FORMULATION, DEVELOPMENT AND EVALUATION OF NOVEL FILM FORMING SPRAY: CITRONELLA LEAVES

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Article History: Received: 29.03.2023 **Revised:** 12.05.2023 **Accepted:** 30.06.2023

Abstract:

The intent of this study was to develop a topical citronella oil film-forming spray that could enhance the healing process of wounds. Film-forming sprays have a number of benefits over conventional topical preparations, including consistent medication distribution and dose, improved bioavailability, reduced risk of irritation, continuous drug release, and faster wound healing through moisture control. Polymers and excipients employed in film-forming sprays contribute to improved preparation qualities and active ingredient stability. Different excipient and polymer combinations will produce films with varying properties. 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 its 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, grittiness free in appearance. The evaluation investigations revealed that the PH becomes similar to that of normal skin and has ability to evaporate swiftly resulting in lesser skin irritation when sprayed on wounds. Spray is more convenient to use, can be applied easily thus improve patient acceptance and compliance.

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

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DOI: 10.31838/ecb/2023.12.s3.574

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]. 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]. Both *Cymbopogon nardus* and *Cymbopogon winteriness*, which are indigenous to tropical Asia and are frequently used as herbs and flavoring agents in a variety of foods and beverages, are the main sources of citronella oil. *Cymbopogon nardus* contains citronella oil with citronellal, geraniol, and citronellol as active substances. These compounds remove the intra-cellular hydrogen ions, causing immobility and eventually cell death in bacteria.[1]

The oil is yellowish and has stimulant, diaphoretic, insecticidal, antibacterial, antiseptic and stimulant properties. The monoterpene aldehyde citronellal, its equivalent oxidation product citronellol, and geraniol are the three main components of citronella, and they all have insect-repellent properties whose modes of action are as food deterrents, contact repellents, and killers. The following substances are also biologically active or biocidal: camphene, linalool, limonene, pinene, and borneol. The poisoning of adult insects, interference with reproduction, and harm to the integuments as a result of its irritating qualities are further effects[13].The primary compound of citronella oil, citronellal, is an oily liquid that is clear to yellow in colour, boils at 206^0C, and is soluble in alcohol and fixed oils but insoluble in glycerin and water.

It is commonly found in balm mint. Citronella oil is used in some industrial formulations as an insecticidal repellent, primarily against the mosquito that transmits malaria. Citronella oil has potent anti-inflammatory, antioxidant, and nociceptive properties. In addition to these properties, oil causes the central nervous system to relax. Successful cardiovascular activity evaluations of citronella oil have also been conducted in many researches. These properties are a direct result of the oil's main ingredients, linalool, citronellal, citronellol, and elemol[12]. Water soluble substances like phenolic components that are present in the residual water are also extracted along with the essential oil. The residual and distilled water known as hydrosol can be used as the low-cost food preservatives or flavoring agent[15].

Figure1 .Citronella leaves

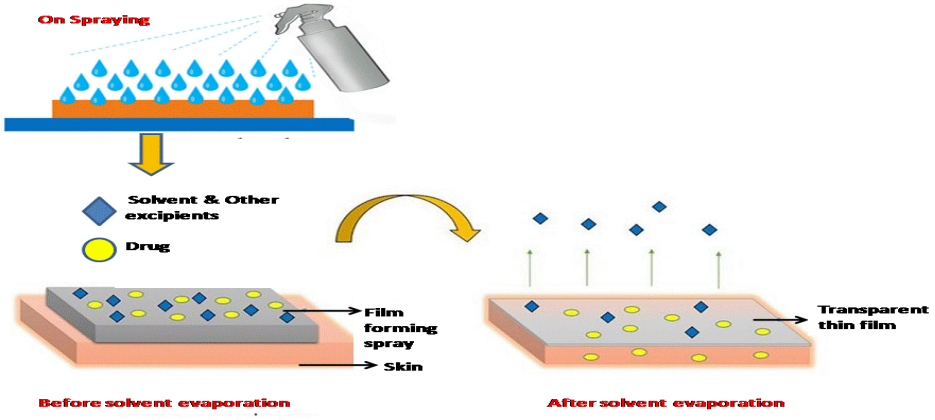


Figure 2. Mechanism of action of Film forming spray

2. Methods

1. Citronella leaves were procured from 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 skin, and a superior excipient was selected for the subsequent trial.
3. **Selection of solvent system:** Citronella oil is insoluble in glycerin and water but soluble in organic solvents like alcohol and fixed oils. Different concentrations of ethanol were utilised as solvents. Ethanol are 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 citronella film-forming spray. The different film-forming polymers were such as PVPK30 and HPMCE3 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.

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	-	-	-	-	-
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. Major Focus was on breakable of film and white spot on the surface.

Ingredients	**Formulation w/w**			**Function**
	F1	F2	F3	
PVPK30	3.0		3.0	Film forming agent
HPMCE5	-	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
Citronella oil	0.03	0.03	0.03	Active ingredient
Purified water	37.98	37.98	37.98	Solvent
Ethanol	54.0	54.0	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. Tea tree oil was dissolved in ethanol and added into a polymeric solution The plasticizer was then added and the final weight was adjusted with water. the screening of the excipients (polymers and plasticizers) in formulation, water was used for adjusting the final weight. The topical film forming sprays from Citronella were developed, other ingredients such as methyl salicylate and menthol were used as counter irritant that both dissolved in ethanol, mixed well to formulate spray.

Evaluation of film forming spray formulations:
Physical properties: Citronella film forming spray

was kept at room temperature (302°C) for 0, 7, 14 and 28 days, clarity of solution, thickness of film and white spot on surface were visually observed.

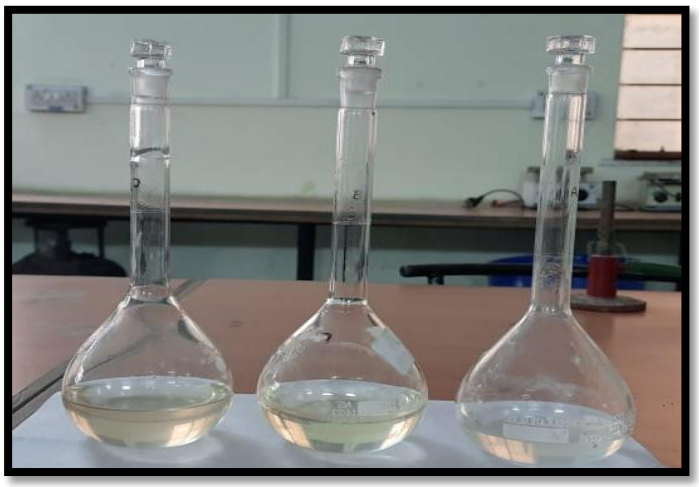
Evaporation time: Film forming spray was spread on a bagasse paper that is suspended from a sensitive balance in a fume hood. Analytical elements balancing is used to calculate the weight loss of the bagasse paper/solvent liquid as a function of time as the solvent evaporates.

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. Citronella 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, PEG400 as plasticizer), and F3 (PVP K30 as polymer, PEG400 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 andF3),

Figure 4: Topical film forming spray

Figure 5: Topical film forming spray

Table: Physical appearance so film forming spray formulation

Formulation	**Days**			
	0day	**7days**	**14days**	**28days**
F1dfyuth	Clear, thin film, smooth	clear, thin film, smooth	clear, light yellow solution, thin film, smooth	clear, light yellow solution, thin film, smooth
F2	Clear, thin film, smooth	clear, thin film, smooth	clear, light yellow solution, thin film, smooth, white spot	clear, light yellow solution, thin film, smooth, white spot
F3	Clear, thin film, smooth, white spot	clear, thin film, smooth, white spot	clear, thin film, smooth	clear, thin film, smooth

Table: Evaluation of film forming spray formulation

Formulation	**Evaluation**					
	Evaporation Time (second)	Volume per Spray (g)	PH			
F1	18.61	0.11	5.17	5.32	5.78	5.81
F2	14.72	0.11	5.09	5.18	5.45	5.67
F3	27.78	0.11	6.40	6.38	6.40	6.40

4. Discussion

Ethanol and purified water were the chosen solvents. Both solvents were affordable, accessible, and safe solvents utilised 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.F32 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 Citronella activities. Methyl salicylate and menthol provided heating and cooling sensation after application of spray (around5min)**.** 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

Citronella oil is a valuable blend of oxygenated molecules and hydrocarbons that is appealing to the cosmetics, perfumery, and flavouring industries. Citronella 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. Tantri L. Nareswari*, Fidela O. Vrince, Erga Syatri, Formulation and Evaluation of Citronella oil (Cymbopogon nardus (L.) cream for Acne Treatment, IJDDT Volume 13 Issue 1, January - March 2023 Page 419-422.
2. Swati N. Deshmukh, Vanita Gade, Aniket Garud, Rahul Dumbre, Bhagyashri Warude, Sunita Maharaj, Swapnali Girme 2022, 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 ;2015,22 (8):, page-969–987. doi:10.3109/10717544.2013.879355.
12. Chang R-K, Raw A, Lionberger R, Yu L,Generic development of topical dermatologic products: formulation development, process development, and testing of topical dermatologic products. AAPS J. ;2013,15(1), page-41–52. doi:10.1208/s12248-012-9411-0.
13. Radhakrishnan A, Kuppusamy G, Karri VVSR., Spray bandage strategy in topical drug delivery. J Drug Deliv Sci Technol. ,2018,43. page-113–121. doi:10.1016/j.jddst.2017.09.018.
14. Krishna P. Solanki, Meghal A. Desai, Jigisha K. Parikh, Microwave intensified extraction: A holistic approach for extraction of citronella oil and phenolic compounds, Chemical Engineering and Processing - Process Intensification, Volume 146, December 2019, 107694.
15. Krishna P. Solanki, Meghal A. Desai, Jigisha K. Parikh, Microwave intensified extraction: A holistic approach for extraction of citronella oil and phenolic compounds, Chemical Engineering and Processing - Process Intensification, Volume 146, December 2019, 107694.