FORMULATION DEVELOPMENT AND EVALUATION OF NOVEL HERBAL FILM FORMING SPRAY FROM CINNAMON OIL

Gulab Shankarrao Shinde[1*], Dr. Pankaj Sharma[2], Dr. Jaya Sharma[3], Dr. Rahul Dumbre[4], Dr. Navin Kumar Singhal[5], Dr.Swati Deshmukh[6]

Article History: Received: 09.03.2023 **Revised:** 12.05.2023 **Accepted:** 30.06.2023

Abstract:

The intent of this study was to develop a topical Cinnamon oil film-forming spray that could enhance the healing process of wounds. In comparison to conventional topical preparations, film-forming sprays have a number of benefits, including uniform drug distribution and dose, enhanced bioavailability, a decreased risk of irritation, continuous drug release, and quicker wound healing through moisture control. Polymers and excipients used in film-forming sprays help to increase the properties of preparations and the stability of active ingredients. Different excipient and polymer combinations will result in films with various characteristics. Therefore, it is necessary to look at the various categories of polymers and excipients, as well as their assessment criteria, in order to create a film-forming spray that is more effective. The chosen literature comprised studies on the development and assessment of film-forming sprays with potential medical applications that use plasticizers and polymers as film-forming matrices. This article contains the various polymer and excipient types and their concentrations, spraying type, assessments, and crucial variables in determining the spray ability and film characteristics. The review comes to the conclusion that the developed film-forming spray formulation was clear, and grittiness free in appearance. The evaluation investigations revealed that the pH becomes similar to that of normal skin and has the ability to evaporate swiftly resulting in lesser skin irritation when sprayed on wounds. The spray is more convenient to use, can be applied easily thus improve patient acceptance and compliance.

Keywords: Topical drug administration, film-forming spray, and Cinnamon oil.

[1*,2,3]Apex University, Jaipur.
[4,6]CAYMET's, Siddhant College of Pharmacy, Sudumbare, Pune.
[5]Rajasthan Pharmacy College, Jaipur.

***Corresponding Author:**
Gulab Shankarrao Shinde[1*]

Research Scholar-Apex University, Jaipur,
Postal Address: At/Post: Ghansargaon, Tal-Renapur, Dist-Latur-413527.

Email:[1*]shindegss@gmail.com

DOI: 10.31838/ecb/2023.12.s3.575

1. Introduction:

Topical routes of drug delivery aim for systemic or local effects and offer a number of benefits, such as avoiding first-pass metabolism and the effect of low pH and digestive tract enzymes, as well as a significant amount of surface area.[2-8]

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 on contact with the skin, leaves behind a film of excipients along with the drug upon solvent evaporation. The formed film can either be a solid polymeric material that acts as a matrix for sustained release of drug to the skin or can be a residual liquid film that is rapidly absorbed in the stratum corneum.

The film forming system is applied directly to the skin and it forms a thin, transparent film in situ upon solvent evaporation. After application of the formulation to the skin, the composition of the film-forming system changes significantly due to the loss of the volatile components of the vehicle which results in formation of residual film on the skin surface. In this process, the concentration of the drug increases reaching saturation level and with the possibility of reaching super saturation level on the skin surface. Super saturation results in the enhanced drug flux through the skin by increasing the thermodynamic activity of the formulation without affecting the skin's barrier, thereby reducing the side effects or irritation. The concept of supersaturation be explained by modified form of Fick's law of diffusion. [12, 13]

In recent decades, various innovations have continued to be developed to obtain efficient and effective spray preparations. One of them is a film-forming spray (FFS) which has been applied in multiple fields, such as the food industry, cosmetics, pharmaceuticals, plantations, etc.[14] Drugs used topically are typically produced in a patch, gel, lotion, cream, ointment, or spray, in order to increase therapeutic effectiveness and pharmacokinetic characteristics.[9-11]

Cinnamomum zeylanicum Blume, a member of the family Lauraceae, is a tropical evergreen tree, native to Sri Lanka and the Malabar Coast of India, Medicinally, cinnamon is used in the treatment of diarrhea, flatulent dyspesia, poor appetite, low vitality, kidney weakness and rheumatism, influenza, cough, bronchitis, fever, arthritic angina, palpitations, hypertension and nervous disorders, stimulating the circulatory system and capillary circulation, spasms, vomiting and controlling infections, reducing blood sugar levels in diabetics and as a skin antiseptic. Cinnamon is rich in essential oils and tannins which inhibit microbial growth. The most important chemical constituents of cinnamon are volatile oil (cinnamaldehyde, eugenol, cinnamic acid and weitherhin), mucilage, diterpenes and proanthocyanidins .[1,16,17]

Figure1. Barks and dried flowers of *Cinnamomum zylenicum*

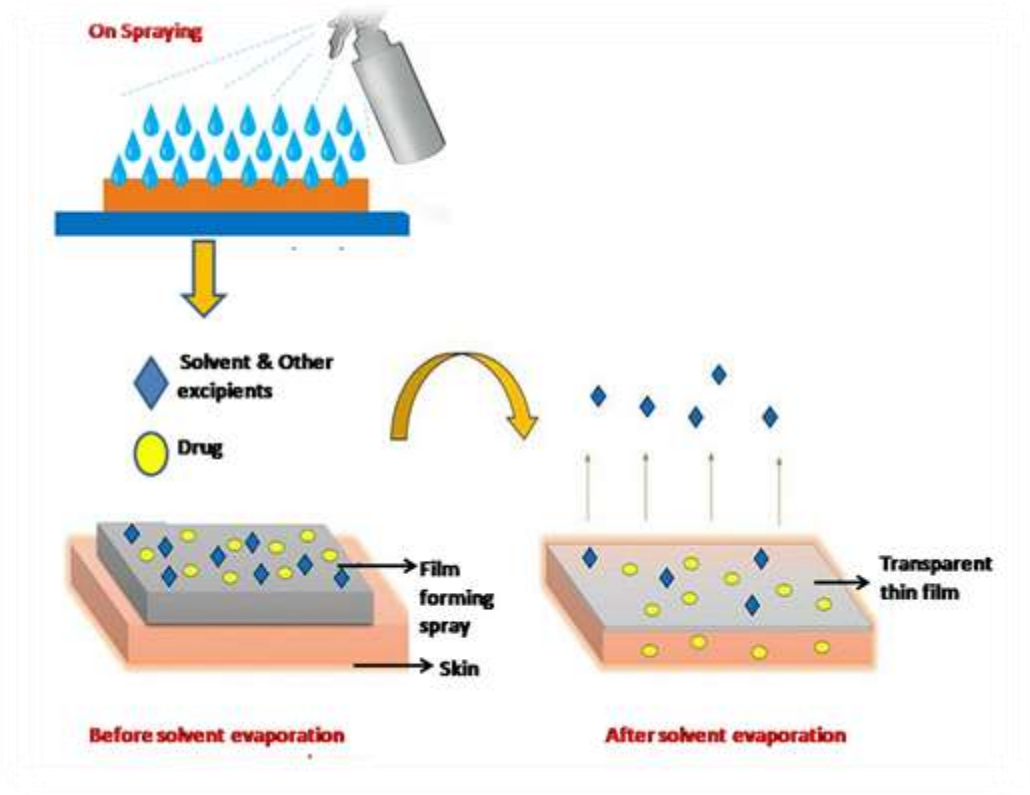

Figure 2. Mechanism of action of Film forming spray

2. Methods

1. Cinnamon bark was procured from a neighborhood market situated in Chinchwad, Pune.
2. Excipients for film-forming spray are optimized by choosing and examining the kind and concentration of the solvent system, polymer, plasticizers, and additional excipients like methyl salicylates and menthol. Sprays' impact on physical appearance was examined visually, tested on the skin, and a superior excipient was selected for the subsequent trial.
3. **Selection of solvent system:** Cinnamon oil is insoluble in glycerin and water but soluble in organic solvents like alcohol and fixed oils. Different concentrations of ethanol were utilized as solvents. Ethanol is harmless solvents that are frequently used in solutions and topical treatments.
4. **Selection of polymer type and its concentration:** PVP K30 and HPMC E5 were chosen for the study of their ability to produce cinnamon film-forming spray. The different film-forming polymers were such as PVP K30 and HPMC E5 at varying weight concentrations of 1, 2, 3, 4, and 5%, as indicated in Table.1 The polymer was selected based on the physical characteristics of the film. Major focus was on a thickness formation of film, smooth, clear texture and quick-drying.[11]

Table 1: Preparation of film forming spray using various type and concentration of polymers

Ingredients	**Formulation (%w/w)**									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
PVP K30	1.0	2.0	3.0	4.0	5.0	-	-	-	-	-
HPMC E5	-	-	-	-	-	1.0	2.0	3.0	4.0	5.0
Purified water	49.5	49.0	48.5	48.0	47.5	49.5	49.0	48.5	48.0	47.5
Ethanol	49.5	49.0	48.5	48.0	47.5	49.5	49.0	48.5	48.0	47.5

Selection of the type of plasticizers:
Propylene glycol (PG) and Polyethylene glycol 400 (PEG 400) were selected for investigation of their flexibility of film forming spray at the concentration of 1.0 % by weight as shown in Table 2. Apply film-forming spray to skin. The polymer was selected based on the physical characteristics of the film. The major focus was on the breakable of film and white spots on the surface.

Table 2: Formulation of film-forming spray using various types of plasticizers using Cinnamon essential oil.

Ingredients	**Formulation (%w/w)**			**Function**
	C1	C2	C3	
PVP K30	3.0	3.0	-	Film forming agent
HPMC E5	-	-	2.0	Film forming agent
Propylene glycol	-	1.0	-	Plasticizer
Polyethylene glycol 400	-	1.0	1.0	Plasticizer
Methyl salicylate	3.0	3.0	3.0	Active ingredient
Menthol	1.0	1.0	1.0	Active ingredient
Cinnamomum zylenicum oil	0.02	0.02	0.02	Active ingredient
Purified water	37.98	40.98	37.98	Solvent
Ethanol	54.0	52.0	54.0	Solvent

Preparation of film forming spray:
The spray was made using a simple solution approach. First, a polymeric solution system was created by dissolving polymers in ¾th of water and stirring with a magnetic stirrer. Cinnamon oil was dissolved in ethanol and added into a polymeric solution The plasticizer was then added and the final weight was adjusted with water. Following the screening of the excipients (polymers and plasticizers) in formulation, the topical film forming sprays from Cinnamon were developed, other ingredients such as methyl salicylate and menthol were used as counter-irritants that both dissolved in ethanol, mixed well to formulate the spray.

Evaluation of film-forming spray formulations:
Physical properties: Cinnamon film forming spray was kept at room temperature (30 ± 2°C) for 0, 7, 14 and 28 days, clarity of solution, thickness of film and white spot-on surface were visually observed.
Evaporation time: Film forming spray was spread on a bagasse paper that is suspended from a sensitive balance in a fume hood. Analytical elements balancing is used to calculate the weight loss of the bagasse paper/solvent liquid as a function of time as the solvent evaporates.
Volume per spray: The spray formulations were also subjected to the following quantitative testing. The average weight per dosage is an essential quantitative quantity to consider. Ten sprays were actuated into a glass beaker, and the volume per spray was estimated using analytical balance.
pH estimation: A 30 ml glass beaker was filled with approximately 20 mL of film forming spray solution. The pH of each ten sprays for 0,7,14 and 28 days values were measured.

3. Results:

All of the film forming spray formulations F1-F3 had obvious clear physical appearances. Cinnamon oil was dissolved in ethanol to generate a clear solution; suitable formulations were F1 (PVP K30 as polymer, PG as plasticizer), F2 (HPMC E5 as polymer, PEG 400 as plasticizer), and F3 (PVP K30 as polymer, PEG 400 as plasticizer). The spray solution was kept in a tightly sealed container with a spray pump, as indicated in Figure 1. Tables 3 and 4 show the results of the examination of film forming spray formulations.

F1 F2 F3

Figure3. Physical appearances of film forming spray formulation (F1, F2 and F3),

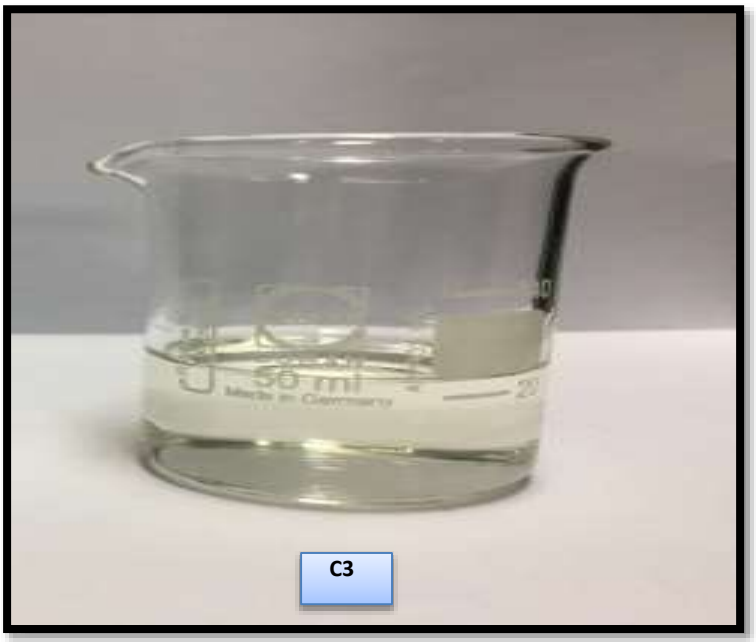

Figure 4: Cinnamon oil film forming spray formulation

Figure 5: Topical film forming spray

Table 3: Physical appearance so film forming spray formulation

Formulation	**Days**			
	0day	**7days**	**14days**	**28days**
C1	clear, thin film, smooth	clear, thin film, smooth	clear, light yellow solution, thin film, smooth	clear, light yellow solution, thin film, smooth
C2	clear, thin film, smooth, white spot	clear, thin film, smooth, white spot	clear, light yellow solution, thin film, smooth, white spot	clear, light yellow solution, thin film, smooth, white spot
C3	clear, thin film, smooth	clear, thin film, smooth	clear, thin film, smooth	clear, thin film, smooth

Table 4: Evaluation of film forming spray formulation

Formulation	**Evaluation**					
	Evaporation Time (Second)	**Volume Per Spray (Gm)**	**pH**			
			0 day	**7 days**	**14 days**	**28 days**
C1	16.61	0.11	5.11	5.30	5.70	5.81
C2	14.72	0.11	5.09	5.18	5.45	5.67
C3	23.89	0.11	6.66	6.58	6.62	6.60

4. Discussion

Ethanol and purified water were the chosen solvents. Both solvents were affordable, accessible, and safe solvents utilized in solution formulations. When water and ethanol blended together, clear (F1, F2,F3) was produced. F1 and F2 changed to bright yellow-clear after 14 days. The effect of solvent on evaporation time was investigated . It was concluded that a ratio of 37.08:54.00 (water: ethanol) was the best solvent
system for spray formulations since it evaporated quickly (within 30 seconds) when applied to skin.

PVP K30 and HPMC E5 were selected as the film-forming polymers PVP (polyvinylpyrrolidone) K30 is an amorphous, hygroscopic polymer. They are soluble in water and organic solvent

As the concentration of PVP K30 was increased from 1% to 5% by weight, the viscosity was gradually increased. A greater polymer concentration produced a more viscous gel and enhanced the tightness of the swelling hydrogel network. When compared to the other polymers, HPMC E5 grew from 1.0% to 5.0% by weight, the viscosity steadily increased, and at concentrations 3.0-5.0% by weight, a white spot appeared. Spray

formulations F1 and F3 were developed with PVP K30 ranging from 1.0 to 5.0% by weight, with PVP K30 at 3.0% by weight exhibiting thin, smooth, and transparent films. F3 was developed using HPMC E5 at 1.0 to 5.0% by weight, while HPMC E3 at 2.0% by weight gave acceptable films. All formulations F1-F3 were indicated slow drying films. Therefore, the formulations were developed to improve rate of drying time by varies concentration of solvent.

The formulations F1-F3 were prepared to examine the effect of different plasticizers. Propylene glycol and PEG 400 were selected for investigation of their flexibility of spray formulation using 1.0% by weight. The results indicated that similar of film appearance, clear film, smooth surface and not break. F1-F3 gave clear solutions while after 14 days F1 and F2 gave light yellow solution those compose of PVP K30 as polymer and detected an unstable of pH. F3 gave clear solution and presented white spot after applied. Film forming sprays were developed by adding methyl salicylate and menthol as counterirritant for synergist Cinnamon activities. Methyl salicylate and menthol provided heating and cooling sensation after application of spray (around 5min)**.** The films on skin will be easily washed off with water**.** Comparing the physical characteristics of films**,** evaporation time and pH, formulation F3 was found to be better as compared to other formulations**.**

5. Conclusion

Cinnamon oil is a valuable blend of oxygenated molecules and hydrocarbons that is appealing to the cosmetics, perfumery, and flavouring industries. Cinnamon oil possesses anti-inflammatory, anti-oxidant, and anti-nociceptive properties. This formulations are diminishes the sense of pain in the region to which it is applied. The process for preparing film forming spray was simple. The resulting film forming spray formulations were transparent, grittiness free, and flexible . The assessment investigations revealed that it has the ability to evaporate quickly on application, pH becomes equivalent to that of normal skin, and no skin irritation..

6. References:

1. Mohammad Reza Farahpour, Amir Amniattalab, and Hadi Hajizadeh,Evaluation of the wound healing activity of Cinnamomum zeylanicum extract on experimentally induced wounds in rats ,African Journal of Biotechnology ,18 October, 2012,Vol. 11(84), pp. 15068-15071,
2. Swati N. Deshmukh, Vanita Gade, Aniket Garud, Rahul Dumbre , Bhagyashri Warude , Sunita Maharaj, Swapnali Girme,Novel Film Forming Spray from Tea Tree Leaves with Special Emphasis on Development, Formulation and Evaluation, *Journal of Positive School Psychology* 2022, Vol. 6, No. 5, 5179 – 5184.
3. Moura Li, Dias A.M. ,Carvalho E, Desousa H.C.,Recent advances on the development of wound dressings for diabetic foot ulcer treatment-a review, *Acta Biomater*,2013,;9(7);Page-7093-114.
4. Zorec B, Miklavcic D, Pavselj N, Préat V., Active enhancement methods for intra- and transdermal drug delivery: a review. *Zdr Vestn*;2013,82(5): Page-339–356.
5. Cristiano MC, Cilurzo F, Carafa M, Paolino D., Innovative vesicles for dermal and transdermal drug delivery. In: Lipid Nanocarriers for Drug Targeting. Elsevier;2013, Page-175–197. doi:10.1016/B978- 0-12-813687-4.00004-9.
6. Sharadha M, Gowda DV, Vishal Gupta N, Akhila A. R. , An overview on topical drug delivery system – updated review. *Int J Res Pharm Sci*;2020,11(1), page-368–385. doi:10.26452/ijrps. v11i1.1831.
7. Kaur J, Kaur J, Jaiswal S, Gupta G., Recent advances in topical drug delivery system. *Pharm Res*. 2016;6(7).
8. Leppert W, Malec–Milewska M, Zajaczkowska R, Wordliczek J.,Transdermal and topical drug administration in the treatment of pain. Molecules.;2018,23(3), page-:681. doi:10.3390/molecules23030681.
9. Dayan N. Delivery system design in topically applied formulations: an overview., In: Delivery System Handbook for Personal Care and Cosmetic Products. Elsevier;2005, page-101–118. doi:10.1016/B978- 081551504-3.50009-2.
10. Ruela ALM, Perissinato AG., Evaluation of skin absorption of drugs from topical and transdermal formulations. *Brazilian J Pharm Sci*.2016;52(3), page-527–544. doi:10.1590/s1984-82502016 000300018.
11. Garg T, Rath G, Goyal AK, Comprehensive review on additives of topical dosage forms for drug delivery. *Drug Deliv* ;22 (8):2015, page-969–987. doi:10.3109/10717544.2013.879355.
12. Mcauley W.J., Caserta F., Hoboken N.J., Film-forming and heated systems. In: Novel delivery systems for Transdermal and Intradermal drug delivery, Donnelly RF, Singh TRR. John Wiley & Sons,

United states; 2015, P 97-107.

13. .Frederiksen K, Guy R.H, Petersson K., The potential of polymeric film-forming systems as sustained delivery platforms for topical drugs., Expert Opin. *Drug Deliv*. 2015;13 (3):349–360.
14. Radhakrishnan A, Kuppusamy G, Karri VVSR.,2018, Spray bandage strategy in topical drug delivery. J Drug Deliv Sci Technol. ,43. page-113–121. doi:10.1016/j.jddst.2017.09.018.
15. 15.Jakhetia V, Patel R, Khatri P, Pahuja N, Garg S, Pandey A, Sharma S. "Cinnamon: A Pharmacological Review". *Journal of Advanced Sciences and Research,*, 2010, 1(2); 19-23.
16. Mau JL, Chen CP, Hsieh PC ., Antimicrobial effect of extracts from Chinese chive, cinnamon and corni fructiis. J. Agric. Food. Chem.,2001, 49:183-188.
17. .Amara AA, El-Masry MH, Bogdady HH , Plant crude extracts could be the solution: Extracts showing in vivo antitumorigenic activity. Pak. J. Pharm. Sci.,2008, 21:159-171.