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A REVIEW ON FILM-FORMING SPRAY SOLUTIONS

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Abstract: Drug delivery through the skin is crucial for local and systemic effects. The physicochemical properties of the medicine, the patient's compliance, the ability to stick to outermost layer of skin during treatment in order to facilitate the drugs adsorption. Film-forming sprays provide several benefits over traditional topical therapies, includes uniform distribution of drugs and dosage, improved bioavailability, less irritation, prolonged drug release, and accelerated healing of wounds through moisture management. To effectively treat wounds and disorders of the body's tissues, the medication must be left at the treatment location for the whole duration of the injury. Drug delivery methods known as "topical film forming systems" are administered topically, adhere to the body, and create a delicate, transparent film that carries active components to bodily tissue. It is advised to use them as emollients or protective agents to skin. In film-forming sprays, polymers and excipients enhance preparation qualities and boost the durability of active components. Different properties will be produced in films depending on the polymer and excipient used. Consequently, various polymer and excipient kinds, in addition to them. The review states that in situ layer or viscoelastic polymers, whether natural or synthetic, can be used to maximise topical medication supply.

Index Terms **- Topical medication delivery, film-forming solution, polymer.**

I. INTRODUCTION

The human body's most extensive organ is the skin. External impacts such as UV radiation, physical and chemical assaults, encounters dangerous microbes, and physical discomfort are all protected by it [1,2]. Because of its poor permeability to micro and macromolecules, it also acts as a barrier against them in the environment. Although transdermal drug delivery has made a substantial contribution to medical practise, it has yet to fully realise its potential as a substitute for oral drug administration and hypodermic injections [3]. Topical drug delivery is designed to achieve either systemic or localized effects and offers several advantages, including bypassing initial metabolic processing, avoiding the impact of acidic conditions and enzymatic activity in the digestive system, and leveraging the extensive available skin surface [4]. The primary pathway for drug absorption through the skin is the stratum corneum, a 10-micrometer-thick layer of non-living, keratinized epidermal cells that acts as a protective shield [5]. Drug permeation is a term used

to describe the process by which medications pass through the skin. Hence, the transportation of medication molecules across the skin presents a challenge [6]. Topical medications are often designed as a spray, gel, cream, ointment, lotion, patch or other dosage method to improve pharmacokinetic properties or therapeutic efficacy [7]. Compared to other topical doses, sprays provide a number of benefits, such as being simple to apply, having a minimal risk of causing irritation, being sterile, providing excellent coverage for an area or wound, distributing the medication evenly when applied, and having a variable dose [8]. Compared to conventional topical applications, a thin, adhesive layer develops, which can extend the duration of contact and the drug's ability to permeate, leading to a sustained release of the medication. This can also prevent crystallization, making more of the medication accessible to provide therapeutic advantages [9]. FFS (film forming system) is a novel technique that can replace conventional skin applications and skin-absorbed preparations. It's a liquid medication format that, upon applying to the skin or another surface, undergoes in-situ film formation. These formulations consist of the drug and additives in a carrier, which, upon contact with the skin, evaporates, leaving behind a film comprising both excipients and the drug. A solid polymeric substance can be formed as a resulting film, which serves as a drug release matrix for controlled drug delivery, or a liquid film can be left behind, which is rapidly absorbed by the stratum corneum [10]. We discuss the strategies utilized for constructing a restricted medication release FFS to enhance therapeutic effectiveness, along with the prospective future advancements of this technology within the pharmaceutical industry. [10,11].

Methodology

Skin anatomy

The human skin consists of two primary layers: the epidermis and the dermis. At the outermost surface is the stratum corneum, and beneath it lie the four epidermal layers [11]. The dermis, which lies inside the skin's epidermis, assures that the skin is flexible and that the body's temperature is maintained. It predominantly consists of collagen fibres mixed with elastic fibres, enveloped by a matrix. Within the dermis are blood vessels, lymphatic pathways, and sensory nerves. The stratum corneum constrains the extent of drug absorption based on its permeation ability. Medications can be transported through the stratum corneum using routes such as trans-epidermal, trans-follicular, and trans-glandular pathways. They enter the skin to varied depths depending on the medication and formulation [12].

Mechanism

The film-forming system is administered directly to the skin and, upon the solvent evaporating, forms a thin, see-through film in place. The formulation undergoes significant transformation once applied to the skin because of the evaporation of volatile elements within the carrier, resulting in the formation of a lasting film on the skin's surface. Throughout this procedure, concentration of the drug increases. until it reaches saturation, with the possibility of achieving supersaturation. By enhancing the thermodynamic activity of the skin without compromising its protective barrier, supersaturation results in an increased drug flux. This formulation can be applied without inducing irritation or adverse effects. [13,14].

Supersaturation can be explained using a modified version of Fick's law of diffusion. Fick's law of diffusion is represented by the equation:

J = DKCv/h

In this equation:

J stands for the rate of drug permeation (flux).

D represents the diffusion coefficient of the drug.

Cv is the concentration of the drug.

h signifies the thickness of the barrier to diffusion.

The rate of drug penetration through the skin and concentration of drug is directly proportional, as shown by this equation. But when all of the medication is dissolved in the car, this is the case. This equation asserts that the connection between drug flux and the system's thermodynamic activity, linked to saturation, is a straightforward and direct relationship [15]. Thermodynamic instability is however increased as the supersaturation grows. FFS eliminates the instability issue by generating supersaturated systems right away after skin application. Consequently, compared to other transdermal dosing forms, it enhances drug penetration through skin [16,17].

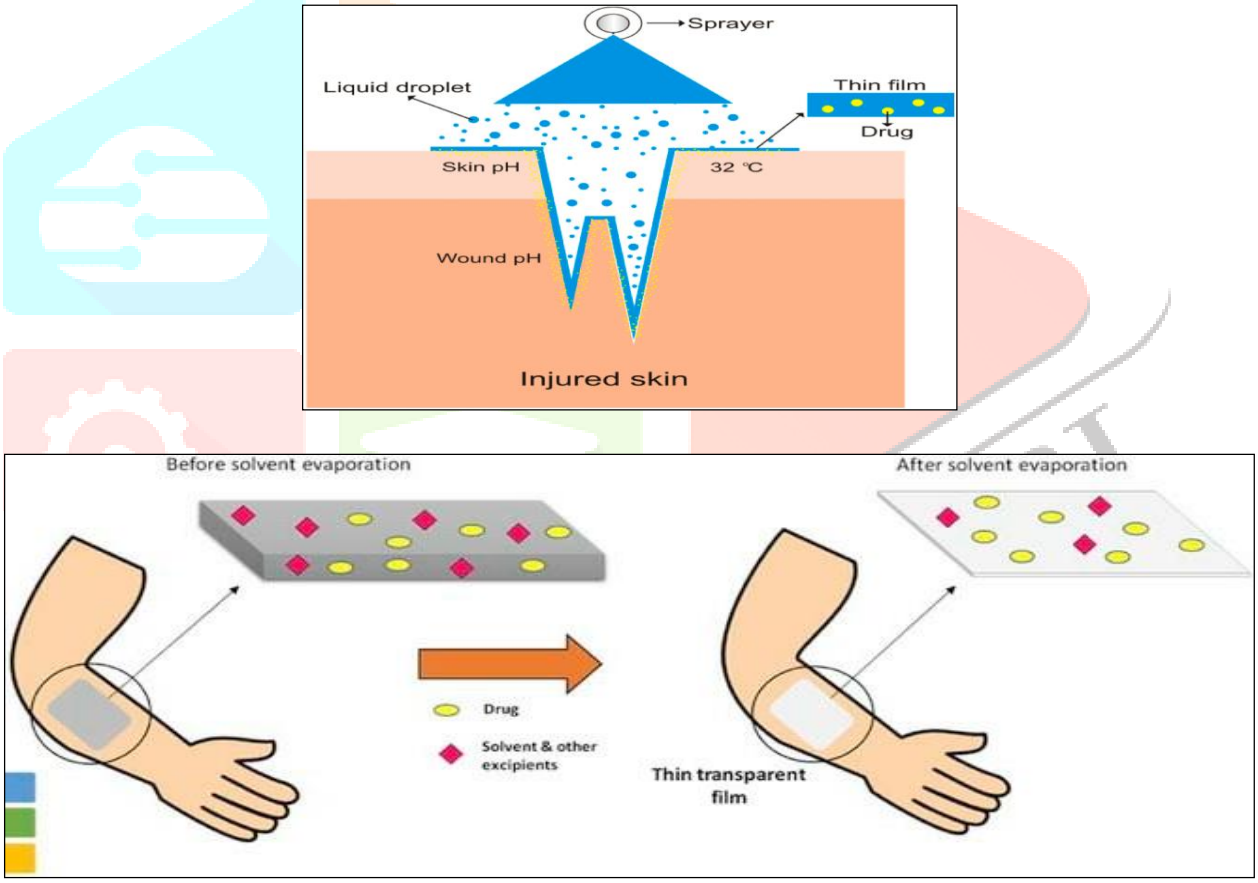

Fig.1 Mechanism of film forming system

Features of the film-forming mechanism

The film-forming formulation can be applied to the skin, irrespective of its shape and size, and possesses the capability to adhere for an extended duration, outperforming traditional semi-solid preparations. In Figure 1, it is evident that the film-forming system creates a nearly transparent and rapidly drying film upon application. In Figure 3(B), it can be observed that once dried, the resulting film is non-tacky, pliable, and can be easily peeled off. This film exhibits exceptional adhesion to the skin, providing resistance to being wiped off. Consequently, the low chance of the active components transferring to other individuals or clothing is significantly reduced[18].

Utilizations of Film-Forming Systems

In the beginning, film-forming systems were predominantly utilized within the domain of surgical procedures and the field of wound management. These systems, in the form of gels or solutions, were used as surgical adhesives to close surgical incisions. Film-forming agents employed for this objective may encompass both naturally occurring substances, like fibrin, or artificially created compounds, such as cyanoacrylates. This wound management formulations were specifically created to be either devoid of medicinal ingredients or to incorporate antimicrobial agents, which serve the purpose of averting infections within the wounds. However, this technology has found applications beyond medical use. It has been employed in non-medical contexts, including the transport of active ingredients in cosmetic products, such as the use of formation of silicone films technologies in the preparations of cosmetic ointments and creams. It has also been utilized in transparent peel-off masks for treatments related to moisture for the skin acne treatment, and more. Furthermore, the technology exhibits the capability to be used as a foundational material for a range of protective membranes employed in industrial environments. These protective membranes play a crucial role in safeguarding workers from contact with substances like cleansers, corrosive materials, alkaline solutions, dangerous compounds, infrared heat, ultraviolet radiation, and the like. Illustrative instances of such utilization encompass both water-attracting and water-repellent lotions and salves, in addition to creams designed for shielding against ultraviolet radiation 18,19.

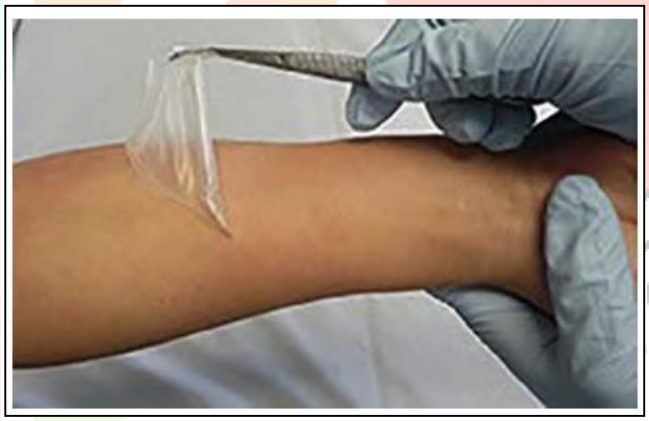

Fig. 2 Applications of film forming systems

Components

The most popular kind of film-forming systems are film-forming solutions. The main components are the drug, plasticizers, and other excipients are combined with a volatile medium for polymer dissolution or dispersion [20].

1. Drug

For topical application via film-forming systems, drugs must exhibit specific characteristics that are independent of the dosage form. These drugs are typically highly potent, facilitate rapid absorption through the skin, cause minimal discomfort, and demonstrate relative resistance to an enzyme residing in the epidermis. The skin penetration pathway that a drug follows is contingent on additional drug traits, including its partition coefficient. The permeability of a drug through human skin is influenced by its molecular weight, and smaller molecules tend to penetrate the skin more readily than larger molecules. [14]. Whether designed

for topical use or transdermal application, the drug should possess the capability to permeate the stratum corneum effectively, considering the lipid-rich composition of this skin layer. Medications with a pronounced lipophilic quality generally exhibit superior skin penetration compared to their hydrophilic counterparts [21,22].

2. Polymers

The FFS relies on polymers, and there exists a variety of polymer types that can be harnessed for fabricating these systems. These polymers may be employed independently or in collaboration with other film-forming polymers to generate the desired film attributes. At the skin's temperature, these polymers should harmonize to create a see-through and supple film. Such as Hydroxypropyl methylcellulose, Polyvinyl pyrrolidine, Chitosan, Silicones Polydimethylsiloxane [23,24].

3.Solvent

When crafting films, the choice of solvents holds considerable importance. The solvent employed in film-forming apparatus has a dual impact on drug permeation and drug solubility. Since these solvents are so often used, their long-term safety. Such as isopropanol, Ethanol, benzyl alcohol, butanol, propylene glycol, Ethyl acetate [25-27].

4. Plaster

To enhance the film's flexibility and bolster its tensile strength, plasticizers are introduced into the film-forming systems. These plasticizers need to be compatible with the polymers in use and should not readily permeate the skin. A few instances of plasticizers include propylene glycol, glycerine, polyethylene glycol, sorbitol, triethyl citrate, dibutyl phthalate and so on [28,29].

Comparison

FFS solves the instability issue by generating supersaturated systems right away after skin application. Therefore, in comparison to other transdermal dose forms, it enhances medication penetration through skin. The study examined the efficiency of the film-forming solutions in delivering ethinylestradiol. In an in-vitro setting, the absorption of ethinylestradiol via the skin of humans was assessed, comparing a readily accessible in store patch to the permeation from the film-forming solution, both with and without an enhancer. The film-forming formulations demonstrated superior ethinylestradiol penetration when compared to the commercial patch. Without the enhancer, the formulation carried more than double the amount of ethinylestradiol compared to the marketed patch. The formulation provided nearly sevenfold the quantity of ethinylestradiol as the commercial patch when used with the enhancer. As a result, these methods show promise for improving drugs describes how film-forming technologies outperform patches and ointments. All three systems have different drug permeability patterns. If there is patch transdermal the medication is kept in a reservoir, which is where the medicine is taken into the body and released slowly. the topical patch is designed to reach the capillaries from whence it is delivered to the systemic circulation. the skin in order to take localised effect on the target tissue. Drugs they are active when mixed into semisolids and on the skin. Reach the place of action by penetrating the skin's surface or deeper layers. Drug systemic

delivery, however, is constrained for a number of reasons. Both semisolids and liquids can be used as film forming processes. cans and patches[30,31].

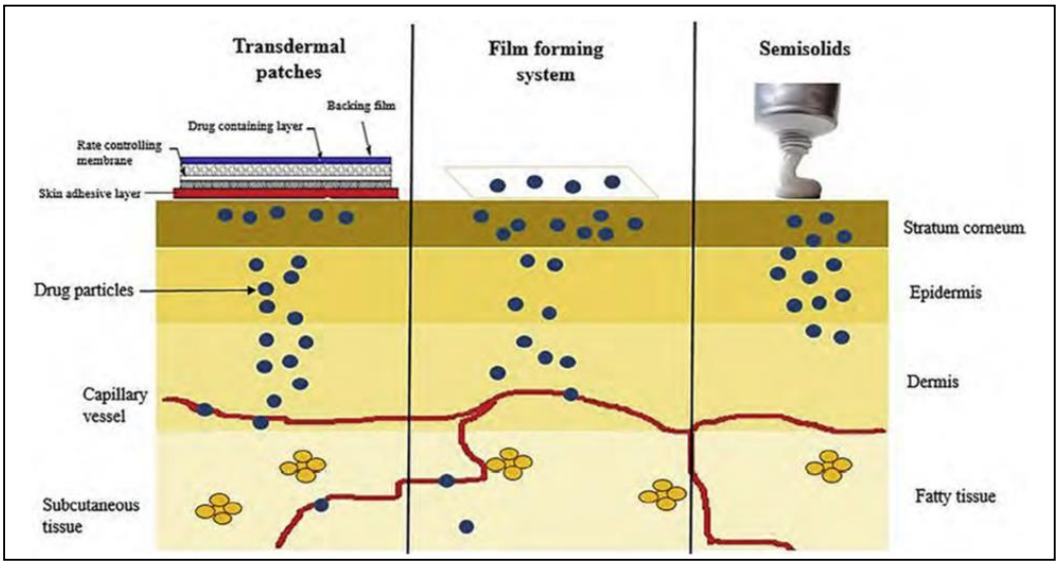

Fig. 3 Comparison

Evaluation

Film formation

Film-forming systems are administered on either a Petri dish or a section of pig ear skin that has been excised. The evaluation of the film formation's excellence is conducted and categorized as one of the following: fully and consistently formed, inadequately or unevenly developed, with or without any particulate matter from the film-forming polymer. The visual characteristics of the film are denoted as either see-through or non-transparent, adhesive or desiccated, detachable or non-detachable [32].

Drying duration

The formulation is applied to a volunteer's inner forearm sides in order to measure the drying time. A glass slide is lightly placed on the film after a predetermined amount of time. The film is considered dry when there are no visible traces of liquid remaining on the glass slide after removal. To prevent the patient from having to wait for a long time, an effective FFS should include a minimum drying time [33].

Stickiness

The film's adhesion level is determined by gently pressing the dried film against cotton wool. The adhesiveness is classified as follows: "high" when there is a notable building up of fibers on the film, "medium" when there is a slender layer of fibers, and "low" when there is minimal or no fibre adherence. This evaluation is of utmost importance because the formulation must exhibit low adhesiveness to prevent it from adhering to the attire of the patients [34].

Measurement of the permeability of water vapour

Water vapor permeability quantifies the volume of water that traverses a defined film area within a specified timeframe. These measurements play a pivotal role in unravelling how the film's behaviour affects skin characteristics such as stratum corneum hydration, blood circulation, and skin temperature. To conduct this evaluation, films are fashioned via a solvent evaporation technique on a Teflon surface and then allowed to air-dry at room temperature for a period of 72 hours. Subsequently, circular specimens are excised from these thoroughly dried film sheets. To create test samples, glass vials with openings are filled with distilled water, covered with circular film segments, and tightly sealed using both a silicone ring and an aluminium

vial cap to prevent any leakage. The vial's initial weight is recorded, following which it is transferred into a desiccator, thus establishing an environment with either a 58% relative humidity level or exceedingly low relative humidity (approximately 0%). These vials are kept at a controlled temperature for a continuous span of 72 hours and are subjected to periodic weighing at predetermined intervals. By evaluating the reduction in weight of the vials (denoted as W in grams), the determination of water vapor permeability is derived, reflecting the amount of water that passes through the film relative to both the film's surface area and the duration of exposure [35-36].

In-vitro Drug Release Study (Diffusion study)

A custom-designed laboratory device, mimicking a Franz diffusion cell, was utilized to investigate the drug release profile from a gel that forms a film. This custom diffusion cell consisted of two distinct parts: the donor compartment and the receptor compartment, separated by a diffusion barrier made of an egg membrane. The donor compartment, with a 24mm internal diameter, remained unsealed at one end and was exposed to the surrounding environment. The receptor compartment was purposefully designed to facilitate the collection of samples. The experiment employed a phosphate buffer solution with a pH of 5.8 as the diffusion medium. To commence the experiment, 1ml of the drug-infused film-forming gel was deposited into the donor compartment, positioned a top the drug-release membrane. This membrane acted as a barrier, separating the donor compartment from the receptor compartment, with the egg membrane in between. The membrane had been pre- saturated in phosphate buffer solution (PBS) for 24 hours. A secure connection between the donor and receptor compartments was established using a clamp, and the donor compartment was situated so that the egg membrane made contact with the diffusion medium. The entire assembly was affixed to a magnetic stirrer. The receptor compartment held 100ml of PBS and was set on a thermally regulated magnetic stirrer to maintain a constant temperature of 37 ± 0.5 degrees Celsius. It was continuously agitated at a rate of 50 revolutions per minute. At specified time intervals, 1ml samples were retrieved and subsequently subjected to drug content analysis using a UV spectrophotometer at its maximum absorption wavelength (λ max) against a blank. In order to maintain consistency in the receptor phase, an equivalent volume of phosphate buffer was added each time a sample was withdrawn [37-39].

Ex vivo permeation study

Ex-vivo permeation investigations are undertaken to explore the impact of the skin's protective characteristics on the evolving film-forming system. To achieve this objective, a Franz diffusion cell or a Keshary–Chien diffusion cell is utilized. In these experiments, a segment of rat skin is positioned between the dual compartments of the diffusion cell, with the outermost epidermal layer, the stratum corneum, oriented toward the donor compartment, while the underlying dermal layer faces the receiver compartment. The film-forming concoction is subsequently administered onto the skin's surface, and as it dries, it gives rise to a slender film. The receiving section is loaded with phosphate-buffered saline at a pH of 7.4, with the temperature rigorously controlled at 37 ± 0.5 degrees Celsius. At designated time intervals, samples (portions) are obtained, and their constituents are scrutinized utilizing a suitable spectroscopic technique. These trials aid researchers in evaluating the interaction of the evolved film with the skin's protective layer and its impact on the passage of substances[13, 16,40,41-45].

Permeation Analysis

Flux is the quantity of drug that enters a receptor compartments per unit area and travels across the membrane per unit time. Flux is measured in mass, area, and time units[36,43].

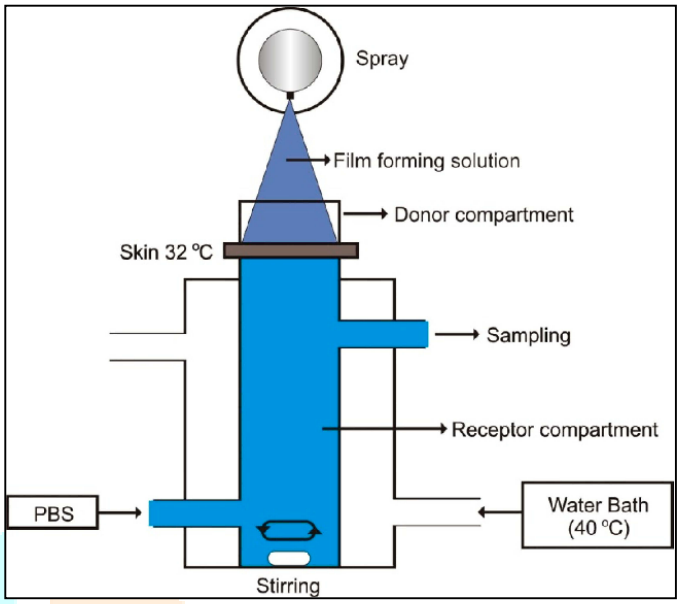

Fig. 4 Keshary–Chien diffusion cell

II.CONCLUSION

The film-forming system stands as a groundbreaking foundation for dispensing medications to the skin, providing a versatile strategy for conveying drugs through both surface application and skin absorption. These systems are characterised by their simplicity and several advantages, including transparency, lack of greasiness, reduced skin irritation, resistance to removal, prolonged drug presence, enhanced dosage adjustability, increased compliance among patients, and a visually appealing design.. Despite significant research efforts in this field, there is limited available data on the efficiency of drug delivery using these systems. Consequently, there are relatively few products available in the market. Further research is essential to substantiate the viability of the film-forming system as a transdermal drug delivery method. However, the initial findings are promising and support the continued development of this innovative technology for delivering drugs topically.

III. CONFLICTS OF INTEREST

The authors affirm that they have no competing interests.

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