

## A REVIEW OF SYNTHETIC SPRAY BANDAGE

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### **Abstract:**

To formulate Spray Bandage to get good protective and therapeutic activities for a longer duration of time and form film which act as a protective barrier for open wound or another tropical disease. It is easy to use and apply by spraying directly on the affected area. It forms film within a few seconds and has good patient compliance. Curcumin is useful in various activities such as anti-tumor, antioxidant, anti-arthritis, anti-amyloid, anti-inflammatory, bacterial infections, wound healing, and tissue repairing. Curcumin has low GI stability hence it is given through a topical drug delivery system for sustained release of the drug. In other words, a bandage film formed in situ on a skin surface by actuating a hydrophilic polymer and a low volatile plasticizer with the solvent system. They are commonly used to guard and prevent infection of topical abrasion and cut which exist in minor level. By changing the spray drug concentration, it can also be considered as a drug delivery film on the skin to the systemic circulation. Different spray devices were designed and evaluated with simulation, from simple ideas to complex device shapes. This article discusses the types and concentrations of polymers and excipient sprayer type's evaluations and critical parameters in determining the spray ability and film forming spray. The review concludes that both natural and synthetic polymers that have in situ film or visco elastic property can be used to optimize topical drug delivery.

**Key words:** Spray Bandage, Diclofenac, FFS (film forming spray), Visco elastic, synthetic.

### **Introduction:**

Bandaging is the process of covering a wound or an injured part. Topical drug delivery might be the least one important as it is not directly connected to mainstream fluids and vital organ but it's the main important gateway for microbes in environment to reach into the body. So, in one recent advancement in TDDS has managed to cover up after injury treats.

The skin is the most readily accessible organ of the body and acts as a barrier against the micro and macromolecules of the environment because of its low permeability to such substances [1]. The skin of an average adult body has approximately 2 m<sup>2</sup> surface area and it receives about one-third of the total blood circulating throughout the body [2]. The goal of drug administration through skin is for topical treatment of skin diseases or for transdermal absorption of drugs in the systemic circulation [3].

Carbomer resins have been considered extensively by many researchers and scientists, since they provide a wide range of applications as thickening agents, emulsifying agents, suspending agents and tablets compressed matrix forming agents, which is particularly used in controlling drug release. [4] And it is used for making of spray bandage.

Spray bandage or Film Forming System [FFS] is a novel approach that can be used as an alternative to conventional topical and transdermal formulations. It is defined as a non-solid

dosage form that produces a film *in situ*, i.e. after application on the skin or any other body surface. These systems contain the drug and film forming excipients in a vehicle which, upon contact with the skin, leaves behind a film of excipients along with the drug upon solvent evaporation [5].

As the wound healing process continues to be better understood, systems that actively control the spatial and temporal profile of drug release would be extremely beneficial for wound care treatment.[6]

**Limitations of Current Wound Care Technologies**

Most of the current wound technology are passive and they do not respond to various injuries / wounds. Also, current wound healing techniques has slow rates of healing and that's one major limitation that leads to development of antibiotic resistant bacteria. [7]

**Need of Spray bandage –**

As there are drawbacks in current available topical drug delivery system, it should possess advantages like compact package, easy to wash, easy to apply, and painful application on burnt wound, etc.[8]

**Film forming systems**

Dermal and transdermal application of drug via liquid or semisolid formulation has major problem by rubbing or washing off the formulation resulting the failure to achieve therapeutic use. sprays, gels, or emulsions may be Formulated. [9]

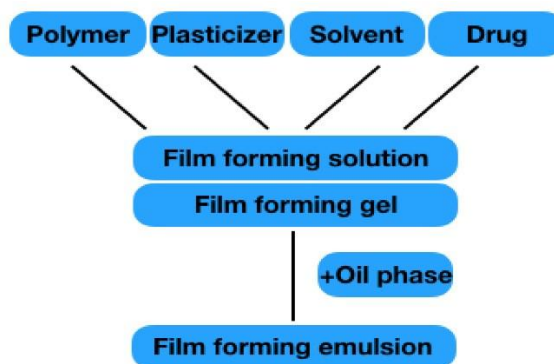


Fig. 1 Illustration of different film- Forming solution/gel.

**Mechanism of spray bandage**

Film forming system is applied directly to the skin and it forms a thin, transparent film *in situ* Upon solvent evaporation as shown in Fig. 1

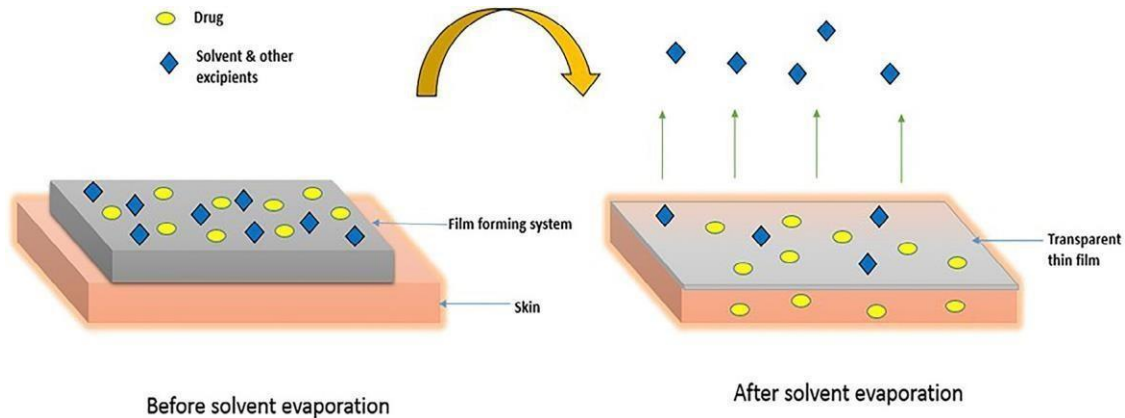


Fig. 2 Mechanism of film formation in different spray bandage

The concept of super saturation can be explained by the modified form of Fick's law of diffusion. Fick's law of diffusion is given by Eq. (2.1):

$$J = DKCv \quad (2.1)_h$$

Where

$J$  = rate of drug permeation per unit area of skin per unit time (flux)

$D$  = diffusion coefficient of drug  $Cv$  = concentration of drug  $h$  = thickness of barrier to diffusion

From this equation, it is clear that the rate of drug permeation across the skin is proportional to the concentration of the drug. However this is true when all the drug is dissolved in the vehicle.

Equation (2.2) describes the modified form of Fick's law of diffusion:

$$J = \alpha D / \gamma h \quad \dots (2.2)$$

Where  $\alpha$  = thermodynamic activity of drug within formulation

$\gamma$  = thermodynamic activity of drug within membrane

According to this equation, the flux of the drug is directly proportional to the thermodynamic activity of the system, which is related to saturation. However increasing the super saturation increases thermodynamic instability.

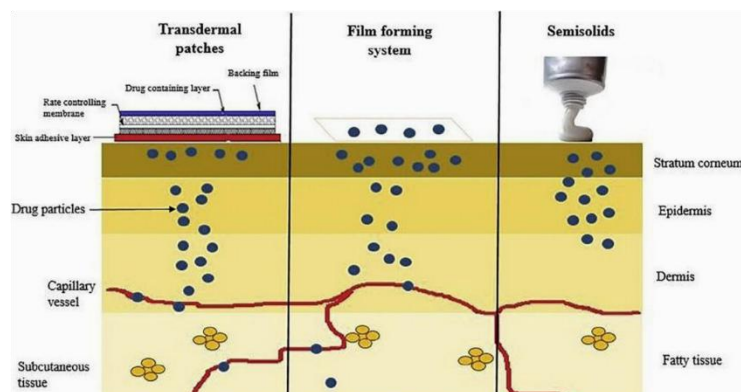


Fig.3 Release profile of topical and transdermal drug delivery system (TDDS)

FFS creates supersaturated systems immediately after application to the skin, overcoming the problem of instability. Thus it improves the drug permeation through skin compared to other transdermal dosage forms. Without enhancer the formulation transported more than double the ethinylestradiol than the marketed patch. With enhancer, the formulation delivered about seven times as much ethinylestradiol as that of the marketed patch. Thus these systems prove to be useful in enhancing the drug permeation. [10]

### Polymers Used in Film-Forming Sprays

Polymers play a significant role in the success of FFS preparations. Aside from being a drug release controller, polymers also act as the film-forming base. Polymers can also prevent the transformation of molecules, such as the formation of unexpected crystals. General considerations in the selection of polymers are its ease of being washed away by water, stability, biodegradability, and non-irritating properties. Polymers used in FFS can be natural or synthetic, as long as they have in situ gel or viscoelastic properties. Viscoelastic polymers start at a thick consistency but can become elastic when placed under pressure (sprayed) and return to a thick consistency after the pressure is removed. [11]

### Natural and Semisynthetic Polymers

#### 1. Cellulose

Ethyl cellulose forms films that are easily washed away with water. The concentration of ethyl cellulose that produces films with excellent characteristics is 5.02–5.25% and is generally combined with Eudragit. Hydroxypropyl methylcellulose (HPMC) is reported to have a slow drying time. Films of cellulose and chitosan blends were prepared using trifluoroacetic acid (TFA) as a co-solvent for the two polysaccharides. Analyses of X-ray Diffractograms, scanning electron micrographs, and the mechanical properties of the films suggest that cellulose and chitosan are intimately. [12]

## 2. Chitosan

Aside from being a filmmaker, chitosan also has antimicrobial, antioxidant, and mucoadhesive activity, making it suitable for use in topical drug delivery. Chitosan has a relatively high surface tension. Surfactants are usually used to improve the solubility of chitosan.

## 3. Cyclodextrin

Cyclodextrin is known to maintain drug stability from crystal deformation. Cyclodextrin is also reported to have a small impact on increasing the viscosity of the film forming solution, so it is easy to spray.

## 4. Gellan Gum

Gellan gum (GG) has viscoelastic properties so that it is easily delivered using a spray system. The viscoelastic nature allows GG to melt in consistency when sprayed and return to its original texture after being on the surface of the skin.

## 5. Xanthan Gum

Based on research conducted by Shilin Wang, the sprayability of xanthan gum was strongly influenced by its viscosity. Xanthan gum is an extracellular polymer produced mainly by the bacterium *Xanthomonas campestris*. [13] The addition of surfactants in the xanthan gum solution decreased the surface tension and reduced the size of the droplet. Interestingly, the viscosity and flow properties were not significantly changed.

### Synthetic Polymers –

**Carbopol** – Carbopol also has thixotropy flow properties. Carbopol itself forms an amorphous hydrogel that is good for open wounds because it can donate or absorb wound moisture. Carbopol polymers are high molecular weight, cross linked, acrylic acid based polymer. These are polymers of acrylic acid cross-linked with polyalkenyl ethers or divinyl glycol. Each particle can be viewed as a network structure of polymer chains interconnected via cross-linking. [14]

**Eudragit** – Eudragit is available in various types with different purposes for use. Generally this synthetic polymers are used as a additive to tablet for modifying drug release. Also increase drug permeation in the skin. These polymers allow the active in your solid dosage form to perform during the passage of the human body. The flexibility to combine the different polymers enables you to achieve the desired drug release profile by releasing the drug at the right place and at the right time and, if necessary, over a desired period of time. [15]

**Lutrol** – Similar to Carbopol but produces more inform dose of each spray. Better drug release compared to Carbopol. Systems containing only Lutrol contain the drug in the form of particles of reduced size and in a crystalline form. [16]

**Plasdone** – Plasdone can increase testosterone permeation better than other polymers.

**Kollidon** – Widely used in pharmaceutical world. Kollidon increase solubility and permeability and control drug release. Among synthetic excipients, polyvinylpyrrolidone (povidone), marketed under the brand name Kollidon®, is one of the most important substances in the

pharmaceutical and cosmetic industries. Starting from the soluble Kollidon® grades which were synthesized by W. Reppe in 1939, several products followed, including insoluble grades, copolymer sates and sustained release preparations for numerous applications. [17]

**Excipients used in Film forming System –**

Besides polymers, other excipients are also added for the purpose of improving the quality of the preparation and its therapeutic efficiency. The following is a list of excipients (Table) commonly used in film-forming systems.

No	Excipient	Function	Concentration (% b/v or v/v)	Sprayer
1.	Azone	Permeation enhancer	1–5	MDS
2.	Camphor:menthol (1:1)	Permeation enhancer	4–10	Ordinal
3.	Cyclomethicone	Co-solvent	0.5	MDS
4.	Dimethyl ether	Propellant	39–59.8	MDS
5.	Ethanol	Volatile solvent	7.5–50	MDS
6.	Ethanol:acetone (8:2)	Solvent	Ad. 100	Ordinal
7.	Ethanol:acetone:methylal (2:1:2)	Solvent	Ad. 100	MDS
8.	Ethanol:PG:water (4:1:1)	Solvent	Ad. 100	Ordinal
9.	Ethanol:water (1:1)	Solvent	Ad. 100	Ordinal
10.	Glycerol	Stabilising agent and plasticiser	10–30	Ordinal and electro spray
11.	Hydrofluoroalkane	Propellant	76.7–87.2	MDS
12.	IPA	Volatile solvent	30	MDS
13.	IPA:water (8:2)	Solvent	90	Ordinal
14.	IPA:ethanol (1:1)	Solvent	Ad. 100	MDS
15.	IPM	Permeation enhancer	2.5–5	MDS
16.	LA	Permeation enhancer	5	MDS
17.	Myristyl lactate	Penetration enhancer	0.5	MDS
18.	NaCl	Cross-linker	0.1–0.5 (Molar)	Ordinal
19.	NMP	Permeation enhancer	5	MDS
20.	PEG-200	Plasticiser	0.25	Ordinal
21.	PEG-400	Plasticiser	0.45–10	Ordinal
22.	PG	Plasticiser and permeation enhancer	0.25–9	Ordinal and MDS
23.	Tween 80	Surfactant	5	Electrospray

Table.1 Excipients used in FFS

**Cross linkers**

The use of cross linkers can affect the elasticity, viscosity, solubility, glass transition, and film stiffness of the polymer. The use of NaCl as a cross linker in Gellan gum also affects the gel’s sensitivity to temperature, so that film formation is better and faster. NaCl also increases cell encapsulation in Gellan gum. The crosslinking amylose–xanthan-coprocessed excipient using 6% STMP is more suitable for use in controlled release dosage forms, particularly when the polymer ratio is 1:1.[18]

### Permeation Enhancers

Eutectic blends are often used as enhancers to drug permeation. One of the most potent eutectic blends is a mixture of camphor and menthol. Camphor and menthol form a hydrophobic mixture, so it is suitable as a penetration enhancer for drugs that are also hydrophobic. However, camphor and menthol can cause leaching and the formation of pores in the skin. [19]

### Plasticizers and Stabilizing Agents

Plasticizers are used in the film forming systems to impart flexibility to the film and improve the tensile strength of the film formed. [20]

In the film formation, the plasticizer maintains elasticity and prevents cracking of the film. Plasticizers can also maintain the stability of active substances and increase the permeation of drugs. Polyethylene glycol (PEG) and propylene glycol (PG) are reported to have a role in increasing the permeation of antifungal drugs.

### Solvents

The solvents used in the FFS system include both volatile and non-volatile solvents. The aim is to balance the film drying rate. Films that dry out too quickly and form a hard film make it difficult for drugs to escape and penetrate. [21]

### Methods

Spray containers and filling method

#### 1. Cold Filling -

- Both the product concentrate and propellant must be cooled to temperature of -30 to -40° F.
- The chilled product concentrates quantitatively metered into an equally cold aerosol container.
- The liquefied gas is added, the heavy vapours of cold liquid propellants displace the air present in that container.
- The concentrate is added to the cold propellant in the mixing vessel, and the entire formulation is mixed to ensure homogeneity. [22]

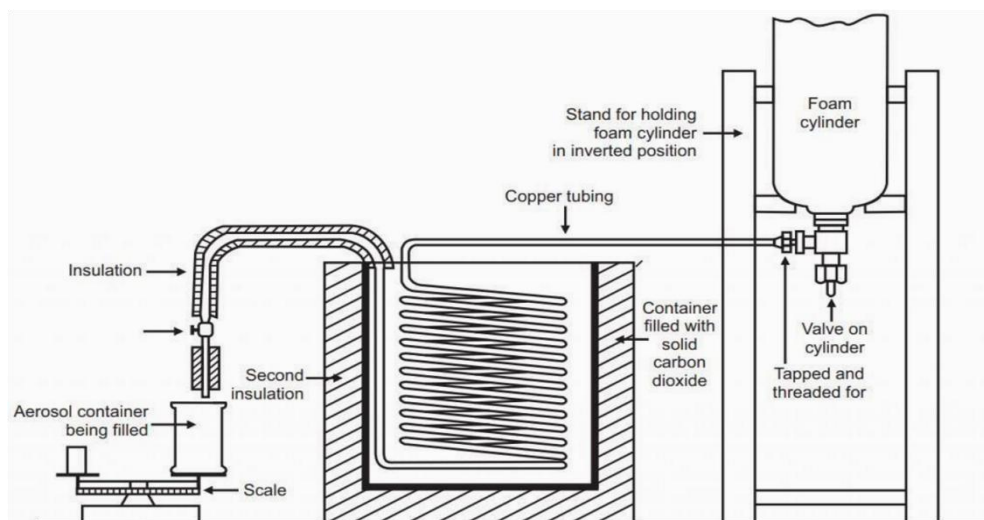


Fig. 4. Aerosol cold filling process apparatus

## 2. Pressure filling process –

- This process used for filling aerosol containing hydrocarbon propellants •The product concentrate is placed into container and valve sealed.
- The propellant is forced through valve under pressure, after this container immersed into water bath at 130<sup>0</sup> F for 54 0C ) in order to check any leakage and strength of container.

There are two different methods for pressure filling

- 1) Single stage pressure filling: the concentrate and propellant are combined in mixing vessel & held under pressure.
  - 2) Two stage pressure filling: the concentrate is dispensed into an open aerosol containers.
- [23]



Fig. 5 Pressure filling apparatus using spray film.

### Evaluation parameters of spray film.

1. pH
2. Viscosity
3. Tonicity
4. Bioadhesive strength of the film
5. Water washability
6. Fluid affinity
7. Rheological Properties

#### 1) pH

The pH value is measured and adjusted to improve the stability of the active substance or make it suitable for the area of application. For skin pH ranging from 4–6, the pH of diabetic wounds ranges from 6.5–8, whereas faster healing time for burns occurs below pH 7. [24]



## **2) Viscosity**

Each type and concentration variation of the polymer will result in a different viscosity. The viscosity of the film forming solution will affect its spray ability, so this is an important parameter, especially in MDS. [25]

## **3) Tonicity**

The application of film-forming solution to certain parts of the body such as wound and eye mucosa requires the tonicity adjustment of the film-forming solution. Nonisotonic preparations can cause mucosal irritation and eye pain. For this reason, the tonicity of the preparations needs to be calculated and adjusted using the Kahar method. [26]

## **4) Bio adhesive strength of the film**

Measurement of the bio adhesive strength of the film can be done by attaching a film to the surface of the mouse skin (2 x 5 cm). Then, the skin is hydrated with 0.5 mL distilled water. The film is allowed to interact with the tissue surface for 5 minutes the total force (F) To detach the film from the surface of the skin is recorded. The Bioadhesive strength (Fb) is calculated per unit area (A) of the film. [27]

## **5) Water washability**

The ease of film wetting is assessed in the dried film. The film is washed with water and assessed in ordinal scale, i.e. easily washed, moderately washed, and poorly washed.<sup>34,40</sup> The ease of sprinkling with water will be useful if the film-forming solutions contact with sensitive areas in the body such as eyes and mouth. [28]

## **6) Fluid Affinity**

This test is carried out to see how the ability of the film formed to absorb moisture from the wound or provide moisture to the wound. An adequate supply of moisture to the injury will speed healing, but excess moisture can cause erosion of the wound tissue. [29]

## **7) Rheological Properties -**

Flow testing aims to determine whether a compound is thixotropic or not. A mixture can easily pass through the sprayer nozzle repeatedly if it has these flow properties. This flowing property allows thinning of the film-forming solution as it shifts along past the nozzle (stressed) and returns to its original viscosity after being sprayed (stress is lost).. [30]

## **Advantages**

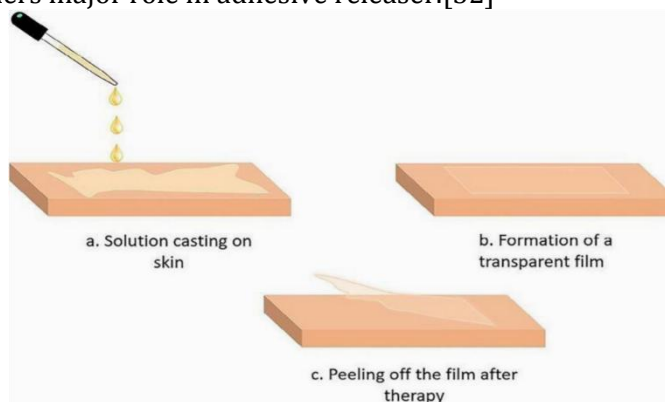
- There is less chance for infection since the wound is sealed shut.
- These products are waterproof, so you can shower or bathe without worry.
- The seal lasts for 5 to 10 days. It will fall off naturally after it has done its job.
- Using these products may also reduce the size of scars that form at the injury site. [31]

## **Disadvantages -**

- Causes a slight burning when applied
- May cause bacterial growth in moisture conditions
- Over-spraying may affect dermal layers.

### Applications

- Liquid bandages can stick better than plastic or fabric adhesive bandages too many hard-to-bandage areas, such as knuckles and between fingers.
- Doctors and veterinarians may also use these materials to repair some cuts to internal organs or to close surgical incisions.
- Soldiers can use the dressing to patch large, bleeding wounds until further medical care is available,
- The use most products are intended for the handling and treatment of wounds.
- Common injuries that can be treated can be incised wounds such as surgical or sharp object contact, burns, diabetic wounds.
- Major role in skin protector from irritation and wound cover in protector.
- Diglycol polymers used in sensitive skin protector.
- Siloxane copolymers major role in adhesive releaser.[32]



(A)



(B)

Fig 6.- Appearance of film forming system: (A) Formation of transparent film on application; (B) Non-tacky, flexible, easily peel able film after drying

Film forming solutions can be applied with an applicator to the skin and allowed to dry. Film forming spray is manufactured as a metered dose pump dispenser to provide fixed amount of drug and it is sprayed on the topical site to form a film. These systems form a stable fast drying, non-irritating invisible film from which the drug is available for transdermal therapy.

Following administration, the film can be peeled off once the desired results are obtained or for the termination of therapy.[33]



Fig. 7 Spray bandage application

#### **Conclusion:**

The film forming system presents novel platform to deliver drug now a days consuming time of healing and more safety. These film forming systems are simple and offer advantages of transparency, non-greasy, lower skin irritation, wipe off resistance, longer retention, greater increased dosage flexibility, improved patient compliance and aesthetic appearance Although considerable work has been done on these systems, not much data are available on its delivery efficiency. Hence the marketed products available are less. Additional research is necessary to prove the relevance of film forming system as transdermal dosage form, but the obtained results are encouraging for further development of this novel topical drug delivering technology.

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