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Research Article

Formulation and Evaluation of a Topical Spray-based Foam Containing Aloe Vera and Silver Sulfadiazine to Treat First and Second-degree Skin Burns

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I N F O

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A B S T R A C T

Introduction: Skin burns of the first and second degrees are frequent wounds that need quick and efficient care to speed up healing and avoid complications. For the treatment of severe burns, the goal of this study was to create a novel topical spray-based foam formulation incorporating silver sulfadiazine and aloe vera.

Method: The formulation was created to offer improved medication distribution, increased wound site adhesion, and maximum therapeutic efficacy. To hasten tissue regeneration and lessen discomfort, aloe vera, known for its anti-inflammatory and wound-healing capabilities, was added to the foam. A broad-spectrum antimicrobial drug called silver sulfadiazine was also added to stop infection, a frequent side effect of burn wounds.

Results & Conclusion: To create a stable and user-friendly product, the foam formulation was created utilising a combination of surfactants, propellants, and polymers.

Keywords: Foaming Spray, Aloe Vera, Silver Sulfadiazine, Skin Burn Diseases

Introduction

In dermatological applications, solutions, suspensions, creams, gels, ointments, and lotions are the most often utilised forms. The most popular way to provide dermatological therapy is still through a topical drug delivery device. Foam is suitable for dermatological and gynaecological applications because it has high patient acceptability, excellent spreadability, maximal efficacy, and increased compliance. The foam works with a variety of active ingredients, including small and big molecules, medications that are sensitive to water, suspensions of water-soluble and oil-soluble substances, and drugs that are sensitive to air and light.[1] Comparable cost to other topical formulation types is the key benefit of foam, along with very high patient satisfaction. Additionally, excessive rubbing onto the skin is not recommended with foam formulations because they have exceptional spreadability and instantaneous absorption is not required.[2] Burns constitute a common type of injury among people. They can be described as unwanted, highly drastic traumatising injuries that can occur to any person at any moment in

time and any place. The cause of burns may be due to radiation, exposure to chemicals, cold, friction, heat, and other electric sources. However, the majority of the major injuries are caused due to heat exposure from fire or hot liquids or solids. During the burn, the injuries destroy the tissue due to the transfer of energy. The reasons associated with the cause of burns involve both pathophysiological and physiological factors.[3] The common causes of burn injuries are automobile accidents, building fires, hot liquids, construction accidents, defective products, chemicals, and electrical and industrial malfunction. Based on the site and depth of the burn, the victim undergoes severe potentially harmful complications like respiratory failure, shock, infection, and electrolyte imbalance. Other than the physical complications produced in the body, emotional and psychological distress and deformities may be observed.[4]

Classification of Burn Wounds

Burn wounds can be categorised based on their depth, aetiology, or severity. As per the depth of the wounds, they are classified as follows:

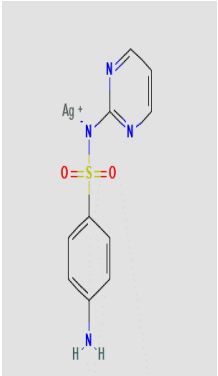
1. **First-degree burns:** Skin injuries fall under this category. In these, only the epidermis, the outermost layer of the skin, is affected.
2. **Second-degree burns:** In these skin burn wounds, the deep layer (hypodermis) of the skin is affected.
3. **Third-degree burns:** These types of skin burns damage the entire structure completely such as joints, muscles, and nerves.[5]

The severity of the burn symptoms might increase during the next few hours or days from the time of occurrence of the burn, depending on the severity of the burn damage. Pain, peeling skin, blisters, white or burnt skin, and swelling are some of the symptoms.

Drug Profile of Silver Sulfadiazine

The drug profile of silver sulfadiazine has been shown in Table 1.

Table 1.Basic Information about Silver Sulfadiazine[6]

S. No.	Parameter	Specification
1	BCS class	IV
2	State	Solid state
3	Structure	
4	Colour	White powder
5	Physical state	Solid powder
6	Melting point	285 ºC
7	Solubility	8.96 ug/mL
8	Log P value	0.19
9	pKa	6.99 (strongest acid)
10	Therapeutic class	Antibiotics
11	Route of administration	Topical
12	Dose	0.5%, 1.0%

BCS: Biological Classification System

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Biological Profile of Aloe Vera[7]

The biological profile of aloe vera, also known as Aloe barbadensis, is as follows:

Biological Source

Aloe vera is derived from the succulent plant Aloe barbadensis, primarily from the gel-like substance found in its leaves.

Family

Asphodelaceae

Geographical Source

It is generally cultivated worldwide in various regions with suitable climates.

Chemical Constituents

Aloe vera contains a varied range of chemical constituents, including polysaccharides (e.g. acemannan), enzymes (e.g. bradykinase, amylase, and lipase), anthraquinone compounds (e.g. aloin and emodin), sterol (e.g. beta-sitosterol and lupeol), and phenolic compounds (e.g. salicylic acid, cinnamic acid, and coumarins).

Medicinal Uses

- Topical application for wound healing, burns, and skin conditions such as dermatitis and psoriasis
- Anti-inflammatory effects that are helpful in reducing swelling and inflammation
- Antimicrobial activity against bacteria, fungi, and viruses
- Antioxidant activity that protects against oxidative damage and promotes skin health

Materials and Methods

List of Materials

Silver sulfadiazine was purchased from Macsen Laboratories and aloe vera was purchased from Mahogany Organics Private Limited. Propylene glycol, polyethylene glycol 400, glycerine, and cocamidopropyl betaine were purchased from Chemdyes Corporation. Sodium benzoate was obtained from Sigma Life Science. HPMC and Tragacanth gum were obtained from Oxford Lab Fine Chem LLP.

List of Equipment

The various equipment needed for the process have been mentioned in Table 2.

Table 2.List of Equipment[8]

S. No.	Name of Instruments	Manufacturer/ Source
1	UV spectrophotometer (UV-1900)	Shimadzu, Japan
2	Weighing balance	Shimadzu, Japan
3	Water-jacketed Franz diffusion cell	Remi Equipment, Mumbai
4	FTIR	Shimadzu, Japan
5	DSC	Shimadzu, Japan

FTIR: Fourier Transform Infrared Spectroscopy, DSC: Differential Scanning Colorimetry

Method for Preparation

The preparation was done using a simple solution method. In a nutshell, a magnetic stirrer was used to continuously agitate water until the surfactant was dissolved. Following the addition of the stabiliser and glycerin, water was used to get the final volume up to 10–15 ml. This process of preparation was used for trial batches.[9] The detailed composition of ingredients used in the preparation has been shown in Table 3.

Table 3.Composition of Ingredients[10]

Ingredients	NF_1 (%)	NF_2 (%)	NF_3 (%)
Glycerine	8	8	10
Sodium lauryl sulphate	2	-	-
Polyethylene glycol 400	-	9	-
Tween 80	-	3	-
Cocamidopropyl betaine	-	-	10
Purified water	Sufficient amount	Sufficient amount	Sufficient amount

NF_1–NF_3: Batch names

Trials Batches for Selecting Different Methods

The process for creating oil-in-water emulsions was optimised as shown in Table 4 to prevent pronounced foam creation, which could result in the loss of foaming and emulsifying ingredients.

All the excipients were measured accurately and dissolved in distilled water, except the foaming agent, which formed the aqueous phase. The aqueous phase was kept in a water bath to bring it to 50 °C. The oil phases were measured accurately and put in a second beaker. The oil phase was heated at 55 °C. The aqueous phase was combined with the oil phase slowly while mixing continuously. The emulsion was kept on a magnetic stirrer until foam was formed. The foaming solution was then transferred to an appropriate container. This preparation procedure was for trial batches NF8 to NF15. The details of excipients used for these trial batches have been shown in Table 5 and the final optimised batch formulation of foaming spray has been shown in Figure 1.

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Table 4.Trial Batches for Optimised Batch[10]

Batch	Oil Phase	Water Phase	Incorporation	Foam Generation
NF_4	Heated oil phase at 55 °C	Added foaming agent and heated to 55 °C	Incorporated the water phase into the oil phase	Strong foam was generated
NF_5	Heated oil phase at 55 °C	Added foaming agent and heated to 55 °C	Incorporated the oil phase into the water phase	Strong foam was generated
NF_6	Added foaming agent and heated to 55 °C	Heated to 55 °C	Incorporated the water phase into the oil phase	Strong foam was generated
NF_7	Added foaming agent and heated to 55 °C	Heated to 55 °C	Incorporated the oil phase into the water phase	It was prevented from producing a lot of foam.

NF_4–NF_7: Batch names

Table 5.Trials batches for Selecting Excipients[10]

Ingredients	NF_8 (%)	NF_9 (%)	NF_{10} (%)	NF_{11} (%)	NF_{12} (%)	NF_{13} (%)	NF_{14} (%)	NF_{15} (%)
Silver sulfadiazine	-	-	-	-	-	-	-	0.6
Aloe vera	-	-	-	-	-	-	-	0.79
PEG 400	4	4	4	4	4	4	4	4
Cocamidopropyl betaine	15	15	24	10	15	15	18	18
Olive oil	1	1	0.5	1	1	1	1	1
Glycerine	-	10	10	10	10	10	10	10
HPMC	-	-	-	4	-	-	-	-
Tragacanth gum	-	-	-	-	1	-	-	-
Sodium alginate	-	-	-	-	-	2	-	-
Propylene glycol	-	-	-	-	-	-	3	3
Purified water	Sufficient amount							

NF8–NF15: Batch names
PEG: Polyethylene Glycol
HPMC: Hydroxy Propyl Methyl Cellulose

Figure 1.Optimised Batch NF15

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Drug Identification

Determination of Aloe Vera Absorption Maxima (λ_{max}: 283 nm) in Water by UV Spectrophotometry

10 mg of the drug was dissolved in 10 ml of water to create a stock solution. Several solutions were made ranging in concentration from 100 g/ml to 1000 g/ml and were scanned with a UV spectrophotometer (between 200 nm and 400 nm).

Determination of Silver Sulfadiazine Absorption Maxima (λ_{max}: 255 nm) in 10% Ammonia by UV Spectrophotometry

10 mg of the drug was dissolved in 10 ml ammonia (1000 µg/ml). A series of solutions were prepared ranging in concentration from 2 µg/ml to 24 µg/ml and a 100 µg/ml solution was prepared containing 10% ammonia. These were scanned with a UV spectrophotometer between 200 nm and 400 nm.

Fourier Transform Infrared Study

The potential chemical interactions were examined using a Bruker TENSOR 27 FTIR Spectrophotometer (Karlsruhe, Germany) with a spectrum resolution of 1 cm-1. The data were gathered between 4000 and 400 cm^{-1}.[11]

Differential Scanning Calorimetry Study

The sample of pure drug as well as that of physical mixture were analysed for Differential Scanning Calorimetry (DSC) study.[12]

Evaluation Parameter

Appearance[13]

The colour and uniformity of the prepared foamable emulsion were visually examined.

pH Measurement[14]

The pH values of the formulation were measured using a digital pH meter. The measurements were carried out in triplicate after calibration and then the average of the three readings was recorded.

Bubble Size Measurement[14]

The bubble sizes were manually measured for at least 100 bubbles per foam sample using the ImageJ software after digital photographs of the foams were taken. The analysis programme was applied to high-quality (300 pixels per inch) and highly magnified photos in order to reduce measurement error. To determine a size distribution, every bubble inside a certain area was counted. These numbers were recorded as mean bubble diameters (mm) and standard deviation (SD), along with graphs showing the distribution of their sizes.

Foam Stability[15]

The Thorlabs high-resolution camera was used to measure the real foam decay (FD) in the sample. This streamlined technique evaluates the variation in foam heights (mm), both immediately on foaming and after three minutes. Visual measurements were made using the captured images.

Drug Content[16]

After sufficient dilution with water at 256 nm, 1 ml of the spray solution was obtained, and its absorbance was assessed using a UV spectrophotometer. The standard plot was used to calculate the concentration and percentage (theoretical value) for the drug content.

In Vitro Study[13]

The Franz diffusion cell was used for the *in vitro* study. The phosphate buffer (pH 7.4) was placed within the receiver chamber. A foamable emulsion was added to the cellophane membrane's surface. The temperature was maintained at 37 °C. The solution in the receiver chamber was stirred using a magnetic stirrer. 0.5 ml of the receiver compartment's solution was pipetted out at regular intervals, which was promptly replaced with brand new 0.5 ml of the receiver medium.

Result and Discussion

UV Spectrophotometry[17,18]

Aloe Vera Absorption Maxima (λ^{max}: 283 nm) in Water by UV Spectrophotometry

Figures 2 and 3 show the overlay and the calibration curve of aloe vera, respectively.

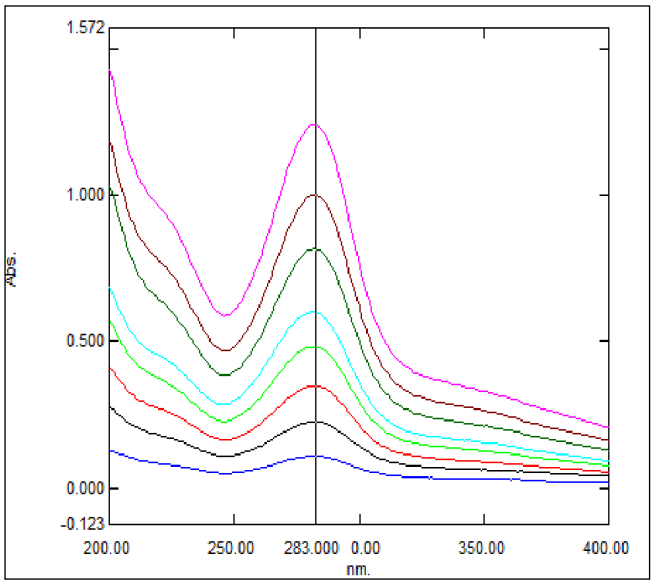

Figure 2.Overlay of Aloe Vera

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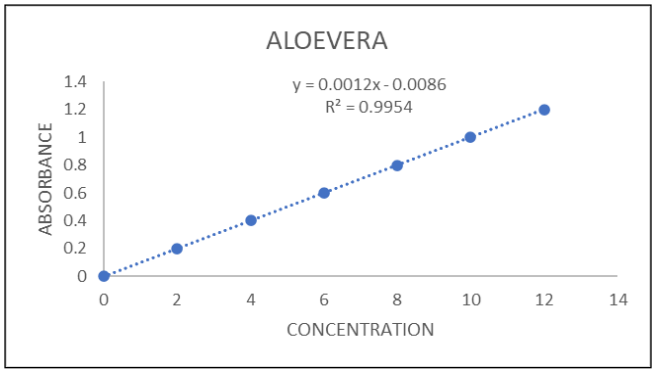

Figure 3.Calibration Curve of Aloe Vera

Silver Sulfadiazine Absorption Maxima (λ^{max}: 255 nm) in 10% Ammonia by UV Spectrophotometry

Figures 4 and 5 show the overlay and the calibration curve of silver sulfadiazine, respectively.

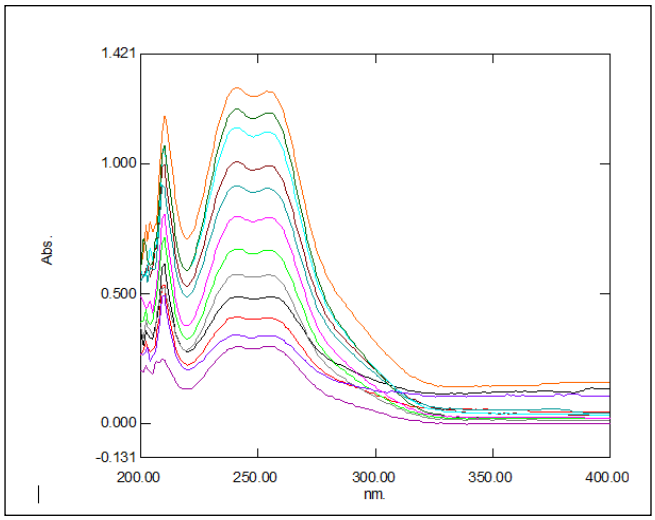

Figure 4.Overlay of Silver Sulfadiazine

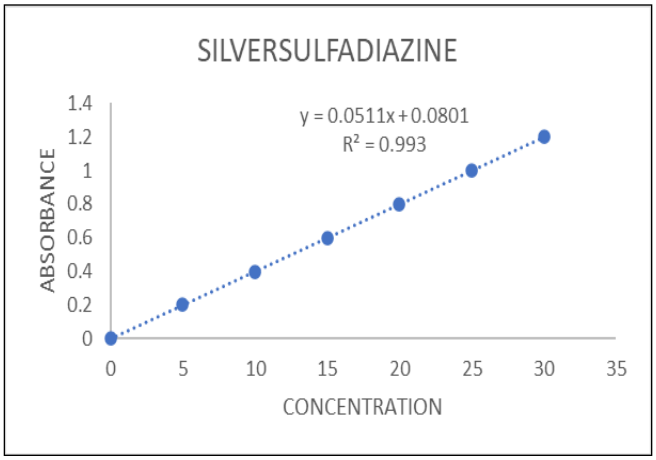

Figure 5.Calibration Curve of Silver Sulfadiazine

Fourier Transform Infra-Red Spectrophotometry (FTIR) of Silver Sulfadiazine

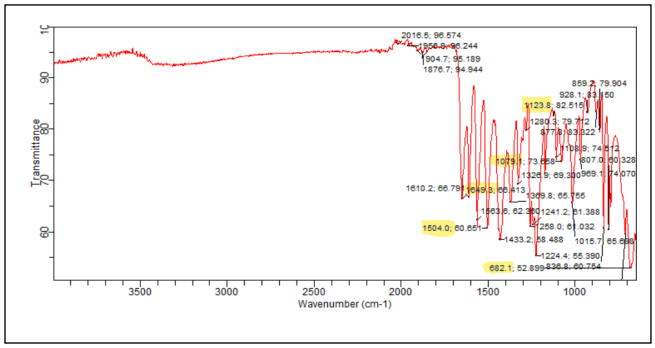

Figure 6.Silver Sulfadiazine FTIR

Figure 6 and Table 6 show the FTIR representation and interpretation of silver sulfadiazine, respectively.

Table 6.FTIR Interpretation of Silver Sulfadiazine[18]

Functional Group	Observed Wave Number (cm^{-1})
C-H	1504
C-N	1123
S=O	1079
C-S	682

Differential Scanning Calorimetry (DSC) Study

A sample medication, weighing 20 mg, was hermetically sealed in an aluminium pan and subjected to a 20 ml/min nitrogen gas purge while being heated at a rate of 2 °C per minute from 0 to 300 °C. The DSC sepctrum of silver sulfadiazine has been shown in Figure 7.

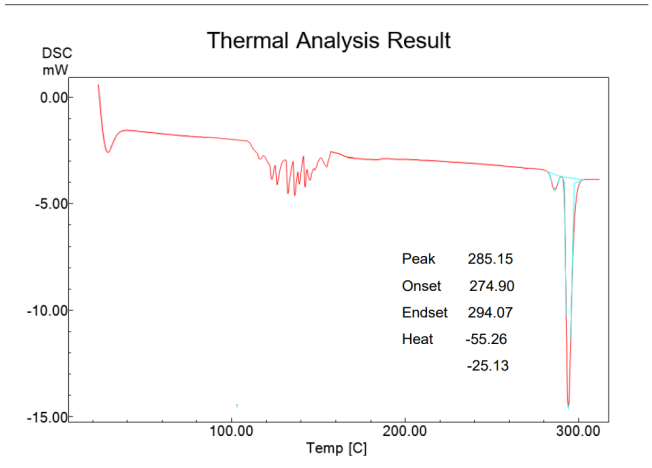

Figure 7.DSC Spectrum of Silver Sulfadiazine

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Evaluation of Foam

The properties of the finalised foam sample were assessed and have been shown in Table 7.

Table 7.Evaluation of Foam[18]

S.No.	Parameter	Result
1	Physical appearance	White in colour
2	pH	6.4
3	Bubble size (mm)	0.191 ± 0.014
4	Drug content	SSD: 98.0% ± 0.12
		Aloe vera: 97.0% ± 1.02
5	*In vitro* study	78.0%
6	Foamability and stability	FE (%): 944
		FVS (%): 96

Conclusion

In conclusion, the successfully developed topical spray-based foam containing aloe vera and silver sulfadiazine is useful in the treatment of first and second-degree skin burns. The optimised formulation was prepared using different trial and error methods. Aloe vera has been shown to promote wound healing and reduce inflammation. To confirm the security and effectiveness of this unique drug delivery method and to ascertain its therapeutic application, additional clinical research is required.

Source of Funding: None

Conflict of Interest: None

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