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"A REVIEW ARTICLE ON MUCOADHESIVE BUCCAL BILAYER TABLET".

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Abstract— The mucus layer that covers the mucosal epithelial surface interacts with mucoadhesive drug delivery systems, and mucin molecules lengthen the dosage form's stay at the absorption site. The situation in which two materials, at least one of which is biological in nature, are kept together for extended periods of time by interfacial forces is known as bioadhesion. Since mucosal layer lines many parts of the body, such as the gastrointestinal tract, urogenital tract, vaginal tract, eye, ear, and nose, it represents prospective sites for the attachment of any bioadhesive systems. The mucoadhesive bilayer tablets include two different therapeutic molecules that each exhibit a unique set of effects at their respective locations.

Keywords :- mechanism of permeation, bioadhasion, polymer, bilayer tablet, NDDS, Novel Drug.

INTRODUCTION

Due to the GIT's enzymatic activity and various pH levels, the oral route of drug delivery has a number of issues with drug delivery and bioavailability. Poor bioavailability of the medicine is caused by hepatic first-pass metabolism, which is caused by the drug being transported directly to the liver by the blood that circulates in the GIT. But even so, the oral route is the most popular medication delivery method because to its low cost, convenience of administration, and high level of patient compliance. Either altering the formulation or the administration method will solve the issues.

Since parenteral administration is the only recognised route that overcomes numerous problems associated with orally ineffective medications, pharmaceutical scientists have been investigating transdermal and transmucosal routes as alternatives during the past few decades. Due to its relatively immobile smooth muscle, adequate vascularization, and speedy recovery after stress exposure for both local and systemic effects, the buccal cavity was discovered to be the most practical and simple site for transmucosal administration. Bypassing the first pass metabolism and providing direct access to the systemic circulation through the internal jugular vein results in excellent bioavailability.

The interest in developing new medication administration methods has increased due to the improvement of drug bioavailability. One such method is the buccal drug delivery route employing bio adhesive dosage forms. The medicine can be administered buccally to prevent the rapid first-pass metabolism and drug degradation in the GIT environment. One possible route for big, hydrophilic, unstable proteins, polysaccharides, and tiny medicinal molecules is the buccal route.

The delivery can be divided into two groups in the oral mucosa: local delivery, systemic delivery, etc.

Dental caries, stomatitis, mouth ulcers, and oral infections are all treated with local therapy.

Treatment for chronic disorders like hypertension and depression is part of systemic therapy.

Advantages of buccal drug delivery systems

- Ease of administration, so dosage form easily administered and even removed easily.
- Allows localization of the drug in the oral cavity for a prolonged period of time.
- Provides systemic delivery of drugs with high first pass metabolism, thereby offering an increase in bioavailability.
- Bioavailability enhancement may results into the dose reduction.
- The buccal mucosa is highly perfused with blood vessels hence offers greater permeation than the skin and hence increase the absorption and ultimately bioavailability.
- Drugs which are unstable or sensitive to acidic environment of the stomach or enzymatic or alkaline environment of the intestine can delivered by buccal route.
- Its ability to recover after local treatment is

pronounced, hence allows a wide range of formulations to be used.

- It can be made unidirectional to ensure only buccal absorption.

Disadvantages of buccal drug delivery system

- Drugs which causes irritation to oral mucosa and having a bitter, unpleasant taste or odour cannot be administered.
- The drugs which are absorbed by passive diffusion can be administered.
- Drugs which are unstable at buccal pH, cannot be administered by this route.
- Surface area available for absorption is less.
- Only small dose drug can be administered.
- Eating and drinking may become restricted.
- Over hydration may lead to formation of slippery surface and structural integrity of the formulation may get disrupted by this swelling and hydration of the bioadhesive polymers.
- Drugs swallowed with saliva loose the advantages of buccal route.
- The buccal mucosa is relatively less permeable than the small intestine, rectum, etc.

NEED AND OBJECTIVE

The most common method of drug delivery is through the oral route, which has benefits like ease of administration but also serious drawbacks like poor bioavailability due to hepatic metabolism (first pass) and the propensity to produce high and low blood levels quickly, necessitating high and/or frequent dosing, which can be both expensive and inconvenient for patients.

As a result of the aforementioned factors, new drug delivery systems must be developed. These systems will enable temporary placement within the body, which will reduce the size and quantity of dosages while improving the safety and therapeutic efficacy of medications.

Drugs (or other therapeutic chemicals) are transported through the buccal mucosa for systemic action, which is known as transmucosal drug delivery.

The medication chosen for the ongoing investigation is the anti-gout medication Febuxostat.

The molybdenum pterin centre, which is the active site on xanthine oxidase, is blocked non-competitively by feuxostat, a non-purine selective inhibitor of xanthine oxidase.

To progressively oxidise both xanthine and hypoxanthine to uric acid, xanthine oxidase is required. Because febuxostat prevents xanthine oxidation, less uric acid is produced.

Because febuxostat inhibits xanthine oxidase in both its reduced and oxidised forms, it is difficult to remove from the molybdenum pterin site.

The half-life of februxostat is 5-8 hours. Due to first pass metabolism, it only has a 50% overall bioavailability in the body.

When compared to oral administration, transmucosal delivery of medications that undergo first pass metabolism can increase bioavailability, decrease dose frequency, and preserve the antigout profile for a longer period of time.

The Febuxostat satisfies the physicochemical, pharmacokinetic, and pharmacological requirements for optimum drug molecule characteristics for buccal distribution.

The goal of current research is to create better drug delivery methods that will improve dosage, therapeutic effects, and patient compliance. Therefore, buccal tablets of Febuxostat were created for regulated distribution in the current investigation.

MECHANISM OF PERMEATION VIA BUCCAL MUCOSA:

Oral mucosa has a lower degree of permeability than skin and intestinal mucosa. Buccal membrane is shown to be more permeable when differences in permeability between various oral area organs are taken into account.

Drug penetration is prevented by the buccal mucosa. Drug administration is influenced by buccal absorption and the efficacy of this barrier. Since the buccal mucosa is less permeable than the intestinal epithelium, the use of permeation enhancers in buccal drug delivery dosage forms has been thoroughly studied.

The buccal mucosa is somewhat leaky epithelia and is situated between the intestinal mucosa and the epidermis. The buccal mucosa's permeability is thought to be 4–4000 times higher than that of the skin.

The mouth cavity has a permeability hierarchy of sublingual, buccal, and palatal. The relative thickness and level of keratization are used to determine the rank order.

A drug's permeability coefficient is used to gauge how easily it can pass across a membrane. The degree of keratinization of these tissues, the drug's physicochemical characteristics (such as molecular weight, size, and lipophilicity), and the membrane thickness (i.e., its inverse to thickness) all affect the permeability coefficient.

The so-called membrane coating granules (MCG), which come in two varieties, are thought to be the source of the intercellular material responsible for the permeability barrier in the oral mucosa. Both keratinized and non-keratinized tissues are involved.

Keratinized tissues with lamellar lipid stacks, including sphingomyelin, glucosylceramides, and ceramides, are less permeable than non-keratinized tissues with cholesterol esters, cholesterol, and glycosphingolipids as non-lamellar lipid components.

BIOADHESIVE OR MUCOADHESIVE POLYMER

Water-soluble or water-insoluble, bioadhesive polymers produce swellable networks connected by cross-linking agents. The polymer should have the right balance of polarity and fluidity to allow for both mutual adsorption and interpenetration of the polymer and mucus. This will ensure that the polymer is adequately wetted by the mucus.

The following characteristics of an ideal polymer for a mucoadhesive drug delivery system are desirable:

Molecular mass ought to be high.

It must be flexible to work with mucus-selected polymers to provide the appropriate strength. These functional groups must be able to create hydrogen bonds.

It should be cross-linked in such a way as to have a good swelling index and sufficient swelling to improve the interpenetration of the polymer and mucin.
The polymer should not be poisonous and should not be absorbed by the gastrointestinal tract (GIT).
It shouldn't aggravate the mucous membrane.
The mucin epithelial cell surfaces should ideally form a potent non-covalent bond with it.
It should have site specificity and attach fast to wet tissue.
It should make it simple to incorporate the medicine and not obstruct its release.
The polymer doesn't break down while being stored or while it's being used.
The polymer must to be reasonably priced.
Examples include carbopol934, carbopol914p, HPMC k4 and k15, among others.

BIOADHESION

According to the American Society of Testing and Materials, adhesion is the condition in which two surfaces are held together by interfacial forces, which can include valence forces, interlocking action, or both.
The word "bioadhesion" refers to the attachment of a drug carrier system to a specific biological surface for the purpose of drug delivery. The biological surface might be mucus on the surface of a tissue or epithelial tissue. Mucoadhesion is the term used to describe a phenomena where an adhesive attaches to a mucus coat.
"A substance that can interact with biological materials and be retained on them or holding them together for a prolonged period of time" is the definition of a bioadhesive.
Type I: Bioadhesion is defined as adhesion between biological things that doesn't use synthetic materials. For instance, cell aggregation and fusion.
Type II: Bioadhesion is exemplified by the attachment of cells to culture dishes or to a range of materials, such as metals, woods, and synthetic materials.
Bioadhesion, also known as Type III, is the attachment of artificial materials to biological substrates, such as the adhesion of polymers to the skin or other soft tissues.

Various Techniques involved in bilayer tablet formulation

OROS push pull technology:

This method primarily consists of two or three layers, of which one or more layers are necessary for the medicine and the remaining layers are push layers. The primary components of the drug layer are drugs and two or more diverse agents. As a result, the medication in this layer is in a poorly soluble form. Osmotic and a suspending agent have also been added. The core of the tablet is encased in a semi-permeable membrane.

L-OROS technology:

The solubility issue was addressed by this system. Alza created the L-OROS system, which involves manufacturing a lipid soft gel product with a medicine in a dissolved condition before coating it with a barrier membrane, an osmotic push layer, and a semi-permeable membrane with an exit hole.

EN SO TROL technology:

Solubility enhancement of an order of magnitude or to create optimized dosage form Shire laboratory use an integrated approach to drug delivery focusing on identification and incorporation of the identified enhancer into controlled release technologies

Duros Technology:

An exterior cylindrical titanium alloy reservoir makes up the system. High impact strength and enzyme protection are provided by this reservoir. The DUROS technology is a tiny medicine delivery system that resembles a minuscule syringe and continuously dispenses a tiny amount of concentrated medication over the course of several months or an entire year.

DUREDAS technology:

Dual release of a medicine from a single dosage form is made possible by the DUREDAS or Dual Release medicine Absorption System (Elan Corporation), which makes use of bilayer tableting technology. The tablets are made by combining a controlled release hydrophilic matrix complex and an immediate release granulate (for a quick beginning of action) in two distinct direct compression stages.
Fluid from the GI tract is progressively absorbed by the controlled release matrix, which keeps its integrity. The hydrophilic polymers expand and change into a porous, viscous gel, acting as a barrier between the medicine and the fluid it is in contact with.

CHARACTERIZATION OF BILAYER TABLET

Particle Size Distribution

The particle size distribution can be measured by sieving method

Angle of Repose

The fixed funnel method can be used to measure angle of repose. It controls the powder's flow characteristics. It is described as the greatest angle that can be produced between the powder pile's surface and the horizontal.
The funnel, which was fastened to a stand at a specific height (h), was opened to let the powder pass through. The formula Tan =h/r, where h and r are the height and radius of the powder cone, can be used to compute the angle of repose by measuring the height and radius of the resulting pile of powder (r).

Moisture Sorption Capacity

All disintegrates have the ability to absorb moisture from the air, which has an impact on medicines that are sensitive to moisture. The ability to absorb moisture can be tested by evenly distributing 1 g of material in a Petri dish, keeping it in a stability chamber at 37°C with 100% relative humidity for two days, and determining the quantity of moisture uptake by comparing the weights.

Density

Bulk density can be determined by tapping method. It is determined by pouring the weighed powder (sieve #20) into a measuring cylinder and initial weight was noted and the initial volume of powder is called bulk volume.

EVALUATION OF BILAYER TABLET :

Tablet Thickness and Size

Thickness and diameter of tablets are important for uniformity of tablet size. Thickness and diameter can be measured by venire caliper.

Tablet Hardness

The hardness of tablets determines how resistant they are to shattering during storage, transportation, and handling prior to use. The Monsanto hardness tester was used to gauge the hardness of each formulation's tablet. kg/cm2 is a unit of measurement for hardness.

Friability

Tablet strength is a measure of friability. A friabilator (Aarson) can be used to determine a tablet's degree of friability. It's stated as a percentage (%). The tablets are dropped from a height of 6 inches into a plastic chamber that rotates at 25 revolutions per minute for 4 minutes or up to 100 times. The friabilator was filled with pre-weighed tablets and rotated 100 times. It is calculated using the formula percent loss = [(initial weight - final weight of tablets)/initial weight of tablets] x 100.

Uniformity of Weight

To make sure a tablet has the right amount of medication, it is frequently possible to determine the weight of the tablet being created. Twenty pills were chosen at random, and each one was weighed separately before the average weight was determined and the individual weights were compared to it. The tablets complied with the USP requirement that no tablet may differ by more than twice the percentage restriction and that no tablet may differ by more than 2 times the percentage limit on any given day.

CONCLUSION:

For the effective creation of new mucoadhesive drug delivery systems, this overview of mucoadhesive dosage forms may be helpful. The discovery of new mucoadhesives, device design, mucoadhesion processes, and permeation enhancement are some of the uses for mucoadhesive drug delivery systems. Mucoadhesive drug delivery will become even more crucial as a result of the massive flood of new drug molecules brought on by drug discovery.

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