

A Review Article on Mucoadhesive Bilayer Tablet

Vaibhavi A. Kalambe, Dr. Amit R. Jaiswal, Harsha O. Indoriya, Aastha B. Padawe

P. R Pote Collage of Pharmacy, Amravati

vaibhavikalambe@123gmail.com

Abstract: *Mucoadhesive bilayer tablets have gained significant attention as an advanced drug-delivery approach designed to enhance therapeutic efficacy, patient compliance, and site-specific delivery. These systems are composed of two functional layers: a drug-loaded layer that enables sustained release, and a mucoadhesive layer that promotes intimate contact with the mucosal surface, thereby prolonging residence time and improving drug absorption. The effectiveness of such systems depends largely on the selection of suitable mucoadhesive polymers, including natural, semi-synthetic, and synthetic materials such as chitosan, sodium alginate, hydroxypropyl methylcellulose, and carbomers, which provide the necessary adhesion strength and modulate release kinetics. This review consolidates current knowledge on the mechanisms of mucoadhesion, formulation strategies, polymer characteristics, manufacturing techniques, and evaluation parameters used in the development of mucoadhesive bilayer tablets. Overall, mucoadhesive bilayer tablets represent a versatile and promising platform with the potential to improve bioavailability, reduce dosing frequency, and support patient-centered drug-delivery solutions*

Keywords: Mucoadhesive, bilayer tablet, mucoadhesive bilayer tablet, history, mucous membrane, mucoadhesion, polymer

I. INTRODUCTION

Mucoadhesive drug delivery has many benefits, such as avoiding first-pass metabolism, easy administration, enhancing permeation, preventing enzymatic degradation, and fewer dose-related side effects. They are applied in the oral cavity, for local and systemic drug delivery. This delivery route is used for conventional dosage forms to improve the therapeutic performance of the drug. Oral mucoadhesive drug delivery systems have very popularity in the pharmaceutical industry ^[1]

Mucoadhesive Drug Delivery System

A mucoadhesive drug delivery system is a dosage form designed to adhere to the mucosal surfaces of the body, thereby prolonging the residence time of the drug at the site of absorption and enhancing bioavailability^[2]

Bilayer Tablet Technology

A bilayer tablet consists of two distinct layers, usually containing two different drugs or two release profiles (e.g., one immediate-release and one sustained-release layer). It is primarily used for chronotherapeutic, combination, or controlled-release drug delivery

Objective

- To separate incompatible drugs in one dosage form
- To provide biphasic drug release (e.g., immediate + sustained release)
- To allow combination therapy for improved patient compliance

Advantages

- Enables controlled or sustained release
- Improved stability for incompatible drugs
- Reduced dosing frequency



- Better therapeutic efficiency^[3]

General properties of bilayer tablets ^[4]

- Should be free from damages like chips, discolouration and cracks
- Should be elegant
- Should possess chemical stability
- Should possess ability of withstanding mechanical property

Following are the general steps involved in the preparation of bilayer tablets ^[5]

- Filling of first layer
- Compression of first layer
- Ejection of upper punch
- Filling of second layer
- Compressing the second layer
- Ejection of prepared bilayer tablet.

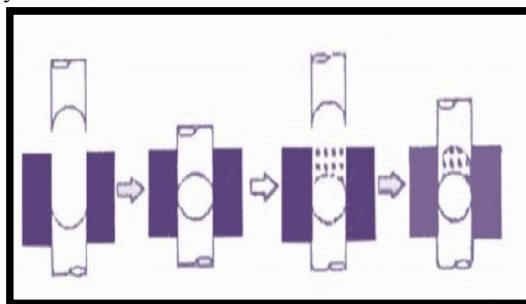


FIG NO 1: Techniques of bilayer tablets ^[6]

1. OROS® push-pull technology

This technology mostly includes two or three layers, among which the first one or two layers contain the active pharmaceutical ingredient and the last one is the push layer. The drug layers are only composed of the drug and a few excipients and are made of poorly soluble material. It could also additionally include a suspending and osmotic agent. A semipermeable layer keeps the tablet core separate from its surroundings.

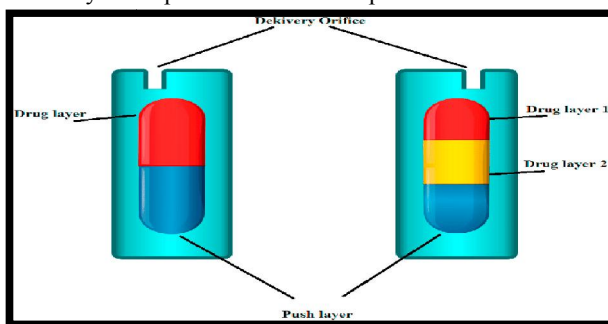


FIG NO: 2 OROS push pull technology ^[7]

2. L-OROS™ technology

This technology is made by Alza and solves a major problem of solubility. The drug was first developed in the form of lipid soft gel in a dissolved state. It was then covered by a barrier membrane, followed by the osmotic push layer, and after that, the semipermeable membrane was punctured for an exit cavity.



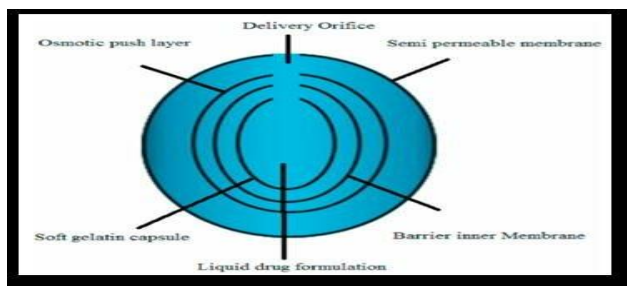


FIG NO: 3 L-OROS technology ^[8]

3 DUROS technology (Alza corporation)

The Duros technology relies on the implant technique and acts as a substitute for the transmission of numerous therapeutic substances, which ranges from peptides, proteins, and various other biochemical substances. Also known as “Miniature drug dispensing technology”, this system works similarly to a miniature syringe that releases drugs continuously and consistently in a concentrated form for a longer period. In the human body, the therapeutic compounds are protected due to these cylinders, hence, making it resistant to human tissues for a long period. For the annual palliative treatment of advanced prostate cancer, Viadur (leuprolide acetate implant) this technology is employed.

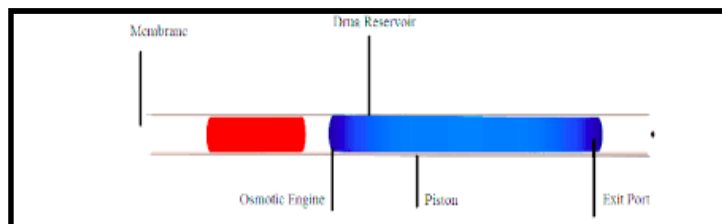


FIG NO 4: DUROS technology ^[9]

4. Elan drug technologies’ dual release drug delivery system (DUREDAS™ technology)

Dual drug delivery system (DUREDAS) is a technology employed by Elan corporations for two distinct discharge amounts or double discharge from a solo dosage. This technology provides a combination release pattern of drug i.e. immediate or sustained release. This technology produces a tablet through two independent direct compression steps which combine the immediate-release layer with the hydrophilic layer in a single tablet. This generates a complex controlled-hydrophilic matrix that remains compact and gradually absorbs liquid from the gastrointestinal tract (GI tract). The hydrophilic matrix upon absorption of fluid turns in sticky, permeable gel, which acts like obstacles between the dosage and the adjacent fluid, as the gel expands more the surrounding fluid, penetrates the drug, hence, dissolving it

5. ENSO TROL technology

An integrated approach is used by the Shire laboratory for the drug delivery system by properly identifying and incorporating the enhancer to get the optimized dosage form in the controlled release system. This approach helps to increase solubility



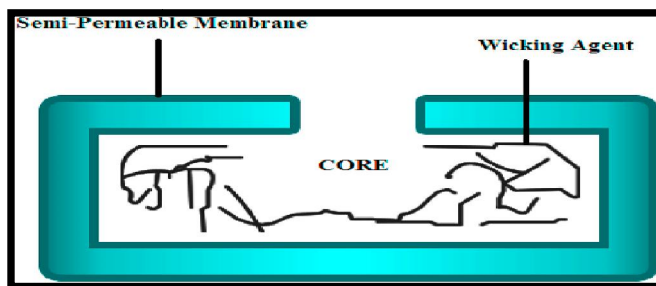


FIG NO: 10 ENSO TROL technology ^[10]

6. Geminex technology

This technology helps massively in increasing the therapeutic effectiveness of the drugs while also minimizes their side effects. It delivers one or more drugs having different release rates through a single dose. It is extremely beneficial for patients as well as the industry and is largely used by pen west in for cardiovascular diseases, CNS disorders, diabetes, cancer, and central nervous system (CNS) disorders

7. Programmable oral drug absorption system (PRODAS)

PRODAS, also known as multi particulate drug technology (Elan Corporation), encapsulates mini-tablets of controlled drug release, with size ranging from 1.5 to 4 mm. The technology is a combination of multi- particle and hydrophilic matrix tablet technologies and is used for providing the combined benefits of these drugs in one dose. PRODAS technology is beneficial in the targeted delivery of the drugs for targeting to GIT. Different release rates of the mini-tablets, such as immediate, delayed, or controlled release, are combined in the form of a single dosage for providing the wanted release rate. The Minitab are sometimes combined with various APIs for forming products with anticipated release patterns

CHALLENGES IN FABRICATION OF BILAYER TABLET

following are the challenges in preparing bilayer tablets.

Delamination

Both the layers should adhere after the process of compression.

Production yields

Lower yields are reported in bilayer tablet than in single tablets as the process of dust collection is required which leads to loss.

Cross contamination

Cross contamination of layers may also occur if mixing of layers occurs.

Cost

Production of bilayer tablets is expensive as compression steps, stability and interaction is to checked.[44,45]

APPLICATIONS

- ♣ suitable for sequential release of two drugs in combination and Separating Two Incompatible Substances is done by bilayer tablet.
- ♣ Patient Convenience and Compliance is more pronounced.
- ♣ The shortcoming of the single layered tablet is improved by beneficial technology known as bilayer tablet
- ♣ The loading dose and sustained dose of the same or different drugs are delivered through the bilayer tablets



Mucoadhesive Bilayer tablet^[11]

A mucoadhesive bilayer tablet is a two-layered dosage form designed to adhere to a mucosal surface (such as buccal, nasal, or vaginal mucosa) and deliver the drug in a controlled manner.

One-layer acts as the mucoadhesive layer, ensuring the tablet sticks to the mucosal membrane.

The second layer serves as the drug-release or backing layer, which may provide controlled release and prevent drug loss into the oral cavity



Fig no 11: Mucoadhesive bilayer tablet^[12]

Objectives

- To prolong drug residence time at the absorption site
- To improve bioavailability by bypassing first-pass metabolism
- To control the rate of drug release
- To protect the drug from enzymatic degradation

Advantage

- Avoids hepatic first-pass metabolism (useful for peptides, hormones, etc.)
- Provides prolonged therapeutic effect
- Offers localized or systemic action depending on design
- Enhances patient compliance

History of Mucoadhesive Bilayer Tablet

1. Early Concepts (1940s–1970s) — Birth of Bioadhesion

The concept of bioadhesion—the ability of certain materials to stick to biological tissues—was first explored in the 1940s in the field of dentistry and surgery, where natural gums and synthetic polymers were used for tissue adhesion and wound closure.

In 1970, the first scientific studies on bioadhesive polymers for drug delivery began, marking the beginning of mucoadhesive drug delivery research.

These studies focused mainly on hydrogels and natural polysaccharides such as gelatin, pectin, and cellulose derivatives^[13]

2. Development Of Mucoadhesive Drug Delivery System [1980]

During the 1980s, researchers started designing mucoadhesive dosage forms (tablets, gels, and films) to improve drug absorption through mucosal tissues (especially buccal and nasal routes).

The term “mucoadhesion” was formally introduced to describe adhesion to mucus or mucosal surfaces.

Polymers like Carbopol, HPMC, and chitosan were identified as effective mucoadhesive materials^[14]

3. Emergence of Bilayer Tablet Technology (Late 1980s–1990s)

In parallel, bilayer tablet technology evolved as a method to combine two different release profiles (e.g., immediate and sustained release) or to separate incompatible drugs within a single dosage form.



Pharmaceutical companies started using bilayer compression machines to improve drug delivery precision and flexibility.

The combination of mucoadhesion and bilayer tablet technology was a natural next step to achieve localized, sustained delivery at mucosal sites^[15]

4. Integration into Mucoadhesive Bilayer Systems (2000s)

The 2000s saw the development of mucoadhesive bilayer tablets, where:

One layer contained mucoadhesive polymers to ensure attachment to the mucosa.

The other acted as a drug release or backing layer to control release direction and duration.

This approach was widely used for buccal, vaginal, and nasal delivery systems, offering improved bioavailability and prolonged retention time.

Example drugs formulated this way include glipizide, metoprolol, and propranolol^[16]

5. Recent Advances (2010–Present)

Current research focuses on novel mucoadhesive polymers (e.g., thiolated chitosan, carbomer derivatives) and nanotechnology-based bilayer systems.

Modern 3D printing and hot-melt extrusion techniques allow precise control over layer thickness, drug distribution, and adhesion strength.

The systems are being developed for systemic peptide delivery, targeted cancer therapy, and oral mucosal vaccines^[17]

Anatomy of Mucous Membrane^[18]

Mucous membrane is the main site of administration for bioadhesive systems. A mucosa consists of two to three layers: (1) an epithelium, (2) lamina propria, (3) a layer of smooth muscle called the muscularis. They are characterized by a layer of epithelium, whose surface is covered by mucus. Mucin, a glycoprotein of mucus, is responsible for the structure of mucus membrane. Thickness of mucus can vary from 50-500µm in the stomach to less than 1 µm in the mouth cavity

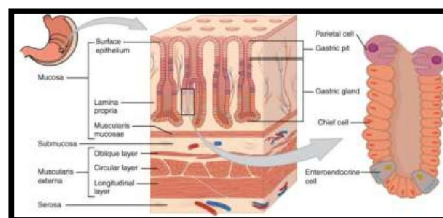


Fig no 2: Mucous membrane^[19]

Composition of mucus layer

The mucus consists of glycoproteins, fats, salts and about 95% of water by mass, making it a highly hydrophilic system. Mucus glycoproteins are high molecular weight proteins possessing attached oligosaccharide units containing, L-fucose, D-galactose, N-acetyl-D-glucosamine, N-acetyl-D-galactosamine and Sialic acid.

Functions of mucus layer

Mucous membranes have absorptive, secretory, and protective functions. Mucous layer is protective because of its hydrophobicity.

It influences the bioavailability of drugs as it hinders the tissue absorption of drugs and other substrates.

It strongly bonds with the epithelial cell surface as a continuous gel layer i.e. helps in adhesion.

It has key part in the lubrication of the mucosal membrane and maintenance of its moisture.

They are often covered with mucus secreted by goblet cells, multicellular mucous glands, or both. The mucus traps bacteria and foreign particles, which keeps them from invading the tissues and aids in their removal from the body



Mechanism of Bioadhesion^[20]

For bioadhesion to occur, three stages are involved:

1. An intimate contact between a bioadhesive and a membrane either from a good wetting of the bioadhesive and a membrane or from the swelling of bioadhesive.
2. Penetration of the bio-adhesive into the tissue takes place
3. Inter penetration of the chains of the bioadhesive with mucous takes place. Low chemical bonds can then settle.

The bonding between the mucus and the biological substance occurs chiefly through both physical and chemical interactions results from enlargement of the adhesive material and chemical bonds due to electrostatic interaction, hydrophobic interactions, hydrogen bonding and dispersion forces

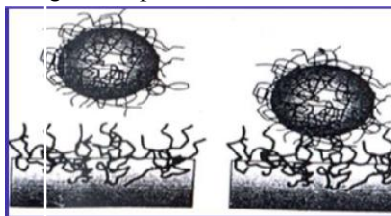


Fig:3 Inter penetration of bioadhesive and mucus polymer chain^[21]

Theories of Bioadhesion or Mucoadhesion

Several theories have been proposed to explain the fundamental mechanism of adhesion.

a) **Wetting Theory:** Wetting theory is predominantly applicable to liquid bioadhesive systems and analyzes adhesive and contact behaviour in terms of a liquid or a paste to spread over a biological system. The work of adhesion [expressed in J/m²] being defined as energy per cm² in terms of surface and interfacial tension (released when an interface is formed).

According to Dupres equation, work of adhesion is given by

$$W_A = \gamma_B - \gamma_A + \gamma_{AB}$$

Where, A and B refers to the biological membrane and the bioadhesive formulation respectively.

The work of cohesion is given by

$$W_C = \gamma_B$$

For a bioadhesive material B spreading on a biological substrate, the spreading coefficient is given by:

$$S = \gamma_B + \gamma_A - \gamma_{AB}$$

γ_{AB} should be positive for a bioadhesive material to adhere to a biological membrane. For a bioadhesive liquid B adhering to a biological membrane A, the contact angle is given by:

$$\cos \theta = \frac{\gamma_B + \gamma_A - \gamma_{AB}}{\gamma_B}$$

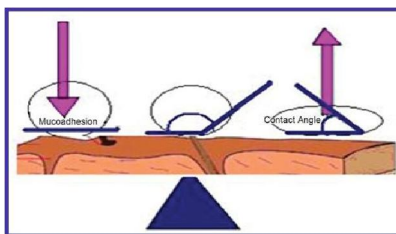


Fig 4: Mucoadhesion process with permeation^[22]

b) **Diffusion Theory:** According to this theory, the polymer chains and the mucus mix to a sufficient depth to create a semi-permanent adhesive bond. The exact depth to which the polymer chains penetrate the mucus depends on the diffusion coefficient and the time of contact. This diffusion coefficient, in turn, depends on the value of molecular weight between cross links and decreases significantly as the cross-linking density decreases.



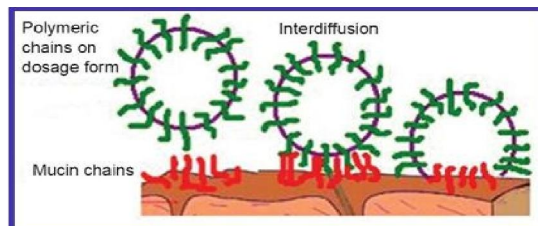


Fig 5: Secondary interaction between mucoadhesive device and mucus^[23]

c) Electronic Theory: According to this theory, electronic transfer occurs upon contact of an adhesive polymer and the mucus glycoprotein network because of differences in their electronic structure. This results in the formulation of an electronic double layer at the interface; adhesion occurs due to attractive forces across the double layer.

d) Fracture Theory: According to Fracture theory, adhesion is related to separation of two surfaces after adhesion. The fracture strength is equivalent to adhesive strength as given by,

$$G = (E\varepsilon / L)^{1/2}$$

Where: E = Young's module of elasticity

ε = Fracture energy

L = Critical crack length when two surfaces are separated

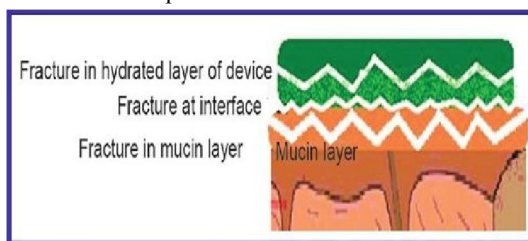


Fig 6: Fractures occurring for Mucoadhesion^[24]

e) Adsorption Theory: According to this theory, after an initial contact between two surfaces, the materials adhere because of surface forces acting between the atoms in the two surfaces. Two types of chemical bonds such as primary covalent (permanent) and secondary chemical bonds (including electrostatic forces, Vander Waals forces and hydrogen and hydrophobic bonds) are involved in the adsorption process.

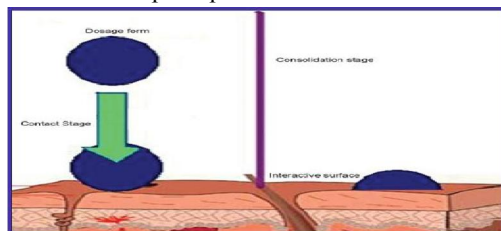


Fig 7: The process of consolidation^[25]

Components

Mucoadhesive Layer Contains polymers like:

Chitosan

Carbopol 934P

HPMC (Hydroxypropyl methylcellulose)

Sodium alginate

Backing Layer Usually water-insoluble, made of:

Ethyl cellulose

Polyethylene

Eudragit RL/RS^[26]



CLASSIFICATION OF POLYMERS ^[27]

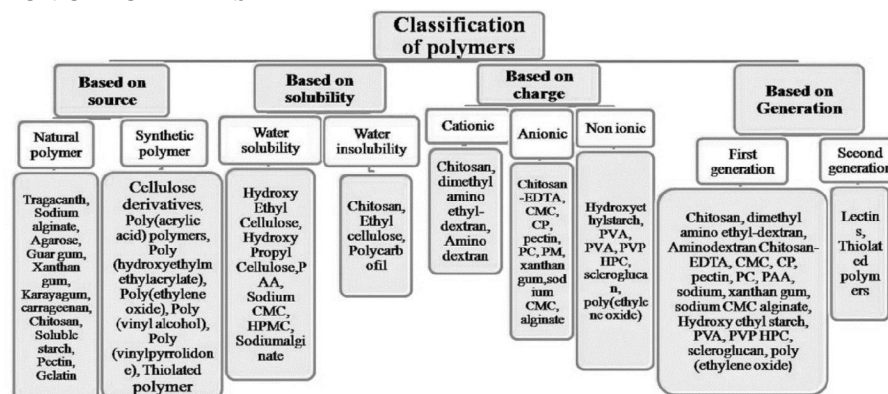


Fig:8 Polymers Used in Mucoadhesive Bilayer Tablets ^[28]

Polymer Name: Carbopol (Carbomer 934, 940, 974P)

Type (Natural / Synthetic): Synthetic, anionic polymer of acrylic acid

Function in Tablet: Mucoadhesive polymer (adhesive layer)

Explanation / Properties: Provides strong adhesion due to $-\text{COOH}$ groups forming hydrogen bonds with mucin. Excellent swelling capacity and bioadhesion. ^[29]

Polymer Name: polycarbophil

Type (Natural/Synthetic): Anionic synthetic polymer

Function in Tablet: Mucoadhesive polymer

Explanation/Properties: Similar to Carbopol but less acidic. Forms hydrogen bonds with mucin glycoproteins; used for prolonged retention ^[30]

Polymer Name: Sodium Carboxymethyl Cellulose (Na-CMC / SCMC)

Type (Natural/Synthetic): Anionic cellulose derivative

Function in Tablet: Mucoadhesive & swelling polymer

Explanation/Properties: Hydrophilic polymer that swells and forms gels. Moderate adhesion strength, enhances drug release control. Often used in combination with Carbopol ^[31]

Polymer Name: Chitosan

Type (Natural/Synthetic): Cationic natural polysaccharide

Function in Tablet: Mucoadhesive + permeation enhance

Explanation / Properties: Binds electrostatically to negatively charged mucin. Biodegradable, biocompatible, and enhances drug absorption. Used in buccal and nasal mucoadhesive tablets ^[32]

Polymer Name: Hydroxypropyl Methylcellulose (HPMC)

Type: Nonionic cellulose derivative

Function in Tablet: Matrix former / release controller

Explanation / Properties: Controls drug release by gel formation. Provides moderate mucoadhesion and mechanical strength. Used in drug layer or sometimes in both layers ^[33]

Polymer Name: Sodium Alginate

Type (Natural/ Synthetic): Anionic natural polysaccharide

Function in Tablet: Mucoadhesive & matrix former

Explanation / Properties: Swells in aqueous media and adheres to mucosa. Biocompatible and forms stable gel matrices for sustained release ^[34]



Patient Types / Situations Suitable for Mucoadhesive Bilayer Tablets

Mucoadhesive bilayer tablets are an advanced dosage form designed to enhance drug delivery through the buccal or other mucosal routes. They are particularly beneficial for specific patient populations and therapeutic conditions where conventional oral dosage forms are less effective or impractical^[35]

Patients with swallowing difficulties (dysphagia, elderly, paediatric, or bedridden patients)

Patients who have difficulty swallowing tablets or capsules—such as children, elderly individuals, or those bedridden due to illness—benefit greatly from mucoadhesive bilayer tablets. These dosage forms adhere to the buccal mucosa and deliver the drug without the need for water or swallowing, improving compliance and convenience^[36]

2. Patients requiring systemic drug delivery with avoidance of first-pass metabolism:

Many drugs suffer from extensive first-pass hepatic metabolism, leading to low bioavailability when administered orally. Mucoadhesive bilayer tablets bypass the gastrointestinal tract and hepatic metabolism by allowing direct absorption through the oral mucosa. This is beneficial for drugs such as propranolol, nifedipine, and carvedilol, improving therapeutic efficacy and consistency in plasma drug levels^[37]

3. Patients needing local treatment for oral conditions:

For localized diseases such as oral candidiasis, gingivitis, aphthous ulcers, or periodontal infections, mucoadhesive bilayer tablets offer prolonged drug contact at the affected site. This ensures a higher local drug concentration and extended therapeutic effect compared to mouthwashes or gels^[38]

4. Patient requiring controlled or sustained drug release

Mucoadhesive bilayer tablets, typically consisting of an adhesive layer and a drug-release layer, provide controlled, unidirectional drug delivery over extended periods (e.g., 8–12 hours). This reduces dosing frequency, improves patient adherence, and maintains steady-state plasma levels—ideal for chronic disease management such as hypertension or diabetes^[39]

5. Patients with gastrointestinal disturbances or nausea/vomiting:

In patients unable to tolerate oral medications due to nausea, vomiting, or gastrointestinal surgery, the buccal route provides an alternative for drug administration. Since the drug is absorbed directly through the mucosa, it avoids^[40]

6. Patients requiring rapid onset of therapeutic action:

For emergency situations such as angina pectoris or breakthrough pain, mucoadhesive bilayer tablets allow for fast transmucosal absorption of drugs like nitroglycerin or fentanyl. The high vascularization of the buccal mucosa enables rapid entry of the drug into systemic circulation, leading to a quicker onset of action than conventional oral tablets. Degradation in the stomach and intestine^[41]

1. Direct Compression (Most Common)^[42]

Procedure:

Prepare two separate powder blends:

Mucoadhesive layer → contains drug + mucoadhesive polymers (e.g., HPMC, Carbopol, PVP).

Backing layer → hydrophobic or non-adhesive material (e.g., ethyl cellulose).

Compress the first layer lightly.

Add second layer on top.

Perform final compression to form the bilayer tablet.

Advantages: Simple, cost-effective, no solvents required



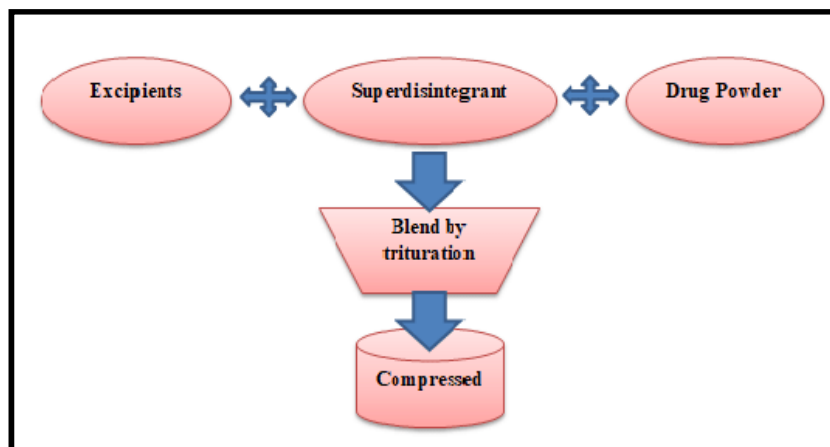


FIG NO:9 Direct compression method^[43]

2. Wet Granulation Method

Procedure:

Drug and excipients for each layer are granulated separately using a binder solution.

Dry, mill, and blend the granules.

Compress the granules in two steps to form the bilayer.

Advantages: Enhanced flow and compressibility for poorly flowing powders

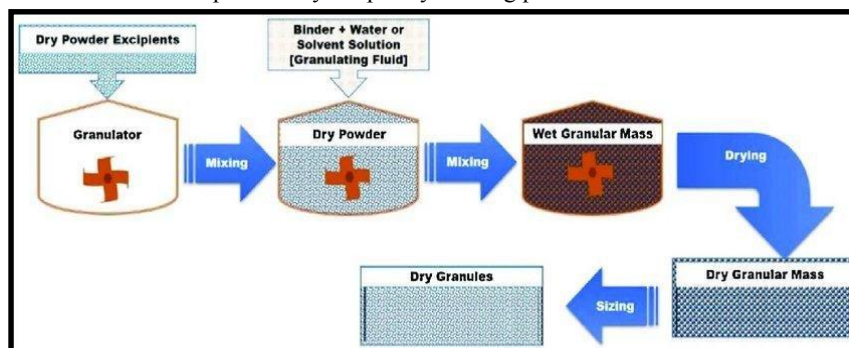


FIG NO: 10 Wet granulation method^[44]

3. Dry Granulation (Slugging or Roller Compaction)

Used when the drug is moisture- or heat-sensitive.

Procedure:

Convert each layer's blend into slugs or ribbons.

Mill into granules.

Compress bilayer tablets similarly to direct compression.

Advantages: Avoids heat and solvents



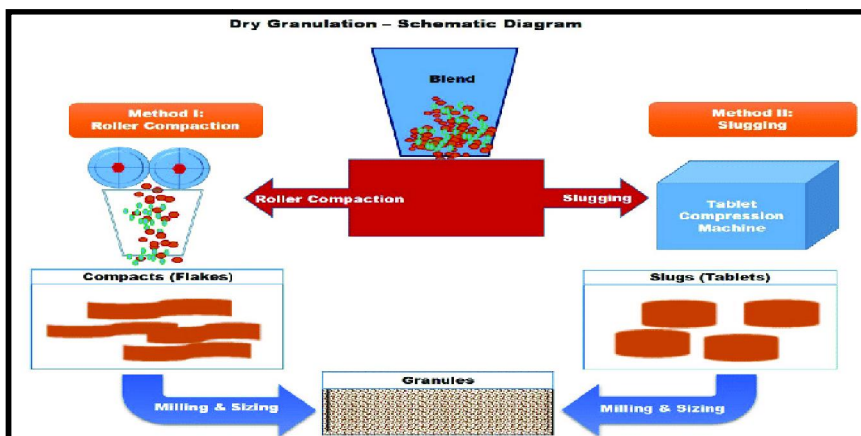


FIG NO: 11 Dry granulation] method ^[45]

4. Hot-Melt Extrusion (HME) for Backing Layer

Used especially when the backing layer requires hydrophobic polymers.

Procedure:

Backing layer prepared by melting polymer + drug/excipients through extrusion.

Combined with a separately prepared mucoadhesive layer and compressed.

Advantages: Precise control of drug release; good for sustained release

Figure 1

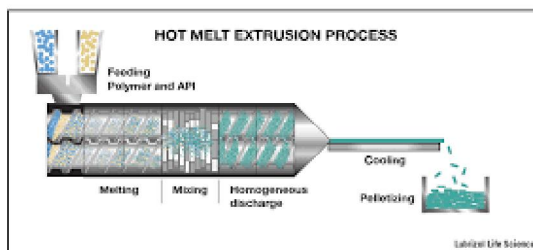


FIG NO: 12 Hot melt extrusion ^[46]

5. Compression-Coating (Press Coating)

A core tablet (e.g., backing layer) is placed inside a die.

Mucoadhesive polymer blend is added around/over it.

Compressed to form a bilayer or coated tablet.

Advantages: Good for protecting sensitive drugs in one layer

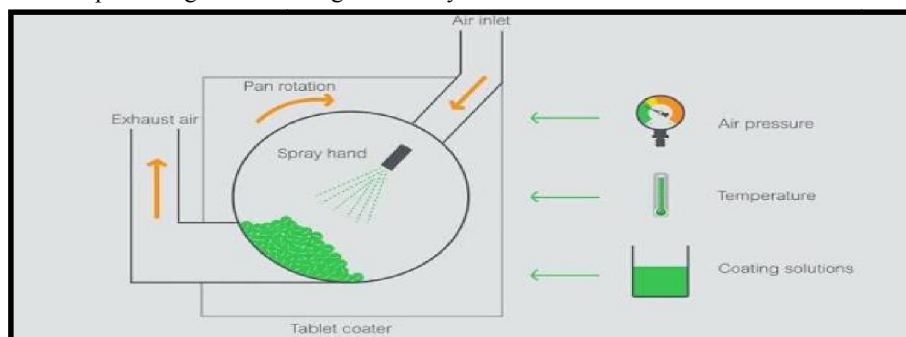


FIG NO : 13 Compression coating ^[47]



6. Solvent Casting + Compression

Less common; used when mucoadhesive layer needs film-forming polymers.

Procedure:

Prepare mucoadhesive polymer film by solvent casting.

Place film on backing-layer tablet.

Light compression bonding is applied.

Advantages: Very strong mucoadhesion; good for tablets

EVALUATION OF MUCOADHESIVE BILAYER TABLET ^[48]

Some of the general test for evaluating mucoadhesive bilayer tablets are the following

- Tablet Thickness and Size
- . Tablet Hardness
- Friability
- Uniformity of Weight
- Drug content
- Swelling index
- Mucoadhesion strength
- Compatibility studies

REFERENCES

- [1]. Shaikh S, Shaikh Z, Khan GJ, Patel SM. A review on mucoadhesive drug delivery system. European Journal of Pharmaceutical & Medical Research. 2017;4(11):247-52.
- [2]. Andrews GP, Lavery TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009;71(3):505–518.
- [3]. Shiyani B, Gattani S, Surana S. Formulation and evaluation of bilayer tablet of metoclopramide hydrochloride and ibuprofen. AAPS PharmSciTech. 2008;9(3):818–827.
- [4]. Sloan P, Picardo M, Schor SL. The structure and function of oral mucosa. Dental update. 1991 Jun 1;18(5):208-12.
- [5]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews. 1994 Jan 1;13(1-2):43-74.
- [6]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews. 1994 Jan 1;13(1-2):43-74
- [7]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews. 1994 Jan 1;13(1-2):43-74
- [8]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews. 1994 Jan 1;13(1-2):43-74
- [9]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews. 1994 Jan 1;13(1-2):43-74
- [10]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews. 1994 Jan 1;13(1-2):43-74
- [11]. Gupta A, Garg S, Khar RK. Mucoadhesive buccal drug delivery systems. Indian Drugs. 1992;29(13):586–593.
- [12]. Procaccini M, Palazzo V, Mastroianni L, Orefici M. Flurbiprofen collutory in oral surgical pathology. Minerva Stomatologica. 1996 Sep 1;45(9):421-5.
- [13]. Park H, Robinson JR. Mechanisms of mucoadhesion of poly (acrylic acid) hydrogels. Pharmaceutical research. 1987 Dec;4(6):457-64.



- [14]. Smart JD. The basics and underlying mechanisms of mucoadhesion. Advanced drug delivery reviews. 2005 Nov 3;57(11):1556-68.
- [15]. Shiyani B, Gattani S, Surana S. Formulation and evaluation of bi-layer tablet of metoclopramide hydrochloride and ibuprofen. Aaps Pharmscitech. 2008 Sep;9(3):818-27.
- [16]. Semalty M, Semalty A, Kumar G, Singh D, Saraf S. Formulation and characterization of mucoadhesive buccal films of glipizide. Indian J Pharm Sci. 2008;70(1):43-48
- [17]. Khutoryanskiy VV. Advances in mucoadhesion and mucoadhesive polymers. Macromol Biosci. 2011;11(6):748-764.
- [18]. Bhatt DA, Pethe AM. Mucoadhesive drug delivery systems: an overview. Journal of pharmacy research. 2010;3(8):1743-7.
- [19]. Bhatt DA, Pethe AM. Mucoadhesive drug delivery systems: an overview. Journal of pharmacy research. 2010;3(8):1743-7.
- [20]. Jain NK, editor. Controlled and novel drug delivery. New Delhi: CBS publishers & distributors; 1997
- [21]. Jain NK, editor. Controlled and novel drug delivery. New Delhi: CBS publishers & distributors; 1997
- [22]. Jain NK, editor. Controlled and novel drug delivery. New Delhi: CBS publishers & distributors; 1997
- [23]. Jain NK, editor. Controlled and novel drug delivery. New Delhi: CBS publishers & distributors; 1997
- [24]. Jain NK, editor. Controlled and novel drug delivery. New Delhi: CBS publishers & distributors; 1997
- [25]. Jain NK, editor. Controlled and novel drug delivery. New Delhi: CBS publishers & distributors; 1997
- [26]. Andrews GP, Lavery TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009;71(3):505-518.
- [27]. drug delivery. Eur J Pharm Biopharm. 2009;71(3):505-518.
- [28]. Andrews GP, Lavery TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009;71(3):505-518.
- [29]. Andrews GP, Lavery TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009;71(3):505-518.
- [30]. Shaikh S, Shaikh Z, Khan GJ, Patel SM. A review on mucoadhesive drug delivery system. European Journal of Pharmaceutical & Medical Research. 2017;4(11):247-52
- [31]. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. J Control Release. 2011 Feb 10;153(2):106-116.
- [32]. . Park Jain NK, editor. Controlled and novel drug delivery. New Delhi: CBS publishers & distributors; 1997
- [33]. K, Robinson JR. Mechanisms of mucoadhesion of poly(acrylic acid) hydrogels. Pharm Res. 1987 Jul;4(6):457-464.
- [34]. Smart JD. The basics and underlying mechanisms of mucoadhesion. Adv Drug Deliv Rev. 2005 Nov 3;57(11):1556-1568
- [35]. . Lehr CM, Bouwstra JA, Schacht EH, Junginger HE. In vitro evaluation of mucoadhesive properties of chitosan and some other natural polymers. Int J Pharm. 1992 Mar;78(1-3):43-48.
- [36]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Adv Drug Deliv Rev. 1994 Jun;13(1-2):43-74
- [37]. Andrews GP, Lavery TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009 Aug;71(3):505-518.
- [38]. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. J Control Release. 2011 Feb 10;153(2):106-116.
- [39]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Adv Drug Deliv Rev. 1994 Jun;13(1-2):43-74.
- [40]. Perioli L, Ambrogi V, Giovagnoli S, Ricci M, Blasi P, Rossi C. Mucoadhesive bilayered tablets for buccal sustained release of flurbiprofen. AAPS PharmSciTech. 2007 Sep;8(3):E20-27
- [41]. Andrews GP, Lavery TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009 Aug;71(3):505-518.



- [42]. Smart JD. The basics and underlying mechanisms of mucoadhesion. Adv Drug Deliv Rev. 2005 Nov 3;57(11):1556–1568.
- [43]. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15–30.
- [44]. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15–30
- [45]. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15–30
- [46]. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15–30
- [47]. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15–30
- [48]. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews. 1994 Jan 1;13(1-2):43-74

