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MUCOADHESIVE DRUG DELIVERY SYSTEM: A PROMISING STRATEGY FOR ENHANCED BIOAVAILABILITY

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Abstract
Mucoadhesive drug delivery systems (MDDS) have gained considerable attention as an effective approach to address the shortcomings of conventional drug delivery methods, particularly issues such as poor oral bioavailability, rapid drug elimination, and the need for frequent dosing. By adhering to mucosal surfaces, these systems prolong the residence time of dosage forms at the site of absorption, leading to enhanced drug uptake and sustained as well as controlled release profiles. MDDS are formulated using natural or synthetic polymers that interact with mucosal tissues through physicochemical mechanisms including hydrogen bonding, electrostatic interactions, and polymer chain interpenetration.

Keywords: *Mucoadhesion, mucoadhesive drug delivery, polymers, theories and mechanism of mucoadhesion, Factors affecting mucoadhesive.*

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1. INTRODUCTION

The concept of mucoadhesion was introduced in the field of controlled release drug delivery systems in the early 1980s. Mucoadhesive drug delivery systems have emerged as sophisticated pharmaceutical platforms that fundamentally alter the way medications interact with biological surfaces. Over the past 40 years, researchers have utilized the concept of mucoadhesion to apply it significantly in prolonging the residence time and achieving controlled release effects of bioadhesive dosage forms through various mucosal routes [1]. The prolonging of the residence time of the dosage of within ten gastrointestinal tracts. This would reduce the need for multiple dosing, resulting better patient compliance. The biological surface can be epithelial tissue or the mucus coat on the surface a tissue [2].

1. Anatomy and Physiology of Oral Mucosa

The delivery of drugs is provided by both systemic and local pathways. A large surface area of mucous membrane is contained in the oral cavity for the complete absorption of various drugs. The total surface area of the oral cavity, lined by mucous membranes, is approximately 100 cm^2.Several parts of the oral cavity include:

i). The floor of the mouth (sublingual)
ii). The buccal mucosa (cheeks)
iii). The gums (gingiva)
iv). The palatal mucosa
v). The lining of the lips.

Several distinct patterns of maturation in the epithelium of the human oral mucosa are revealed by light microscopy, based on various regions of the oral cavity. A subsurface layer of connective tissues (dermis for skin and lamina propria for oral mucosa), containing fibroblasts, macrophages, mast cells, blood vessels, and nerve endings, is embedded in the extracellular matrix (ECM) to provide the epithelium with structural support and nutrients required for continuous renewal, supporting the stratified epithelium [3].

2. MUCO ADHESIVE DRUG DELIVERY SYSTEM

In the previous few years, the mucoadhesive drug delivery system has become popular and gained substantial attention for both local and systemic medication delivery due to exceptional approachability, avoiding first-pass metabolism, large blood supply, safety, and more patient acceptability with enhanced and better treatment. This review aims to explore the increasing knowledge of the characteristics of oral mucosal remodeling in allergic (food allergy,

respiratory allergy) or non-allergic (i.e., celiac disease, a food-induced autoimmune) diseases [4].

3. MECHANISMS OF MUCOADHESION

The mucoadhesion process is initiated through two stages, involving the connection between the mucoadhesive material (formulation) and the mucous membrane. Mucoadhesion involves attaching the drug, along with a suitable carrier, to the mucous membrane. The complex phenomenon of mucoadhesion involves wetting, adsorption, and interpretation of polymer chains [5].

4. THEORIES OF MUCOADHESION

Several theories have been proposed to explain the phenomenon of cohesion. Cohesion is defined as the interaction between a mucoadhesive polymer and the mucosal layer.

4.1 DIFFUSION THEORY [6].

The basis of "Diffusion theory" lies in interaction between strands of mucin and polymer chains. This theory describes that the polymer and mucous chains penetrate to a sufficient depth and are driven by a concentration gradient to form a semi-permanent adhesive bond.

4.2 WETTING THEORY [7].

This theory is predominantly relevant to liquid systems or bio adhesives with low viscosity. This theory defines the affinity of bioadhesive polymer to the surface in order to spread over it and develop intimate contact with the biological surfaces.

4.3 ADSORPTION THEORY [8].

According to this theory, when the two surfaces come in contact, the atoms present in two surfaces form chemical bonds due to the surface force acting between them and the adhesion of materials occur.

4.4 ELECTRONIC THEORY [9].

The electronic theory indicates that an attractive electrostatic force occurs when glycoprotein mucin network interacts with bio-adhesive material that results in electrons transfer through the adhesive boundary.

4.5 MECHANICAL THEORY [10].

In this theory the adhesion of two surfaces occurs, because the rough surface is filled by a mucoadhesive fluid.

5. FACTORS AFFECTING MUCOADHESIVE DRUG DELIVERY SYSTEMS

The mucoadhesive drug delivery systems are affected by polymer related factors, environmental factors, and physiological factors, which are the followings:

5.1 Polymer-Related Factors

5.1.1 Molecular Weight

The mucoadhesion force of a mucoadhesive polymer essentially depends on its molecular weight and polymeric linearity. In general, for the linear polymers (e.g., polyethylene glycol), the mucoadhesive property is proportional to their molecular weight [11].

5.1.2 Spatial Confirmation

The spatial conformation of a molecule is an important factor for the mucoadhesion strength. The mucoadhesive strength of a polymer depends on the spatial arrangement of polymers, i.e. whether they are helical or linear [12].

5.1.3 Concentration of Active Polymer

Optimum concentration of active polymer is required. In remarkably concentrated system, beyond a certain optimum level, the adhesive strength declines drastically because the coiled molecules become separated from the medium so the length of chain available for permeation become limited.

5.2 Environment-Related Factors

5.2.1 Moistening

Moistening provides an ideal environment for the mucoadhesive polymer to distribute over the surface of mucin and creates a particle size suitable for polymer penetration into mucin. The result of moistening of polymer is to provide a close contact of particles with the mucosa [13].

5.2.2 Presence of Metal Ions

Combining with charged groups of polymers and/or mucous can reduce the number of interaction sites and the strength of mucoadhesive bonding.

6. CLASSIFICATION OF MUCO ADHESIVE POLYMERS

6.1 On the Basis of Charge

6.1.1 Anionic Polymers

Anionic polymers possess negatively charged functional groups, such as carboxyl or sulfonic acid moieties.

Example: Carbopol

6.1.2 Cationic Polymers

These polymers have positively charged functional groups, such as amino groups. Examples include chitosan and polyethyleneimine (PEI). Cationic polymers can interact with the negatively charged mucus layer through electrostatic interactions. [14]

Example: Chitosan

6.2 On the Basis of Origin

6.2.1 Natural Polymers

Natural polymers are those that occur naturally and are derived from living organisms. These polymers are generally biodegradable, biocompatible, and non-toxic, making them suitable for pharmaceutical applications [15]. Example: Pectin

7.ROUTES OF MUCOADHESIVE DRUG DELIVERY SYSTEM

Systems for mucoadhesive drug delivery prolong the time the dose form is left at the application site, improving absorption. For systemic and local effects via oral, buccal, nasal, rectal, and vaginal routes, various such systems have been created recently.

7.1 Buccal Drug Delivery System [16]

An alternative to oral administration for medications affected by the first-pass effect is buccal drug delivery. Long regarded as an ideal location for medication administration, the stratified squamous epithelium in

the buccal mucosa is supported by connective tissue lamina propria.

7.2 Oral Drug Delivery System

Mucoadhesive systems developed for oral administration aim to provide controlled and sustained drug release while maintaining adhesion as the dosage form transits through the gastrointestinal tract.

7.3 Vaginal Drug Delivery System

The uterus is connected to the outside of the body by the vagina, which acts as a fibrovascular conduit. Lamina propria and squamous epithelium are used to line it.

7.4 Gastrointestinal Drug Delivery System

The oral route is undoubtedly the most desired way of administration, but there are some serious risks with it, including hepatic first-pass metabolism, drug degradation during absorption, the presence of mucus on GI epithelia, and rapid mucus turnover.

8.EVALUATION PARAMETERS OF MUCOADHESIVE DRUG DELIVERY SYSTEM

a. Methods of mucoadhesive strength measurement
b. Methods determining tensile strength
c. Falling liquid film method
d. B. Swelling index
e. C. Thumb method
f. D. Electrical conductance

8.1 Methods of mucoadhesive strength measurement

8.1.1 Methods determining tensile strength

There is uniform distribution of stress over the adhesive joint in tensile and shear experiments, while the stress is focused at the edge of the joint in the peel strength. Thus, the mechanical properties are measured through tensile and shear measure, while the peel strength measures the peeling force [17].

8.1.2 Falling liquid film method

In the falling liquid film method, the mucous membrane is positioned inside a longitudinally cut stainless steel cylindrical tube.

8.2 Swelling index

The amount of swelling is quantified in terms of % weight gained by the formulation. It is calculated using following formula:

Swelling index (S.I.) = (Wt.-Wo/Wo)

Where,

S.I = Swelling index;

Wt. = Weight of tablet at time t;

Wo = Weight of tablet before placing in the beaker.

8.3 Thumb method

This is used for the qualitative determination of peel adhesive strength of the polymer and is useful in the development of buccal adhesive delivery systems [18].

8.4 Electrical conductance

A modified rotational viscometer has been used to measure the electrical conductance of different semisolid mucoadhesive ointments.

9. APPLICATIONS OF MUCOADHESIVE DRUG DELIVERY SYSTEM

9.1. Buccal Drug Delivery [19].

Buccal drug delivery systems take advantage of the rich blood supply and relatively immobile mucosal surface of the oral cavity to enhance drug absorption and improve therapeutic efficacy.

9.2. Vaginal Drug Delivery

Vaginal formulations benefit from extended residence time through mucoadhesion. Semi-solid preparations, including gels and creams, provide improved distribution and intimate contact with vaginal mucosa.

10. CURRENT SCENARIO [20].

Mucoadhesive drug delivery systems are attaining popularity around the world, with more inventors and researchers working on the design and development of new adhesive devices. A large number of new formulations are being developed on a daily basis, and their demand is increasing, examples are mucoadhesive formulations and the use of peptides as drugs.

11. FUTURE CHALLENGES AND OPPORTUNITIES

Buccal drug delivery research has grown and advanced dramatically over the last few years. The buccal mucosa presents great potential for systemic delivery of drugs which are ineffective via orally administration and also a feasible and attractive alternative to administer the protein and peptide drugs non-invasively. As a result of broad research in this field many novel devices such as nanoparticulate devices, buccal sprays, and phospholipid vesicles. Different techniques have been used to create sustained or controlled delivery systems [21].

12. CONCLUSION

Mucoadhesive drug delivery systems offer innovative solutions to traditional drug delivery challenges by improving the drug retention. Novel polymeric systems have remarkable potential in improving therapeutic outcomes across various routes of administration. This overview of mucoadhesive dosage forms serves as a valuable guide for the rational design and development of advanced mucoadhesive drug delivery systems, encompassing both the creation of novel mucoadhesive polymers and the design of suitable delivery devices.

13. AUTHOR CONTRIBUTIONS

All authors are contributed equally.

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None

15. DECLARTION COMPETING INTEREST

The authors have no conflicts of interest to declare.

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