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Development and Evaluation of a Silver Nitrate and Neomycin Sulfate Topical Spray for Burn Treatment

Jaydip Gohil[a], Kuldip Bhadka[a], Udit Vaghasiya[a], Vijay Vekariya[b], Vishal Vora[b]*

[a]Reserch Scholar, Department of Pharmacy, Shree H N Shukla Institute of Pharmaceutical Education and Research, Rajkot, Gujarat, India.
[b]Assistant Professor, Department of Pharmacy, Shree H N Shukla Institute of Pharmaceutical Education and Research, Rajkot, Gujarat, India.

A B S T R A C T :

Despite advancements in burn treatment, a gap persists in the availability of a single, easy-to-apply spray formulation that combines silver nitrate and neomycin sulfate. This study aimed to develop and evaluate a novel topical spray formulation integrating these active ingredients for enhanced burn healing and antimicrobial efficacy. The formulation was prepared using a simple solution method and optimized through multiple trials to achieve desirable physical stability, appearance, and odor. Various evaluation tests were conducted, including pH measurement, spray pattern and angle assessment, leak and evaporation tests, skin irritation studies, and antimicrobial activity analysis. The optimized formulation exhibited a pale yellow color, a neutral pH range (6.6–7.4), a consistent spray pattern (2.85–3.12 cm diameter), and a controlled spray angle (~75°). Minimal leakage was observed over a seven-day period, and the formulation demonstrated rapid evaporation and skin compatibility, with no significant irritation reported. The antimicrobial efficacy, assessed using the zone of inhibition method against Staphylococcus aureus and Escherichia coli, confirmed strong antibacterial activity, with inhibition zones ranging from 21–28 mm and 15–20 mm, respectively. These results suggest that the developed spray formulation is a promising alternative for burn care, offering ease of application and effective antimicrobial protection.

Keywords: Burn treatment, Topical spray formulation, Silver nitrate, Neomycin sulfate

1. Introduction

Burn injuries represent a significant global public health challenge, with approximately 7 million cases reported annually in India alone, leading to 1.4 lakh deaths and 2.4 lakh cases of disability (Gupta et al., 2010). Burns are characterized by damage to the skin or underlying tissues caused by thermal, chemical, electrical, or radiation exposure. The severity of burns is classified into four degrees, ranging from superficial (first-degree) to full-thickness (third-degree) and deep tissue involvement (fourth-degree), each requiring distinct therapeutic approaches (Jeschke et al., 2020). Effective management of burn wounds necessitates not only promoting tissue regeneration but also preventing microbial infections, which are a leading cause of complications in burn patients (Rowan et al., 2015).

Topical drug delivery systems (TDDS) have emerged as a promising strategy for burn treatment due to their ability to deliver therapeutics directly to the affected site while minimizing systemic side effects (Zhao et al., 2024). TDDS offers several advantages, including bypassing first-pass metabolism, sustained drug release, and improved patient compliance (Hmingthansanga et al., 2022). Among various topical formulations, sprays are particularly advantageous for burn care due to their ease of application, uniform coverage, and reduced mechanical irritation compared to creams or ointments (Sevgi et al., 2013). Non-pressurized sprays, in particular, are environmentally friendly, cost-effective, and suitable for delivering combination therapies (Pawar & Jalwal, 2021).

Silver nitrate and neomycin sulfate are two well-established agents with complementary mechanisms of action in burn wound management. Silver nitrate exhibits potent antiseptic and cauterizing properties, making it effective in preventing infections and promoting wound healing (Dai et al., 2010). Its mechanism involves the release of silver ions, which disrupt microbial cell membranes and inhibit DNA replication (More et al., 2023). Neomycin sulfate, an aminoglycoside antibiotic, provides broad-spectrum activity against Gram-positive and Gram-negative bacteria, further reducing the risk of infection in burn wounds (Blanchard et al., 2015). The combination of these agents in a spray formulation could synergistically enhance wound healing while addressing microbial contamination.

Despite the availability of various burn treatments, there remains a gap in formulations that combine silver nitrate and neomycin sulfate in a single, easy-to-apply spray dosage form. Current therapies often require multiple applications or lack the convenience of a spray delivery system (Tiwari & Pathak, 2023). This project aims to develop and evaluate a novel topical spray formulation incorporating silver nitrate and neomycin sulfate for burn healing and antimicrobial activity. The formulation will be assessed for physical stability, spray characteristics, and efficacy against common burn

pathogens. The development of such a formulation aligns with the growing demand for patient-friendly and effective topical therapies in burn care. By leveraging the benefits of TDDS and the therapeutic synergy of silver nitrate and neomycin sulfate, this research seeks to contribute to improved clinical outcomes for burn patients.

2. Materials and Methods

2.1. Materials

The materials used in this study include silver nitrate, neomycin sulfate, and de-ionized water. Silver nitrate was purchased from MOLYCHEM (Mumbai, Maharashtra, India), a reputable supplier known for providing high-quality chemicals for pharmaceutical research. Neomycin sulfate, another key ingredient, was sourced from CHEMDYES CORPORATION (Rajkot, Gujarat, India). De-ionized water, which serves as the solvent in this formulation, was obtained from Central Drug House (P) Ltd (Delhi, India).

The apparatus required for the preparation and evaluation of the spray formulation includes a magnetic stirrer, beaker, weight balance, measuring cylinder, and volumetric flask. These instruments are essential for accurately measuring, mixing, and preparing the spray formulation.

2.2. Methods

2.2.1. Formulation of Topical Spray

The spray formulation was prepared using a simple solution method. Silver nitrate, the primary pharmaceutical active ingredient, was first dissolved in de-ionized water using a magnetic stirrer. Next, neomycin sulfate, in its pure powder form, was dissolved in de-ionized or double-distilled water, also with the aid of the magnetic stirrer. Various concentrations of silver nitrate and neomycin sulfate were tested to determine the optimal formulation. The solutions of both ingredients were mixed in equal amounts, resulting in a spray solution, which was then filled into a glass container bottle for storage.

Trial 1

In the first trial, the formulation consisted of 20 mg of silver nitrate, 0.5 g of neomycin sulfate, and 1.5 g of de-ionized water. However, the formulation produced an unpleasant odor, which led to the rejection of this trial as it did not meet the desired results.

Trial 2

For the second trial, adjustments were made to the concentrations, with 15 mg of silver nitrate and 0.25 g of neomycin sulfate, along with 1.75 g of de-ionized water. Despite these changes, the formulation developed a light dark color, likely due to exposure to sunlight, which caused the trial to fail as well.

Final formulation

The final formulation that passed all the criteria contained 20 mg of silver nitrate, 0.5 g of neomycin sulfate, and 1.5 g of de-ionized water. This formulation was found to have a good appearance, odor, and passed physical tests such as irritation and skin rashes. Additionally, a fragrance was added to mask the unpleasant odor from earlier trials.

2.2.2. EVALUATION TEST FOR SPRAY FORMULATION

2.2.2.1. Physical Appearance/Clarity

The spray formulation was visually examined for physical appearance, clarity, color, odor, and the presence of any turbidity. These characteristics were assessed to ensure the formulation met aesthetic and functional requirements.

2.2.2.2. pH Measurement

The pH of the final formulation was determined using a calibrated digital pH meter (Dynalab Enterprise). This test is crucial to ensure the formulation's compatibility with the skin and its stability over time.

2.2.2.3. Spray Pattern

The spray pattern was evaluated by spraying the formulation onto a white paper at a distance of 3.0–4.0 cm. To enhance visibility, 1% methyl red was dissolved in the formulation. After spraying, the diameter of the spot was measured using a scale, and the process was repeated 3-4 times to calculate the average measurement.

2.2.2.4. Spray Angle

The spray angle was determined by spraying the formulation onto a piece of white paper placed on a board. The distance from the nozzle to the paper was 10–15 cm. The spray dots formed were measured, and for calculating the Spray Angle, the formula involves finding the inverse tangent (also known as arctangent) of the ratio of the height of the spray from the nozzle to the average radius of the spray pattern. In simpler terms, you divide the distance from the nozzle to the paper by the radius of the circular spray pattern formed on the paper. Then, you take the arctangent of that value to determine the angle at which the spray is distributed.

2.2.2.5. Leak Test

The leak test evaluated the ability of the container to store the formulation without leakage. The initial weight of the filled container was recorded, and after the container was kept upright for one day, the weight was measured again to check for any loss of formulation.

2.2.2.6. Evaporation Time

The evaporation time was determined by spraying the formulation on a piece of white paper and measuring the time it took for the spray to dry. The average of three measurements was recorded as the evaporation time.

2.2.2.7. Skin Irritation Test

The skin irritation test was performed on five healthy human volunteers. Approximately 1 to 3 ml of the spray formulation was applied to a 2 cm^2 area of skin. The volunteers were monitored for any signs of irritation, redness, or adverse reactions. This test is essential to ensure the formulation's safety for human use.

2.2.2.8. Average Weight Per Dose

To calculate the average weight per dose, the filled spray container was weighed initially (W1). After delivering five sprays in succession, the final weight (W2) was recorded. For Average Weight per Dose, the formula involves subtracting the final weight of the spray container (after dispensing a certain number of sprays) from its initial weight (before dispensing). The result is divided by the number of sprays delivered to find the average weight of the formulation dispensed with each spray. This helps in determining how consistent the amount of spray dispensed is with each use.

2.2.2.9. Antimicrobial Activity

The antimicrobial activity of the optimized formulation was evaluated using the zone of inhibition method. Test cultures of Staphylococcus aureus and Escherichia coli were spread on agar plates, and wells were prepared in the agar. The formulation was poured into the wells, and the plates were incubated at 37°C for 24 hours. The zone of inhibition around each well was measured to assess the formulation's antimicrobial efficacy. This test is vital to ensure that the formulation can effectively prevent infection in burn wounds.

3. Results

3.1. Physical Appearance

The spray formulation was observed visually, and the color was noted to be pale yellow or light yellow. The solution appeared clear without any visible precipitate, indicating good solubility and stability. The odor was mild, resembling a subtle fish-like scent, which was not overpowering. It was also observed that the solution's appearance could be influenced by temperature changes, as extreme temperatures might have affected the formulation.

3.2. pH

The pH of the spray formulation was measured by taking approximately 20 ml of the solution in a small glass beaker. A digital pH meter was used to record the pH after immersing the electrode for one minute. The results for different batches of the formulation showed pH values of 6.6, 7.1, 6.9, and 7.4, indicating that the formulation was slightly acidic to neutral. These pH levels are within the acceptable range for topical formulations, suggesting that the spray is likely to be safe for application on the skin.

3.3. Spray Pattern

The spray pattern was evaluated by spraying the formulation onto white paper at a lab scale. The spray pattern was observed and measured three to four times to ensure consistency. The measurements for the spray pattern diameter, in centimeters, were recorded as follows: 2.85 cm, 3.03 cm, 2.95 cm, and 3.12 cm. The spray exhibited uniform distribution, indicating good spray characteristics for application.

3.4. Spray Angle

The spray angle of the formulation was determined by spraying it from a fixed distance onto a white surface and calculating the angle based on the spray pattern. The spray angle was found to be between 74.80° and 75.92°, with an average of 75.10°. This indicates that the formulation dispenses in a fairly consistent and controlled manner, allowing for efficient coverage during application.

3.5. Leak Test

The leak test was conducted by filling a glass bottle with the spray formulation and recording its initial weight. The bottle was then kept in an upright position for seven days to observe any potential leakage. After seven days, the weight of the bottle was checked, and it was found that the formulation volume had slightly decreased. For example, an initial volume of 20 ml was recorded, and after seven days, the volume had decreased to 19.85 ml. This minor decrease in volume suggests that the formulation container had minimal leakage, ensuring its stability during storage.

3.6. Evaporation Time

The evaporation time of the spray formulation was measured by spraying it onto a white paper and recording the time it took for the spray to dry completely. The results were noted using a stopwatch, and the average time for evaporation was calculated. This test is crucial in determining how quickly the formulation dries on the skin after application.

3.7. Skin Irritation Test

The skin irritation test was performed on five healthy human volunteers. A small quantity (1 to 3 ml) of the spray formulation was applied to an area of 2 cm^2 on the skin. The volunteers were observed for any signs of irritation, redness, or discomfort over a period of time. No significant irritation or adverse reactions were noted, suggesting that the formulation is safe for use on the skin.

3.8. Average Weight per Dose

To determine the average weight per dose, the initial weight of the filled spray bottle (W1) was recorded, followed by spraying five doses and recording the final weight (W2). The difference between the initial and final weights was divided by the number of sprays delivered. The average weight per dose for different samples was found to range from 0.81 gm to 0.88 gm. This indicates that the formulation dispenses a consistent amount with each spray, ensuring uniform delivery.

3.9. Antibacterial Activity

The antimicrobial activity of the spray formulation was evaluated using the zone of inhibition method against Staphylococcus aureus and Escherichia coli. Agar plates were prepared with the bacteria, and wells were made for the formulation. The spray formulation was added to the wells, and the plates were incubated at 37°C for 24 hours. The zone of inhibition, which indicates the formulation's effectiveness in preventing bacterial growth, was measured. The results showed a clear antibacterial effect, with inhibition zones for S. aureus ranging from 21 mm to 28 mm and for E. coli ranging from 15 mm to 20 mm, depending on the concentration of the spray formulation. This demonstrates the formulation's efficacy in combating common bacterial pathogens associated with burn wounds.

4. Discussion

This study aimed to develop a topical spray formulation combining silver nitrate and neomycin sulfate for burn wound treatment. The formulation showed satisfactory physical characteristics, with a pale-yellow color, mild fish-like odor, and clear appearance, indicating good solubility and stability. These properties are consistent with those observed in other silver-based formulations, which are known for their stability in aqueous solutions (Dhaka et al., 2023).

The pH of the formulation, ranging from 6.5 to 7.5, aligns with the skin's physiological pH and supports its potential for safe topical use (Lukić et al., 2021). The spray pattern and angle were consistent with optimal drug delivery, ensuring uniform coverage of the wound area, which is crucial for effective treatment (Angsusing et al., 2025). The formulation demonstrated minimal leakage during the leak test, indicating good container integrity, and an appropriate evaporation time, which is vital to reduce bacterial growth during application (Chang et al., 2013; Pandya et al., 2017).

Skin irritation testing revealed no significant irritation, suggesting the formulation's safety for topical use, which is consistent with findings from previous studies on silver-based and neomycin sulfate formulations (Banna et al., 2022). The antibacterial activity was strong against Staphylococcus aureus and Escherichia coli, pathogens commonly associated with burn infections, confirming the formulation's potential for infection control (Banna et al., 2022).

5. Conclusion

The results of this study suggest that the developed spray formulation is promising for burn wound care. It exhibits good physical properties, such as clarity, mild odor, and stability, along with a safe pH level for topical use. The spray demonstrates a consistent pattern, angle, and average weight per dose, ensuring efficient application. The formulation has passed stability tests, including the leak test and skin irritation test, indicating its safety and reliability. Furthermore, its antimicrobial activity against S. aureus and E. coli suggests its potential effectiveness in preventing infections in burn wounds. Thus, the developed formulation holds potential for improving burn care treatments.

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