

Preparation and Evaluation of Novel Floating Mucoadhesive Antidiabetic Tablets

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Abstract: *In the present study, Metformin an anti - diabetic drug is formulated in the form of floating mucoadhesive tablets to improve its bioavailability. Various polymers used as rate controlling and mucoadhesive polymers in designing the tablets. Various formulations were prepared by using different concentration of polymers. The pre - compression blend of Metformin mucoadhesive tablets were characterized with respect to bulk density, angle of repose, tapped density, carr's index and hausner's ratio and all the results indicated that the blend had good flow property and better compressibility. The swelling studies were performed and the results indicated that all the formulations had good swelling index. The Floating and Mucoadhesive both are coming under the novel drug delivery system in which they considered as predominantly more effective as compared to alternative drug delivery system because this formulation having direct contact with a biological system. This review also describes the studies to assess the effectiveness and implementation of floating systems, and applications of mucoadhesive systems. Regardless of age, diabetes is a complicated group of health conditions that impact many individuals. Researchers from all around the world have looked into and created various drug - delivery methods that try to cure this condition because of how prevalent it is. Current treatments for DM are characterised by shorter half - lives, which means that patients must take bigger dosages daily, which is not ideal. Therefore, medications with extended stomach residence durations need to be designed for continuous release, which can help the drug's effects last longer. For this reason, the medication should stay in the stomach or upper gastrointestinal system for prolonged periods of time.*

Keywords: Floating, Bioadhesive, Effervescent, Colloidal system. Mucoadhesive tablets, floating, Mucoadhesive polymer

1. Introduction

Regardless of age, diabetes is a complicated group of health conditions that impact many individuals. Researchers from all around the world have looked into and created various drug - delivery methods that try to cure this condition because of how prevalent it is. Current treatments for DM are characterised by shorter half - lives, which means that patients must take bigger dosages daily, which is not ideal. Therefore, medications with extended stomach residence durations need to be designed for continuous release, which can help the drug's effects last longer.

Davis first studied the idea of "drugs that float and deliver" in 1968. According to this theory, drugs with a bulky density one that is lower than gastric juice's density (1.004 g/cm³) can stay in the gastrointestinal tract for a longer period of time, increasing their bioavailability and reducing their rate of elimination or degradation while still having a localised effect. The first - line medication of choice for the treatment of type 2 diabetes has been proven to be metformin. It should be given early upon the diagnosis of this metabolic disease, together with diet and exercise, according to generally recognised standards. Additionally, all other oral hypoglycemic medications can be safely and effectively used with this medication to have a beneficial additive effect. The primary goal of the current study is to develop

methods for treating diabetes in humans.

Diabetes

Diabetes mellitus, sometimes known as just diabetes, is a metabolic condition that raises blood sugar levels. Insulin is a hormone that transports sugar from the blood into your cells where it can be stored or utilized as fuel. When you have diabetes, your body can't utilise the insulin it does manufacture or doesn't produce enough of it.

They are instead related to the diseases that develop as a result of chronic diabetes mellitus. Macrovascular illnesses, such as coronary heart disease and peripheral artery disease, as well as microvascular diseases, such as retinal and renal vascular diseases, as well as neurological disorders are among them. [2]

Causes

The beta cells that release insulin are found in the pancreatic islets of Langerhans, which are collections of cells. The purpose of insulin in the body is to cause cells to take up glucose so that the cells may utilise this sugar's ability to produce energy. Diabetes patients may have malfunctioning beta cells, which reduces insulin output, or their muscle and adipose cells may be resistant to the effects of insulin, which reduces these cells capacity to absorb and utilise glucose.

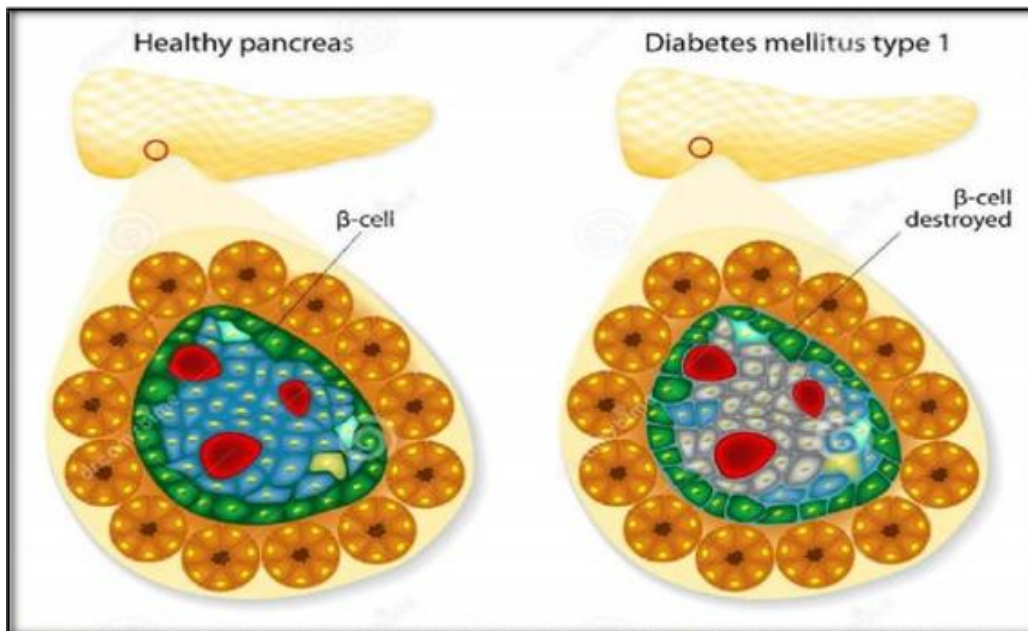


Figure 1: Islet of Langerhans. The general symptoms of diabetes include [5]

- heightened hunger
- heightened thirst
- Slimming down
- urinating a lot
- hazy vision

Types of diabetes

There are several varieties of diabetes.



Figure 2: Types of diabetes

Novel drug delivery systems

A unique technique that combines creative development, formulations, new technology, and novel methodology for delivering pharmaceutical substances throughout the body as necessary to safely accomplish its targeted pharmacological effects is known as a novel drug delivery system. It could also increase drug potency, manage drug release with a lasting pharmacological impact, and scientific site - targeting inside the body. It entails the creation of brand - new, enhanced, and safer medications with lengthy half - lives and significant therapeutic indices.

Floating drug delivery system

The bilayer floating tablet plays the primary function in the floating drug delivery system, which is the key strategy for extending the gastric residence duration in the stomach. It is utilized for systemic applications in diabetes and is more effective for treating local infections including peptic ulcer,

gastritis, Zollinger - Ellison syndrome, indigestion, and other local diseases connected to the gastrointestinal tract. For medications with a short half - life and acid liability, FDDS offers protection.

Mucous membranes

Mucous membranes (mucosae) are the moist surfaces lining the walls of various body cavities such as the gastrointestinal and respiratory tracts. They consist of a connective tissue layer (the lamina propria) above which is an epithelial layer, the surface of which is made moist usually by the presence of a mucus layer. The epithelia may be either single layered (e. g. the stomach, small and large intestine and bronchi) or multilayered/stratified (e. g. in the oesophagus, vagina and cornea).

Mucoadhesion

In the field of pharmaceutical sciences, mucoadhesion is the condition in which interfacial forces hold a substance and mucus or a mucous membrane together for extended periods of time. [13] Mucoadhesive drug delivery systems are appealing and adaptable in the creation of dosage forms because to the variety of administration routes, including ophthalmic, nasal, buccal and gingival, gastrointestinal (oral), vaginal, and rectal.

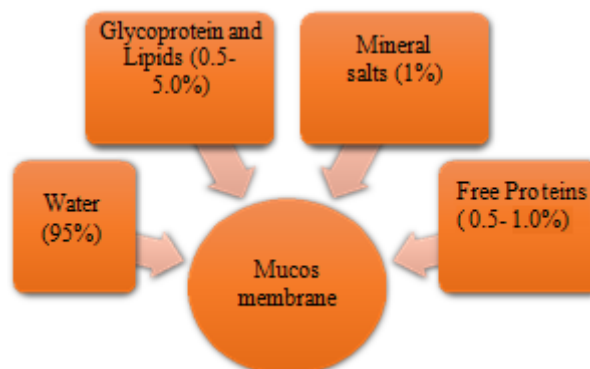


Figure 3: Composition of Mucous Membrane Preparation of Floating mucoadhesive:

The Floating mucoadhesive tablets containing Metformin, were prepared by direct compression method. Various batches were developed by changing the ratio of polymers. Sodium bicarbonate is used to enhance the floating behavior of tablets. Talc and Magnesium stearate are used as lubricant and glidant. Lactose is used as a filler to maintain the bulk of the formulations.

Route of administration

Mucosadhesive dosages was administered orally. This is

systemic delivery of drugs through the mucosal membranes lining the floor of the mouth. Local delivery: This is drug delivery into the oral cavity.

Polymers used:

- Hydroxypropyl methyl cellulose ether [HPMC]
- Propylene glycol
- Tween 80 (Polysorbate 80)
- Chitosan

Table: Some Mucoadhesive Polymers

Natural	Synthetic	Biocompatible	Biodegradable
Sodium alginate	Polyvinyl alcohol, Polyamides, Polyalkylene glycols, Polycarbonates	Ester of hyaluronic acid	Polylactides
Pectin	Esters and halides, Polymethylmethacrylic acid	Polyvinyl acetate	Polyglycolides
Trgacanth	Methyl cellulose, Ethyl cellulose Hydroxypropyl methyl cellulose	Ethylene glycol	Poly (lactide - co - glycolides), Polycaprolactones
Gelatin	Sodium corboxymethyl cellulose	-	Polyphosphoesters, Polyanhydrides
Caragenan	-	-	Chitosan, Polyphosphazenes

Role of Polymers in Floating drug delivery

The currently available polymer - mediated noneffervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyancy principles, appear to be an effective and rational approach to the modulation of controlled oral drug delivery. This is evident from the number of commercial products and a myriad of patents issued in this field. The FDDS become an additional advantage for drugs that are absorbed primarily in the upper segments of GI tract, i. e., the stomach, duodenum and jejunum. Some of the unresolved, critical issues related to the rational development of FDDS include (1) the quantitative efficiency of FDDSs in the fasted and fed states; (2) the role of buoyancy in enhancing GRT of FDDS; and (3) the correlation between prolonged GRT and SR/PK characteristics. [16]

Evaluation of mucoadhesion In vitro techniques:

The best approach to evaluate mucoadhesive microspheres is to evaluate the effectiveness of the mucoadhesive polymer to prolong the residence time of drug at the site of absorption, thereby increasing absorption and bioavailability of the drug. The quantification of the mucoadhesive forces between polymeric microspheres and the mucosal tissue is a useful indicator for evaluating the mucoadhesive strength of microspheres. In vitro techniques have been used to test the polymeric microspheres against a variety of synthetic and biological tissue samples, such as synthetic and natural mucus, frozen and freshly excised tissue, etc.

The different in vitro methods include the following.

(i) Tensile stress measurement using Wilhelmy plate technique:

The Wilhelmy plate technique is traditionally used for the measurement of dynamic contact angles and involves the use of a microtensiometer or a microbalance. The CAHN dynamic contact angle analyzer (model DCA 322, CAHN instruments, Cerritos) has been modified to perform adhesive microforce measurements. By using the CAHN software system, three essential mucoadhesive parameters can be analysed. These include the fracture strength, deformation to failure, and work of adhesion. [24]

(ii) Shear stress measurement:

The shear stress measures the force that causes a mucoadhesive to slide with respect to the mucus layer in a direction parallel to their plane of contact. Adhesion tests based on the shear stress measurement involve two glass slides coated with a polymer and a film of mucus. Mucus forms a thin film between the two polymer coated slides, and the test measures the force required to separate the two surfaces. [25]

(iii) Miscellaneous methods:

Other techniques for evaluation of mucoadhesive strength include adhesion number, in vitro wash - off test for microspheres, falling liquid film method, [26] everted sac technique, [27] novel rheological approach [28] and flow - through approach. [29]

Evaluation of Mucoadhesive tablet properties

Weight variation Twenty tablets (n = 20) from each batch were weighed using electronic balance and their average weight was calculated.

Friability Hardness Drug content

Mucoadhesion test Swelling test

In vitro dissolution studies Compatibility study

Pre compression evaluation:

Solubility Studies

Drug - excipient compatibility studies Pre - compression Evaluation Compressibility index

Hausner's ratio Angle of repose

Theories and Mechanisms

Mucoadhesion could be explained by some theories that include the electronic theory, the wetting theory, the adsorption theory, the diffusion theory, the mechanical theory, the cohesive theory, and the fracture theory. [30, 31]

Electronic Theory

The electronic theory explains the presence of attractive forces between the biological and the adhesive system surfaces due to the formation of an electrical double layer

produced from the electron transfer among the surfaces [32]

Wetting Theory:

The wetting theory is applied to adhesive systems with low viscosity and high affinity to the substrate. It correlates the adhesion strength to the contact angle of the low - viscosity system, the spreadability coefficient (the difference in the surface energies between the biological surface and the liquid), and the work of adhesion (the energy needed to separate the two phases). In general, at contact angles close to zero, the adhesion strength is benefited due to the increased contact area. In addition, higher individual surface energies are correlated with a better adhesive strength of the interface [33].

Adsorption Theory

The adsorption theory approaches the presence of intermolecular forces, namely, hydrogen bonding and Van der Waals force that act between the biological substrate and the adhesive material. Despite the isolated interaction being weak, the combined effect of several forces could lead to strong interactions [34].

Diffusion Theory

The diffusion theory presumes the polymer chain interpenetration through the substrate surface, forming a network structure. The depth of penetration depends on the polymer diffusion coefficient, flexibility and mobility of the mucin structure, the polymer-substrate contact time, the mutual solubility, and the similarity in the chemical structures [34].

Mechanical Theory

The mechanical theory assumes the diffusion of the low - viscosity polymeric system to an irregular and rough biological surface which must increase the surface area available for interaction, forming an interlocked structure that benefits the adhesion process, as well as viscoelastic and plastic dissipation of energies [30]

Advantage of mucoadhesive drug delivery system

Mucoadhesive drug delivery gives rapid absorption and good bioavailability due to its considerable surface area and high blood flow. Drug delivery across the mucosa bypasses the first - pass hepatic metabolism and avoiding the degradation of gastrointestinal enzymes.

Disadvantages of mucoadhesive drug delivery systems:

Occurrence of local ulcerous effects due to prolonged contact of the drug possessing ulcerogenic property.

Application of mucoadhesive drug delivery system

Over the years, mucoadhesive and bioadhesive systems have been used for nasal, ocular, buccal, vaginal, rectal and oral drug delivery. In early studies of mucoadhesion, different methods were developed or modified from other areas of adhesion research.

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