oral mucosa in general is somewhat leaky epithelia intermediate between that of the epidermis and intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin. As indicative by the wide range in this reported value, there are considerable differences in permeability between different regions of the oral cavity because of the diverse structures and functions of the different oral mucosa. In general, the permeability’s of the oral mucosa decrease in the order of sublingual greater than buccal and buccal greater than palatal. This rank order is based on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa being relatively thin and on-keratinized, the buccal thicker and nonkeratinized, and the palatal intermediate in thickness but keratinized. It is currently believed that the permeability barrier in the oral mucosa is a result of intercellular material derived from the so-called ‘membrane coating granules’ (MCG). When cells go through differentiation, MCGs start forming and at the apical cell surfaces they fuse with the plasma membrane and their contents are discharged into the intercellular spaces at the upper one third of the epithelium. This barrier exists in the outer most 200µm of the superficial layer. Permeation studies have been performed using a number of very large molecular weight tracers, such as horseradish peroxides and lanthanum nitrate. When applied to the outer surface of the epithelium, these tracers penetrate only through outermost layer or two of cells.

When applied to the sub mucosal surface, they permeate up to, but not into, the outermost cell layers of the epithelium. According to these results, it seems apparent that flattened surface cell layers present the main barrier to permeation, while the more isodiametric cell layers are relatively permeable. In both keratinized and non-keratinized epithelia, the limit of penetration coincided with the level where the MCGs could be seen adjacent to the superficial plasma membranes of the epithelial cells.

Fig: 1: Buccal Mucosa Structure
Since the same result was obtained in both keratinized and non-keratinized epithelia, keratinization by itself is not expected to play a significant role in the barrier function. The components of the MCGs in keratinized and non-keratinized epithelia are different, however. The MCGs of keratinized epithelium are composed of lamellar lipid stacks, whereas the non-keratinized epithelium contains MCGs that are non-lamellar. The MCG lipids of keratinized epithelia include sphingomyelin, glucosyl ceramides, ceramides, and other non-polar lipids, however for non-keratinized epithelia, the major MCG lipid components are cholesterol esters, cholesterol, and glycosphingolipids. Aside from the MCGs, the basement membrane may present some resistance to permeation as well, however the outer epithelium is still considered to be the rate limiting step to mucosal penetration. The structure of the basement membrane is not dense enough to exclude even relatively large molecules.

1.5.3. Environment:
The cells of the oral epithelium are surrounded by an intercellular ground substance, mucus, the principle components of which are complexes made up of proteins and carbohydrates. These complexes may be free of association or some maybe attached to certain regions on the cell surfaces. This matrix may actually play a role in cell-cell adhesion, as well as acting as a lubricant, allowing cells to move relative to one another. Along the same lines, the mucus is also believed to play a role in bioadhesion of mucoadhesive drug delivery systems. In stratified squamous epithelia found elsewhere in the body, mucus is synthesized by specialized mucus secreting cells like the goblet cells, however in the oral mucosa; mucus is secreted by the major and minor salivary glands as part of saliva. Up to 70% of the total mucin found in saliva is contributed by the minor salivary gland. At physiological pH the mucus network carries a negative charge (due to the sialic acid and sulfate residues) which may play a role in mucoadhesion. At this pH mucus can form a strongly cohesive gel structure that will bind to the epithelial cell surface as a gelatinous layer. Another feature of the environment of the oral cavity is the presence of salivary glands. Saliva is the protective fluid for all tissues of the oral cavity. It protects the soft tissues from abrasion by rough materials and from chemicals. It allows for the continuous mineralization of the tooth enamel after eruption and helps in remineralization of the enamel in the early stages of dental caries. Saliva is an aqueous fluid with 1% organic and inorganic materials.

The major determinant of the salivary composition is the flow rate which in turn depends upon three factors: the time of day, the type of stimulus, and the degree of stimulation. The salivary pH ranges from 5.5 to 7 depending on the flow rate. At high flow rates, the sodium and bicarbonate concentrations increase leading to an increase in the pH. The daily salivary volume is between 0.5 to 2 liters and it is this amount of fluid that is available to hydrate oral mucosal dosage forms. A main reason behind the selection of hydrophilic polymeric matrices as vehicles for oral transmucosal drug delivery systems is this water rich environment of the oral cavity.

1.5.4. Absorption via buccal mucosa:
There are two permeation pathways for passive drug transport across the oral mucosa: Para cellular and Tran cellular routes. Permeants can use these two routes simultaneously, but one route is usually preferred over the other depending on the physicochemical properties of the diffusant. Since the intercellular spaces and cytoplasm are hydrophilic in character, lipophilic compounds would have low solubilities in this environment. The cell membrane, however, is rather lipophilic in nature and hydrophilic solutes will have difficulty permeating through the cell membrane due to a low partition coefficient. Therefore, the intercellular spaces pose as the major barrier to permeation of lipophilic compounds and the cell membrane acts as the major transport barrier for hydrophilic compounds. Since the oral epithelium is stratified, solute permeation may involve a combination of these two routes. The route that predominates, however, is generally the one that provides the least amount of hindrance to passage.

1.5.5. Promoting buccal absorption: Absorption enhancers:
Absorption enhancers have demonstrated their effectiveness in delivering high molecular weight compounds, such as peptides, that generally exhibit low buccal absorption rates. These may act by a number of mechanisms, such as increasing the fluidity of the cell membrane, extracting inter/intracellular lipids, altering cellular proteins or altering surface mucin. The most common absorption enhancers are azone, fatty acids, bile salts and surfactants such as sodium dodecyl sulfate. Solutions/gels of chitosan were also found to promote the transport of mannitol and fluorescent-labeled dextrans across a tissue culture model of the buccal epithelium while Glyceryl monooleates were reported to enhance peptide absorption by a cotransport mechanism.
1.5.6. Prodrugs:
Hussain et al., delivered opioid agonists and antagonists in bitter less prodrug forms and found that the drug exhibited low bioavailability as prodrug. Nalbuphine and naloxone bitter drugs, when administered to dogs via the buccal mucosa, causes excess salivation and swallowing. As a result, the drug exhibited low bioavailability. Administration of nalbuphine and naloxone in prodrug form caused no adverse effects, with bioavailability ranging from 35 to 50% showing marked improvement over the oral bioavailability of these compounds, which is generally 5% or less.

1.5.7. pH:
Shojaei et al., evaluated permeability of acyclovir at pH ranges of 3.3 to 8.8, and in the presence of the absorption enhancer, sodium glycocholate. The in vitro permeability of both pH extremes (pH 3.3 and 8.8), as compared to the mid-range values (pH 4.1, 5.8, and 7.0) 5

1.6. Buccal mucosa-site for drug delivery:
Controlled drug delivery systems specifically designed for buccal cavity, where the drug releases in a controlled manner. The drug can be administered for local or systemic action. These systems are generally based on the polymers including bioadhesive polymers. The various dosage forms including buccal bioadhesive tablets, laminated film, hydrogels, buccal patches, chewing gums and hollow fibers have been designed to extend the time of drug release from buccal cavity.

The absorption of drug through buccal mucosa can be increased using some absorption enhancers. Different peptides including insulin can be delivered to or through buccal cavity using control drug delivery systems. Buccal control drug delivery can be achieved in three ways; delivery through buccal mucosa, delivery through sublingual mucosa and local delivery to mouth. Local delivery includes the systems designed mainly to deliver drugs to periodontal pocket. Bioadhesion is a major approach involved in the designing of buccal controlled drug delivery systems. Theoretically, acyclovir was found to be pH dependent with an increase in flux and permeability coefficient at maximum buccal residence time can be in the order of several days. But it has been observed that usually it does not exceed several hours, possibly due interference with drinking, eating and talking.

1.7. Factors Affecting Buccal Absorption:
The oral cavity is a complex environment for drug delivery, as there are many interdependent and independent factors which reduces the absorbable concentration at the site of absorption. Membrane Factors: This involves degree of keratinization, surface area available for absorption, mucus layer of salivary pellicle, intercellular lipids of epithelium; basement membrane and lamina propria. In addition, the absorptive membrane thickness, blood supply/lymph drainage, cell renewal and enzyme content will all contribute to reducing the rate and amount of drug entering the systemic circulation.

1.7.1. Environmental Factors:
1.7.1.1. Saliva: The thin film of saliva coats throughout the lining of buccal mucosa and is called salivary pellicle or film. The thickness of salivary film is 0.07 to 0.10mm. The thickness, composition and movement of this film effects buccal absorption.

1.7.1.2. Salivary glands:
The minor salivary glands are located in epithelial or deep epithelial region of buccal mucosa. They constantly secrete mucus on surface of buccal mucosa. Although, mucus helps to retain mucoadhesive dosage forms, it is potential barrier to drug penetration

1.7.1.3. Movement of oral tissues:
Buccal region of oral cavity shows less active movements. The mucoadhesive polymers are to be incorporated to keep dosage form at buccal region for long periods while withstanding tissue movements during talking and if possible during eating food or swallowing.

1.8. Oral Mucosal Dosage Forms:
Various drug delivery systems are their which uses the oral mucosa as a drug delivery site such as – fast dissolving tablets, orodissolving films, fast caps, buccoadhesive film and tablets, chewing gums etc.

(a) Fast Dissolving Tablet (FDT):
Recently fast dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery system, because they are easy to administer and lead to better patient compliance. They also impart unique product differentiation thus enabling use as line extension for existing commercial products. FDTs can be prepared by various techniques like direct compression, sublimation, melt granulation, moulding, volatilization and freeze drying. Some of patented technologies are zydis, orasolve, durasolv, flash dose, wowtab, flash tab etc. some drugs which are poorly water soluble and have a variable bioavailability and bio-inequivalence related to its poor water solubility. The solubility of drug was increased by various methods to make a fast dissolving tablet like solid dispersion technique, by cocrystallization with beta – cyclodextrin. Because fast dissolving systems dissolves or disintegrate in patient’s mouth, thus the active constitute come in contest with the taste buds and hence taste masking of the drugs become critical to patient compliance. Taste masking can be done by various methods like addition of sweeteners, or by mass extrusion technique using eudragit E100. Recently various comparative studies were done between fast dissolving and conventional formulations. In an acceptance survey of FDT in allergic patients it is observed that if given the choice 93 % would choose FDT formulations

(b) Fast Dissolving Films:
However, the fear of taking solid tablets and the risk of choking for certain patient population still exist despite their short dissolution/disintegration time. Recent development in novel drug delivery system aims to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration. One such approach is rapidly dissolving film. It consists of a very thin oral strip, which releases the active ingredient immediately after uptake into the oral cavity. Rapid film combines all the advantages of tablets (precise dosage, easy application) with those of liquid dosage forms (easy swallowing, rapid bioavailability). The delivery system is simply placed on a patient’s tongue or any oral mucosal tissue. Instantly wet by saliva, the film rapidly hydrates and dissolves to release the medication for oromucosal absorption. One or a combination of the following processes can be hot melt extrusion, solid dispersion extrusion, rolling, semisolid casting, and solvent casting.

(c) Fast Caps:
A new type of fast dissolving drug delivery system based on gelatine capsules was developed. In contrast to conventional hard capsules, the fast caps consist of gelation of low bloom strength and various additives to improve the mechanical and dissolution properties of the capsule shell. The advantage of these fast disintegrating capsules are high drug loading, possible solid and liquid filling, no compression of coated taste-masked or extended release drug particles/pellets, good mechanical properties, simple manufacturing, mechanical stability and requirement of special packaging.

(d) Buccoadhesive Film and Tablets:
Recent years have seen an increasing interest in the development of novel muco-adhesive buccal dosage forms. These are useful for the systemic delivery of drugs as well as for local targeting of drug to a particular region of the body. Water soluble drugs are considered difficult to deliver in the form of sustained or controlled release preparations due to their susceptibility to “dose dumping phenomena “. Attempts have been made to regulate their release process by use of mucoadhesive polymers in order to achieve a once-a-day dose treatment

(e) Medicated Chewing Gums:
Medicated chewing gum is an attractive alternative for drug delivery system with several advantages including convenience for administration, individually controlled release of active substance and effective buccal drug administration for the treatment of local oral disease and systemic action. Mainly chewing gum is used to promising controlled release drug delivery system. Medicated chewing gums are currently available for pain relief, smoking cessation, travel illness and freshening of breath. A hydrophobic gum was used for the formulation of chewing gum. A new chewing gum device in the form of a three layer tablet has been also developed. In vitro release study of chewing gum requires special apparatus and instrumental setting.

1.9. Preparation methods

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There are different methods of preparation, among all solvent casting method and spraying methods are widely used.

1.9.1. Solvent casting method:
Films were prepared by solvent casting method where solution I was prepared by dissolving polymer in solvent with stirring to produce a clear solution and kept for 1 h to remove all the air bubbles. Another portion of solution II was prepared by dissolving pure drug and plasticizer in specific proportion of solvent. The solutions I and II were mixed and stirred for 1 h. The solutions were cast on to Petri dish and were dried. The films was carefully removed from the Petri dish and checked for any imperfection and cut according to size required for testing.

1.9.2. Spray technique:
A solvent system containing a film former and other excipients are sprayed onto suitable carrier system; dried films are peeled off to get the film. The carrier substrates used are glass, non-siliconized kraft paper, polyethylene paper. Some of the FDA approved fast dissolving buccal films are:

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<tr>
<th>S.No</th>
<th>Drug</th>
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<td>1.</td>
<td>Buprenorphine And Naloxone</td>
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<td>Zuplenz</td>
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<td>Zelapar</td>
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1.10. Evaluation:
The prepared buccal patches are evaluated in terms of Physical characteristics of patches, Physical appearance, Surface texture, Thickness uniformity of films, Uniformity of weight of patches, Swelling studies, In vitro biadhesion measurement, Percentage moisture loss, Surface pH, Folding Endurance, Content Uniformity Of Patches, Invitro release studies, Exvivo buccal permeation study .

REFERENCES