Film-Forming Spray Systems: Formulation Science, Mechanisms of Film Formation & Characterization

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ABSTRACT
When compared to traditional topical preparations, film-forming sprays have a number of benefits, including more uniform drug distribution and dose, higher bioavailability, a decreased risk of irritation, sustained drug release, and rapid healing of wound through moisture control. Polymers and excipients used in film-forming sprays help to increase the properties of preparations and the stability of active ingredients. Different excipient and polymer combinations will result in films with various characteristics. Therefore, it is necessary to look at the various categories of polymers and excipients, as well as their assessment criteria, in order to create a film-forming spray that is more effective. The research on polymers as film-forming elements and the medical use of these sprays was included in the literature review. This article covers the various polymer and excipient kinds and concentrations, sprayer types, assessments and crucial variables that affect sprayability and film properties.
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INTRODUCTION

Topical drug administration avoids first-pass metabolism, low pH, gastrointestinal enzymes, and has a large surface area.[1] Topical drugs are delivered as patches, gels, lotions, creams, ointments, sprays, or lotions to improve therapeutic efficacy or pharmacokinetics.[2] Patch preparations can be overused and leave drug residues, which is concerning.[3] Patch treatments might cause hypersensitivity, itching, and blistering.[4] Hard-to-stabilize or often crystallizing drugs hinder industrial scale-up.[5] Additional semisolid drugs may adhere to garments and infect additional wounds when applied with fingers.[6] Sprays provide many advantages over other topical dosages, including ease of use, low irritation risk, sterility, great skin or wound coverage, equal medication dispersion after application, and variable dosage.[6,7] FFS contains organic solvent-dissolved activators, enhancers, and polymers. In recent decades, many spray preparation innovations have improved efficiency and effectiveness. Film-forming spray (FFS) is utilized in food, cosmetics, pharmaceutical, and plantation sectors. Compared to previous topical preparations, a thin, non-sticky layer forms, extending drug contact time, increasing permeability, and inhibiting crystallization[6,8]. Continuous drug release can increase therapeutic pharmaceutical availability.[9] Nozzle type, aperture size, spray pressure, and liquid composition affect FFS sprayability. FFS's viscoelastic, in situ gel, pH, and thermally sensitive properties must be studied to determine polymers, solvents, and excipient selection criteria.The polymer, excipient, and sprayer types used in FFS and the assessment standards needed to establish FFS quality for improved development are examined in this analysis.[10]

Mechanism of a Film-Forming Spray: FFS drug delivery systems spray a solution at a therapeutic site and employ the polymer as a matrix to form a film.[10] After the film is produced, the polymer matrix will release the medicine, like a patch.[11] Films stick to the skin or wound better than topical patches and other medicines because tiny droplets of the film-forming solution can enter deep indentations. Naturally, medications can reach their target tissues more easily. Drug dosages in film-forming sprays can be adjusted by solution volume to manage systemic or local effects. An FFS distributes drugs evenly and well. Simple use may increase patient compliance. Water easily removes the thin film.[12] This thin, non-sticky film makes patients more comfortable while doing activities than patches, ointments, gels, etc.[13] To maintain equilibrium, the thin coating allows wound moisture to permeate. Patch preparations and abnormal wound humidity might cause irritation or infection.[14] Droplets are created by spraying film-forming fluid using any sprayer. Medical applications depend on sprayer conditions and intended use.

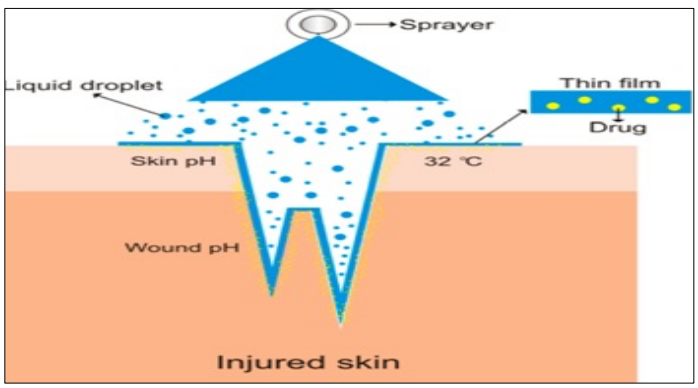

Figure 1: Mechanism of Film Forming Spray

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Types of Film Forming Sprays:

Ordinal Spray: Ordinal sprays employ plastic or aluminum containers with 1.2 mm dip tubes and 0.3 mm apertures. This spraying method requires no specific technology. Average spray angle is 78.69-87.39°.Spraying 150.11-0.35 g or - mL film-forming solution is common.[15,16] Ordinary spray bottles leak 0.01–0.03%.16Ordinal spray force depends on polymer type and concentration. Ordinal sprays can prepare extracts.[17]

Metered Dose Spray: The metered dosage spray (MDS) features variable spray output. This device delivers transdermal or transmucosal drugs to the systemic compartment. Film-forming sprays must be evaluated based on spray volume, which is related to medication dose. Normal spray force is also affected by polymer type and concentration. Extracts can be made with ordinary spray.[17] the container's usage location, particle dispersion uniformity, and bottle design.[18] FFS sprays typically range from 90 to 102 mL. MDS averages 83.51° spray angle. Average MDS container leakage is 0.01–0.02%.[19]

Electrostatic Spray: Electrostatic spray (ES) is commonly used in agricultural pesticide application. Drift reduction by ES improves deposition efficiency, droplet formation speed, coverage uniformity, and loss.[20] ES performance depends on solution viscosity, surface tension, and electrical resistivity.[21] ES cannot be sprayed on solutions with conductivities below 108–105 S/m. ES droplets averaging 6.3–26 m in diameter.[22]

Ultrasonic Spray: It can provide ultrasonic spray film-forming solutions. Thin-film droplets can be nanoscale. The ultrasonic spray nozzle produces uniform droplets fewer than 10 m at low and high pressures. The ultrasonic spray has 1–10 m droplets with a 0.5 mm nozzle. The electrode resonates at 10 MHz. Ultrasonic sprays provide layer-by-layer (LBL) coating films with higher particle size homogeneity in the medical industry.[23] Each sprayer has polymer-specific traits. The FFS process uses natural and synthetic polymers.

Polymers Used in Film-Forming Sprays: Success in FFS preparations depends on polymers. Polymers are film-forming bases and medicine release controllers. Polymers can prevent unexpected crystal formation with molecular transitions.[24] Polymers are chosen for their water-washability, stability, biodegradability, and non-irritability. FFS uses natural or manmade polymers with in situ gel or viscoelastic properties. Water-washable, stable, biodegradable, and non-irritating polymers are chosen.[25] Natural or manufactured polymers with gel or viscoelastic qualities can be employed in FFS. The pH-sensitive will create a solution at a certain pH and gel if the system pH changes.[26] Viscoelastic polymers are thick at initially but become elastic when sprayed and return to thick when released.[27]

Natural and Semisynthetic Polymers:

Cellulose: Ethylcellulose films are water-removable.[27] Excellent films are made with 5-5.25% ethyl cellulose and Eudragit. Slow drying is found with hydroxypropylmethylcellulose (HPMC). Film characteristics are best at 2%. At these concentrations, HPMC forms transparent, thin, smooth coatings.[28] The thixotropic flow rate of Na-CMC makes it thinner under pressure, making it simpler to pass through the nozzle and return to its normal consistency after spraying. Maximum Na-CMC spray concentration is 2.5%. 1.5% Na-CMC produces the best films with constant doses and great sticking. Na-CMC also stabilizes and controls medication release, improving therapeutic efficacy.[29]

Chitosan: Chitosan is a filmmaker, antibacterial, antioxidant, and mucoadhesive, making it suitable for topical drug administration.[30] Chitosan has high surface tension.[31] With concentration and molecular weight, chitosan's surface tension increases, making it hard to dissolve in water. Chitosan solubility is often improved with surfactants.[32] Tween 80 reduces surface tension while making FFS from chitosan.Low chitosan surface tension increases deacetylation and concentration, although the result is not statistically significant.[33] Chitosan drug stability and solubility can be improved using PEG 400.[34] Electrostatic spraying is possible because chitosan conducts well as its molecular weight increases. Chitosan viscosity decreases after deacetylation. Due to these properties, chitosan can generate films with denser droplet densities and smaller droplet sizes of 4-27 m. At higher deacetylation, chitosan becomes hydrophilic. Hydrophilia does not match water vapour permeability. Deacetylation increases chitosan's tensile strength but not its elongation.[35]

Cyclodextrin: Cyclodextrin protects pharmaceuticals from crystal deformation and slightly increases film forming solution viscosity, making it easier to spray.[35]

Gellan Gum: Gellan gum (GG) is viscoelastic and can be sprayed. Because of its viscoelasticity, GG dissolves when sprayed and returns to its normal texture following contact with the skin. Spraying gel droplets with GG encapsulates and delivers cells in situ. Spray systems benefit from GG's thermosensitivity. When it touches surfaces hotter than 30-40 °C, such the skin and eyes, it easily turns from solution to gel because to its thermosensitivity.[36] GG is pH-sensitive, hence adding NaCl as a crosslinker can raise yield stress. In a 0.1% NaCl solution, high acyl GG thickens at 78 °C, while low acyl GG viscosifies at 35 °C. Low-acyl GG releases drugs better than high-acyl GG.[37]

Xanthan Gum: Shilin Wang found that viscosity affected xanthan gum sprayability. Surfactants reduced xanthan gum solution surface tension and droplet size. Interestingly, viscosity and flow did not change. Increasing xanthan gum concentration lowered spray angle and solution coverage.[38]

Deacetylated Chitin: It is utilized in concentrations between 0.5 and 1.5 and is odourless, white, or creamy-white powder or flakes. In addition to its viscosity-increasing properties, it serves as a coating agent, disintegrant, film-forming agent, mucoadhesive, and tablet binder. It is only weakly soluble in water; at pH values above around 6.5, it is nearly insoluble in ethanol (95%), other organic solvents, and neutral or alkaline solutions.[22,23]

Randomly Methylated B-Cyclodextrin: It appears as fine crystalline powders that are white, nearly odourless, and have a faintly sweet flavour. Certain compounds of

cyclodextrin are amorphous powders. It serves as a stabilizing and solubilizing agent, in concentration range of upto 5 %.[35]

Ethylated Cellulose: After drying, it becomes hygroscopic and is a white, yellowish-white, or grayish-white powder or granule. It is nearly insoluble in toluene, ether, ethanol (95%), acetone, and hot water (over 60°C). A colloidal solution is created when it dissolves in cold water. It serves a variety of purposes, including coating, suspending, thickening, binding tablets, and raising viscosity in concentration range of 0.1-10 %.[16,28]

Hydroxypropylcellulose:
It is a tasteless, odorless powder that ranges in hue from w hite to slightly yellow. It is readily soluble in water below 38°C, forming a smooth, clear, colloidal solution, and almost insoluble in aliphatic hydrocarbons, aromatic hydrocarbons, carbon tetrachloride, petroleum distillates, glycerine & oils. In concentration upto 5 %, it works as a coating agent, emulsifying agent, stabilizing agent, suspending agent, tablet binder, thickening agent & viscosity increasing agent.[35]

Hypromellose: It is a white or creamy white, fibrous or granular powder that has no taste or odour. It forms a viscous colloidal solution when dissolved in cold water; it is nearly insoluble in ether, chloroform, and 95% ethanol, but soluble in ethanol and dichloromethane mixes, methanol and dichloromethane mixtures, and water and alcohol mixtures. It can be used as a coating agent, film-former, stabilizing agent, suspending agent, tablet binder, viscosity-increasing agent, and rate-controlling polymer in concentration range upto 5 % for prolonged release.[35]

Hypromellose Phthalate: It is found as granular powder or as free-flowing, white to slightly off-white flakes. It has a taste that is hardly perceptible and is odourless or mildly acidic. At concentrations up to 5%, it acts as a film-forming agent.[35]

Synthetic Polymers:
Carbopol: Carbopol flows thixotropically.An amorphous hydrogel, carbopol can contribute or absorb wound fluids, making it effective for open wounds.Carbopol's viscoelasticity increases drug diffusion. Carbopol and Poloxamer operate better together than alone. The polymer combination produces a film with good drug release at 0.05% and high sprayability (spray angle, drying period, and uniform content per spray).Carbopol is known for its heat-resistant gels.[39]

Eudragit: Eudragit comes in many forms for various uses. Typically, synthetic polymers are added to tablets to regulate drug release.[40] Eudragit also promotes skin medicine absorption, therefore its application in topical formulations is growing.[41] Eudragit RSPO and RLPO do not form translucent and lustrous films like Eudragit EPO, E 100, S 100, RL 100, and RS 100. Eudragit EPO, E 100, RL 100, and RS 100 films are water-resistant. After applying to the skin, Eudragit S100 forms a film that can be removed with water. Because Eudragit S100 dissolves above pH 7. Eudragit S100 is skin-friendly. Eudragit RS sprayed on a silicone membrane generated a thick coating, according to in vitro permeability studies. Methylphenidate crystallisation likely lowered permeability. Methylphenidate penetration was greater with Eudragit RS than E.Eudragit L100 films also fail to inhibit testosterone crystallisation. Sprayability, adhesiveness, and flexibility are Eudragit RS 100's strengths. At 10.05% with ethyl cellulose 5.02%, Eudragit RLPO produces better films than concentrations over 15%, which limit water washing.[42]

Lutrol: Lutrol F-127 has similar film characteristics and spray patterns to Carbopol 940, but it produces a more uniform drug dose with a lower standard deviation.Lutrol F-127 films release drugs better than Carbopol 940. No skin irritation has been reported.[42]

Plasdone: Plasdone works better than other polymers at testosterone penetration. Plasdone > Eudragit EPO > PVP K30 Most efficient testosterone permeation sequence was Eudragit RL. Because the polymer blocked testosterone crystallisation, it increased flow.[43]

Kollidon: Kollidon is a synthetic polymer used in pharmaceuticals. Kollidon is available in solid, semisolid, and liquid forms with different characteristics. Kollidon controls medication release and increases solubility and permeability in liquid and semisolid formulations.44Kollidon® 30 reportedly produces translucent, thin, well-dispersed films. Kollidon® 30's pH didn't change after 28 days of storage. Kollidon® 30 and VA64 suppress testosterone crystallisation as antinucleants.Drug penetration via the skin increases with Kollidon® 30 films.[44]

Carbomer 940: It is a white powder that is "fluffy," acidic, hygroscopic, and has a faintly distinctive smell. It dissolves in water and, once neutralized, in glycerin and 95% ethanol. It serves as a tablet binder, suspending agent, emulsifying agent, release-modifying agent, bioadhesive, and viscosity-increasing agent in concentration range of 0.25-0.5%.[39]

Butyl Methacrylate EPO: It can be acquired as an organic solution, an aqueous dispersion, or a dry powder. The most widely used organic solvent is a 60:40 blend of acetone and propan-2-ol. It is used as film former, tablet binder, tablet diluent in concentration upto 5% [12, 47]

Pluronic F-127: It usually appears as cast solids or as white, waxy, freely flowing prilled grains. They are essentially tasteless and doorless. Poloxamer 124 is a colourless liquid at ambient temperature. In the concentration range of 0.05-2.0 percent, it serves as a dispersing agent, emulsifying and co-emulsifying agent, solubilizing agent, tablet lubricant, and wetting agent.[19]

Povidone: It is a fine, hygroscopic, odorless or nearly odorless powder with a white to creamy-white tint. In concentrations up to 5%, it serves as a disintegrant, dissolving aid, suspending agent, and tablet binder. It is nearly insoluble in ether, hydrocarbons, and mineral oil, but easily soluble in acids, chloroform, ethanol (95%), ketones, methanol, and water.[48]

Kolliphor P 407: It usually appears as cast solids or as white, waxy, freely flowing prilled grains. They are

essentially tasteless and odourless. Poloxamer 124 is a colourless liquid at ambient temperature. In the 0.05–1% concentration range, it serves as a dispersing agent, emulsifying and co-emulsifying agent, solubilizing agent, tablet lubricant, wetting agent, etc.69

Excipients Used in Film-Forming Sprays:

Crosslinkers: Crosslinkers affect polymer elasticity, viscosity, solubility, glass transition, and film stiffness. NaCl as a cross linking agent in gellan gum increases temperature sensitivity, resulting in faster film formation. Cell encapsulation in gellan gum is improved by NaCl. [45]

Permeation Enhancers: Eutectic mixes often boost drug absorption. Strongest eutectic combinations are camphor and menthol.[46] Camphor and menthol are hydrophobic, making them good penetration boosters for hydrophobic drugs. However, camphor and menthol cause leaking and skin pores. Camphor and menthol provide a warm, then chilly, sensation that rises gradually. In a Franz diffusion cell with nylon membranes, a eutectic mixture of camphor and menthol greatly enhances fluconazole, clotrimazole, and voriconazole penetration. Hydrophobic camphor and menthol interact with stratum corneum lipids to increase drug penetration.[46] Azone > isopropyl myristate (IPM) > propylene glycol (PG) > N-methyl-2-pyrrolidone improves testosterone permeability.[47] Lauryl lactate (LA) > IPM > azone > PG permeation enhancers enhanced dexketoprofen permeability.[48] This implies that these compounds' ability to promote drug penetration varies by drug. However, hydrophilic drugs benefit from azone. The combination of azone with PG increases its penetration.[49-50] Laurocapram (1-5 %v/v), Camphor (2-5 %v/v), Menthol (2-5 %v/v), Estergel (2.5–5 %v/v), Tetradecyl Lactate (0.5 %v/v), etc. are some examples of permeation enhancers.

Plasticizers and Stabilizing Agents: Plasticizers provide films flexibility and prevent cracking. Plasticizers stabilize active compounds and improve medication penetration.[51] PEG and PG improve antifungal medication absorption. Besides being a plasticizer, PG is a solubilizer that helps drugs pass through the skin.[52] Concentration is important since PG affects film-forming solution viscosity. PG mixed with ethanol and water did not hinder testosterone crystallization. PG concentrations below 5% improve drug permeability.[53] PEG 400 may increase film-forming solution spray volume. Spray volume increases with PEG 400 content. Increased PEG 400 levels increase spray coverage. Because PEG is a non-volatile solvent, vapor pressure drops.[54]

Glycerine is used as stabilising agent and plastisizer (10-30 % v/v), Polyglycol 200 (0.25 %v/v) & Polyglycol 400 are used as plasticisizer (0.45–10 %v/v), Trimethyl Glycol is used as plastisizer and permeation enhancer (0.25-9 %v/v) & Polysorbate 80 is used as surfactant (5 %v/v).

Solvents: The FFS system uses volatile and nonvolatile solvents. The purpose is film drying control. Films that dry quickly and harden make it hard for drugs to penetrate. The active component is dissolved to saturation in the solvent to simplify drying. [54] Cyclotrisiloxane (0.5 %v/v), Ethanol (7.5-50 %v/v), Acetone (15-20 %v/v), Dimethoxymethane (30-40 % v/v) & Isopropyl alcohol (30 %v/v) are some examples of solvents.

Evaluation of Film-Forming Sprays:

pH: To make the active chemical more stable or suitable for the application, its pH is evaluated and adjusted. For 4-6.[55] pH skin. Burns heal faster below pH 7.32.57 than diabetes wounds 6.5-8.[56] The preparation adjusts pH to prevent wound irritation and physiological changes during healing.[57] The pH of the dosage might also affect cutaneous medication absorption based on ionisation.[58]

Viscosity: Each polymer and concentration change affects viscosity. Film-forming solution viscosity impacts sprayability, making it important in MDS. Increasing film-forming fluid concentration reduces spray coverage.[59]

Tonicity: Adjust the tonicity of film-forming solution while applying it to wounds and ocular mucosa. Nonisotonic formulations may cause mucosal and ocular irritation. Therefore, the Kahar method must be employed to determine and change pharmaceutical tonicity. Material isotonic concentration is estimated using the equation below.[60]

$$C_b = \frac{C_i}{1.92\ [\sum^{(C_n x \Delta T f_n)}]}$$

Where,

C_b = isotonic concentration of the material,

C_i= starting concentration of the material,

$\sum(C_n x \Delta T f_n)$ = sum of the multiplication of the concentration and the value of each ingredient's freezing point depression.

Rheological Properties: Chemical thixotropy is determined via flow testing. A mixture with good flow can pass through the sprayer nozzle repeatedly. This flowing characteristic thins the film-forming solution as it passes the nozzle (stressed) and recovers to its usual viscosity after spraying.[61] The rising and descending curves form the hysteresis circle, which defines thixotropic behavior. A rheometer in rotation model with a logarithmic shear rate increase of 1-900 s1 and back from 900-10 s1 may determine this flow. This test is done at room and film-forming solution storage temperatures. Testing flow characteristics utilizing oscillation time sweep and amplitude sweep in various excipient concentration and temperature ranges can help reveal how excipient and temperature affect gel consistency.[62]

Bio-adhesive Strength of the Film: Attaching a 2 x 5 cm film to mouse epidermis measures its bioadhesive capacity. The skin is moisturised with 0.5 mL distilled water. The tissue surface is exposed to film for 5 minutes. The force (F) needed to remove the film off the skin is measured. Film bioadhesive strength (Fb) is calculated per area (A).[63]

$$F_b = \frac{F}{A}$$

Tensile Strength and Elongation of the Film: A film's tensile strength (TS) resists pressure.TS testing determines whether the film is abrasion-resistant and flexible enough to follow skin movement without cracking. Use this equation to calculate TS.[64]

$$TS = \frac{F_m}{LxW}$$

Where,

F_m = Maximum pressure that the film can withstand before ripping,
L = Its thickness
W = Its original width.

Elongation (EB), which measures film elasticity, can be calculated using the equation below after stretching.

$$EB = \frac{l_{max} - l_0}{l_0} \times 100$$

Where,
l_0 = Initial length of the film
l_{max} = Total length of the film before it is torn when pulled.

Water Washability: Wetting ease is assessed for dry film. Water-washed film is rated readily, moderately, and poorly. Simply spraying with water will help if film-forming substances hit sensitive body regions like the eyes and mouth.[64]

Fluid Affinity: This test determines whether the film can absorb or hydrate the wound. Moisture helps the lesion heal, but too much might degrade wound tissue.[65]

Surface Morphology of the Film: This test measures the film's microscopic form, surface roughness, and homogeneity using SEM or TEM.[66]

Film Formation/Drying/Evaporation Time: Drying time is measured to determine how quickly the film forms once the solution is sprayed. Sometimes the solution is sprayed on the glass and permitted to air out at room temperature. In other studies, activated silica gel and dye are applied on the glass plate to facilitate absorption. Using a film-forming solution on the skin lets you measure drying time. A glass plate is placed against the film without pressing it to check for drying. A film is dry when water doesn't stick to the glass. Because skin has pores and body warmth, this method may take longer to dry than the film drying time test using glass plates.[66-67]

Stickiness: The dry film is gently pressed using cotton wool. Viscosity depends on cotton wool fibers on the film. Film adhesiveness is high if the attached fiber is thick, medium if thin, and low if no fibre is attached. Stickiness determines whether the film will stick to clothing or other objects, hence it needs care while moving.[67]

Spraying Force: This test determines film-forming fluid spraying pressure. Stable Micro Systems' TA.XT Plus texture analyzer can be used.[67]

Spray Angle, Pattern, and Droplet Size Distribution: Paper soaked with indicator reagents makes spray patterns easy to notice. This depends on the solvent and filmforming solution pH. Solvent-sensitive paper clarifies spray droplet size distribution and pattern. Measure the pattern diameter to compute the spray angle and area covered.[67-68]

$$Spray\ angle\ (\theta) = tan^{-1}\frac{l}{r}$$

Where,
l = Distance between the paper surface and the nozzle
r = Radius of circle.
Typically, the nozzle is 15 cm from the paper. Higher spray angles make film-forming fluid spreading harder.[68]

Drug Content per Spray and Uniformity: Each spray's dose uniformity is measured by weight or volume, and its active ingredient concentration in the film-forming solution is utilized to compute its amount. The active substance level can be measured by collecting and instrumenting the sprayed solution.[68] To determine spray volume, weigh the solution that forms the film in the sprayer, not the fluid flowing out of the nozzle. Because spray droplets are so small and easily carried by the wind, they are unlikely to be collected and weighed. This equation measures spray volume:20

$$V = \frac{W_t - W_0}{D}$$

Where,
V = Volume of Spray
W_t = Weight of film forming solution after spraying
W_0 = Weight of film forming solution before spraying
D = specific gravity of film forming solution

Potential Drug Aggregation: Sprayability will alter with particle size. Size exclusion chromatography (SEC) and zeta potential determine drug aggregation potential.[68]

In vitro Drug Penetration/Release Study: In Franz diffusion cell tests, compartment separators are usually cellulose (0.45 m), nylon (0.22 mm), or silicone membranes. Used media is pH 7.4 phosphate buffer. The donor compartment receives the film-forming solution after compartment system completion. An tool measures cell fluid diffusion at regular intervals. An identical volume of fluid is added after sampling.[68]

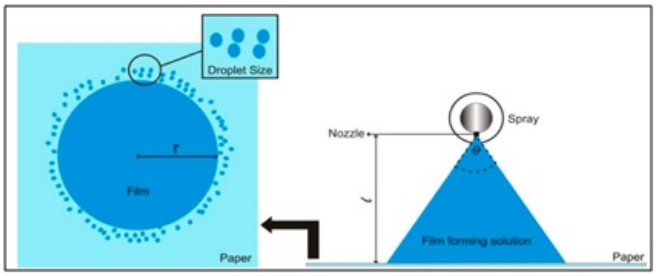

Figure 2: Measurement of spray angle and observation of spray patterns.

Ex vivo Skin Permeation Study: Drug penetration on mouse or rabbit abdomens can be studied using Franz diffusion cells. A cotton swab dipped in propanol or isopropanol removes any leftover fat tissue, then the skin is cleansed with regular saline. Diffusion media include phosphate buffer pH 7.4 and acetate pH 6.0. Medium flow on the receptor compartment side is produced via flow-through cells linked to silica tubes at 0.3–0.6 mL/hr. The donor compartment receives the film-forming solution after compartment system completion.After taking aliquots from the receptor compartment at set intervals, an equipment measures drug levels. Aliquots extracted to maintain sink conditions are replaced by a fresh diffusion medium. Fluorescence can be used to measure drug permeation through the epidermal layer in addition to the other methods. Using a microscope, fluorescent samples can be inspected. [68-69]

In vivo Skin Irritation Test: Test animals like mice and rabbits are shaved and given the film-forming fluid. hours to 7 days after application, irritation, inflammation, erythema, oedema, papules, flakiness, and dryness occur.[69]

Stability Study: Various storage conditions are used to analyze active ingredient particle size, chemical and 3D structures, levels, and therapeutic efficacy. Thermal analysis can identify metastable active compound recrystallization. The antinuclear polymer keeps the medicine crystalline. Multiple trials will assess the medication concentration and metered-dose spray pattern. Maintaining dosage while storage is crucial.[69]

CONCLUSION:

Various polymers can be used to construct FFS systems. Ideal polymers create in-situ films (pH- and thermo-sensitive) or are viscoelastic. Hydrogel, mesquite gum, gelatin, Poloxamer 407, and other thermo- and pH-sensitive polymers could be employed in FFS systems.Since it produces a film in situ and contains antibacterial, antioxidant, anti-inflammatory, anticancer, tissue regeneration inductor, and wound healing capabilities, chitosan is a unique natural polymer for FFS. Chitosan is biodegradable and compatible with many drugs and the body. Drug solubility and potency can be improved with chitosan molecules.

FFS could be a promising medicine delivery technique with many benefits. Natural or synthetic polymers can be used as drug matrices and film formers to improve active component stability and therapeutic efficacy.Sprayers create droplets for more equal medicine distribution and dosing. Additionally, each sprayer has unique testing requirements.

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