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Topical Sprays: A Review of Formulation Stratgies, Evaluation and Applications in Drug Delivery (Past, Present and Future)

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Abstract:

- ***Aim:***

This review aims to present a clear and comprehensive understanding of topical spray drug delivery systems, with emphasis on their formulation approaches, evaluation methods, mechanism of skin delivery, and their growing role in dermatological therapy.

- ***Objectives:***

The main objective is to explore how topical sprays have evolved from conventional aerosol-based products to more advanced systems such as pump sprays, film-forming formulations, and nano-carrier assisted delivery systems. It also focuses on highlighting their advantages over traditional semisolid dosage forms like creams and ointments, along with discussing key formulation ingredients, skin penetration enhancement strategies, evaluation techniques, and clinical applications in various skin conditions.

- ***Results:***

Literature analysis shows that topical sprays provide several practical and therapeutic benefits, including easy and hygienic application, uniform spreading over the skin, rapid drying, and improved patient comfort and compliance. Advanced systems such as film-forming sprays and nano-based formulations further improve drug delivery by enhancing penetration through the stratum corneum, increasing skin retention, and enabling controlled and sustained release. Evaluation studies indicate that parameters such as droplet size, spray pattern, drying time, dose uniformity, and skin permeation play a crucial role in determining the overall performance and effectiveness of these formulations.

- ***Conclusion:***

Topical spray systems have emerged as a promising and efficient approach in modern dermatological drug delivery. Ongoing innovations in formulation design and delivery technology are expected to further enhance their therapeutic performance, safety, and acceptance in both pharmaceutical and cosmetic applications.

Keywords: *Topical Sprays, Dermatological Drug Delivery, Film-Forming Systems, Nanocarriers, Skin Permeation, Patient Compliance.*

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I. INTRODUCTION

The largest organ of the body is skin and serves as a protective shield against germs, harmful chemicals, sunlight, and physical damage. It also plays an important role in maintaining body temperature and preventing excessive water loss, helping the body function properly and stay healthy and allowing sensations like touch, pain, and temperature to be felt. The surface of the skin has a slightly acidic nature with a pH typically ranging between 4 and 5.6, which is due to sweat and natural oils. This mild acidity

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serves to protect the skin by limiting the growth of harmful microbes and supporting healthy skin function[1].

The skin is made up of three layers includes ; the epidermis, dermis, and subcutaneous tissue. These layers helps maintain body temperature by providing insulation, and protects the body from physical injury by cushioning underlying tissues. [2-4].

Topical drug delivery involves applying a medication directly to the skin to produce its effect at the desired site. This route helps avoid passage through the digestive system and reduces first-pass metabolism in the liver, which can improve drug availability and minimize unwanted systemic side effects. Because the skin covers a large surface area, it provides a convenient and effective route for treating various skin disorders.

However, successful delivering of drugs through the skin can be difficult because the outermost layer of the skin, called the stratum corneum which acts as a protective barrier and limits the passage of many drug molecules into the deeper layers. Therefore, topical formulations must be carefully designed to enhance drug penetration while maintaining product stability, safety, and patient convenience [5].

In recent years topical sprays have become a popular and advanced option for delivering drugs through the skin.[5 Proper optimization of these factors can enhance drug delivery, improve treatment effectiveness, and support better outcomes in skin disorders and wound healing [6].

- *Evolution of Topical Spray Dosage Forms*

The evolution of topical spray dosage forms has been driven by advancements in pharmaceutical technology and the growing demand for more convenient and patient-friendly treatment options. In the past, topical therapy mainly relied on creams, ointments, and lotions. While these formulations often had major limitation, such as the possibility of contamination during application by hand [5].To address this issue, topical sprays were developed as a more convenient and hygienic alternative.

Early topical spray products were mainly designed as pressurized aerosol systems that used propellants such as chlorofluorocarbons (CFCs) to generate fine spray droplets. These formulations allowed quick application, uniform distribution of the medication, and improved patient convenience. However, due to the harmful effects of chloro fluorocarbons s on the ozone layer, they were gradually replaced with safer and more environmentally friendly propellants, including hydro fluoro alkanes and liquefied petroleum gas [9].

With further advancements in technology, non-pressurized pump spray systems were introduced, eliminating the need for propellants and making the products safer, more portable, and easier to use. These spray systems gained widespread popularity in both pharmaceutical and cosmetic applications because they are cost-effective, user-friendly, and convenient. In addition, metered-dose spray devices were developed to deliver a precise and consistent amount of medication with each spray, ensuring accurate dosing and improved treatment reliability [9].

Further improvements in topical spray technology resulted in the introduction of film-forming sprays. These formulations are designed to form a thin layer on the skin after application as the solvent evaporates. The resulting film helps keep the drug at the application site for a longer time, supports gradual drug release, and may reduce the need for repeated applications. Because of these advantages, film-forming sprays are becoming more widely used in the treatment of fungal infections, wound healing, and several long-term skin disorders [5].

Recent developments in topical spray technology have enabled the use of advanced nano-carrier systems, including nano-emulsions, liposomes, solid lipid nanoparticles, and polymeric nanoparticles to improve drug delivery through the skin. These innovative systems help improve drug solubility, enhance penetration through the skin barrier, and enable controlled and targeted drug delivery. As a result, topical sprays have progressed from simple aerosol products to sophisticated drug delivery systems that offer improved therapeutic effectiveness and better patient acceptance [10].

- *Overview of Topical Sprays:*

The improved patient comfort is beneficial in particular for treating large, sensitive, painful, or hairy areas of the skin where rubbing a formulation may be difficult or uncomfortable. The fine droplets produced by the spray can also reach irregular skin surfaces and wound areas effectively, supporting both protection and treatment of the affected site [7]. They are easy to use, allow accurate and adjustable dosing, and help distribute the medication evenly over the skin, which can improve medication adherence and improved treatment outcome [8].

- *Basic Working Mechanism of Topical Sprays*

The primary function of topical sprays is to deliver medication directly to the skin or mucosal surface, allowing the drug to act at the target site without passing through the digestive system. This direct route of administration can improve local drug availability and reduce unwanted systemic effects. After application, the spray forms fine droplets that spread over the skin surface, facilitating drug deposition, absorption, and therapeutic action at the desired site.

The working mechanism involves the following steps listed in figure 1:

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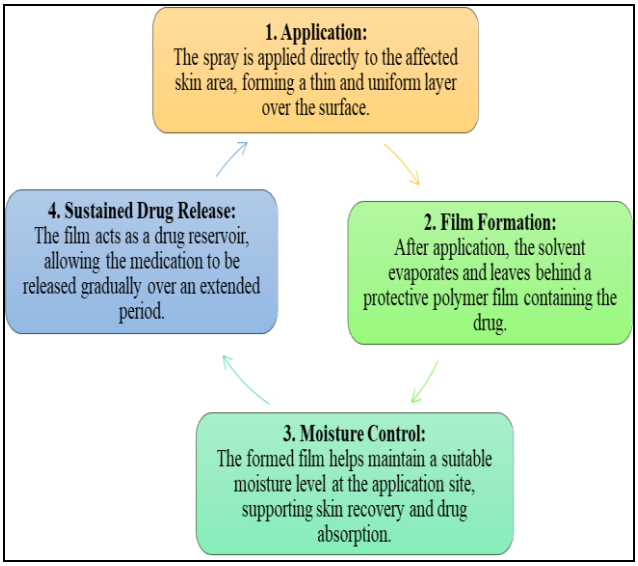

Fig 1 Basic Working Mechanism of the Topical Sprays

This combination of processes makes topical sprays an effective and modern drug delivery system.

➢ *Role of Stratum Corneum in Topical Sprays*

The outermost layer of the skin is the stratum corneum which serves as primary protective barrier of the skin. The stratum corneum consists of dead skin cells embedded within a lipid-rich matrix, which helps preventing excessive loss of water and protects the body from harmful external substances. The stratum corneum regulates the movement of drug molecules from topical sprays into the deeper layers of the skin, thereby influencing drug absorption in the topical spray delivery. As the main barrier to drug absorption, it significantly influences the effectiveness of topically applied medications. Therefore, successful topical spray formulations must be designed to overcome this barrier and enhance drug delivery while maintaining skin safety. According to Barry (1983), the stratum corneum is the key skin barrier that regulates and restricts drug absorption following topical application [12]. Drugs that have a small molecular size and are able to dissolve to some extent in skin lipids can pass through the skin more easily. In general, smaller and moderately lipophilic drug molecules show better skin penetration and absorption. Therefore, the effectiveness of topical drug delivery largely depends on the size and lipid solubility of the drug. Williams and Barry (2012) reported that molecular size and lipophilicity are two of the most important factors influencing drug permeation through the skin [13].

To improve the penetration of drugs through stratum corneum, topical sprays often contain penetration enhancers such as ethanol, propylene glycol, surfactants, and terpenes. These ingredients help increase the permeability of the skin and improve drug absorption. In film-forming sprays, the solvent evaporates after application and leaves a thin film on the skin, which helps keep the drug in contact with the application site for a longer time and improves drug retention. Research findings suggest that the film-forming systems can enhance both the residence time as well as drug penetration through the skin [5]. Therefore, proper formulation design is important for improving topical drug delivery while maintaining skin safety.

➢ *Factors Influencing Topical Permeation:*

The extent to which a drug penetrates through the skin is influenced by several physicochemical characteristics of the drug molecule. These include:

- *Physicochemical Properties of the Drug*

✓ Partition coefficient
✓ Degree of ionization
✓ Drug solubility
✓ Drug concentration
✓ Particle size
✓ Polymorphic form
✓ Molecular weight [14, 15]

- *Penetration Enhancers*

✓ Solvents
✓ Surfactants
✓ Bile salts
✓ Binary system
✓ Miscellaneous chemicals [16 - 21]

- *Physicochemical Properties of a Topical Drug Delivery System*

✓ *Drug Release Characteristics and Formulation pH:*

The effectiveness of topical drug absorption depends on how readily the drug is released from the formulation and transferred into the skin. The pH of the formulation can also influence drug ionization and permeation, thereby affecting overall absorption.

✓ *Composition of Drug Delivery System:*

The formulation composition can also affect drug penetration through the skin. For example, low-molecular-weight polyethylene glycols may reduce the permeation of the drug.

✓ *Nature of the Vehicle:*

A lipophilic (oil-loving) vehicle generally helps the drug pass through the skin more easily, while a lipophobic (water-loving) vehicle may reduce penetration of drugs through the skin [11].

- *Physiological and Pathological Condition of Skin*

✓ *Reservoir Effect of Horny Layer:*

The stratum corneum (horny layer) serves as a temporary reservoir for some drugs, storing a portion of the applied medication and slowly releasing it over time. This reservoir effect occurs because some drug molecules bind to the skin layers, which can affect the permeation of drugs into the skin. Pre-treating skin with certain surfactants may improve drug penetration.

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✓ *Lipid Layer of Film:*

The skin surface lipid layer contributes to moisture retention and helps preserve the barrier properties of the stratum corneum, thereby protecting the skin. When this lipid layer is removed or damaged, the skin barrier becomes weaker, which can change the absorption and drug penetration into the skin. This shows that skin lipids play an important role in transdermal drug delivery.

✓ *Skin Hydration:*

Increased hydration of the stratum corneum enhances skin permeability, making it easier for drug molecules to penetrate through the skin.

✓ *Skin Temperature:*

When temperature of the skin rises, the rate at which substances pass through the skin also rises. This happens because higher temperature provides extra thermal energy, which enhances the movement of molecules and improves their ability to diffuse through the skin layers.

✓ *Regional Variation:*

Skin permeability differs across various body regions due to differences in skin thickness and barrier function. Drug penetration is generally lowest through the thick skin of the sole (plantar region) and gradually increases through the forearm, scalp, thigh, scrotum, and behind the ear (posterior auricular area).

✓ *Pathologic Injuries to the Skin:*

When the stratum corneum (the outermost protective layer of the skin) damaged or disrupted due to injury, the skin's barrier function weakens. As a result, substances can pass through the skin more easily, leading to an increase in permeability.

✓ *Cutaneous Drug Metabolism:*

The systemic absorption and distribution of drugs applied through the skin are partly affected by the blood flow (cutaneous perfusion) beneath the application site, as well as the structure and accessibility of nearby blood vessels and tissues.

➢ *Mechanism of Drug Absorption Through Skin*

Drug absorption through the skin primarily occurs by diffusion of drug molecules across the stratum corneum, the skin's main protective barrier. In most cases, this process occurs through passive diffusion, where drugs naturally move from an area of higher concentration on the skin surface to a lower concentration in the deeper layers. In some cases, drugs can also pass through small skin appendages like hair follicles and sweat glands, known as the appendageal or shunt pathway. Additionally, processes like solvent evaporation and drug retention within the skin can further improve drug penetration and enhance therapeutic effectiveness, especially in topical spray formulations.

- *Passive Diffusion*

Passive diffusion is the primary mechanism responsible for this process as conceptualized in figure 2. It depends on the physical and chemical properties of drugs such as molecular weight, lipid solubility, and water solubility, and follows fick's law of diffusion. The drug molecules mainly travel through the lipid-rich spaces between skin cells (intercellular pathway) and, to a lesser extent, directly through the skin cells themselves (transcellular pathway). Since the stratum corneum is rich in lipids, drugs that have moderate lipophilicity and a molecular weight below 500 Daltons are usually absorbed more efficiently through the skin [22,23].

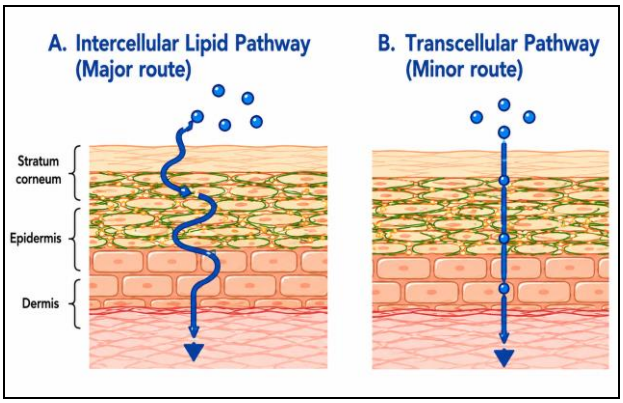

Fig 2 Mechanism of Drug Absorption by Passive Diffusion

- *Appendageal (Shunt) Pathway*

The appendageal pathway refers to drug transport through structures such as hair follicles, sebaceous (oil) glands, and sweat ducts. Although this route contributes only a small portion of overall skin absorption, it becomes especially important for certain types of drugs.

It is particularly useful for hydrophilic (water-loving) molecules, larger drug molecules, and particulate delivery systems that may not easily pass through the main skin barrier. This pathway is also highly relevant in topical spray formulations, where fine droplets can settle around hair follicle openings and sweat glands as represented in figure 3. This allows the drug to penetrate more effectively into these regions, leading to better localized delivery and increased drug accumulation within the hair follicles [24].

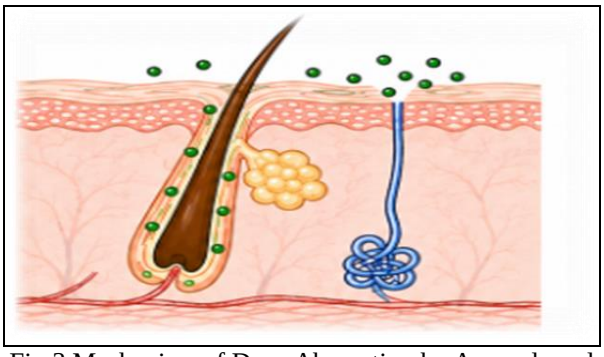
Fig 3 Mechanism of Drug Absorption by Appendageal (Shunt Pathway)

- *Role of Solvent Evaporation in Topical Sprays*

Topical sprays often contain volatile solvents like ethanol and isopropyl alcohol that evaporate quickly after application. This evaporation increases the drug

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concentration on the skin surface, creating a temporary supersaturated state as shown in figure 4, that improves drug penetration into the stratum corneum. These solvents can also slightly disrupt skin lipids, which increases permeability and enhances drug absorption [22,23].

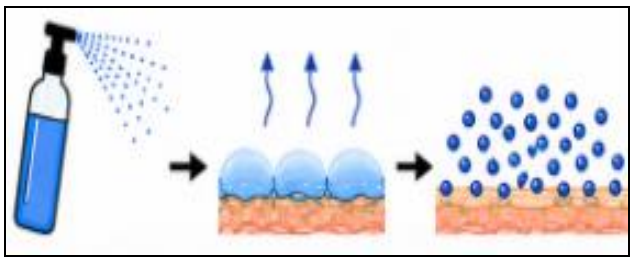

Fig 4 Mechanism of Drug Absorption by Role of Solvent Evaporation in Topical Sprays

- *Skin Retention and Reservoir Effect*

Skin retention is a significant mechanism in topical therapy, particularly for sprays intended for local dermatological action. After penetration, drugs may remain retained within the stratum corneum and viable epidermis due to partitioning into skin lipids, binding to keratin, and accumulate within appendageal structures such as follicles. In film-forming topical sprays, solvent evaporation results in polymeric film formation on the skin, which acts as a drug reservoir as depicted in figure 5, and prolongs drug residence time, thereby enhancing skin retention and sustained drug release while reducing systemic absorption [5].

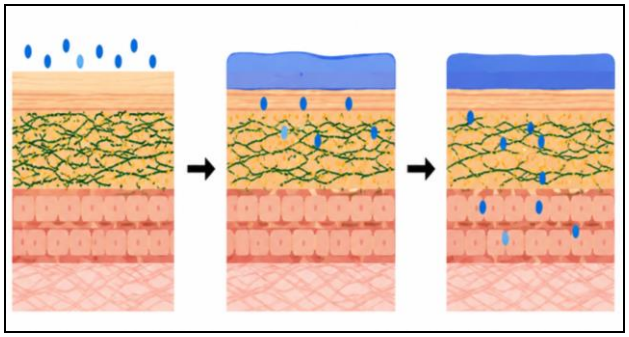

Fig 5 Skin Retention and Reservoir Effect

Thus, the combined effects of passive diffusion, appendageal penetration, solvent evaporation-induced supersaturation, and skin retention determine the therapeutic efficiency of topical spray drug delivery systems.

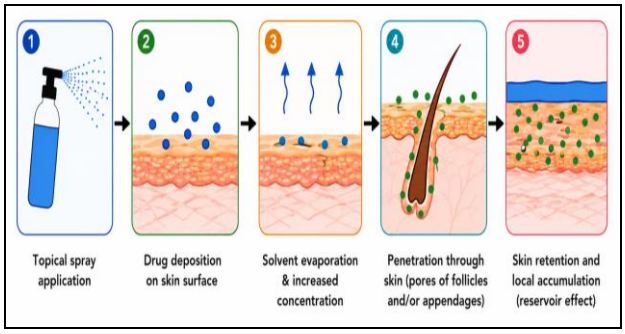

Fig 6 Overall Mechanism of the Topical Spray

➢ *Classification of Topical Sprays*

Topical sprays are classified as five varieties based on delivery system, formulation type, film formation, advanced delivery approaches and therapeutic applications as shown in figures 7 to 11 respectively.

- *Based on Propulsion in Delivery System*

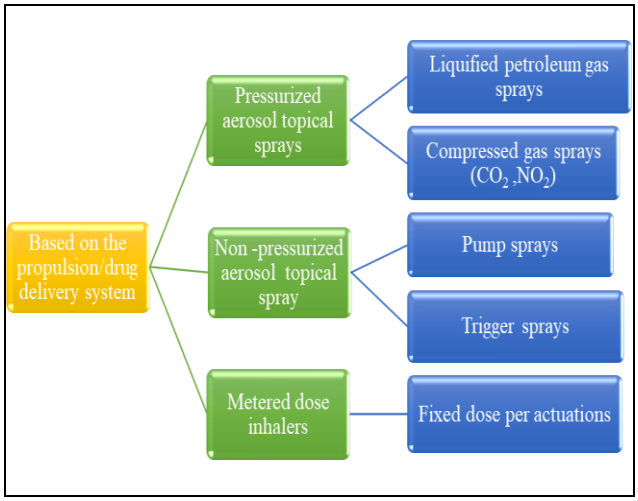

Fig 7 Classification of Topical Sprays Based on the Propulsion in Drug Delivery System

- *Based on the Formulation Type*

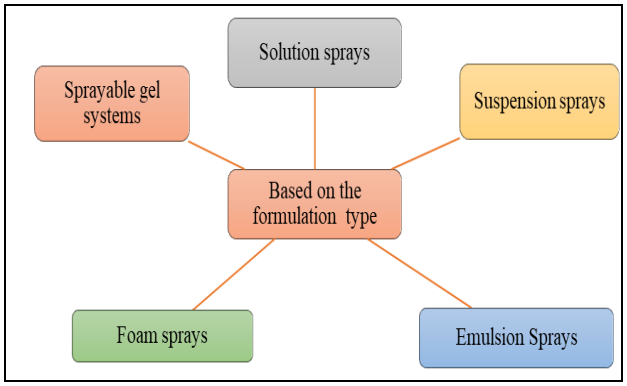

Fig 8 Classification of Topical Sprays Based on the Formulation Type

- *Based on Film Formation and Subsequent Drug Release Behaviour*

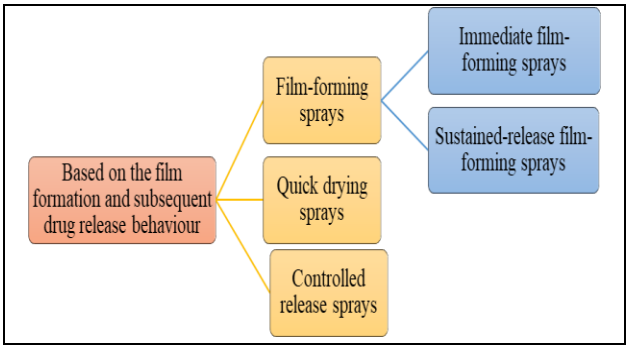

Fig 9 Classification of Topical Sprays Based on the Film Formation and Subsequent Drug Release Behaviour

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- *Based on an Advanced Drug Delivery Approach*

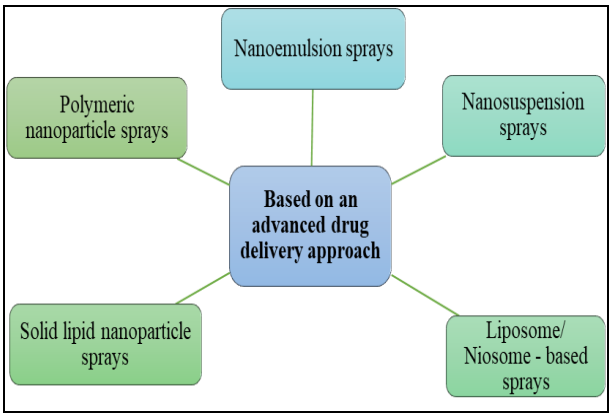

Fig 10 Classification of Topical Sprays Based on the Advanced Drug Delivery Approaches

- *Based on Therapeutic Application*

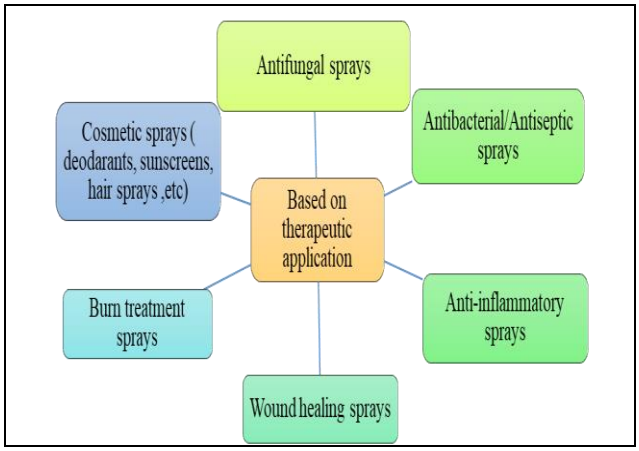

Fig 11 Classification of Topical Sprays Based on the Therapeutic Applications of Topical Sprays

➢ *Components of Topical Spray Formulations*

The topical sprays made of some typical ingredients depending on requirement for their functionality and effective usage for patient compliance enlisted in table 1.

Table 1 Basic Components of Topical Spray Formulations

S. no	Components	Definition	Function	Examples
1.	Active pharmaceutical ingredient (API)	These are the active drug substances in topical sprays responsible for producing the intended therapeutic effect on the skin by reaching the targeting area.	Proper selection of APIs ensure effective drug delivery and absorption when carefully formulated with excipients.	Diclofenac diethylamine, itraconazole, miconazole, etc.
2.	Solvents and co-solvents	These are the substances incorporated into topical spray formulations to increase the solubility of active ingredients.	For complete dissolution of the drug, improving homogeneity, and enhancing drug availability for skin penetration.	Methanol, Propylene glycol, isopropyl alcohol, ethanol, etc.
3.	Film-forming polymers	These are specialized polymers incorporated to produce a smooth and uniform film on the skin after application and solvent evaporation.	They enhance the adhesion, prolong drug retention at the application site, and support sustained and controlled drug delivery.	Hydroxypropyl Methylcellulose, Polyvinylpyrrolidone. Eudragit, etc.
4.	Plasticizers	Plasticizers are liquids or soft waxes that improve flexibility, durability, and texture.	Prevents brittleness and cracking, ensuring a smooth, long-wearing application.	Glycerine, triethyl citrate, and castor oil, etc.
5.	Penetration enhancers	These are the chemical compounds that improve the absorption of active ingredients in topical sprays by facilitating their penetration through the	Works by disrupting the lipid matrix of the outer skin layer or improve drug solubility or support greater diffusion across the skin.	Dimethyl sulfoxide, ethanol, propylene glycol, oleins, terpenes, surfactants, etc.

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		skin's barrier.		
6.	Surfactants	These are the chemical agents that reduce surface tension, helping the spray spread evenly and mix oil- and water based ingredients.	They improve spreading on the skin, keep ingredients uniformly mixed, and enhance delivery of APIs	Tweens, spans, lecithin, sodium lauryl sulfate, sorbitan esters, etc.
7.	Preservatives	They inhibit the growth of microorganisms such as bacteria, fungi, and molds, thereby protecting the product from microbial contamination.	Their primary function is to preserve the integrity, stability, and safety of the product during storage.	Benzalkonium chloride, parabens (methylparaben, propylparaben), phenol, chlorhexidine, honey, and vitamin E (tocopherol).
8.	Antioxidants	Antioxidants are substances that protect cells and tissues from oxidative damage by reducing the harmful effects of unstable molecules known as free radicals.	Helps to protect the skin from environmental damage, support skin repair, and maintain overall skin health.	Vitamin C, Vitamin E, Vitamin A, Coenzyme Q10, carotenoids, polyphenols, curcumin, resveratrol, green tea extract, aloe vera extract, grape seed extract, and flavonoids.
9.	Humectants	Humectants are defined as hygroscopic substances that attract and retain moisture.	They are used in topical sprays to keep the product moisturized and preserve its effectiveness.	glycerine, sorbitol, and sodium pyrrolidine carboxylic acid
10.	Emollients	Emollients are used to soften, smoothening, and moisturizing the skin by forming a protective layer that reduces water loss.	Emollients used in topical sprays to soften and moisturize the skin.	Isopropyl myristate, isopropyl palmitate, ethyl oleate, cetyl palmitate, Glyceryl monostearate

➢ *Preparation Methods, Mixing Procedures, Filling Processes & Packaging Considerations of Topical Sprays*

- *Solution-Type Topical Sprays*

✓ Solution sprays are prepared by dissolving the drug and other ingredients in suitable solvents such as ethanol or propylene glycol to obtain a clear and uniform solution.
✓ The ingredients are mixed under stirring until completely dissolved, followed by pH adjustment and filtration to remove particles.
✓ The final solution is filled into pump spray bottles or aerosol containers using accurate filling systems.
✓ Airtight and solvent-resistant containers are preferred to prevent evaporation and maintain spray quality [1].

- *Suspension-Type Topical Sprays*

✓ Suspension sprays are used for poorly soluble drugs and contain fine drug particles dispersed in a liquid medium.
✓ The drug is micronized and mixed with wetting and suspending agents to maintain uniform dispersion and prevent settling.
✓ The formulation is filled into spray containers with suitable nozzles to avoid clogging.
✓ These products are usually labelled “shake well before use” because particles may settle during storage [25].

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- *Emulsion-Based Topical Sprays*

✓ Emulsion sprays contain both oil and water phases and are suitable for drugs with mixed solubility.
✓ The oil phase and aqueous phase are prepared separately and mixed using high-speed stirring or homogenization to form a stable emulsion.
✓ The formulation is then filled into spray containers under controlled conditions to avoid contamination or phase separation.
✓ Proper packaging helps maintain emulsion stability and spray performance [10].

- *Film-Forming Topical Sprays*

✓ Film-forming sprays contain polymers that form a thin film on the skin after solvent evaporation.
✓ The polymer, plasticizer, and drug are dissolved in volatile solvents and mixed until a uniform solution is obtained.
✓ These formulations are filled into airtight spray containers to minimize solvent loss.
✓ Film-forming sprays improve drug retention, prolong release, and provide better skin adherence [5].

- *Pressurized Aerosol Sprays*

✓ Pressurized aerosol sprays contain the formulation along with a propellant inside a sealed container.
✓ The drug concentrate is prepared first and then combined with propellants such as LPG or HFA under controlled conditions.
✓ Filling may be carried out by cold filling or pressure filling methods.
✓ Strong and corrosion-resistant containers are required to safely withstand internal pressure [9].

- *Foam Sprays*

✓ Foam sprays are formulated using surfactants and foaming agents that produce foam during application instead of fine droplets.
✓ The formulation is prepared as a solution or emulsion and filled into aerosol containers fitted with foam actuators.
✓ Proper propellant selection is important to maintain foam consistency and stability.
✓ Barry, 1983 highlighted the use of foam-based topical systems for enhanced dermal application and drug delivery [12].

- *Nano-Based Topical Sprays*

✓ Nano-based topical sprays contain nanosized carriers such as nano-emulsions, nanosuspensions, liposomes, or solid lipid nanoparticles to improve drug penetration and retention.
✓ These systems are prepared using techniques like homogenization, ultrasonication, or milling to reduce particle size.
✓ The formulations are filled under controlled conditions to maintain nanoparticle stability.
✓ Protective packaging is required to avoid light, temperature, and aggregation-related instability.

Shakeel et al. and Manca et al. reported improved skin permeation and therapeutic efficacy using nano-based topical delivery systems [10,26]. The figure 12 represents the combined view of formulation technologies.

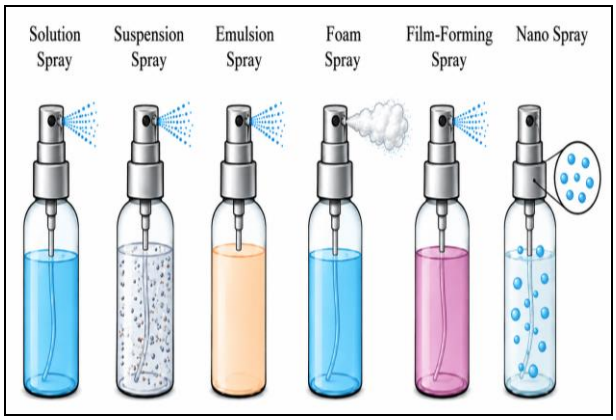

Fig 12 Formulation Technology Types in Topical Sprays

- *Spray Device Technology in Topical Sprays*

Topical spray drug delivery systems use different spray devices depending on whether the formulation is pressurized or non-pressurized. These devices are designed to provide uniform drug distribution, easy application, and improved patient convenience.

- *Pressurized Topical Sprays (Aerosols)*

Pressurized topical sprays are formulations packed in sealed containers under pressure that release the medication as a fine mist, foam, or spray when activated. These systems help provide uniform drug application over the skin surface. Allen et al. (2011) explained that aerosol systems contain the product concentrate and propellant within a pressure-resistant container for spray delivery [25]. The main components of pressurized sprays include the container, propellant, concentrate, valve, and actuator.

- *Main Components of Pressurized Sprays*

The pressurized spray packaging certainly contain some components which are visualized in figure 13.

✓ *Container:*

Containers are commonly made of aluminium, stainless steel, glass, or coated plastic to safely withstand internal pressure.

✓ *Propellant:*

Propellants provide the pressure required to expel the formulation from the container. Commonly used propellants include hydrocarbons, carbon dioxide, nitrogen, and nitrous oxide.

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✓ *Concentrate:*
The concentrate contains the active drug along with other excipients. The drug may be dissolved, suspended, or emulsified within the formulation.

✓ *Valve:*
The valve controls the release of the formulation from the container and helps regulate the spray pattern and dose delivery.

✓ *Actuator:*
The actuator is the spray button attached to the valve. When pressed, it directs the formulation onto the skin as a spray, foam, or stream.

Lachman et al. (2009) described aerosol spray systems as devices capable of delivering drugs in the form of fine droplets, foams, or streams depending on valve and actuator design [27].

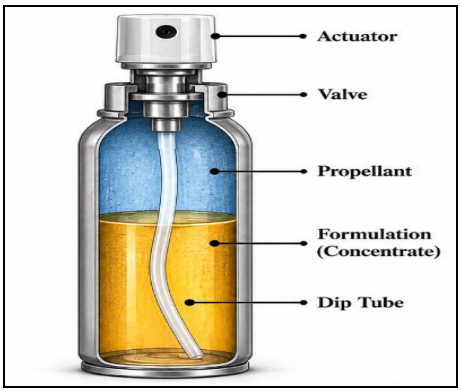

Fig 13 Pressurized Topical Spray System

- *Types of Pressurized Systems*

✓ *Two-Phase Systems:*
These systems contain the drug dissolved in the liquefied propellant along with vaporized propellant.
✓ *Three-Phase Systems:*
These systems contain the drug in suspension or emulsion form along with propellants. Foam aerosols are common examples of three-phase systems [25].

➢ *Non-Pressurized Topical Sprays*
Non-pressurized topical sprays mainly use pump spray systems and are widely preferred because they are simple to use, cost-effective, and environmentally friendly since they do not require propellants. The components of non pressurized system is clarified in figure 14.

- *Main Components*

✓ *Container:*
These formulations are usually packed in plastic or glass bottles, commonly polyethylene terephthalate containers, which do not need to withstand internal pressure.

✓ *Pump Dispenser:*
The spray is delivered using a finger-operated pump mechanism that converts mechanical force into a fine spray or liquid stream without using propellants. Some pumps can also provide a fixed dose with each actuation.

✓ *Product Concentrate:*
The formulation contains the active drug along with excipients such as solvents, polymers, penetration enhancers, and plasticizers to improve spray performance and skin delivery.

✓ *Actuator:*
The actuator directs the spray onto the skin and helps control the spray pattern, angle, and volume during application.

Aulton and Taylor et.al., (2018) reported that pump spray systems provide controlled and convenient topical drug application without the use of propellants [28].

Fig 14 Non -Pressurized Topical Spray System

II. LIMITATIONS AND CHALLENGES OF TOPICAL SPRAY DRUG DELIVERY SYSTEMS

Topical spray formulations offer significant advantages in dermatological therapy; however, they also face several formulation and device-related limitations that may affect product performance, safety, and patient acceptability.

➢ *Drug Crystallization*
One of the common challenges in topical spray formulations is drug crystallization after solvent evaporation. Rapid evaporation of volatile solvents such as ethanol may cause drug precipitation on the skin surface, reducing drug penetration and therapeutic efficacy. Crystallization may also produce an unpleasant gritty feeling on the skin and affect the uniformity of dosing. Lane (2013) explained that supersaturation can improve penetration initially but may also lead to crystallization of the drug on the skin [29]. The plasticizers, surfactants can

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avoid this problem to certain extent by their judicial selection.

➢ *Irritation Due to Alcohol-Based Solvents*

Alcohol-based solvents are widely used in topical sprays because they improve drug solubility and provide quick drying. However, repeated use may cause dryness, irritation, burning sensation, and disruption of the skin barrier. Alcohol can extract lipids from the stratum corneum and disrupt the skin barrier, leading to increased trans-epidermal water loss. This issue becomes more prominent in chronic therapy where repeated application is required, reducing patient compliance. Williams and Barry (2012) reported that solvents such as ethanol can alter stratum corneum lipids and increase skin irritation [13].

➢ *Nozzle Clogging*

Nozzle clogging may occur in suspension sprays or polymer-containing formulations due to drug particles or dried residues blocking the spray opening. This can affect spray pattern, dose uniformity, and patient convenience. Clogging can also occur due to drying of formulation residues around the nozzle tip after repeated use. This issue reduces product reliability and affects patient convenience. Allen et al. (2011) discussed that improper particle dispersion and polymer deposition may reduce spray performance [25]. The proper solvent combination may prevent this problem.

➢ *Poor Adhesion and Low Residence Time*

Low-viscosity sprays may show poor adhesion on the skin surface, resulting in reduced contact time and rapid loss of formulation due to rubbing or sweating. Film-forming sprays are developed to improve skin adhesion and prolong drug residence time. Although film-forming sprays are designed to overcome this limitation, improper polymer selection or low polymer concentration can still result in weak films and poor adhesion. An author reported that film-forming systems improve skin retention and controlled drug release [5].

➢ *Flammability of Aerosol Sprays*

Pressurized aerosol sprays using hydrocarbon propellants such as liquified petroleum gas are highly flammable and require careful handling during manufacturing, storage, and use. Flammable aerosols must be labeled with warnings, and exposure to heat sources or open flames can cause serious hazards. Additionally, aerosol containers may explode if exposed to high temperatures, making storage conditions critical. Lachman et al. (2009) highlighted that aerosol products require proper safety precautions because of propellant flammability [27].

➢ *Stability Issues*

Topical spray formulations may face stability problems such as oxidation, phase separation, sedimentation, polymer precipitation, and pressure loss during storage. Compatibility between the formulation, container, and propellant is important to maintain product quality and shelf-life. Some authors discussed that the formulation stability as a major consideration in spray film-forming systems [9].

In emulsion sprays, phase separation and creaming may reduce product stability. Film-forming sprays may experience polymer precipitation or viscosity changes over time. Furthermore, aerosol sprays require compatibility between formulation components, propellant, and container materials to avoid corrosion, leakage, or loss of pressure. These stability issues can ultimately reduce shelf-life and therapeutic performance.

III. EVALUATION OF TOPICAL SPRAYS

➢ *Physical Evaluation of Topical Sprays*

- *Appearance and Clarity:*

Physical appearance (colour, presence of particulates) and clarity are primary quality attributes to ensure the formulation is free from visible particles or phase separation, which can affect aesthetics and uniformity. Clear sprays typically indicate good solubility and homogeneity of components [5].

- *pH:*

pH measurement ensures compatibility with skin (ideal pH ~5–7) to minimize irritation. pH evaluation helps predict the irritation potential and stability of the spray formulation [30].

- *Viscosity:*

Viscosity affects spray ability and droplet formation; lower viscosity often provides better spray coverage, while excessively high viscosity can clog the nozzle and reduce spreadability [30].

- *Density / Specific Gravity:*

Density and specific gravity influence spray performance, delivery rate, and droplet size distribution. Consistent density ensures repeatable dosing and spray pattern [1].

- *Drug Content:*

Uniform drug content ensures each actuation delivers the stated amount of drug. Assay methods (e.g., UV-Visible spectroscopy, High performance liquid chromatography etc) quantify active concentration to confirm formulation consistency [1].

➢ *Spray Performance Evaluation*

- *Spray Pattern:*

Spray pattern tests evaluate the distribution area of the spray plume on a surface, indicating uniformity of dispersion — critical for even drug delivery [1].

- *Spray Angle:*

The angle of the spray plume determines the coverage area; wider angles may lead to broader distribution.

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Measurement of spray angle is essential for optimizing targeted delivery [1].

- *Spray Rate:*

Spray rate measures the mass or volume dispensed per second or per actuation, affecting dose accuracy and patient compliance [1].

- *Droplet Size Distribution:*

Droplet size influences absorption and skin deposition; smaller droplets generally enhance uniform coverage and penetration. Measurements can be done via laser diffraction or microscopy [1].

- *Dose Per Actuation:*

Ensures reproducible drug delivery per spray — vital for dose control. This is assessed by measuring drug amount emitted in multiple actuations [1].

- *Discharge Time:*

The time taken to empty the spray container or to release a fixed number of doses indicates consistency and helps assess device reliability [1].

➢ *Film Evaluation (for Film-for Ming Sprays)*

- *Drying Time:*

The time required for the sprayed formulation to form a dry film on the skin is critical for patient convenience and drug retention. Shorter drying times improve adherence and reduce risk of smudging [5].

- *Film Thickness:*

Film thickness affects drug release and mechanical properties; it is measured after drying using micrometers to ensure adequate protective coverage [31].

- *Tensile Strength:*

Tensile strength reflects mechanical integrity of the formed film; higher values indicate stronger films resistant to cracking [31].

- *Flexibility:*

Film flexibility is evaluated by stretching tests to ensure the film does not crack under movement; flexible films enhance comfort and durability [31].

- *Stickiness:*

Stickiness testing assesses adhesion tendency of the film to surfaces (e.g., clothes), where low stickiness is desirable to prevent unwanted adhesion [31].

➢ *In-Vitro* Drug Release Studies

- *Franz Diffusion Cell:*

In-vitro drug release testing from topical sprays or films is done by Franz diffusion cell which simulates drug release through membranes under controlled conditions [31].

- *Release Kinetics:*

The drug release data are fitted to different kinetic models, such as zero-order, first-order, and Higuchi models, to understand how the drug is released and to predict its performance *in vivo* [31].

➢ *Ex-Vivo Skin Permeation Study*

- *Animal/Human Skin:*

Excised animal or human skin mounted on diffusion cells assesses permeation through real biological barriers, providing closer *in-vivo* relevance than synthetic membranes [31].

- *Permeation Flux:*

Permeation flux (Microgram per Square Centimeter per Hour) quantifies the rate of drug permeating through skin over time, indicating formulation efficiency in delivering actives across the barrier [31].

➢ *Skin Retention Studies*

- *Drug Deposition Analysis:*

After permeation experiments, residual drug in the skin layers (stratum corneum, epidermis, dermis) is quantified to assess local retention, often using extraction and spectrophotometric or chromatographic analysis [31].

➢ *Antimicrobial/ Antifungal Studies*

- *Zone of Inhibition:*

A common microbiological assay where sprays or films are applied on agar plates inoculated with pathogens; inhibition zones indicate antimicrobial/ antifungal efficacy and are measured in millimeters [1].

➢ *Stability Studies*

- *ICH Guidelines:*

Stability testing is performed as per International Council for Harmonization guidelines (e.g., Q1A) including long-term and accelerated conditions to assess drug and formulation integrity over time [5].

- *Accelerated Stability:*

Formulations are kept at high temperature and humidity conditions (e.g., 40 Degree Celsius /75% Relative Humidity) to quickly evaluate their long-term stability and predict how they will perform during storage [5].

- *Freeze-thaw Cycles:*

Samples are repeatedly cycled between cold and room temperatures to test physical stability (phase separation, precipitation) and robustness against temperature stress [5].

- *Leakage Test:*

For aerosol sprays, leakage tests ensure container and valve integrity under pressure, preventing loss of formulation or propellant [1].

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➢ *Safety Studies*

- *Skin Irritancy:*

Evaluated in animal models or volunteers by observing erythema and edema after application; non-irritant formulations show minimal signs [1].

- *Sensitization:*

Assesses potential allergic reactions upon repeated exposures using established protocols like the Draize or Local Lymph Node Assay, ensuring formulation safety [1].

IV. THERAPEUTIC APPLICATIONS OF TOPICAL SPRAYS

Topical spray formulations are widely used in dermatology because they provide non-contact application, uniform drug distribution, rapid drying, and better patient convenience compared to conventional creams or ointments. These systems are useful for treating fungal infections, inflammatory disorders, wounds, burns, pain, and cosmetic skin conditions. Topical spray systems improve patient compliance and provide effective local drug delivery through easy and hygienic application [9].

➢ *Antifungal Sprays*

Antifungal topical sprays are commonly used for fungal infections such as tinea corporis and tinea pedis. These sprays deliver the drug directly to the infected area and provide better coverage over large or hairy skin surfaces where creams may be difficult to apply. Spray formulations also reduce direct touching of infected areas and improve patient comfort. Kaur et al. (2021) explained that topical antifungal sprays can enhance local drug concentration while minimizing systemic exposure [33].

Nano-based antifungal sprays such as ciclopirox nanosprays have shown improved skin penetration and better drug retention at the infection site. These systems provide more uniform drug distribution and may reduce irritation compared to conventional semisolid formulations [32].

➢ *Anti-Inflammatory Sprays*

Topical anti-inflammatory sprays are used for conditions such as dermatitis, eczema, and psoriasis. They deliver corticosteroids or non-steroidal anti-inflammatory drugs directly to inflamed skin without the need for rubbing, which may further irritate sensitive areas. Sprays also provide rapid and uniform coverage over affected regions. Butarbutar et al. (2020) reported that film-forming topical sprays improve local drug retention and controlled release while reducing skin irritation [5].

Film-forming anti-inflammatory sprays create a thin polymeric film after application, which helps maintain prolonged drug contact with the skin and improves therapeutic effectiveness.

➢ *Wound Healing Sprays*

Wound healing sprays are designed to deliver antimicrobial agents, herbal extracts, and tissue-regenerating compounds directly onto wounds. Since wounds are sensitive and painful, sprays provide non-contact application and reduce trauma during treatment. Sawatdee et al. (2021) reported that sprays containing *Centella asiatica* extract improved wound healing and accelerated re-epithelialization in experimental studies [34].

Herbal and essential oil-based sprays have also shown antimicrobial and anti-inflammatory activity that supports faster wound closure and improved tissue repair.

➢ *Local Anaesthetic Sprays*

Local anesthetic sprays such as lidocaine sprays are used to provide temporary pain relief before minor dermatological procedures, injections, wound dressing, or superficial painful conditions. These sprays block nerve signal transmission and provide quick local anaesthesia. Becker and Reed (2012) described topical anaesthetic sprays as effective non-invasive systems for reducing pain with minimal systemic absorption [35].

➢ *Burn Treatment Sprays*

Topical sprays are useful in burn management because they allow painless and non-touch application over damaged skin surfaces. Burn sprays commonly contain antimicrobial agents, silver compounds, and wound-healing promoters that help reduce infection and accelerate tissue repair. Dai et al. (2010) reported that topical antimicrobial delivery plays an important role in preventing burn wound infections and improving healing outcomes [36]. Spray formulations also provide uniform coverage over irregular burn surfaces while minimizing secondary trauma during application.

➢ *Cosmetic and Dermatological Sprays*

Topical sprays are increasingly used in cosmetic dermatology for moisturizers, sunscreens, antioxidants, anti-aging agents, deodorants, and herbal skincare products. These sprays provide a light, non-greasy feel and are convenient for application over large skin areas. A reviewer reported that film-forming spray systems can improve hydration, skin protection, and controlled release of cosmetic ingredients [9].

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➢ *Commercial Marketed Products of Topical Sprays*

Table 2 The List of the Commercial Marketed Topical Spray Products

Marketed Product	Drug	Company	Therapeutic use	Formulation type	References
Lamisil Once®	Terbinafine hydrochloride	Novartis, Australia	Antifungal treatment	Film forming solution	[37]
Axiron®	Testosterone	Lilly USA, LLC	Testosterone replacement therapy	Film forming spray	[38]
Medspray® the Patch-in a-Can®	Terbinafine hydrochloride	MedPharm Ltd, UK	fungal skin infections such as tinea pedis and tinea corporis	Film forming spray	[39]
Liqui-Patch Technology	Testosterone hydrocortisone	Epinamics GmbH, Germany	Hormone replacement therapy and anti-inflammatory	Film forming spray	[40]
Evamist®	Estradiol	Ther-Rx Corporation	Hormone replacement	Transdermal topical spray	[41]
Opsite® Spray	Acrylic copolymer	Smith & Nephew	Wound protection	Film-forming spray	[42]
Curanail® Spray	Amorolfine hydrochloride	Galderma	Nail fungal infections	Antifungal spray	[43]
Betadine® spray	Povidone iodine	Mundipharma	Antiseptic wound care	Topical spray	[44]
Pevaryl® Spray Powder	Econazole nitrate	Janssen Pharmaceuticals	Fungal skin infections	Powder spray	[45]
Paxil® Topical Spray	Lidocaine	Various manufacturers	Local anaesthetic / pain relief	Topical aerosol spray	[46]
Nizoral® Spray	Ketoconazole	Janssen Pharmaceutical	Antifungal therapy	Topical spray solution	[47]
Tinaderm® Spray	Tolnaftate	Bayer	Fungal skin infections	Aerosol spray	[48]
Solarcaine® Spray	Lidocaine hydrochloride	Bayer Consumer care	Burn and sunburn relief	Aerosol spray	[46]
Nexcare™ liquid bandage spray	Ethyl acetate + polymeric film former	3M	Minor cuts and wound protection	Film-forming spray	[5]
Tinactin® Aerosol Spray	Tolnaftate	Bayer	Athlete's foot /fungal infections	Aerosol spray	[50]

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Micatin® Spray	Miconazole nitrate	Bayer	Antifungal	Aerosol spray	[49]
Lotrimin® AF Spray	Clotrimazole	Bayer	Tinea infections	Aerosol spray	[48]
Zeasorb-AF® Spray	Miconazole nitrate	Stiefel Laboratories	Antifungal powder spray	Powder spray	[45]
Solarcaine® Cool Aloe Spray	Lidocaine hydrochloride+Aloevera	Bayer	Sun burns and minor burns	Aerosol spray	[46]

➢ *Future Prospects of Topical Spray Drug Delivery System*

- *Personalized Sprays*

Future topical spray systems are expected to provide more personalized treatment based on individual patient needs, skin type, disease condition, and severity. Smart topical sprays may contain stimuli-responsive materials that can control drug release according to changes in pH, temperature, or moisture on the skin surface. These advanced systems may help improve therapeutic effectiveness, reduce side effects, and provide better patient-specific treatment. Mura et al. reported that responsive drug delivery systems have strong potential in personalized dermatological therapy [51].

- *Eco-Friendly Propellants*

Due to environmental concerns associated with older aerosol propellants, modern topical spray formulations are increasingly using safer and eco-friendly alternatives such as hydro fluoro alkanes , nitrogen, and carbon dioxide. Researchers are also focusing on biodegradable propellants and sustainable formulation materials to reduce environmental impact. These greener approaches help improve product safety while maintaining effective spray performance. Montenegro et al., (2020) highlighted the importance of environmentally friendly formulation strategies in modern topical delivery systems [52].

- *Advanced Spray Nozzles*

Modern topical spray devices are being designed with advanced nozzle technologies to improve spray accuracy, droplet size control, and uniform drug distribution. Precision spray systems such as microfluidic and piezoelectric nozzles can produce fine and controlled droplets, which may improve skin deposition and reduce formulation wastage. Advanced nozzles can also help target specific skin areas more effectively and improve patient convenience. Vehring (2008) explained that controlled droplet generation improves deposition efficiency and therapeutic performance [53].

- *Clinical Translation*

Although many advanced topical spray formulations have shown promising results in laboratory and preclinical studies, more clinical studies are still required to confirm their long-term safety, effectiveness, and patient acceptability. Hence, the importance of further human studies and clinical translation for advanced topical spray systems to be addressed for compliance and commercialization [9].

V. CONCLUSION

Topical spray drug delivery systems have become an important advancement in the field of dermatology because they offer a simple, convenient, and effective method of applying medicines directly to the skin. They are particularly useful for treating painful, infected, inflamed, or hairy skin areas where conventional formulations may be difficult to apply traditional creams, ointments, and gels.

The blend of the advanced technologies, proper evaluation of topical sprays is essential to ensure product quality, stability, safety, and consistent drug delivery, which needs continuous research to overcome the limitations.

With ongoing developments in formulation science, nanotechnology, and spray device engineering, topical sprays are expected to play an even greater role in future dermatological treatment. Overall, topical spray systems offer a promising combination of effectiveness, patient convenience, and formulation flexibility, making them a valuable option for modern topical drug delivery. Sprays provide better patient comfort, easier self application, and improved hygiene due to their non-contact nature makes them promising in future.

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