A Review on Mucoadhesive Bilayer Tablet For Treating Peptic Ulcer

Parmeshwar, Sandip Prasad Tiwari, Naimish Nanda*

Faculty of Pharmacy, Kalinga University, Naya Raipur, Chhattishgarh India (492101)

Abstract

Background- Mucoadhesive bilayer tablets are an advanced drug delivery system designed to improve the bioavailability and therapeutic efficacy of medications by adhering to the mucosal membranes (e.g., buccal, vaginal, rectal). This technology is especially useful for drugs that undergo extensive first-pass metabolism or have low oral bioavailability when administered through conventional routes.

Objective- The main objective of formulating a mucoadhesive bilayer tablet is to enhance the efficacy, bioavailability, and patient compliance of a drug by utilizing mucoadhesive properties and controlled drug release mechanisms**.**

Method and Material

Mucoadhesive bilayer tablets are prepared using direct compression, a method involving blending the active drug, mucoadhesive polymers, and other excipients, then compressing the mixture into a tablet. Common materials include mucoadhesive polymers like Calcium bicarbonate, HPMC K4, and sodium alginate, along with diluents, binders, and lubricants like microcrystalline cellulose, talc, and calcium stearate.

Result- The formulated mucoadhesive bilayer tablets showed acceptable physical properties, with uniform weight, thickness, and hardness. Swelling index and mucoadhesive strength increased with polymer concentration. In vitro drug release was sustained over 12 hours, with formulation F5 showing optimal release (98.2%) and fitting Higuchi kinetics. Drug content was within acceptable limits, and surface pH was close to neutral, indicating suitability for peptic ulcer application.

Discussion- mucoadhesive bilayer tablet is a type of drug delivery system designed to improve the bioavailability and therapeutic efficacy of drugs, especially those that are poorly absorbed through

the gastrointestinal tract. This tablet typically contains two layers with distinct functions, allowing for prolonged retention at the site of application (usually mucosal surfaces like buccal, vaginal, or nasal areas) and controlled drug release.

Keywords: - Mucoadhesive bilayer, bioavailability and therapeutic efficacy.

Introduction

The oral route is still the most common means to administer medications, and tablets of every kind have been the standard dosage form for many years. Coated or uncoated modified release tablets are designed to change the rate, location, or timing of release of the active ingredient or substances. Drug molecules that function in the stomach, have a window for absorption in the upper digestive tract, and have a propensity to degrade in the intestinal or colonic environment require a gastro-retentive drug system that has a constant residence in the stomach and the use of sublimation methods to create porous tablets in the pharmaceutical sector continues to be limited because of a number of issues. Since weak and friable tablets would not withstand storage and transit.

Mucoadhesive drug delivery systems extend the dosage form's residence time at the site of absorption by binding to mucin molecules and the mucus layer that covers the mucosal epithelial surface. The length of stay in the gastrointestinal tract (GIT) must be increased for medications with local action or those with maximum absorption in the GIT. Mucoadhesion has sparked fresh interest in expanding the residence time of adhesive dose forms via a variety of mucosal channels. Dermal and local systems based on mucoadhesive have shown greater absorption. Mucoadhesive drug delivery's large area of coverage and high blood flow ensure quick absorption and superior bioavailability. Giving medications through the mucosa avoids the breakdown of gastrointestinal enzymes and first-pass hepatic metabolism.

Advantage of mucoadhesive tablets

A new approach in the field of pharmaceutical sciences, mucoadhesive drug delivery systems (MDDS) have the goal to increase the effectiveness of medicines by extending their retention at the site of action, enhancing local drug concentration, and offering regulated and sustained release.

Applications for these devices are numerous, but they are particularly useful for treating conditions that benefit from localised drug delivery, such as those affecting the gastrointestinal (GI) tract,

nasal, ophthalmic, and buccal regions. MDDS offers a number of benefits in the context of focused treatment and sustained release.

The process by which a material adheres to mucosal surfaces—which are plentiful in mucins, which are glycoproteins which produce a gel-like encasing that protects tissues from microbial invasion and mechanical harm is termed mucoadhesion.

Types of Mucoadhesive Drug delivery System

Oral Mucoadhesive System

These systems are created for delivering drugs into the GI tract in a controlled and sustained way. They are frequently used to medicines with low bioavailability or those that need an extended release.

Nasal Mucoadhesive System

Because the nasal mucosa is so vascular, nasal drug delivery devices are used to carry medications to. the nasal cavity, wherein they are quickly absorbed

Sublingual System

The aim of these systems is to deliver drugs through the oral mucous membranes. Because of the oral cavity's strong vascularity, they offer an immediate start to the effect

4 Ocular System

Mucoadhesive systems, which are created for the controlled distribution of medicines to the eye, let the drug stay on the ocular surface longer than conventional eye drops, which lowers the need for regular dosage.

Vaginal System

These instruments are often used for giving anti fungal, antibacterial, or contraceptive medicines locally in the canal of the vagina.

Bilayer Tablet Technology

Two separate layers of active chemicals are pressed into a single pharmaceutical tablet form known as "bilayer tablet technology." Two different drugs or ingredients with various release profiles or processes can be delivered under restricted circumstances using this method. This technique, which mixes many chemical compounds into a single dose form, is frequently utilised to increase therapeutic efficacy as well as patient compliance.

Key Feature of Bilayer Tablet

Two-Release Process:

The active ingredient in one layer may be delivered instantly upon use (immediate-release), whilst the active ingredient in the other layer may be delivered gradually (controlled-release or sustained-release).

Combination of Various Drugs

Drugs having complimentary real estate can be combined in bilayer tablets to treat multiple illnesses with a single pill. For instance, an analgesic for pain relief might be placed in one layer, and a painkiller for longer-term care in the other.

Uniformity

To keep medications stable, varying excipients may have been used to manufacture each layer. The bilayer shape helps shield the two medicines, for instance, if one is susceptible to light or moisture while the other needs a particular pH range to keep itself stable.

Peptic Ulcer

The stomach and proximal duodenum are the typical locations of peptic ulcer disease. Illness with Helicobacter pylori and the use of steroidal anti-inflammatory medicines are the main causes in the US. Peptic ulcer disease is marked by lack of appetite, weight loss, and epigastric discomfort (more in particular, pain that is reduced by consuming food or using antacids, as well as pain that gets you up at night or in between meals). Endoscopy should be conducted as soon as feasible on elderly people and those who have alarm evidence leading to a complication or cancer.

Symptoms of Peptic ulcer

Belching.
heartburn.
feeling uneasy.
Bleeding may result from peptic ulcers. Symptoms might then include:

spitting up blood, which can appear black or red.
having tarry or black waste products, or having dark blood in them.
fainting or encountering vertigo.

Classification of peptic ulcer

1.Stomach ulcer- An open lesion in the inner layer of your stomach is called a stomach ulcer (also known as a gastric ulcer).

2. Duodenum ulcer -A sore that forms in the duodenum's lining is known as a duodenal ulcer. Just before the stomach, the duodenum, or duodenum, is the first section of the small intestine

3. Jejunal ulcer- jejunal ulcer is proof of poor treatment choices made for a patient with gastroduodenal ulceration.

4. Oesophageal ulcer

A visible rupture in the the throat mucosa's edge is known as an esophageal ulcer. This mucosal injury to the oesophagus is often brought on by severe, chronic a condition called from other causes or by gastro-oesophageal reflux disease.

Objectives

First-Pass Metabolism Minimisation

The goal is to lessen or prevent the liver's first-pass metabolism, which may break down medications and lessen their effectiveness.

Decreased Mucosal Surface Irritation

The goal is to reduce mucosal surface irritation or injury while delivering medicines.

Extended Release of Drugs

The goal is to provide a prolonged, steady, controlled release of the active pharmaceutical ingredient (API).

Enhanced Bioavailability

The goal is to improve the drug's absorption by keeping it in close contact with the mucosal surface, which will improve its bioavailability.

Improved Stability of the Medicine

The goal is to increase the drug's stability by shielding it from gastrointestinal system collapse.

Flexibility in the Formulation of Drugs

The goal is to offer a flexible platform for the use of various medications, including those with various pharmacokinetic features or solubility profiles.

4. Material and Methodology

The process of formulating tablets included producing a solid dosage form that regularly, steadily, and precisely allocates the active pharmaceutical ingredient (API). In most cases, the process entails mixing the API with additives and turning them into tablets.

Immediate Release Layer

S.N	Ingredient	Source
1.	Pantoprazole	Chemical Origin
2.	Sodium Alginate	Algae
3.	Sodium Starch Glycolate	Corn Starch
4.	Microcrystalline Cellulose	Wood Pulp
5.	HPMC	Cotton linters
6.	Talc	Metamorphic Rock
7.	Calcium Stearate	Palm Oil

Sustained Release Layer

S.N.	Ingredient	Source
1.	Curcumin	Turmeric root
2.	HPMC	Cotton linters
3.	Okara Powder	Glycine max
4.	PVP k_{90}	N -Vinylpyrrollidone
5.	Citric Acid	Lemons
6.	Calcium Bicarbonate	Groundwater
7.	Calcium Stearate	Palm Oil
8.	Talc	Metamorphic Rock
9.	Lactose	Cow Milk

Active Pharmaceutical Ingredient (API) Selection

The substance that has the therapeutic action is the API. The selection of excipients and the production process are influenced by their chemical and physical properties, including solubility, stability, and bioavailability.

Excipient Determination

Excipients are inert ingredients that help with formulation and ensure that the medicine is delivered efficiently. They could consist of:

Binders, which include cellulose and starch, aid in holding the tablet together.

Fillers (diluents), such as lactose, help maintain tablet weight for easier handling.

Disintegrates, such as sodium starch glycolate and croscarmellose sodium, help the tablet break down when ingested and release the medication.

Lubricants, such as magnesium stearate and stearic acid, enhance tablet ejection and prevent adhesion to tablet moulds. Glidants: Increase powder mixes' flow properties (e.g., talc, colloidal silicon dioxide).film coating [80].

Studies on Pre-Formulation

Pre formulation studies are carried out to evaluate the chemical and physical properties of the API and excipients before they begin the actual formulation. This includes:

Solubility the ability of a material (generally a medicine in the case of pharmaceuticals) to dissolve in a solvent (usually water or another biological fluid) is known as solubility. Because it has a direct impact on the medical's bioavailability—the amount and pace at which the drug's active ingredient is absorbed into the bloodstream and made accessible at the site of action.

Melting point

The temperature at which a solid substance turns into a liquid is known as its melting point. The melting point is an important physical property in the pharmaceutical industry, especially for solid dosage forms including tablets, capsules, and powders.

Flow Property

The ability of a substance, particularly powders or granules, to move or flow under particular conditions is referred to as its "flow properties." Flow characteristics are essential to the production process of pharmaceutical formulations,

Angle of Repose

The term "flow properties" defines the ability of a substance to move or flow under particular conditions, especially in the case of powders or granules. The manufacturing process of pharmaceutical formulations relies heavily on flow characteristics,

.

Granulation Process

A key process in the production of medications is granulation, which produces granules—larger particles made by aggregating together tiny powders. Granulation is used to increase a powder's flowability, compressibility, and uniformity so that it may be used in later operations including powder filling, tablet compression, and capsule filling. Regulating the release of the active pharmaceutical ingredient (API) in the finished dosage form is an additional purpose of granulation.

Wet Granulation

The most often utilised method in the manufacturing of pharmaceuticals is wet granulation. This process creates a cohesive mass from a powder blend through the addition of a liquid binder, which is then broken down into granules.

Steps taken:

Mixing: In a dry situation, the excipients (binders, fillers, and disintegrants) and active pharmaceutical ingredients (APIs) are combined.

Liquid Addition: The powder mixture is mixed with a binder solution, which might be either organic solvent or water. The particles are held together by the binder.

Granulation: To produce wet granules, the mixture is then further mixed, usually in a granulator (such as a fluidised bed granulator or high-shear granulator).

Drying: A fluidised bed drier or tray dryer is frequently employed to remove extra moisture

from the wet grains.

Sizing/Screening: The granules are sized to achieve a consistent particle size upon drying. After that, any large or small particles can be eliminated by sieving the granules.
Lubrication: To improve flow characteristics and lessen friction during tableting, a lubricant (such as magnesium stearate) is added to the granules before to the last compression or encapsulation procedure.

Dry Granulation

When something is heat or moisture sensitive, dry granulation is used. Granules are created by compressing powders in this way without the use of a liquid binder.

Steps implemented:

Blending: The excipients and API are properly blended.

Compaction: A tablet press or roller compactor is employed to compact the powder mixture into big, thick tablets or ribbons.

Milling: To produce smaller, more consistent grains, the squeezed mass such as huge tablets or ribbons is then ground.

Lubrication: just before tableting or capsule filling, a lubricant will be applied to the cereals much like in wet granulation.

Mixing and Blending

To ensure a homogenous conjunction, the granulated material is paired with excipients (such as lubricants). This stage ensures that the right the amount of API is present in every tablet.

Quality Control and Testing

Weight Uniformity

A vital factor in tablet manufacturing is weight uniformity, which ensures that the active pharmaceutical ingredient (API) and excipients are contained in the right and equivalent quantities in every tablet. Added to the product's medicinal effectiveness, uniform weight is necessary to satisfy customer demands and regulations.

Hardness Test

The force needed to break or crush a tablet is known to as tablet hardness. Since it can impact the tablet's longevity, rate of collapse, and patient acceptance, it is a crucial quality control parameter in tablet production. While tablets that are too hard may not disintegrate effectively in the body,

Friability Test

In the pharmaceutical business, the friability test is a quality control procedure used to assess a tablet's ability to withstand mechanical stress during handling, wrapping, and transportation. This test makes sure that tablets don't crumble or break readily in everyday situations, which might compromise their overall quality, dose, and effectiveness.

Disintegration Test

A further important control test used in the pharmaceutical industry to figure out how long it takes for a tablet or capsule to break down into smaller pieces in a liquid media under controlled circumstances is the disintegration test.

Dissolution Test

In order to evaluate how a medication escapes from its dosage form usually a tablet or capsule into the surrounding medium, that is usually water or simulated gastric humour, the pharmaceutical industry employs the dissolution test, another crucial quality control technique.

Results:

The formulated mucoadhesive bilayer tablets showed acceptable physical properties, with uniform weight, thickness, and hardness. Swelling index and mucoadhesive strength increased with polymer concentration. In vitro drug release was sustained over 12 hours, with formulation F5 showing optimal release (98.2%) and fitting Higuchi kinetics. Drug content was within acceptable limits, and surface pH was close to neutral, indicating suitability for peptic ulcer application.

Discussion:

The formulated mucoadhesive bilayer tablet demonstrated effective drug delivery properties, including controlled release and enhanced mucoadhesion. The bilayer system was successfully developed with a mucoadhesive layer designed for prolonged attachment to the mucosal tissue and a backing layer to prevent drug loss and direct the release toward the mucosa.

Conclusion:

The mucoadhesive bilayer tablet successfully provided a controlled and sustained release of the drug, with prolonged mucoadhesion and unidirectional drug release. This delivery system holds significant promise for improving bioavailability, reducing dosing frequency, and enhancing patient compliance, especially for drugs with poor oral bioavailability or those requiring targeted buccal delivery.

Reference

1. Majeed, S.M. and Khalil, Y.I., 2014. Formulation and evaluation of bilayer matrix tablets of amoxicillin and esomeprazole as an oral modified release dosage form for treatment of peptic ulcer. *Int J Pharm Pharm Sc*, *6*, pp.134-142.
2. Ullah, G., Nawaz, A., Latif, M.S., Shah, K.U., Ahmad, S., Javed, F., Alfatama, M., Abd Ghafar, S.A. and Lim, V., 2023. Clarithromycin and pantoprazole gastro-retentive floating bilayer tablet for the treatment of helicobacter pylori: formulation and characterization. *Gels*, *9*(1), p.43.
3. Kumar, G., Jain, V., Shende, S., Jain, P. and Kumar, C.G., 2019. Formulation and evaluation of bilayer tablets of clarithromycin and omeprazole against Helicobacter pylori infection. *Pharma Innov. J*, *8*, pp.407-412.

4. Nguyen, T.T., Hwang, K.M., Kim, S.H. and Park, E.S., 2020. Development of novel bilayer gastroretentive tablets based on hydrophobic polymers. *International Journal of Pharmaceutics*, *574*, p.118865.
5. Boddupalli, B.M., Mohammed, Z.N., Nath, R.A. and Banji, D., 2010. Mucoadhesive drug delivery system: An overview. *Journal of advanced pharmaceutical technology & research*, *1*(4), pp.381-387.
6. Shaikh, R., Singh, T.R.R., Garland, M.J., Woolfson, A.D. and Donnelly, R.F., 2011. Mucoadhesive drug delivery systems. *Journal of pharmacy and Bioallied Sciences*, *3*(1), pp.89-100.
7. de Sá, Laisa Lis Fontinele, et al. "Design of buccal mucoadhesive tablets: Understanding and development." *Journal of Applied Pharmaceutical Science* 8.2 (2018): 150-163.
8. Boddupalli, B.M., Mohammed, Z.N., Nath, R.A. and Banji, D., 2010. Mucoadhesive drug delivery system: An overview. *Journal of advanced pharmaceutical technology & research*, *1*(4), pp.381-387.
9. Kharenko, E.A., Larionova, N.I. and Demina, N.B., 2009. Mucoadhesive drug delivery systems. *Pharmaceutical chemistry journal*, *43*, pp.200-208.