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TOPICAL SPRAYABLE GEL FORMULATION FOR SKIN: A REVIEW

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ABSTRACT

Due to the use of various formulation components, sprayable gel has so much beneficial advantages over other traditional topical drug delivery systems like cream, patches and ointment in terms of characterization, appearance, easy application, affability, conventional dosage design, reducing likelihood of skin irritation, and adhesive nature on the skin surface from the application site. However, there aren't as many transdermal sprayable gel products on the market as there are for other transdermal drug administration dosage forms. This review article focuses on the current state of sprayable gel formulation and evaluation in the context of its formation, with the effectiveness of choices of drug, penetration enhancers, volatile solvents, polymers and their evaluation parameters to be has to tested for the development of a more efficacious form of a dosage form like sprayable gel. Also discusses the types of polymers and excipients, sprayer types, its factors affecting on formulation and evaluations and analytic parameters for the determination of the ability to spray at the site of application and gel characteristics and with the natural and synthetic gelling agent and its characterization with the polymers and its future aspects via application of the dosage form.

Keywords: Sprayable gel, Dosage form, Skin permeability, in-situ gelling

INTRODUCTION

Being the outermost protective covering and being in constant contact with the outside world, skin is the biggest structure of the human anatomy and one of

the most important resistance mechanisms against infections and mechanical and chemical and thermal threats. A surface epidermis, a deeper dermis, and a subcutaneous hypodermis make up the three primary layers of skin **[1-3]**. The keratinized epithelium that makes up the many layers of the epidermis is active and constantly renewing itself. Because of their capacity to specialize and produce a range of constructural proteins and constructural lipids which required for skin membrane regeneration, keratinocytes the prevailing cell type in the skin membrane has a critical role on the skin action. Melanocytes, it produces iridescence and Langerhans' cells which aid in immunological supervision, are additional epidermal cells. Stratum corneum, the topmost tier of the epidermis, contains corneocytes (enucleated departed cells), which act as a barrier against water loss and component absorption **[4-5]**. The dermis is a broader layer of connective tissue made up primarily of cells and extracellular matrix (ECM), and structural fibers such as elastin and collagen that give the skin its habitual strength and adaptability as well as a vascular systems for supplying it with nutrients. The initial membrane is a highly specialized structure that composite between the epidermis and the dermis. It is made up of various glycoproteins and proteoglycans, and it acts as a circulating obstacle with the layers as well as a stabilizing interface for skin appendages like hair follicles, sweat glands, and nerves. These skin extensions serve a variety of purposes, including keeping the body hydrated and acting as a shield from the environment **[6]**. The hypodermis, a connective tissue that connects the dermis to the underlying tissues and contains fat storage tissues as well as protection for those tissues for example adipose tissues acts as the skin' and heat sensitized ability of the body. The human skin's thickness ranges from 1.5 to 2.5 mm, depending on where in the body it is located anatomically and how it supports the body's weight **[7-8]**.

Heating sketch marks and other mechanical or chemical or physical damage, burns, gene irregularity, other skin diseases or the epidermal skin removing during surgery can all cause skin wounds or injuries. Injury of the skin is to be named epidermal, shallow halfway thickness, profound incomplete thickness, and full-thickness wounds relying upon the profundity of the sore. Albeit certain cases might be trying to definitively characterize with an early assessment, wounds should be perceived as quickly as time permits for the most ideal treatment. Epidermal and shallow fractional thickness wounds can commonly recover without the requirement for remedial mediation on account of oneself abilities to mend of the skin **[9-10]**.

However, the skin's regeneration components are damaged in serious partial and full-thickness wounds, with having absurd recovery along with its own concern to the skin. Consequently require early consideration to forestall a late re-epithelialization, which could empower diseases, bring about sub-par utilitarian and stylish mending results (such contracture and scarring), and stretch the patient's visit in the emergency clinic. A huge surface region wound and critical liquid misfortune might really be lethal. Quick remedial measures can help the patient move around and assist the skin with modifying its design and capability, yet complete capability recuperation probably won't be attainable except if all skin cell types are recuperated **[11]**.

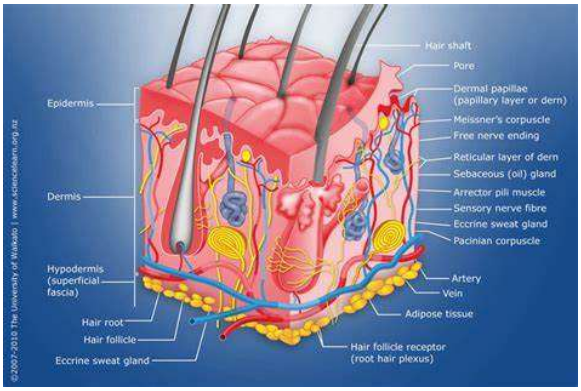

Figure 1: Structure of Skin [12]

Despite the fact that they have innate disadvantages and limitations, conventional skin unites have been utilized for a really long time to recover serious injuries. The coming of tissue designing (TE) and regenerative medication, then again, has given various restorative methodologies for the recovery of skin injuries utilizing different skin substitutes **[13]**.

The use of skin sprays or sprayable gels is also a promising option that is currently not frequently employed in clinical practice however addresses a potential remedial procedure for mending of wound application because to their many benefits, including their adaptability to transport various cell types and materials **[14-15]**.

In terms of safety and tolerability, topical spray gel is thought to be more superior to traditional techniques. Topical spray gel offers adjustable drug dosage distribution, minimizes the likelihood of skin disturbance, and kills the requirement for patients to clean up after application

contrasted with traditional TDD systems. Topical spray gel systems' volatile solvent concentration causes them to dry quickly and leave no occlusive residue behind after application, which speeds up drug absorption via the skin **[16]**.

Figure 2: Topical sprayable gel to be applied on the skin [17]

DRUG DELIVERY MECHANISM FOR SPRAYABLE GEL

When sprayed over the skin, a volatile solvent solution in sprayable gel forms a quickly drying layer. The principal packing material used by the sprayable gel system guarantees the volumetric delivery of the dose that is necessary. The medicine will be carried into the top layers of the skin upon application by the volatile solvent, which will then evaporate and leave behind a gel-like substance. As a result of this activity, the skin retains a significant amount of the drug, serving as a reservoir to release it steadily and gradually into the bloodstream. Once the gel layer has formed, the medication leaves a thin, homogenous film with a high thermodynamic activity that penetrates the skin **[18-20]**.

Sprayable gel in which firstly it will be in a spray form then undergoes gelation under varying physiological conditions. There are 4 mechanisms by which in-situ gelling system can be formed: **[16]**

1. Gel formation due to physiological stimuli:
   a) Temperature causes in situ gel systems
   b) pH causes in situ gelling systems
2. Gel formation due to ion-activated system
3. Gel formation due to physical mechanism:
   a) Swelling
   b) Diffusion
4. Gel formation due to chemical reactions:
   a) Ionic cross-linking
   b) Enzymatically cross linking
   c) Photo-polymerization

1. Gel formation due to physiological stimuli:

A small number of polymers experience significant and abrupt physical and chemical changes as a result of external environmental changes. Stimuli-responsive polymers are those that respond to stimuli. They are also referred to as intelligent,

smart, and stimuli-responsive polymers. These polymers interpret an upgrade as a sign, evaluate the strength of the signal, and adjust their chain confirmation as necessary **[21]**.

a) Temperature causes in situ gel systems:

Naturally responsive polymer frameworks for drug delivery is thermosensitive polymers. This is on the grounds that temperature is very simple to oversee and furthermore helpful for both in vitro and in vivo research. In this innovation, an adjustment of temperature sets off the gelling of the arrangement, which supports the arrival of the medication. These hydrogels are liquid at room temperature (20-25 °C), yet when they connect with organic liquids (35-37 °C), they become gel. A captivating method for moving toward in situ definitions is to utilize biomaterials that change from sol-gel when the temperature climbs. The ideal essential temperature range for such a framework is encompassing and physiological temperature, fully intent on advancing clinical administration and wiping out the prerequisite for outer warming sources other than the body's own intensity to make gelation structure. The thermosensitive sol-gel polymeric structure is planned utilizing three principal strategies. Therefore, they are arranged into the following categories: **[22]**

a. Positively temperature sensitive, which contract upon cooling;

b. Negatively temperature sensitive, which contract upon heating;

c. Thermo-reversible gel.

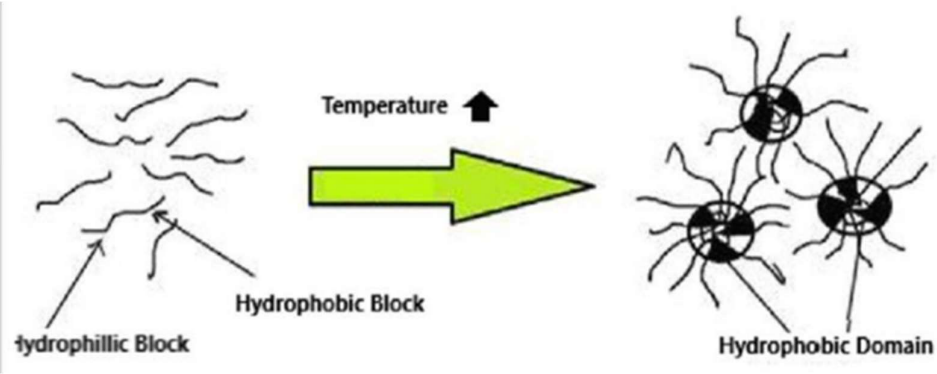

Figure 3: Mechanism of Thermosensitive gelation

b) pH causes in situ gelling systems:

Remembered polymers have an acidic or an alkaline group that, depending on the pH of the environment, either accepts or donates protons. These are now referred to as pH responsive polymers. It is common practise to use this type of mechanism for ocular medication delivery systems. Utilizing gel systems will increase the medication's precorneal time of residence,

improving its bioavailability. The plan exists as an ordinary arrangement at pH 4.4, however gelation happens at pH 7.4, which is, for example, the pH of tear fluid. Polyelectrolytes are polymers with a critical number of ionisable bunches. While polymers having necessary (cationic) groups show reduced swelling, hydrogel swelling increases with an increase in the external pH if pitifully acidic groups (anionic) should appear. The majority of anionic-containing polymers with sensitive pH levels rely on PAA (Carbopol®, Carbomer) and its derivatives. Polyvinyl acetal diethylamino acetate (AEA) arrangements, which are less viscous at pH 4, create hydrogel when the pH is neutral. The polymer cellulose acetic acid derivation phthalate (CAP) latex, polymethacrylic corrosive (PMMA), polyethylene glycol (PEG), faux latexes, and others all exhibit pH-incited gelation **[24-25]**.

2. Gel formation due to ion-activated system:

Here, the bestowed arrangement's inclination to gel is brought about by the ionic strength change. It is broadly recognized that the osmotic angle across the gel's surface decides the pace of gelation. The watery polymer arrangements structure a sensible gel when monovalent and divalent cations, which are as often as possible present in tear fluids, are available. At the point when the plan is implanted in the conjunctival circular drive, the electrolyte presents in the tear fluid, especially Na+, Ca2+, and Mg2+ cations, assume a critical part in the start of gelling. Gel ritual or gellan gum, hyaluronic corrosive, alginates, and different substances are undeniably found in polymers that show osmotically started gelation.

3. Gel formation due to physical mechanism:

a) Swelling: The absorption of the water material from the surroundings and gels as a result. The substance then expands to fill the desired space. Mineral 18-99 is a good example of this kind of material.

b) Diffusion: This strategy involves spreading the dissolvable from the polymer course of action into neighboring tissues, which accelerates the polymer lattice. The dissolvable N-methyl pyrrolidone (NMP) is one that functions admirably in this framework **[26]**.

4. Gel formation due to chemical reactions:

a) Enzymatic cross-linking: This strategy involves spreading the dissolvable from the polymer course of action into neighbouring tissues, which accelerates the polymer lattice. The dissolvable N-methyl pyrrolidone (NMP) is one that functions admirably in this framework. For example, under an enzyme cycle functions effectively under physiological conditions without the requirement for potentially dangerous

substances such initiators and monomers. Increasing the number of enzymes provides a beneficial system for regulating the rate of before the gel forms, the mixture can be injected thanks to gelling.

b) Photo-polymerization: This strategy is normally used to change over biomaterials in situ. At the point when electromagnetic radiation is utilized to make gel, a monomer or responsive macromer and initiator combination is infused into a tissue area. Since acrylates and related polymerizable gatherings photograph polymerize rapidly within the sight of the right photograph initiator, they are much of the time utilized as the polymerizable gatherings on individual monomers and macromers. Especially apparent and UV frequencies are utilized. Short-frequency UV isn't normally utilized in light of the fact that it can enter a little measure of tissue and is risky. At the point when photograph polymerizable designs are acquainted with the ideal area through implantation, they are photocured set up with the guide of fiber optic connections and afterward discharge the drug for a deferred timeframe **[27]**.

c) Ionic cross-linking: Some ion sensitive polysaccharides usually go to phase change due to presence of the various ions **[22-23]**.

IMPORTANCE OF SPRAYABLE GEL SYSTEM

1) Sprayable gel's "Sol-Gel" transition aids in the regulated and prolonged release of the medicines.

2) It helps the body administer medications less frequently.

3) The pills only need to be taken in little doses, so there won't be any drug build-up or negative side effects.

4) It improves the medications bioavailability.

5) The gel formation will lengthen the drug's residence period.

6) The Sprayable Gel Drug Delivery System Reduces Drug Wastage.

7) The best dose form is a gel one that can maintain medication release and stay in contact with the targeted location for a long time **[29-30]**.

PROPERTIES OF SPRAYABLE GEL

1) The gelling agent should ideally be non-reactive, safe, and unable to interact with other formulation ingredients.

2) It must contain an appropriate anti-microbial agent.

3) The topical gel cannot attach to the skin.

4) As the gel's effective crosslink density rises, so does the apparent viscosity or gel strength.

5) It should have excellent stability **[31]**.

ADVANTAGES

1) Offer a regulated and prolonged release of the medication

2) Simplicity of medication administration

3) Drug administration is made simple, and it is possible to provide medication to patients who are unconscious.

4) Better patient comfort and compliance

5) Reduce drug toxicity and dosage frequency

6) Enhanced bioavailable

7) Offer biodegradation and biocompatibility due to the use of natural polymers

8) Cellular functions are supported by the biocompatibility, biodegradability, and physiologically identifiable moieties of natural polymers **[32-33]**.

9) Sprayable gels may also be created with bio-adhesive properties to aid in drug targeting **[34]**.

DISADVANTAGES

1) A lot of fluids are needed.

2) The medication is more prone to deterioration in its sol form.

3) Possibilities of stability issues brought on by chemical deterioration.

4) Eating and drinking may be restricted for a short period of time after taking the medicine.

5) For hydrophobic medicines in particular, the quantity and homogeneity of drug loading into hydrogels may be constrained.

6) Only medicines with a low dosage requirement may be administered.

7) A lower mechanical strength could cause the spray gel to dissolve too soon or to flow away from the intended local spot **[35-36]**.

IDEAL CHARACTERISTICS OF POLYMERS FOR THE PREPARATION OF SPRAYABLE GEL

1) One requirement is that the polymer be able to stick to the transdermal membrane.

2) It should not have any hazardous effects and should be highly compatible.

3) It should behave in a pseudo-plastic manner.

4) The polymer should be able to reduce viscosity as shear rate is increased.

5) Polymer's preferred pseudoplastic tendency.

6) High optical clarity and good tolerance are preferred **[37]**.

FORMULATION COMPONENTS OF SPRAYABLE GEL

These are the formulation components mentioned above:

1) Drug Molecule:

For a sprayable gel formulation, these are the crucial factors to be known:

PARAMETERS	LIMIT
Aqueous solubility	> 1mg ml-1
Lipophilicity	10 < KO/W < 1000
Molecular weight	< 500 Da
Melting point	< 200℃
pH of saturated aqueous solution	pH 5-9
Dose deliverable	< 10 mg day-1

All of the previously mentioned components are believed to be reasonable and great for a medication intended to move beyond the skin's subcutaneous obstruction **[38]**.

2) Penetration enhancers:

Penetration enhancers (PEs) are chemicals added to the Sprayable gel formulation to boost the drug's transdermal flow. PE works by breaking up the subcutaneous layer, which creates a conduit for the medications, or by enhancing the drug's thermodynamic activity and skin partitioning.[39] Two instances of PEs that can likewise be utilized as a dissolvable or vehicle for details are ethanol and propylene glycol. Various scientists have distinguished water, hydrocarbons, acids, amines, amides, esters, surfactants, terpenes, terpenoids, rejuvenating oils, camphor, menthol, sulfoxides, and lipids as PEs. Be that as it may, a decent PE ought to have the accompanying characteristics: **[40-41]**

• It must be chemically and pharmacologically inert.

• It should be stable chemically.

• It needs to be open and typically stable in nature.

• The effects on the skin's characteristics should be reversible after use.

• It must be compatible with the elements of skin and formulation.

• It should not cause any hypersensitivity and comedogenicity.

• It should obtain in terms of taste and odour.

• It should have an appropriate solubility parameter for the both skin and formulation.

3) Volatile solvents:

Solvents both volatile and non-volatile are present in sprayable gel. Non-unpredictable solvents are those with fume strain under 10 mm Hg at similar internal heat level as unstable solvents, which are characterized as solvents with fume pressure more prominent than 35 mm Hg. After a brief amount of time, a volatile solvent evaporates, increasing the drug's thermodynamic activity. Prior to that, an effect known as solvent drag transports the medication into the SC layers. Solvent plays a small yet significant role in the drug's ability to cross the SC. Therefore, choosing the right solvent is crucial for enhancing medication delivery. The chosen solvent ought to make it easier to transport the medicine and have a large amount of drug retaining capacity. By serving as penetration enhancers, this group can also increase the transdermal flow of medications. Alcohols promote medication delivery into the skin via increasing the drug's thermodynamic activity, solvent drag effect, extraction of lipids and proteins, and swelling of the SC layers, among other processes **[42]**.

4) Gelling agents:

When dissolved in a liquid phase, gelling agents are the substances that produce a weakly cohesive internal structure in a colloidal combination. They are either

hydrophilic inorganic compounds or organic hydrocolloids. Gelling agents are utilised in this dosage form at concentrations ranging from 0.5% to 10% **[39]**.

Natural polymers	**Proteins: Gelatin, Collagen** **Polysaccharides: Pectin, Gellum Gum, Alginic acid, Agar, Xanthin, Cassia Tora, Tragacanth, Sodium or Potassium carrageenan, Guar Gum**
Semisynthetic polymers	**Cellulose derivatives: Methylcellulose, Hydroxyethyl cellulose, Hydroxypropyl cellulose, Carboxymethyl cellulose, Hydroxypropyl methyl cellulose**
Synthetic Polymers	**Carbomer: Carbopol-934, Carbopol-940, Carbopol-941,** **Polyacrylamide** **Poloxamer** **Polyvinyl alcohol** **Polyethylene and its co-polymers**
Inorganic substances	**Bentonite** **Aluminium hydroxide**
Surfactants	**Brij-96** **Cetostearyl alcohol** **Sodium lauryl sulphate** **Dodecyl pyridinium iodide** **Sorbitan mono-oleate F Lecithin**

These are called as gel forming substances that can be used in this sprayable gel formulation **[43-45]**.

5) The choice of vehicle/solvent:

As a solvent, pure water is typically employed. Co-solvents, such as alcohol, glycerol, PG, PEG 400, etc., may be employed to improve the solubility of the therapeutic ingredient in the dosage form and/or encourage medication absorption via the skin.

6) Inclusion of buffers:

Gels with aqueous and hydroalcoholic bases may use buffers to regulate the pH of the formulation. Buffer salt solubility is decreased in hydroalcoholic-based vehicles. For instance, citrate and phosphate.

7) Preservatives:

When some preservatives interact with the hydrophilic polymers used to create gels, there is fewer free (antimicrobially active) preservative available in the preparation. In order to compensate for this, the appropriate amount of these preservatives should be raised. Phenolics, parabens, etc. are a few examples **[46]**.

8) Antioxidants:

It might be used in the formulation of medicinal medicines that are vulnerable to oxidative degradation to increase their chemical stability. Its decision is based on the type of vehicle that was utilised to prepare the gel. Since aqueous-based gels make up the majority of gels, water-soluble antioxidants are typically utilised. For instance, sodium formaldehyde sulfoxylate, sodium metabisulphite, etc.

9) Polymers: [47-49]

- **Sodium alginate:** Sodium alginate is a polymer that has a natural origin. In terms of chemistry, sodium alginate is an alginic acid salt that includes residues of β-Dmannuronic and -L-glucuronic acids connected

by 1,4-glycosidic bonds. When di- or trivalent ions are present, an alginates solution in water solidifies (e.g., magnesium and calcium ions). For the preparation of gel-based solutions and the transport of proteins, peptides, and medicines, sodium alginate is frequently utilised. Because of its decomposing and non-toxic characteristics as well as additional adhesive capabilities, alginate salt is regarded as being very desirable. This has demonstrated that where the ionic radical below is low, alginates form cohesive structures. It serves as a water-soluble polymer in pharmacies and also acts as stabilizing and viscosity increasing agent.

- **Pectin:** These polysaccharides, which have anionic characteristics of plant origin and include residues of (1-4)-D-galacturonic acid, can be split into two groups. In the presence of a moderate amount of gel, pectin prevents the creation of a strong gel. A complex polysaccharide called pectin binds to D-galacturonic acid residues mostly in the series (1-4). The two forms of pectin—high methoxy and low methoxy gelation—are based on the methyl esterification of galacturonic acid. At pH 3.5, high methoxy pectin can typically mature. Low-methoxy pectin has a lot of calcium ions and doesn't require an acid or solid substance to function.
- **Xanthan gum:** Xanthomonas campestris produces xanthan gum, an extracellular polymer with a high molecular weight. Polysaccharide has a long chain length and several chains on one side of the trisaccharide. Two units of glucose are found in the main chain. Two units of mannose and one unit of glucuronic acid make up the side chains. When combined with strongly charged polymers, xanthan gum can create a robust gel. By weakening the structure of water, this gum can produce high viscosity solutions even at low concentrations.
- **Pluronic F-127:** Poloxamers, also known as Pluronic, is a line of difunctional copolymers that may be purchased for use in non-ionic organisms and is marketed by BASF Corporation. They are made up of blocks of hydrophilic polyethylene oxide on either side of a centre block of hydrophobic polypropylene oxide. These molecules produce micellar structures when

concentrated in aqueous solvents beyond the critical micellar concentration because of the PEO / PPO ratio of 2:1. These substances are thought to be PEO-PPOPEO copolymers. There are numerous body composition and molecular weight phases of pluronic triblock copolymers. Depending on the body position, certain marks, including F for flake, P for paste, and L for liquid, are allocated. Pluronics or Poloxamers are also susceptible to temperature variations as a result of changes in temperature.

- **Chitosan:** Chitosan is a naturally occurring, elastic polymer that is created when chitin is alkaline-deacetylated. It is hot, rotten, and harmless. Chitosan is a cationic polymer with a biocompatible base that is continuously distributed in strong solutions up to a pH of 6.2. A hydrated gel-like precipitate forms when chitosan in an aqueous solution is neutralised to a pH above 6.2. By adding polyol salt, cationic polysaccharides that are pH-gelling are transformed into potent gel-based pH solutions that form a gel without any chemical alteration or bonding.
- **Carbopol:** Carbopol is a pH-based polymer that, at alkaline pH, forms a tiny viscous gel but does not solidify at acidic pH. In order to increase the viscosity of the Carbopol solution and lessen its acidity, HPMC is used in conjunction with Carbopol. Various water copolymers undergo melting and temperature fluctuations **[50]**.

FACTORS AFFECTING SPRAYABLE GEL DRUG DELIVERY SYSTEM

1) Physiological factors:

Skin qualities such as its thickness, moisture level, and density of hair follicles, are mostly affected by physiological factors. Depending on factors including age, gender, race, anatomical location, general health, and environmental factors like temperature and humidity, these characteristics might show significant individual variation. To lessen the effects of such physiological variability, the rate-limiting step for this medicine distribution should be identified in the composition rather than the physiological barrier.

2) Physical and chemical characteristics of the drug:

The ease of the drug's diffusion through the topical carrier and penetration via the skin or mucosal surfaces is virtually always influenced by its physicochemical qualities. Properties of considerable relevance include

the molecular size as determined by the molecular weight, the partition coefficient between the vehicle and skin, the melting point, stability, and chemical functionality that impact ionisation potential, binding affinity, and drug solubility in the vehicle.

3) Formulation components and their interactions:

How the vehicle formulation impacts the medicine and the place of application serves to illustrate its purpose. The influence on the drug is taken into account along with drug diffusion, thermal activity, stability, and ionic strength of drugs that are weakly basic or acidic. The application site is affected by the modification of barrier characteristics brought on by the simultaneous absorption of formulation constituents and physical occlusion. These techniques promote adjustments that improve drug absorption or skin hydration. The formulation component also impacts the texture and viscosity of the vehicle, which in turn affects the adherence and retention properties of the vehicle **[59]**.

GENERAL METHODS OF PREPARATION

Various methods are involved as a formulation which is mentioned above:

1) Fusion method: This technique uses a variety of waxy compounds as a gellant in non-polar fluids. When sticky materials melted via fusion, drug was introduced. mixed gradually until a homogenous mixture was created.

2) Heating & Cooling method: A mixing container was filled with aqueous medium that had been chilled to low temperature. The gelling ingredient was gradually added while being stirred throughout the whole solution. kept the temperature below ten degrees. Drug was carefully and gently mixed into a solution before being added.

3) Dispersion method: In aqueous medium, a gel - forming agent was disseminated after 30 minutes of stirring at 1200 rpm. In a quasi solvent with a preservatives, the drug was dissolved. With constant stirring, this solution was incorporated into the previous mixture **[60-61]**.

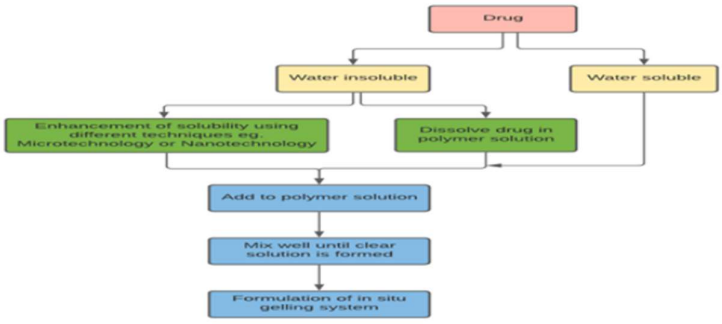

Figure 4: Method of preparation of topical in-situ gelling system [63]

EVALUATION AND CHARACTERIZATION OF SPRAYABLE GEL

1) pH:

The pH value is evaluated and adjusted to optimize the stability in the active constituent or to make it suitable for the application area. with the pH of 4-6 for skin. The pH of diabetic ulcers ranges from 6.8 to 8. Lower pH values (7.32 or less) hasten the healing of burns. The pH of the preparation has been adjusted to prevent irritability and changes in the physiological condition of the Skin. Additionally, the amount of the medication that penetrates the skin depends on the amount of ionisation in the dose **[64]**.

2) Uniformity of drug and drug spray content:

To estimate the dosage uniformity, the mass or amount of each spray is determined. The quantity of the active component is then computed using the chemical's concentration in the solution. Analytical analysis of the sprayed solution's amount of the active component is also possible. In order to calculate how much spray volume is discharged, the weight of the dispersed phase solution that is still within the sprayer instead of the weight of the fluid that comes out of the spray should be measured. Because the spray particles are so small and easily carried by the wind, it is unlikely that all of the spray will be collected for weighing. The following equation is used for measuring spray volume:

$$V = W_t - W_0 / D$$

where V is the spraying volumes, Wt is the solution's weight following spraying, W0 is the solution's initial weight before spraying, and D is the solution's specific gravity as calculated by the pycnometer technique. Sprays are collected, and their drug levels are measured instrumentally at the collecting various spray amounts.[65]

3) Viscosity:

Depends on their type and concentration of the sprayable gel viscosity is a crucial parameter in evaluation of sprayable gel with the application of a Brookfield viscometer.

4) Rheological Properties:

To ascertain if a substance is thixotropic or not, flow testing is used. If a mixture possesses certain flow characteristics, it can readily pass repeatedly through the sprayer nozzle.

Due to its propensity to flow, the dosage form might thin under pressure as it passes through the nozzle before returning to its normal consistency after being administered.

The kind of flow may be identified using a rheometer. This test is conducted at both ambient temperature and the storage

temperature of the dosage form. Testing the flow characteristics utilising the oscillating time sweeps and amplitude sweep method in a range of excipient concentrations and temperatures is another way to ascertain how excipient and temperature effect the change in gel consistency **[66-67]**.

5) Spread ability:

The spreading value affects the therapeutic effectiveness. Spreadability is measured in seconds and is the amount of time it takes for two slides to separate from a gel that is positioned in their interstices under the influence of a specific load. Better spreadability is achieved with shorter gap times between two slides. The spreadability is calculated using the formula below:

Spreadability (S) = M×L / T

Where, M is the weight fastened to the top slide

The size of the glass slides is L.

The amount of time needed to separate the slides is T **[68]**

6) Stability:

Thermal analysis is occasionally used to determine whether or not metastable active compounds recrystallize. The medicine can be kept in its original crystalline form thanks to the antinucleant polymer that is utilised. The amount of medication sprayed per spray and the way it is sprayed will be examined once more in a number of experiments. The dose must be ensured during the storage period **[69-70]**.

7) Skin irritation study:

After being shaved, the dose form is applied onto the skin of target organisms like mice and rabbits. 24 hours to 7 days after application, inflammation, redness, erythema, oedema, papule development, puffiness, and dryness are seen. Below are scores for assessing irritability:

Grading	Description of Irritant Response
0	No response
+	a somewhat favourable response characterised by light erythema at the site of medication administration.
++	erythema, a modestly positive response that may spread in the medication application region, is its defining feature.
+++	A robust, erythematous reaction that may also show oedema.

8) Potential Drug Aggregation:

Sprayability will undoubtedly be impacted by changes in particle size. Size exclusion chromatography (SEC) and zeta potential are two techniques to assess a drug's ability to aggregate **[69-70]**.

9) Spraying Force:

To determine how much pressure is required to spray the dosage form, this test is conducted. The available tool is the TA. XT Plus texture analyser.

10) Homogeneity:

The Sprayable gel was placed in a container and then visually inspected for homogeneity. They underwent examinations to check for aggregates and its appearance **[71-74]**.

11) Grittiness:

The formulations were examined under a light microscope to look for any visible particulate materials that may be observed.

11) Gelling Time:

How much time it is required to form a gel on the skin surface that is called gelling time.

12) Spray pattern, Spray angel, and Droplet Size Distribution:

The spray patterns can easily be seen when paper has been soaked with indicator reagents. This is dependent on the kind of solvent used and the dosage form's pH. The pattern and the spray droplet size distribution will become clearer when written on paper that is solvent-sensitive. The area covered is then calculated by measuring the pattern's diameter **[51-53]**.

Spray Angle (θ) = $\tan^{-1}$ (l/r)

where r is the circle's radius and is the distance between the paper surface and the nozzle. The nozzle is typically around 15 cm away from the paper. The more difficult it is for the gel to disperse when sprayed, the greater the spray angle. The spray pattern is captured at 600x600 dpi to determine the area that is covered (Konica Minolta scanner, bizhub c3350). The size of the droplets is calculated using the particle analysis plugin. Droplet diameter is expressed in mm, from which D10%, D50%, and D90% are calculated **[75-77]**.

13) In vitro Drug release/ Diffusion study:

Franz diffusion cells, cellulose membranes (pore diameter 0.45 m), nylon membranes (pore diameter 0.22 mm), or silicone membranes are frequently used in this test as section separators. After the partition system is ready, the dosage form is put in the receptor compartment using phosphate buffer, pH 7.4. A sample of the fluid that spreads through into the cells is taken at certain intervals, and the apparatus is then utilised to quantify it **[80]**.

APPLICATION OF TOPICAL SPRAYABLE GEL

1) To deliver local action, sprayable gels are administered directly to the skin and improves the bioavailability.

2) It is employed in wide variety of products like cosmetically skin products.

3) Useful in the skin diseases like skin cancer, fungal disorders, etc.

4) Sprayable gel gives better protection than any other conventional dosage form.

5) Gives localization of antibody on the skin surface & improves the penetration through the skin **[81-83]**.

CONCLUSION

Sprayable gel has the ability to enhance medication delivery. Both natural and synthetic polymers can be used as drug

substrates and gel formers to enhance the stability and clinical efficacy of the active component. Sprays assist in forming droplets that have better and more consistent drug dose and dispersion. Additionally, each sprayer has important and detailed testing requirements. To take full advantage of this mechanism, a drug must meet certain requirements, including the right level of aqueous solubility, stability, melting point, pH, and dosing amount. These requirements are crucial for ensuring that the drug is delivered across the subcutaneous tissue and for producing the intended therapeutic effect. This limits the number of medications that can be produced into Sprayable gel formulations. Chemical penetration enhancers and polymers has been added to the formulations to improve the transdermal flow and to improve the mechanism. Sprayable gel formulations provide a wide range of opportunities to achieve a high level of patient compliance and therapeutic efficacy, despite the difficult approach.

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