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Novel Mucoadhesive Film Forming Spray Systems: Mechanism, Formulation Approaches and Therapeutic Perspectives

Damane Madhuri *, Sameer Shafi, Waghmare Pranita, Gadhave Ankita, Swami Shivlila

Department of Pharmaceutics, Shivlingeshwar College of Pharmacy, Almala Maharashtra

A B S T R A C T

Mucoadhesive film-forming sprays (FFS) have emerged as advanced and promising drug delivery systems for mucosal administration owing to their ability to prolong residence time, improve drug absorption, and provide sustained therapeutic action. Conventional dosage forms such as tablets, creams, gels, and ointments often suffer from limitations including poor retention, variable absorption, frequent dosing, and reduced patient compliance. In contrast, mucoadhesive film-forming sprays combine the advantages of mucoadhesive polymers and in situ film formation to enhance localized and systemic drug delivery through buccal, nasal, and vaginal mucosal routes. These systems transform from liquid formulations into thin adhesive polymeric films following solvent evaporation, thereby ensuring uniform drug distribution, improved adhesion, flexibility, and prolonged drug release.The present review discusses the anatomy and physiology of mucosal membranes with particular emphasis on buccal, nasal, and vaginal mucosa, including their permeability, vascularization, mucus composition, and suitability for drug delivery. Various theories and mechanisms of mucoadhesion are also described. Additionally, the formulation aspects of film-forming sprays, including polymers, solvents, plasticizers, penetration enhancers, bioadhesive agents, and preservatives, are comprehensively reviewed. Important physicochemical evaluation parameters such as pH, viscosity, spray angle, mucoadhesive strength, washability, permeability studies, and stability studies are highlighted.Furthermore, the therapeutic applications of mucoadhesive film-forming sprays are discussed. Due to their non-invasive nature, improved patient compliance, and enhanced bioavailability, mucoadhesive film-forming sprays represent a novel and effective platform for mucosal drug delivery and hold significant potential for future pharmaceutical and clinical applications.

Keywords: Mucoadhesion, Film forming spray, Bioavailability, Mucosal drug delivery system, Mucosa, etc.

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*Address for Correspondence:
Dr. Sameer Shafi, Professor and Head Department of Pharmaceutics, Shivlingeshwar College of Pharmacy, almala Maharashtra

INTRODUCTION

Mucosal drug delivery systems have gained popularity as an alternative of the conventional pharmaceutical dosage forms due to the ability to deliver drug across highly vascularized mucosal membranes without the first-pass hepatic metabolism and gastrointestinal degradation. In mucosal drug delivery, there has been significant interest among the various routes of delivery, especially buccal, nasal and vaginal drug delivery systems, which provide rapid drug absorption, improved bioavailability, better patient compliance, and localized and systemic effects. Such routes can be used for the administration of drugs without any invasive procedures and are particularly advantageous for drugs with poor oral bioavailability, low biological half-life or high hepatic clearance [1,2].

There are several drawbacks to conventional dosage forms, such as tablets, capsules, creams, ointments and gels, such as patient discomfort, variable drug absorption, poor residence time, high frequency of dosage and reduced therapeutic efficacy. Enzymatic degradation and first-pass hepatic metabolism in the case of oral administration, and physiological clearance mechanisms and mucous turn-over in the case of topical semisolid formulations, are some of the factors that also restrict the bioavailability of these drugs [3]. These disadvantages have encouraged a wide research in the development of novel mucoadhesive drug delivery systems that aim to extend the time spent at the site and increase the uptake of the drug in the mucosal tissues.

Mucoadhesion: the ability of a polymeric substance to adhere to the mucus film on the surface of the mucosal epithelium. Mucoadhesive polymers interact with mucin glycoproteins by hydrogen bonding, electrostatic force, van der Waals force and chain interpenetration, which increases the retention of a formulation at the application site and the rate of sustained drug delivery [4]. In principle, the process of mucoadhesion can be divided into two important steps: a contact step and a consolidation step, which includes hydration, swelling and entanglement with mucin chains. These characteristics make mucoadhesive systems very useful for enhancing therapeutic efficacy and reducing the loss of the drug as a result of physiological clearance.

Recently, film forming spray systems have attracted a significant amount of interest as next generation mucoadhesive systems for mucosal drug delivery. Film-forming sprays are liquid formulations which when applied, rapidly evaporate the solvent or phase change to form a thin film of polymer. These systems have the benefits of both sprays and mucoadhesive films and boast the following properties: ease of administration, uniform dose distribution, rapid drying, greater flexibility, enhanced adhesion, and longer drug residence time [5]. Film-forming sprays are superior to patches or gels in terms of patient acceptance and provide a good coverage of irregular surfaces while not being uncomfortable

Advantages:

- Prolongs the residence time of the dosage form, thereby enhancing drug absorption and therapeutic efficacy.
- Provides excellent accessibility to the site of administration.
- Improves patient compliance due to ease of use.
- Simple and convenient to administer.
- Increases drug bioavailability by avoiding first-pass metabolism.
- Offers a faster onset of action due to the rich vascularization of mucosal membranes. (6)

Disadvantages:

- Not suitable for administration of high-dose drugs.
- Should not contain toxic or non-absorbable components at the site of application such as buccal or vaginal mucosa.
- Must be non-irritating to the mucosal membrane.
- Requires optimal control of cross-linking density, pH, and hydration level.
- Should exhibit good adhesion to moist tissues with some degree of site specificity.
- Polymer stability is essential; it should not degrade during handling or storage. (7)

Anatomy and Physiology of Mucosal Membranes

Mucosal membranes are highly specialized biological barriers that control drug absorption, protection, lubrication and immunological defense. The three types of mucosa that have become the targets of attention for mucoadhesive drug delivery are the buccal, nasal and vaginal mucosa.The buccal, nasal and vaginal mucosa have been researched extensively as targets for mucoadhesive drug delivery due to their accessibility, permeability and vascularization. The knowledge of the anatomical and physiological properties of these mucosal surfaces is crucial for the effective design of mucoadhesive film-forming sprays.

Composition of the Mucus Layer

The mucous layer is composed of mucin and water. Mucous layer is a very hydrophilic system consisting of about 95% water, glycoproteins, lipids and inorganic salts. Mucus glycoproteins are proteins with high molecular weight, with attached oligosaccharide chains made up of L-fucose, D-galactose, N-acetyl-D-glucosamine, N-acetyl-D-galactosamine and sialic acid. Mucosal membranes are specialised bio-barriers, which control drug absorption, protection, lubrication and immune defence. In the various mucosal routes, the buccal, nasal and vaginal mucosa have gained a great deal of interest in the field of mucoadhesive drug delivery due to its rich vascularization, permeability and easy accessibility. (8)

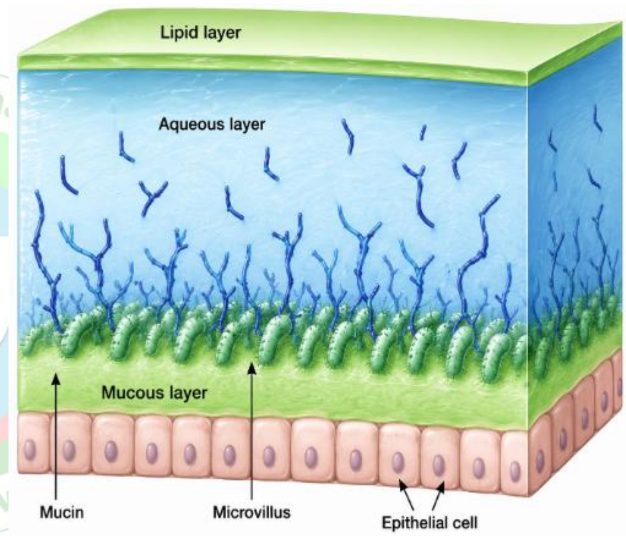

Figure 1: Structure of mucus membrane

Buccal Mucosa

The buccal mucosa is a non-keratinised stratified squamous epithelial membrane in the interior of the cheek and oral cavity. It is very vascular and delivers high systemic drug absorption with bypass of hepatic first pass metabolism. The presence of saliva in the oral cavity softens the mucoadhesive polymers which aids their adhesion and release of the drug. The buccal route is highly utilized for local and systemic delivery of peptides, antifungals, analgesics and antiemetic drugs because of moderate permeability and relatively low level of enzymatic activity [9,10].

Nasal Mucosa

The nasal mucosa is highly vascular and has a large surface area that is ideal for the rapid absorption of drugs and their systemic delivery. It is composed primarily of the columnar (pseudostratified) ciliated epithelium with lumens filled with mucus. The olfactory region allows for direct nose-to-brain delivery of drugs without the involvement of the blood–brain barrier. Mucociliary clearance, however, reduces the residence time of the drug, and this can be increased by the use of film-forming sprays that are mucoadhesive [11,12].

Vaginal Mucosa

The vagina has a stratified squamous epithelium, a mucus layer, and a pH of 3.5–4.5, all of which are kept in place by Lactobacillus species. Hormones affect secretions,
.
thickness and permeability of the epithelia. The use of mucoadhesive film forming sprays for vaginal administration will increase the drug residence time and will allow for a prolonged release of the active ingredients, which are useful for vaginal antifungal therapy, contraception and treatment of sexually transmitted infections (STIs) [13,14] shows in fig.2 and table.1

Table 1: Comparative Table of Buccal, Nasal and Vaginal Mucosa

Parameter	Buccal Mucosa	Nasal Mucosa	Vaginal Mucosa
pH	6.2–7.4	5.5–6.5	3.5–4.5
Surface Area	~50 cm²	~150 cm²	~90 cm²
Epithelium Type	Non-keratinized stratified squa	Pseudostratified ciliated columnar	Stratified squamous
Mucus Thickness	Moderate	Thin	Thick
Residence Time	Moderate	Short	Long
Vascularization	High	Very high	High
Enzymatic Activity	Low	Moderate	Low
Drug Absorption	Good	Excellent	Moderate to good
First-Pass Metabolism	Avoided	Avoided	Avoided
Major Limitation	Saliva washout	Mucociliary clearance	Variable mucus turnover
Delivery Potential	Local & systemic	Systemic & brain targeting	Mainly local delivery

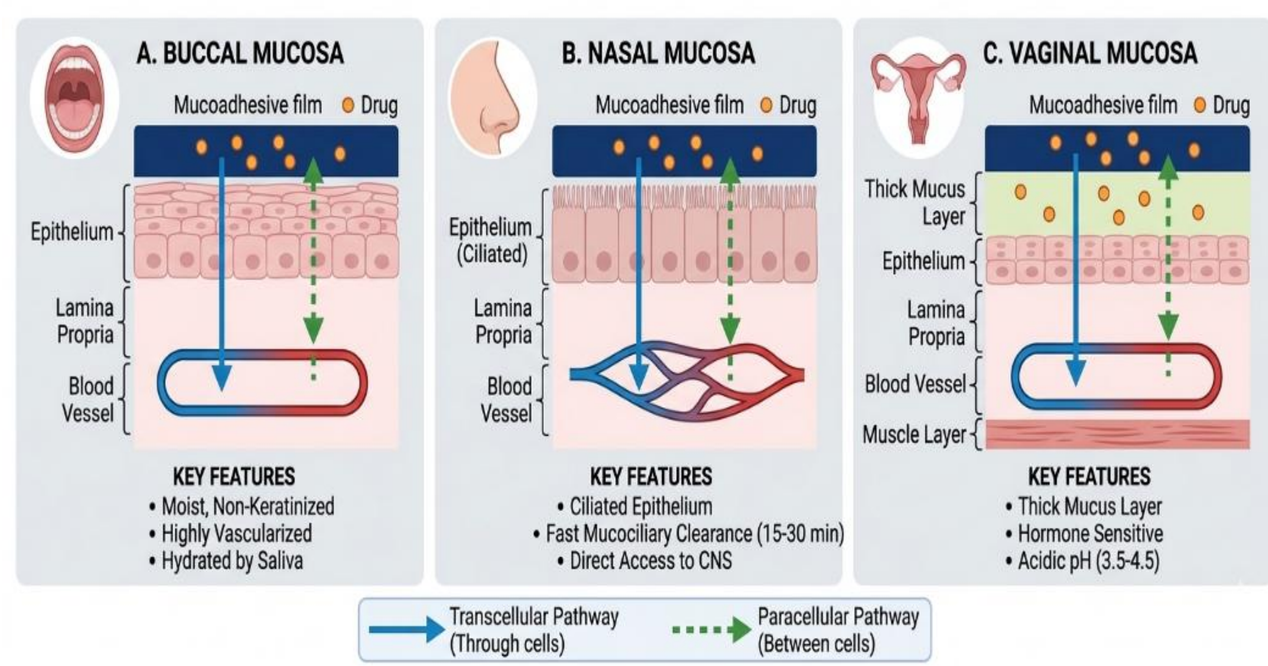

Figure 2: Drug Permeation Pathways in Buccal, Nasal and Vaginal Mucosa

Fundamentals of Mucoadhesion

Mucoadhesion is an occurrence that occurs when a natural or synthetic polymer sticks to the mucous membrane by virtue of the interactions that occur at the interface between the polymer and the mucous layer. For pharmaceutical drug delivery, mucoadhesion is an important property for increasing the time of the formulation's stay at the mucosal surface, which leads to better drug absorption, treatment effectiveness, and controlled drug release. Buccal, nasal, ocular, gastrointestinal and vaginal drug delivery are the broad areas of research for mucoadhesive systems due to its ability of overcoming rapid physiological clearance and enhancing localized as well as systemic drug action [15].

Mucoadhesion Concept

Mucoadhesion can be defined as the adhesion of a polymeric formulation to the mucous membrane that covers biological membranes. The mucin glycoproteins are the primary constituents of the mucus layer, along with water, electrolytes, enzymes, and lipids, which prevent dehydration and microbial invasion of the epithelial tissues. The attachment of mucoadhesive polymers to mucin is a result of several physicochemical interactions including hydrogen bonding, electrostatic attraction, van der Waals forces, and entanglement of polymer chains. The interactions help the formulation stay in the mucosal area for a long time, leading to a better drug retention and prolonged release [16].

Mechanism of Mucoadhesion

Mucoadhesion is an event that is mediated by a series of physicochemical interactions between polymer and mucosal surfaces. A number of theories have been suggested to account for the mechanism of mucoadhesion

Wetting Theory

The principle of wetting will be explained by the tendency of spreading of liquid system over a surface because of their affinity towards the surface. Evaluation of this affinity can be done by using such methods as measuring contact angle. A contact angle close to or as small as zero is required for a good spreadability. The spreading coefficient (SAB) is calculated from the surface energies of the mucus (γB), the device or formulation (γA) and the interfacial energy (γAB) as follows:

$SAB = \gamma B - \gamma A - \gamma AB$ (1)

Increased surface energy of mucus and formulation compared to the interfacial energy leads to a higher work of adhesion (WA). This means that more energy has to be spent to separate the two interacting phases and so there is better adhesion. The work of adhesion is shown in Equation 2:

$WA = \gamma A + \gamma B - \gamma AB$ (2) Gives in fig.3

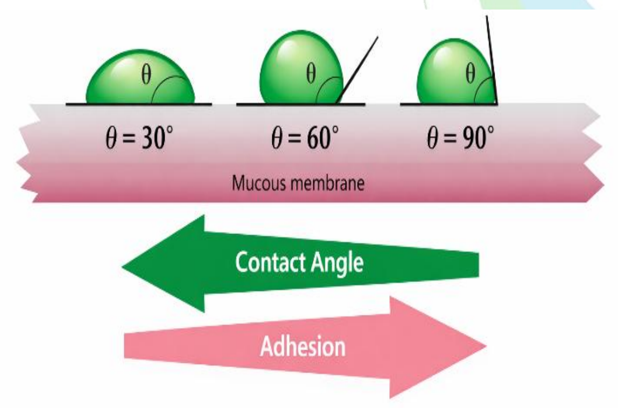

Figure 3 Relationship between Contact Angle and Adhesion on Mucous Membrane

Diffusion Theory

According to diffusion theory, the mucoadhesion is considered to be formed by entanglement of polymer chains and mucin chains, similar to the formation of semi-permanent adhesive bonds. This interpenetration is influenced by various factors such as the diffusion coefficient, stability and type of mucoadhesive chains, contact time, and molecular mobility. The depth of interpenetration needed for efficient bioadhesion is typically from 0.2 to 0.5 µm.

The depth of penetration (L) may be written as shown in Equation 3:

$L = (tDb)1/2$ ………………………….. (3)

where t is the contact time and Db is the diffusion coefficient of the mucoadhesive material in the mucus. The mutual solubility of the interacting materials is also crucial for effective mucoadhesion, as it is essential that the bioadhesive polymer and mucus have similar chemical structures to enhance the chain interaction and mucoadhesion. As shown in Fig.4

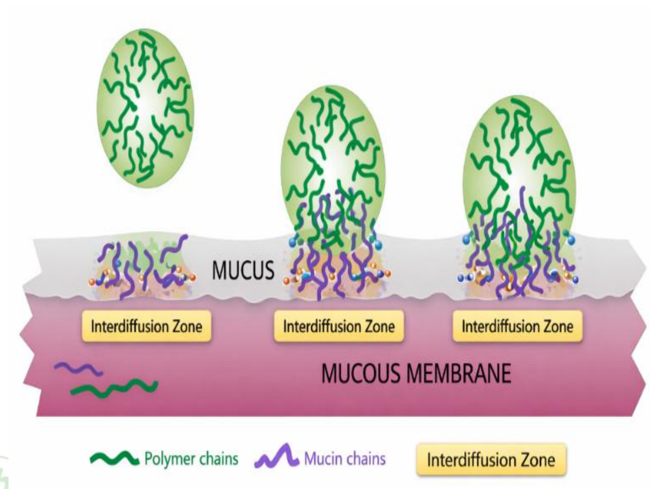

Figure 4: Polymer Mucin Interdiffusion Zones

Electronic Theory

The theory assumes that the biological surfaces have opposite electrical charges to the mucoadhesive materials. When these materials contact each other, electrons transfer between these materials and electronic double layer forms on the interface. The good binding forces created in this double layer layer are involved in the creation of mucoadhesion. (17)

Adsorption Theory

According to the adsorption theory, mucoadhesion can be attributed to secondary chemical interactions between the polymer and the mucus layer. The interactions primarily are hydrogen bonding, Van der Waals forces, hydrophobic interactions, and electrostatic attraction. Of these forces, hydrogen bonding is considered one of the most important forces that contribute to good mucoadhesive properties [18].

Fracture Theory

Theories for adhesion are based on the force necessary to separate two surfaces once adhesion has been established is termed fracture theory. The adhesive strength is regarded as equal to the fracture energy and can be expressed as follows:

$G = (\varepsilon/L)$ ½

Where:

E = Young's modulus of elasticity

εis denoted as the fracture strain or elastic strain at the point of failure

L = critical crack length when surface separation occurs [19]

Stages of Mucoadhesion

The mucoadhesion process generally occurs in two consecutive stages: the contact stage and the consolidation stage.

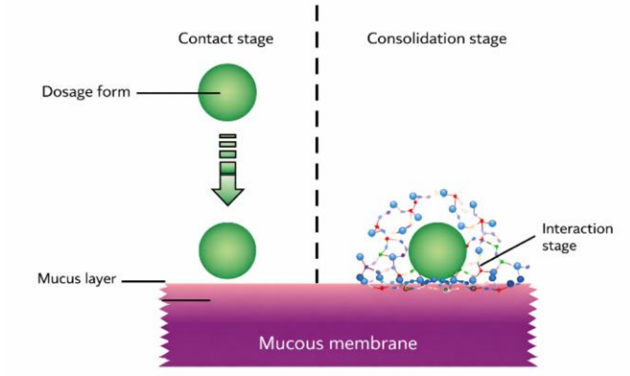

Figure 5: The two steps of mucoadhesion process

Contact Stage

Mucoadhesive drug delivery systems interact with the mucous membrane through the spreading and swelling of the mucoadhesive material, which initiates intimate contact with the mucus layer. The movement of the formulation toward the mucosal surface may occur due to physiological processes such as peristalsis, fluid movement within the organ cavity, or Brownian motion. Once the formulation reaches the mucus surface, both repulsive forces, including osmotic and electrostatic repulsion, and attractive forces, such as Van der Waals interactions and electrostatic attraction, influence the mucoadhesion process [20].

Consolidation Stage

The consolidation stage is characterized by the activation of mucoadhesive compounds in the presence of moisture. Hydration plasticizes the formulation, allowing the mucoadhesive polymer chains to become flexible and interact with the mucus layer through hydrogen bonding and weak Van der Waals forces. This phase of mucoadhesion is mainly explained by the following theories:

Diffusion theory

Dehydration theory

Diffusion theory:

According to diffusion theory, mucoadhesion occurs through the interpenetration of mucoadhesive polymer chains with mucus glycoprotein chains, resulting in the formation of secondary chemical bonds. Polymers containing hydrogen bond-forming functional groups such as hydroxyl (–OH) and carboxyl (–COOH) groups, along with high molecular weight, anionic surface charge, and surface-active properties, exhibit enhanced diffusion and interaction within the mucus layer, thereby promoting mucoadhesion [21].

Dehydration theory:

According to the dehydration theory, materials that rapidly undergo gelation in an aqueous environment upon contact with mucus can induce dehydration due to differences in osmotic pressure. This process promotes closer interaction and mixing between the formulation and the mucus layer, thereby enhancing the contact time with the mucosal membrane. However, this theory is not applicable to solid dosage forms or formulations that are already highly hydrated [22,23].

Film Forming Spray Technology

Film-forming spray systems have developed to be novel platforms for drug delivery and are able to form a thin polymeric film when they are applied to the skin or mucosal surface. In general, these systems are either liquid or semisolid formulations that include film-forming polymers, volatile solvents, plasticizers and other functional excipients. Upon administration, drug is immediately deposited onto the polymer by rapid solvent evaporation and an adhesive film is formed, which results in long residence time and sustained drug release. Film-forming sprays are a highly explored area for buccal, nasal, vaginal and transdermal drug delivery applications due to their ease of application, non-invasive nature, enhanced patient compliance and capacity to form a film on irregular surfaces [24].

Concept of Film Forming Systems

Film forming systems are dosage forms which upon application form a thin polymeric film in situ. The solvent is usually sprayed on the biological surface causing the solvent to evaporate quickly and a clear or cloudy film of the active pharmaceutical ingredient is formed. Formed film is a type of drug reservoir that results in controlled release of the drug for the extended duration.

Film-forming sprays have a number of benefits over conventional creams, gels and ointments, such as:Uniform drug distribution , Rapid drying, Enhanced adhesion, Flexibility, Improved cosmetic acceptability, Reduced dosing frequency, Better patient compliance

Spray film forming and possessing mucoadhesion is especially advantageous as this will increase retention duration at mucosal surfaces, which will also increase the therapeutic effect [25].

Film Formation Mechanism

The mechanism of film formation involves a sequence of physicochemical processes occurring immediately after spray application.

Solvent Evaporation

Once sprayed, a volatile solvent in the formula evaporates quickly once exposed to body heat and air. When the solvent evaporates, it concentrates the polymer on the mucosal surface, and begins the film formation process. The evaporation rate has a significant effect on drying time, film uniformity and patient acceptability [26].

Polymer Precipitation

As the solvent evaporates, the polymer, which is dissolved in the solvent, becomes supersaturated, and precipitates over the mucous surface. Precipitated polymer chains start to aggregate and a continuous matrix of precipitated polymer is formed, which is entrapping drug molecules.

The conditions like solvent composition, polymer concentration, and environment have a significant impact on the precipitation of polymers [27].

Film Maturation

In the film maturing, the polymer chains reorganize and interact by intermolecular forces like hydrogen bonding and chain entanglements, resulting a stable and flexible film. At the same time, hydration and swelling of the polymer increases the mucoadhesion and sustained release of the drug. The following mechanical properties for a mature film are desirable for its therapeutic performance: mechanical strength, elastic properties, adhesion and permeability [28]. Given in Fig.6

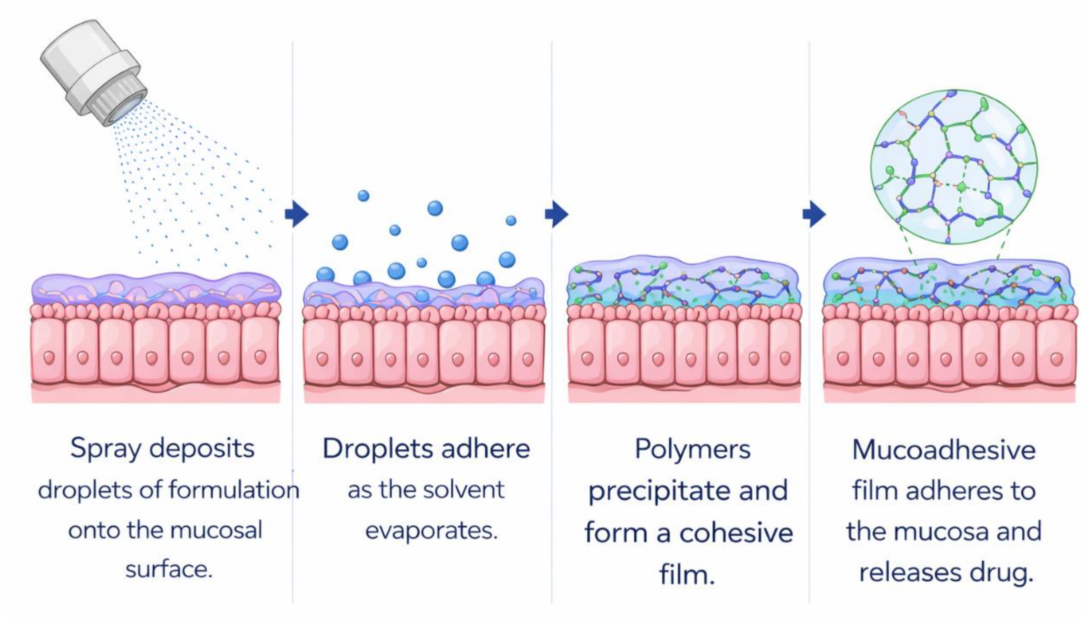

Figure 6: Mechanism of Mucoadhesive Film Formation

Components of Film Forming Sprays

Film-forming sprays contain several excipients that collectively influence sprayability, film formation, adhesion, drug release, and stability.

Polymers

The composition of the buccal film may be prepared in different concentrations with different kinds of polymers according to the desired properties. They consist of natural polymers like hydroxypropyl methylcellulose (HPMC), semi-synthetic polymers like ethyl cellulose and synthetic polymers like polyvinyl pyrrolidone (PVP) [31]. Polymer can also be classified according to their ionic nature, for example, non-ionic polymers like hydroxyethyl cellulose (HEC), anionic polymers like sodium carboxymethyl cellulose (SCMC) and cationic polymers like chitosan [28].

Solvents

Solvents are a vital component of film-forming spray formulations because they are responsible for dissolving the drug and polymer, and help atomize the spray. Once applied, the volatiles are rapidly removed, and a thin film is immediately formed on the mucosal surface. The most used solvents are ethanol, isopropyl alcohol, acetone, water, and ethyl acetate. Choosing an appropriate solvent has a significant impact on drying time, spray properties and precipitation properties of the polymer in the formulation [29].

Plasticizers

For spray film forming formulations, film flexibility and elasticity is provided by plasticizers to increase film flexibility and reduce film brittleness (lower glass transition temperature) of the film. The most frequently used plasticizers are propylene glycol, polyethylene glycol (PEG), glycerol and dibutyl phthalate. The compounds help to enhance the elasticity, mechanical strength and overall patient comfort of the film during its application [30].

Penetration Enhancers

Formulations which include penetration enhancers can increase the permeation of the drug across mucosal barrier through changing the properties of the barrier or by improving the partitioning of the drug into the barrier. Oleic acid, Tween 80, dimethyl sulfoxide (DMSO), menthol and terpenes are the most popular penetration enhancers. These agents help with increased absorption of drugs and increased bioavailability [6].

Bioadhesive Agents

Formulations are made with bioadhesive agents to improve adhesion of the formulation to the mucosal surface to ensure longer retention time and better adhesion at the site of application. Bioadhesive polymers used commonly are Carbopol, chitosan, sodium alginate, hydroxypropyl methylcellulose (HPMC) and polycarbophil. The main interaction between these polymers and mucin is hydrogen bonding and electrostatic interaction that leads to better mucoadhesion [6].

Preservatives

Microbiological stabilisation and storage stability are achieved by the use of preservatives in formulations. These preservatives are typically used: methyl paraben, propyl paraben, benzalkonium chloride and phenoxyethanol. The preservative selected should be compatible with the polymeric components and sensitive mucosal tissues because of their safety and stability [31].

Table 2: Components Used in Film Forming Sprays

Component	Function	Examples
Film-forming polymers	Film formation and sustained release	HPMC, PVA, Eudragit
Mucoadhesive polymers	Enhance adhesion and retention	Carbopol, Chitosan, Sodium alginate
Solvents	Dissolve drug and polymer	Ethanol, Water, Isopropyl alcohol
Plasticizers	Improve flexibility and elasticity	PEG 400, Glycerol, Propylene glycol
Penetration enhancers	Improve drug permeation	Oleic acid, Tween 80, Menthol
Preservatives	Prevent microbial growth	Methyl paraben, Benzalkonium chloride
Drug	Therapeutic activity	Luliconazole, Fluconazole, Lidocaine

Evaluation of FFS

pH

The formulation pH is adjusted to promote the stability of the active pharmaceutical ingredient, and compatibility with the application site. The normal pH of saliva is 5.9 – 7.3. It is, therefore, important to control the pH of a formulation in this physiological range to ensure that it does not cause irritation and does not change the normal oral environment. A pH range of 6.54–6.98 has been reported for the Rizatriptan benzoate buccal films, suggesting that the benefit of Rizatriptan benzoate buccal films is that mucosal irritation is unlikely to occur in such a small range. In the same way, Tizanidine hydrochloride buccal formulations had the range of pH 5.7 to 6.8, which is suitable for buccal administration [32].

Viscosity

The type and concentration of the polymer used, will affect the viscosity of the formulation. It is a crucial parameter as it directly influences the sprayability and performance of the film forming solution, especially of metered dose sprays (MDS). The amount of spray coverage can also be adjusted by changing the film-forming solution concentration. Lower viscosity formulations typically are easier to administer and spray. The viscosity of the clove oil buccal spray formulations ranged from 11.44 cP to 65.83 cP, for instance. Clotrimazole buccal spray formulation had also low viscosity (4.61 – 13.93 cP) due to weak inter- and intramolecular interactions of the fatty acids used in the formulation [33].

Washability and Wettability

The initial evaluation of the wetting and washing properties of the formed film are carried out in the dry state. The film is then washed with water and evaluated on a score sheet with the higher scoring films being more easily washed off and the lower scoring films being less easily washed off. This parameter can be of great significance when solutions that require film forming are applied to sensitive parts of the body like the oral cavity or the eyes, where it is desirable that they can be easily removed with simple rinsing using water. The water washability method was useful in selecting the most suitable formulation in studies on the water washability of the film-forming sprays, Fluconazole and Clotrimazole. [34]

Spray Angle

Spray angle is one of the key parameters that can be used for assessing spray pattern and coverage of film-forming formulations. Using indicator reagents, the spray pattern can be seen when the formulation is sprayed on the sheet of paper. Several factors affect the spray angle such as the type of solvent, the pH of the formulation, the concentration of the solute and the viscosity of its dosage form. The spray coverage area is decreased by an increase in solute concentration and/or viscosity. The spray angle varied from 41.93° to 53.56° in Clotrimazole film-forming buccal spray formulations and a higher concentration of fatty acids led to a decrease in the spray angle of the formulation [35].

$\boldsymbol{\theta} = \mathbf{tan}-(\mathbf{l}/r)$ Eq. 1

In Vitro Oral Drug Permeation Study

Typically an in vitro oral drug permeation study is performed with sheep or goat buccal mucosa at 37 ± 0.2 °C with the use of a Keshary–Chien or Franz diffusion cell. The diffusion cell is made up of interconnected donor and receptor compartments with freshly excised buccal mucosa between the two. The mucosal surface is facing the formulation and is securely clamped between the two compartments. The phosphate buffer (pH 6.8) is added in the donor cell and the phosphate buffer (pH 7.4) is added in the receptor cell. Samples (1 mL) are collected from the receptor chamber at a specific time and the amount of drug is measured at the correct wavelength using a UV spectrophotometer. [36]

Ex Vivo Mucoadhesive Strength

The ex vivo mucoadhesive strength is obtained by the modified balance technique with fresh goat/ sheep buccal mucosa. The mucosa is rinsed with the distilled water and buffer solution pH 6.8 and mounted on a glass vial filled with buffer solution. The formulation comes into contact with the mucosal surface and is kept there for 5 minutes. It is then dropwise added to the other pan of the balance until the formulation comes off the mucosa. The amount of weight needed to separate is noted as the mucoadhesive strength. The study is carried out at 37±1 °C in phosphate buffer (pH 6.8). [37,38]

Stability Study in Human Saliva

Studies of fast dissolving films or mucoadhesive films are conducted with the following stability test as per ICH guidelines. The formulations are kept under accelerated conditions (40 ± 2 °C and 75 ± 5% RH) for up to three months. The films are tested for physical appearance, drug content and disintegration time at preset time intervals. However, after the study period, most formulation parameters are kept unchanged as minor changes were noticed in certain parameters like % elongation, VEE, drug release at 8 hrs etc. [40].

Therapeutic Applications of Mucoadhesive Film-Forming Sprays

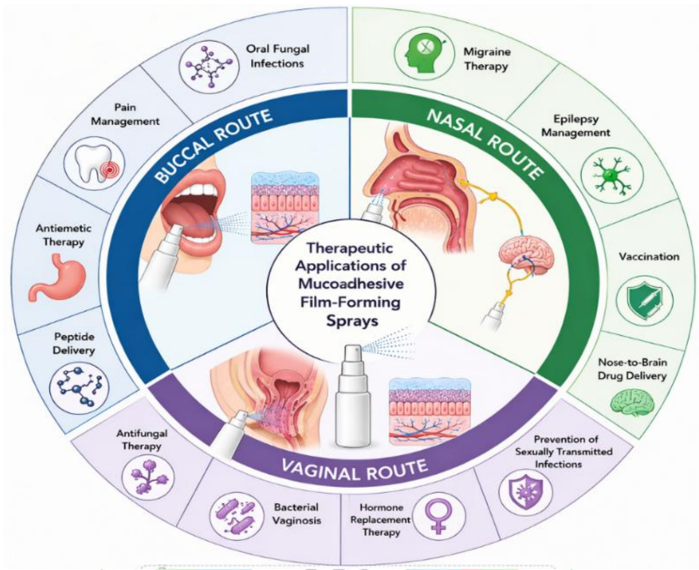

Figure 7: Therapeutic Application of FFS

Mucoadhesive film-forming sprays are widely used for both local and systemic drug delivery through buccal, nasal, and vaginal mucosal routes. These systems form a thin adhesive film after application, which prolongs residence time, improves drug absorption, and provides sustained drug release [41].

Buccal Applications

Buccal film-forming sprays are used for oral fungal infections, pain management, antiemetic therapy, and peptide delivery. Drugs such as fluconazole, lidocaine, ondansetron, and insulin are commonly investigated for buccal administration because the buccal mucosa provides rapid absorption and bypasses hepatic first-pass metabolism [42, 43]. As shown Fig.7

Nasal Applications

Nasal mucoadhesive sprays are useful for migraine therapy, epilepsy management, vaccination, and nose-to-brain drug delivery. The nasal route provides rapid onset of action and direct access to the brain through olfactory pathways, making it suitable for neurological disorders and emergency treatment [44, 45].

Vaginal Applications

Vaginal film-forming sprays are mainly investigated for antifungal therapy, bacterial vaginosis, hormone replacement therapy, and prevention of sexually transmitted infections. Mucoadhesive vaginal films improve drug retention and provide prolonged therapeutic action at the site of infection [46].

Future Perspectives

The development of the mucoadhesive film forming spray has been receiving more and more research interest as an effective drug delivery system because of its ability of prolonged mucosal residence, increased bioavailability and good patient compliance. In future, investigations are anticipated in further development of multifunctional and stimuli-responsive film-forming systems, which can react to the presence of pH, temperature or enzymes at the application site. Nanocarriers like nanoparticles, liposomes, nanoemulsions, and micelles could be included in the film-forming sprays to increase the solubility and permeation of the drug and targeted delivery.

New polymer developments will likely facilitate the development of novel biodegradable, biocompatible and stimuli-sensitive mucoadhesive polymers that have better film forming and controlled release properties. Further formulations are also envisioned to include bioactive materials, peptides, proteins, vaccines and gene delivery systems, which will enhance therapeutic benefits. The use of mucoadhesive film-forming sprays as a direct nose-to-brain delivery system has significant potential in the treatment of neurological diseases like epilepsy, Parkinson's disease, Alzheimer's disease, and migraine.In addition, personalized medicine and technologies of 3D-printing can play a role in creating customized mucosal delivery systems that have optimized drug dosage and release properties. Future formulation development, manufacturing, stability and clinical studies will further consolidate the commercial and therapeutic attributes of the mucoadhesive film-forming sprays in contemporary pharmaceutical drug delivery.

CONCLUSION

Mucoadhesive film-forming sprays represent a promising and advanced approach for mucosal drug delivery through buccal, nasal, and vaginal routes. These systems effectively combine the advantages of mucoadhesion and in situ film formation to improve drug residence time, absorption, bioavailability, and therapeutic efficacy while reducing dosing frequency and enhancing patient compliance. The presence of highly vascularized mucosal membranes enables rapid drug absorption and avoidance of hepatic first-pass metabolism, making these systems highly suitable for both local and systemic drug delivery.

The successful performance of film-forming sprays depends on appropriate selection of polymers, solvents, plasticizers, penetration enhancers, and bioadhesive agents, along with optimization of formulation parameters such as viscosity, pH, sprayability, and mucoadhesive strength. Various theories and mechanisms of mucoadhesion contribute to understanding the interaction between polymers and mucus layers, which is essential for designing efficient formulations.

Overall, mucoadhesive film-forming sprays offer significant advantages over conventional dosage forms and have demonstrated broad therapeutic potential in antifungal therapy, pain management, vaccination, hormone delivery, and brain-targeted drug delivery. With ongoing advancements in polymer technology, nanotechnology, and mucosal drug delivery research, these systems are expected to play an increasingly important role in the development of next-generation pharmaceutical formulations.

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