

Open Access Full Text Article



Review Article

## Silver Sulfadiazine: Action on Burn Wound Sepsis and Infections

Walia Satwinder Singh\*<sup>1</sup>, Prasad D.N.<sup>2</sup>

<sup>1</sup> Department of Pharmaceutical Chemistry, Shivalik College of Pharmacy, Nangal, Punjab, India

<sup>2</sup> Department of Pharmaceutics, Shivalik College of Pharmacy, Nangal, Punjab, India

### Article Info:



#### Article History:

Received 13 May 2022  
Reviewed 18 June 2022  
Accepted 24 June 2022  
Published 15 July 2022

#### Cite this article as:

Walia SS, Prasad DN, Silver Sulfadiazine: Action on Burn Wound Sepsis and Infections, Journal of Drug Delivery and Therapeutics. 2022; 12(4):154-161

DOI: <http://dx.doi.org/10.22270/jddt.v12i4.5419>

#### \*Address for Correspondence:

Singh Walia Satwinder, Department of Pharmaceutical Chemistry, Shivalik College of Pharmacy, Nangal, Punjab, India

### Abstract

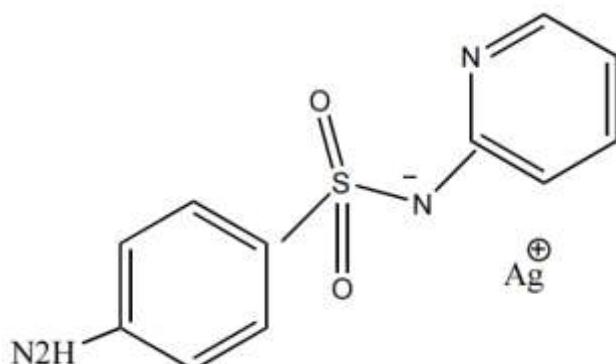
The purpose of this systematic review and meta-review has shifted from assessing the consequences of silver sulfadiazine with most different drugs (SSD) for burn recovery and contamination prevention to different novel dressings, without or with silver. Burn units have to be able to better control sepsis. The degree to which a burn topical antibacterial agent is absorbed determines its effectiveness. Absorption of a topical antibacterial agent may be evaluated against the absorption of a test solute in isolated preparation of the stratum corneum in a cell in an *in vitro* model. Despite the fact that adding silver sulfadiazine (AgSu) to pure deoxyribonucleic acid (DNA) resulted in the formation of silver sulfadiazine (AgSu) the formation of AgSu-DNA complexes, no such complexes were detected in bacteria treated with AgSu. In treated bacteria, AgSu inhibited macromolecular syntheses as DNA synthesis was slightly more sensitive. A tiny amount of sulfadiazine appears to be active in this situation. Pediatric patients were randomly assigned to treatment with either Silva-Sorb® Gel or Silvadene® silver sulfadiazine cream for up to 21 days or to the point of full reepithelialization of the wound.

**Keyword:** Silver, Sulfadiazine, Silvasorb, Bacteria, Burn, Wound.

### INTRODUCTION:

Silver sulfadiazine is an antibacterial medicinal drug this is extensively used to reduce bacterial infections and external contamination. Topical antibiotics are critical in the remedy of burns. Silver sulfadiazine is the maximum famous topical remedy for bacterial infections in second-degree burns. For bacterial infections in second-degree burns, silver sulfadiazine is the maximum common topical remedy. Silver sulfadiazine binds to DNA and damages mobileular membranes. Three deprotonated sulfadiazine molecules encircle a tetra-coordinated silver ion. In 1965, Moyer brought 0.5% silver nitrate (AgNO<sub>3</sub>) burn wound dressings, ushering within the modern generation of burn remedy.<sup>1</sup> In 1968, 1% silver sulfadiazine cream changed into brought as an alternative for those dressings. Avoiding agent-caused electrolyte difficulties, bacterial conversion of nitrate to nitrite, and environmental discoloration are only some of the advantages of AgNO<sub>3</sub> as opposed to AgNO<sub>3</sub>. Regardless, AgNO<sub>3</sub> is an vital a part of burn wound remedy. Silver sulfadiazine is a free chemical aggregate of silver and sulfadiazine that dissociates unexpectedly while it comes into touch with a burn injury. The dissociated silver atom is maximum in all likelihood transported as a silver proteinate via the circulatory system.<sup>2</sup> Topical antiseptic/antibiotic pills are critical in stopping burn wound contamination and, as a end result, burn sepsis in those patients. Topical silver sulfadiazine is a common antibacterial burns prophylaxis remedy. The drug is famous for its tolerability and safety. Burn dressings are usually made from topical silver sulfadiazine and

satisfactory mesh gauze and may be utilized in each inpatient and outpatient settings. It is extensively to be had and inexpensive, making it a famous opportunity for stopping contamination in burn victims. Burns and wounds are often handled with antimicrobial creams containing silver sulfadiazine.<sup>3</sup> It reveals broad-spectrum efficacy in opposition to Gram-bad and Gram-fine micro-organism whilst being quite secure for human cells.<sup>4-5</sup> A twice-each day use of this remedy is commonly required, with a secondary dressing carried out on top (gauze pad).<sup>3-6</sup> As a end result of the low adhesion and inefficient drug penetration within the skin, traditional formulations are simplest utilized in confined circumstances, mainly for long-time period wound remedy, ensuing in low affected person compliance.<sup>7</sup>



Chemical Structure of Silver Sulfadiazine<sup>8</sup>

## INDICATION:

Medical professionals recommend using it once or twice daily, with reapplication as needed, to prevent wound-sepsis in the treatment of burns. Topical antibacterial prophylaxis aims to control microbe colonization in the wound and prevent the development of wound-sepsis while minimizing systemic absorption. Because of its low cost, ease of use, and tolerability, silver sulfadiazine is the most commonly used topical antibiotic medication in burn patients.<sup>9</sup>

## SYSTEMATIC SILVER ABSORPTION:

During the initial healing phase, inflammatory cell infiltration decreases within a few days, whereas infected wounds have prolonged pro-inflammatory and lowered anti-inflammatory cytokine levels. Chronic inflammation reduces the mechanical stability of the provisional matrix, preventing the formation of new blood vessels.<sup>10</sup> The shift from an inflammatory to a proliferative state, as well as the creation of granulation tissue, is delayed greatly.<sup>11</sup> Antibiotic treatment for infected burn wounds, on the other hand, is primarily focused on limiting bacterial colonization while having minimal impact on the healing process. As a result, therapeutic intervention to control infection while also improving the progress of organized healing phases would be a step forward from current strategies. In order to prevent burn wound infection, choosing a carrier system for on-site delivery of an antimicrobial drug at a desired rate of release is crucial. SSD is a popular, FDA-approved topical agent for preventing bacterial colonization in burn wounds. His synergistic approach would improve outcomes from burned patients, accelerating wound healing while preventing fungal infections. His synergistic strategy would enhance burn patient outcomes by speeding up wound healing and reducing fungal infections. The proposed dressing, as stated, can be considered a bioactive dressing. In addition to a medication delivery system, antibacterial agent, and/or growth factor, these dressings are built from biomaterials that play an active part in the wound healing process.<sup>12-13</sup>

## SENSITIVITY TO SILVER:

Silver sulfadiazine-loaded halloysite possesses a negative surface charge in water because of the Si-O-Si group's existence at the nanotube's outer surface.<sup>15</sup> On the interior and outside sides of the tubes, halloysite is made up of various chemical compositions. On the inner (lumen) surface, aluminium and silicon oxides exhibit differing ionisation characteristics and surface charges, as indicated by their colloids' zeta potentials in water.<sup>14</sup> In the case of a 3-year-old Caucasian kid with extensive and superficial cutaneous scald burns totaling 52 percent TBSA on various portions of her body, which were treated with alternating administrations of 5 percent mafenide acetate (MA) solution and AgSD. On postburn day 13, she was administered cefixime, gentamycin, and amphotericin B to prevent the colonization of her burn sites by *Pseudomonas aeruginosa*, *Escherichia coli*, and *Candida tropicalis*. At this point, the majority of the wounds were thought to be in advanced stages of healing. Dark patches were found on the back's deep dermal wound surfaces, indicating an extensive wound infection. There had been no change in vital signs or routine blood tests. As a result, a radical wound excision for invasive sepsis was decided to be postponed pending the results of an urgent workup. Fraser-Moodie discovered a chemical sensitivity to the silver component of AgSD used in burn treatment after a partial-thickness burn of a female patient's right arm caused by a spill of hot cooking fat failed to heal normally while being treated with AgSD dressings.<sup>16</sup> The burned area was red, painful, and weeping after two weeks. After that, the inflammation lasted for more than ten days. After the area was exposed, it began to

heal. When the patient came into contact with metal objects, especially silver and gold, he developed itching and redness. She reacted strongly to AgNO<sub>3</sub> and cetyl alcohol (a component of AgSD cream) in a battery of skin tests, but not at all to the application of a sulfonamide.

## ADVERSE EFFECTS RELATED TO SULFADIAZINE:

Toxicity from the sulfadiazine moiety of AgSD may occur in the burn victim: allergy Methemoglobinemia<sup>17</sup>, immune complex formation<sup>18</sup>, and hemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficiency<sup>18</sup>. An allergic reaction to the sulfadiazine component of AgSD was suspected to be the cause of a nephrotic syndrome in a patient who had a 78 percent TBSA chemical burn injury.<sup>15</sup> There was no previous record of kidney disease. A 16-day pause from a 55-day regimen of AgSD treatments was used for skin grafting. After that, the agent was restarted. Eosinophilia, proteinuria, hematuria, hyaline casts, decreased creatinine clearance, and uremia were the results.<sup>16</sup> An allergic reaction was thought to be caused by an AgSD "rechallenge," which involved stopping and then restarting the sulfadiazine moiety. An electronic microscopic examination of a percutaneous renal biopsy revealed thickening of the glomerular basement membrane. The burns healed, but restoring kidney function needed 9 months of prednisone and cyclophosphamide treatment.

## TOPICAL USE OF SILVER SULFADIAZINE AND ANTIBIOTICS:

Numerous systemic antimicrobials have been developed and used effectively whereas topical antimicrobials are few in number. Since resistant mutants frequently emerge after topical application, use of highly effective, broad spectrum antibiotics has been limited exclusively to systemic use. Silver sulfadiazine (AgSD). Cellulose can be employed in wound dressing compositions because of its ease of extraction, biodegradability, high biocompatibility, and lack of toxicity.<sup>24</sup> Ethyl cellulose (EC), carboxymethyl cellulose<sup>23</sup> (CMC), and hydroxypropylcellulose (HPC) are some of the derivatives of cellulose. Recent research has suggested that combining ethylcellulose with other polymers is an effective way to overcome the innate hydrophilicity of collagen-based fibres, interpreting improved disadvantages as a result of the helpful features of safety, electrospinability, and hydrophobicity. It is one of the most successful developments in topical burn care's long history. Physically, AgSD differs from other silver compounds in that it is stable in powder and ointment form. AgSD does not react quickly with chloride, sulfhydryl groups, or protein, unlike silver nitrate. As a result, its antibacterial activity in the wound is unaffected. Furthermore, unlike sulfonamides, AgSD's action is not inhibited by PABA, a folic acid component, in a competitive manner.<sup>25-26</sup>

AgSD reacted quickly with DNA in vitro, according to more studies. Furthermore, bacteria exposed to radioactive AgSD acquired radioactive silver in proportion to the amount of DNA they contained. When *Pseudomonas aeruginosa* was grown in silver sulfadiazine-containing media and then separated into protein, RNA, and DNA fractions, the DNA fraction had the highest silver uptake. When sulfur-labeled AgSD was used in the growth media, however, no labelled sulfur was detected in the DNA fraction or in the entire bacteria.<sup>25</sup> These findings suggest that silver sulfadiazine's main mechanism of action is at the DNA level

The ability of silver atoms to avoid many phosphate groups in DNA is an often ignored property of this silver binding. The atoms obtain their perch in place of some of the hydrogen bonds connecting the two strands of the double helix. Because the Si-O-Si group exists at the nanotube's outer surface, silver

sulfadiazine-loaded halloysite has a negative surface charge in water.<sup>27</sup> This unexpected reaction appears to be facilitated by the polymeric structure of AgSD.

In wound treatment it is probable that SSD functions by delivering sustained, low concentrations of silver (approximately 1–2 ppm) into the wound environment, and that this interferes with, or modulates, multiple cellular processes.<sup>19</sup>

Trevors (1987) reviewed the possible cellular effects of silver toxicity.

These include:

- a) Silver binds to base pairs in DNA and hence prevents transcription.
- b) Interfering with bacterial respiration and uncoupling ATP synthesis through binding to cell surface components.
- c) Phosphate absorption is inhibited, and components are released (such as glutamine, proline, succinate and phosphate from *Escherichia coli*).

Gupta et al. investigated the influence of halides, such as chloride, on susceptibility to silver in two *E. coli* strains (1998). In vitro research indicated that high chloride concentrations increased the susceptibility of both a silver sensitive and a silver resistant strain to silver, whereas low chloride concentrations revealed differences in the strains' sensitivity.<sup>24</sup>

Silver has been shown to have antibacterial properties as well as good effects on wound healing (Lansdown et al, 1997; Demling and DeSanti, 2001; Kirsner et al, 2002). These are centred on theoretical mechanisms that include:

- Zinc removal from metallothioneines<sup>21</sup>
- Changes in wound metalloprotein levels<sup>22</sup>
- Inflammatory cytokines are influenced. To validate and explain these pathways, more research is needed<sup>23</sup>.

## KEY POINTS <sup>19</sup>

Silver sulfadiazine is a combination of two antibacterial agents: silver and the antibiotic sulfonamide.

SSD is best utilised in topical application; the majority of data is based on the cream; nonetheless, it is increasingly being used to coat medical equipment such as catheters and endotracheal tubes to prevent bacterial development.

SSD has a long history of therapeutic success, particularly in the treatment of burns.

Many of the findings from SSD have been used to justify the use of silver as a topical antibacterial.

## SOLUBILITY:

Equilibrating the chemical in doubly distilled water at 25°C and measuring the saturated solution sulfadiazine by UV spectrometry and silver by atomic absorption spectroscopy<sup>25</sup> were used to evaluate the solubility of silver sulfadiazine. Nesbitt and Sandmann<sup>26</sup> used a silver-ion selective electrode to determine the equilibrated solution for silver. Their measurements were conducted at 25°C in nitric acid. Potassium nitrate buffers and 0.1 ionic strength (pH 2- 3). The data is summarised in Table 1.

Table 1:

Solvent	Solubility (mg/ 100ml)	pH
water	0.34	6.8
water	0.2	—
water, $\mu$ : 0.1	20	2.13
water, $\mu$ : 0.1	2.3	3.85
water*	0.19	6
water*	0.11	7
dimethyl sulfoxide	>35	
10% w/v NH <sub>3</sub> solution	>2.10 <sup>3</sup>	
25% w/v NH <sub>3</sub> solution	>5.10 <sup>3</sup>	

\*calculated

As can be seen from the data, the solubility of silver sulfadiazine increases with the decrease of pH. A solubility of 0.34 mg/ 100 ml corresponds with a 1.10 M solution.

## IDENTIFICATION TESTS:

The detection of the silver ion and the sulfadiazine moiety is used to identify silver sulfadiazine.<sup>26</sup>

### Silver:

The compound is dissolved in a 35 percent ammonia solution or diluted nitric acid solution. When you add hydrochloric acid, you get a curdled, white precipitate. The precipitate dissolves when a 10% ammonia solution is applied to it.<sup>26</sup>

### Sulfadiazine:

The identification can be based on the following tests:

- a) The compound is (partially) dissolved in dilute hydrochloric acid for detection of the main aromatic amine group. An alkaline solution was added after a two-minute soak in a ten percent sodium nitrite solution. An orange or red colour is created in a 5% 2-naphthol solution.<sup>26</sup>
- b) The molecule is suspended in a 5 percent resorcinol solution in % ethanol for detection of the 2-aminopyrimidine moiety. When 95 % sulphuric acid is added, a deep red colour is formed.<sup>23</sup>

## STABILITY:

When silver sulfadiazine is exposed to light, it becomes somewhat yellow within one day and stays that way for at least two years. There were no subsidiary spots or variations in silver or sulfadiazine concentration identified during TLC separation. The chemical remains unaltered after four years at 20°C in the dark.<sup>32</sup>

## ADVERSE REACTIONS AND PRECAUTIONS:

Sulfadiazine (silver) is well tolerated. Application is generally painless, and the preparation does not cause electrolyte disturbances even after prolonged contact with the burned area. In the clinical trials to date, about 2.5% of patients experienced local reactions such as rash, pruritus, or a burning sensation. It is not known whether there is cross sensitivity between silver sulfadiazine and other sulfonamides. In any case, whether or not to continue medication in the face of allergic responses is a clinical choice. Serum sulfadiazine levels may approach those seen after systemic therapy in adults after extended treatment of serious burns. As a result, any of the side effects associated with systemic sulfonamide

formulations might occur. Because of the risk of kernicterus after sulfonamide therapy, topical treatment is not recommended for premature neonates or neonates. No need to monitor serum sulfonamide levels during prolonged therapy, except possibly in patients with renal and hepatic impairment. Adequate fluid intake is recommended, although there is no evidence to date of crystalluria. There is a paucity of information on the use of silver sulfadiazine during pregnancy, as with other new medicines. The medicine should most likely be withheld in the badly burnt pregnant lady on theoretical grounds. However, given the risks of sepsis, the choice to take the medicine during pregnancy is left to the discretion of the doctor. Collagen is one of the useful biomaterials available that is the plentiful extracellular matrix protein in the human body.<sup>33-34</sup>

### SilvaSorb® Gel in Comparison to Silvadene® Silver Sulfadiazine Cream:

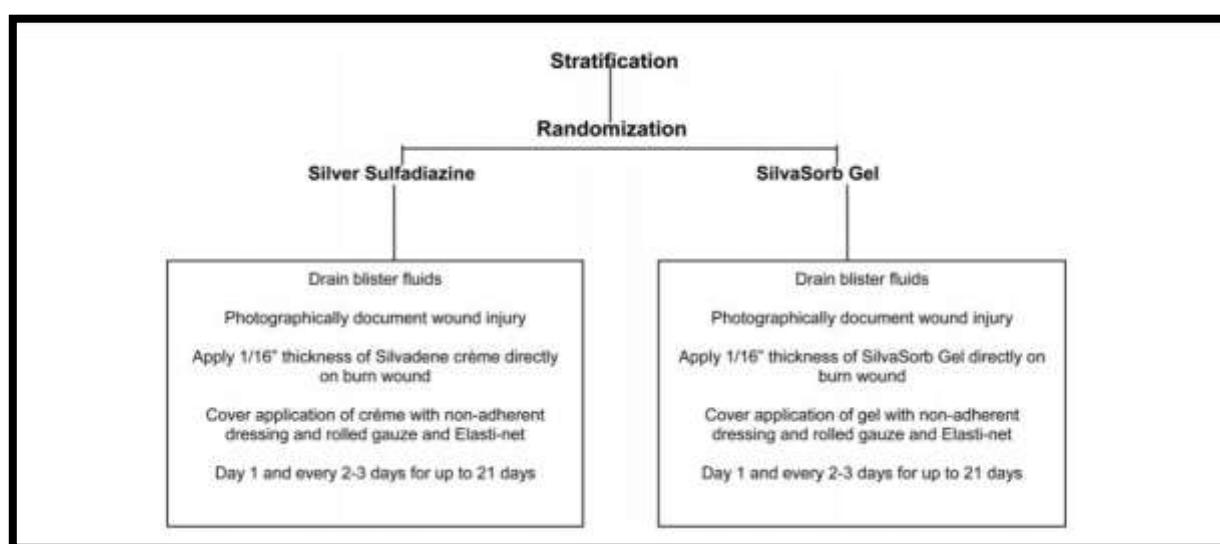
Because of their potential to lower the incidence of wound sepsis, topical antimicrobials have become the standard treatment in the treatment of burn wounds. Silver sulfadiazine (SSD) cream is the gold standard in the treatment of burns due to its relative simplicity of administration, broad effectiveness profile, and availability in most hospital formularies. SSD cream is a water-soluble, soft, white topical that contains 10 mg of antibacterial silver (silver sulfadiazine). SSD includes white isopropyl myristate petrolatum, sorbitan monooleate, sterols, polyoxyl 40 stearate, propylene glycol, and water, in addition to the active antibacterial. SSD cream is a wonderful solution for partial-thickness wounds since it allows them to recover without the need for surgery or skin grafting. The reported side effects of SSD topical therapies, which include allergic responses or sensitivity, frequent and painful dressing changes, delayed healing, and staining/discoloration of the wound bed, complicate wound evaluation and depth estimation, offset the benefits of SSD topical treatments.

Advances in burn management have greatly improved survivability from severe burn injuries, with new wound care products focusing on effective moisture management of infection and better healing, while addressing current treatments' limits and/or negative effects. Newer topical therapies, such as Medline Industries' SilvaSorb® Gel, have been developed to address the potential negative effects of SSD while preserving quick healing, enhancing ease of

administration, reducing bioburden, and improving patient comfort. Burns are difficult and dynamic injuries with a high risk of morbidity and death for patients, as well as considerable complications for families and health-care providers.<sup>36-37</sup> They are characterized as "ultimate inflammatory injuries" and "the most horrific afflictions" on the human body. Because the product lasts three days, no need to replace the dressing each day. The hydrogel is clear, non-irritating, non-sensitizing, and great at managing fluids. In addition, the product's fluid management and wound healing characteristics have been established in vitro, as well as the ability to control wound bioburden without being toxic to host cells such as fibroblasts and keratinocytes.<sup>38</sup> However, SilvaSorb Gel has no longer been significantly studied in a scientific burn setting. As a result, this study was designed to compare SilvaSorb® Gel to the standard of care topical burn treatment, SSD, in the treatment of partial-thickness burn wounds in pediatric patients.

### METHODS:

Patients with superficial and mid-dermal burn wounds who presented to our unit were considered eligible if they were at least 2 months old and not older than 18 years old, and their burn injuries occurred within 36 hours of enrollment. The burn size had to be between 1% and 40% of TBSA, and the patients or their parents could consent to both research participation and therapy until their wounds were completely healed. The trial was supposed to last 21 days, but all of the patients were monitored until they were completely healed. Burn wounds associated with either electrical or chemical injury, deep or full-thickness burns, the subject's prognosis was unlikely for survival beyond the study's duration, the patient's burn site had been previously treated with an antimicrobial agent or enzymatic debriding, the patient had been previously entered into a similar study, or the patient was pregnant were all major exclusions. The progression of burn injuries with an increase in burn depth necessitating wound closure or surgical intervention was a criterion for participants to be removed from the research. Without blinding the physician investigator or any medical workers to the kind of treatment, patients were randomly assigned to a plan of care that included either SSD cream or SilvaSorb Gel. The treatment procedure for each research arm is summarised in Figure 1.<sup>39</sup>



**Figure 1:** Treatment Protocol—SilvaSorb gel vs silver sulfadiazine (SSD). Each product was used in a similar fashion with daily dressing changes until complete reepithelialization was observed.<sup>39</sup>

Patients underwent an initial evaluation that included a medical history, subject demographics, and a baseline assessment of burn damage as part of the research approach. It was planned to keep changing the dressings until the incision was totally healed. Subjects were advised to go to the hospital each to a few days for an evaluation and to finish the necessary dressing change paperwork. Outpatients and/or their guardians were provided the ability to change their own dressings and were given standard burn centre practices instructions as well as advice on how to apply topical

On the wound evaluation, dressing change, and home dressing change forms, as well as in the CRF, the first therapies and each dressing change were reported. During the first treatment and subsequent alterations, details on the therapy application, the status of the burn, the numbers of dressing

changes between assessments, and any adverse findings or occurrences were all recorded. Evaluations, and any adverse findings or occurrences were all noted during the initial treatment and subsequent alterations. The following were some of the study's endpoints that were recorded:

- Reepithelialization will require considerable time to complete.
- Pain during dressing changes as judged by an age-specific pain rating scale shortly after the first postdebridement dressing change
- Number of dressing changes
- Patient satisfaction as measured by a parental or patient questionnaire.

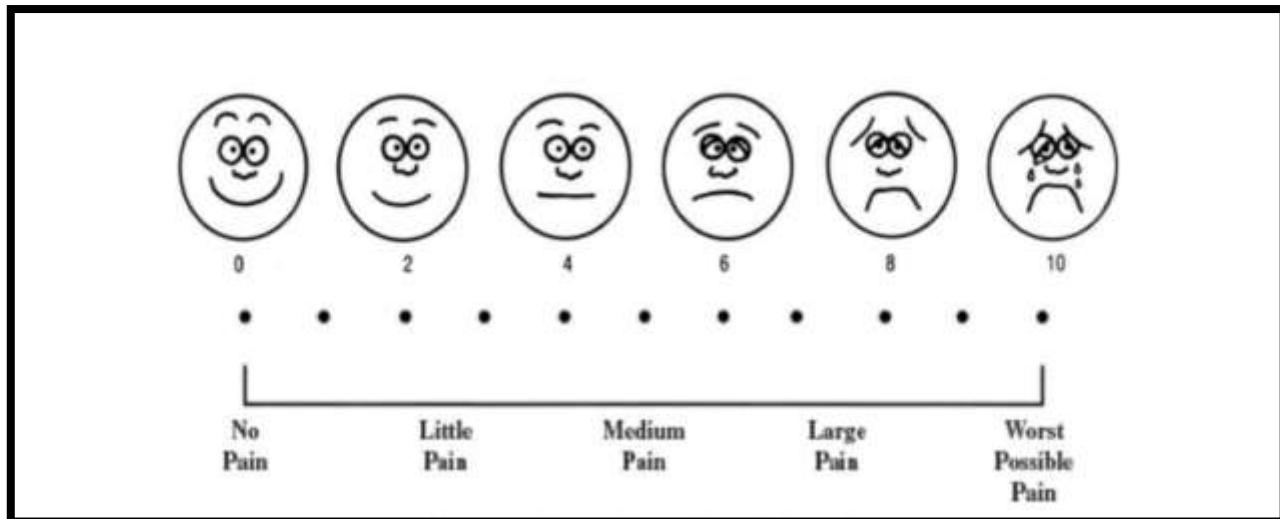


Figure 2: Wong/Baker Faces Pain Scale <sup>39</sup>

The distribution of continuous data, which comprised frequency histograms for continuous variables, was analysed using a descriptive statistical analysis for each of the treatment groups. Transformations were employed to standardise data for statistical analysis in nonnormal distributions. Statistical significance was defined as a two-sided P-value with 90% confidence intervals. For all research outcomes, a P-value of 0.05 or below was considered significant. Blackwelder's approach of assessing equivalence was used to determine if the treatment groups were substantially equivalent in terms of wound infection. The chi-square test was used to determine the proportion of patients who were completely re-epithelialized within 21 days, with an exact test utilised if expected frequencies were low. Comparing the percentage of reepithelialization at 21 days was done with a t-test or Wilcoxon's rank sum test, and the time to full reepithelialization was done with Kaplan-Meier estimates and a log-rank test. The Wilcoxon method was used to calculate the number of dressing changes.

## RESULTS:

The experiment included a total of 24 children who were randomly assigned to one of two treatment protocols: SSD cream (n=12) or Silvasorb gel (n=12). With the exception of patient age, the baseline characteristics were identical in the treatment and control arms of the experiment. Overall, patients in the Silvadene arm were 22.78 months old on average, with a standard deviation of 13.51 months, compared

to 43.00 months old on average, with a standard deviation of 29.10 months in the Silvasorb arm, a significant difference (P=0.0291). Patients in the SSD therapy arm ranged in age from 13 months to 5 years, while those in the Silvasorb treatment arm ranged in age from 9 months to 9 years. In both research arms, the TBSA for wound injury location was similar, ranging from 1 to 10%. An age-specific pain rating scale was used to obtain overall pain ratings. The patients were asked to rate their pain on a scale of 1 to 10 or, in the case of older children, on the Wong-Baker Pain Scale (Figure 2).

Table 2: Pain Rating <sup>39</sup>

Treatment	Mean	Median	SD
SilvaSorb (n = 12)	2.33	2.00	1.07
Silver sulfadiazine (n = 12)	5.33	5.00	1.44
Total (n = 24)	3.83	4.00	1.97

t(22) = -5.80; P = .0001.

The observational pain assessment scale was used to assess pain in newborns and toddlers. The Silvasorb Gel group had considerably lower pain ratings than the SSD group (Table 2), and the difference was statistically significant (2.33 vs 5.33, P 0.0001). In addition, when compared to the same range in the SSD group, proportionately more patients (50 percent) in the Silvasorb cohort experienced reduced pain as measured by a

rating between 1 and 4. (17 percent). Despite the fact that there are no conclusive standard measures for assessing infantile or toddler pain, the two scales employed in this study have been extensively utilised in prior burn studies.<sup>40</sup>

**Table 3: Number of Dressing Changes<sup>39</sup>**

Treatment	Mean	Median	SD
SilvaSorb (n = 12)	13.50	13.00	4.70
Silver sulfadiazine (n = 12)	13.42	10.00	8.26
Total (n = 24)	13.46	11.50	6.57

S = 165.50; P = .383.

Dressing changes were noted throughout the course of treatment, whether inpatient or outpatient. Wound assessment, dressing change (inpatient treatment), and home (outpatient) dressing change forms were all included in the CRF. The frequency of dressing changes varied slightly by treatment arm, but there were almost no differences in the frequency of dressing changes varied significantly by treatment arm, but the overall number of dressings applied was nearly same, as evidenced by the nonstatistically significant P-value of 0.449.(Table 3)

#### MECHANISM OF ACTION:

Silver nitrate is combined with sulfadiazine to produce this compound. Each product's mode of action is the same as the others. Paminobenzoic acid has no impact on antibacterial action, mobileular walls, or folic acid synthesis, and silver salts are launched slowly and have only a bactericidal impact on bacterial membranes (PABA). When tissues and body fluids are exposed to sodium chloride, sulfadiazine is released slowly and can be absorbed systemically from the application site.<sup>41</sup>

#### USES:

This medication is used with other treatments to help prevent and treat wound infections in patients with severe burns. Silver sulfadiazine works by stopping the growth of bacteria that can cause open wound infections. This helps reduce the risk of the bacteria spreading to the surrounding skin or blood, where a serious blood infection (sepsis) can be caused. Silver sulfadiazine belongs to a group of medicines called sulfonamide antibiotics. Silver sulfadiazine should not be used on premature infants or infants during the first 2 months of life due to the risk of serious side effects.<sup>42</sup>

#### DISCUSSION:

In wound healing, silver sulfadiazine is a commonly utilised antibacterial agent. However, only a few research have focused on SSD-containing wound dressings. Topical antimicrobials are still the gold standard in the treatment of partial-thickness burn wounds due to their ability to reduce the risk of wound infections. In the treatment of burns, SSD cream has long been the gold standard. Topical antimicrobials remain the standard of care in the treatment of partial-thickness burn wounds and lower the incidence of wound sepsis due to their capacity to reduce wound sepsis.<sup>35</sup> However, when compared to the study drug, SilvaSorb Gel, the use of SSD was linked to much more pain and patient discomfort in this study. As a result, using SilvaSorb Gel resulted in a higher patient satisfaction rating. The unique polymer microlattice composition of SilvaSorb, which gives more moisture to the wound while reducing exudate, likely to blame for the comfort and satisfaction profile.<sup>37</sup> In addition, the formation of pseudoeschar with the use of SSD could explain why there is more discomfort when the pseudoeschar is removed during dressing changes. The contact permits the silver component to move around and diffuse to the wound

site. In a previous study, the release of ionic silver from the reservoir was recorded at 1.5 parts per million. SilvaSorb gel maintains a high level of ionic silver, which is effective against a wide spectrum of germs while causing minimal harm to healthy tissues in and around the wound site.<sup>38-39</sup> When SilvaSorb Gel is administered as directed every three days, it saves money because less staff is required for dressing changes. This is despite the SilvaSorb Gel's somewhat higher product cost when compared to SSD. However, no adverse events (including infections) were reported in this study, and no significant differences in reepithelialization were discovered. As a result, for these two factors, the two groups were found to be equivalent. To show substantial differences in these areas, a larger research size would be required.

Silver sulfadiazine is a common antimicrobial topical ointment that has several advantages, including ease of use. It has antibacterial properties and does not cause pain during administration. It also has low toxicity and sensitivity. These characteristics, it has become the gold standard among antimicrobial topical medications for burn patients and the most extensively used medicine in the world for the treatment of burn wounds.<sup>42</sup> Large number of treatment options for topicals treating burns, making it difficult for medical professionals to make decisions about the best procedure to adopt. In second and third degree lesions, SSD remains the most frequently used drug due to low cost and high availability. However, even though its consolidated usage, we lack evidence of SSD's effectiveness compared with other new materials in preventing infection and helps re-epithelialize the wound<sup>43</sup> In general, all of the clinical trials compared SSD to another product (20 in total), resulting in a wide range of tested materials and making it difficult to compare the As a result, we divided these treatments into two large groups of dressings: with and without silver<sup>44</sup>, comparing the outcomes of re-epithelialization and infection rate in these groups to the outcomes obtained with SSD.

#### CONCLUSION:

SilvaSorb Gel was found to be safe and effective in the treatment of partial thickness burns, with much less pain and improved patient satisfaction. Although the difference in mean time to reepithelialization between groups was not substantially different (P=0.949), more patients in the SilvaSorb Gel study group reached reepithelialization during the 21-day trial length than those in the Silvadene treatment group. All patients in the SilvaSorb Gel group achieved full reepithelialization before the study's intended 21-day endpoint, but two patients in the Silvadene arm did so at 26 and 28 days, respectively. There were no variations in the number of dressings used. Despite the fact that there were no significant differences in infection rates between the two trial groups, the results suggested that Silvasorb Gel was equivalent to the standard of care in this regard.

Since its first appearance as a cream formulation for topical use some thirty years ago, SSD has become a very valuable antimicrobial agent, especially in burns therapy. It has, through widespread clinical usage, been proven to be remarkably safe with relatively low resistance potential. The advent of a new generation of silver-containing dressings and of SSD impregnation of medical devices has served to confirm the clinical utility of silver and of SSD in modern medicine.

#### ACKNOWLEDGEMENT

I am very thankful to the principal, Shivalik College of pharmacy, Nangal, Punjab and also my guide D.N Prasad for their valuable guidance. I am also thankful to my colleagues for their time-to-time support.

## REFERENCES:

1. Mater BJ. Silver-and Sulfadiazine-loaded nanostructured silica materials as potential replacement of silver sulfadiazine. *Journal of materials chemistry*. 2014; 2:6283. <https://doi.org/10.1039/C4TB00619D>
2. Herndon DN, Hawkins HK, Lee JO, Cox, RA, Kulp, GA, Finnerty CC, Chinkes DL, Jeschke MG, Williams FN. The leading causes of death after burn after injury in a single pediatric burn center. *Critical Care (London, England)*. 2009; 13(6) <https://doi.org/10.1186/cc8170>
3. Atiyeh BS, Costagliola M, Hayek SN, et al. Effect of silver on burn wound infection control and healing. Review of the literature. *Burns* 2007; 33:139-148. <https://doi.org/10.1016/j.burns.2006.06.010>
4. Abdullah ZW, Dong Y, Han N, et al. Water and gas barrier properties of polyvinyl alcohol (PVA)/starch (ST)/glycerol (GL)/halloysite nanotube (HNT) bionanocomposite films. Experimental characterisation and modelling *Compos Part B: Eng* 2019; 174:107033. <https://doi.org/10.1016/j.compositesb.2019.107033>
5. Nejaddehbashi F, Hashemitabar M, Bayati V, et al. Incorporation of silver sulfadiazine into an electrospun composite of polycaprolactone as an antibacterial scaffold for wound healing in rats. *Cell J* 2020; 21:379-390.
6. Stavitskaya A, Batasheva S, Vinokurov V, et al. Antimicrobial applications of clay nanotube-based composites. *Nanomaterials* 2019; 9:708-720. <https://doi.org/10.3390/nano9050708>
7. Vincenzo B, Riccio F, Klosowski AB, et al. Chitosan/nanocellulose-based bionanocomposite films for controlled betamethasone and silver sulfadiazine delivery. *J Appl Polym Sci* 2021.
8. Graziela Louize Polcarpino da Silva, Juliana Bonametti Olivato, Juliano Marini, Priscileila Colerato Ferrari. Antimicrobial dressing of silver sulfadiazine-loaded halloysite/cassava starch-based (bio)nanocomposites. *Journal of Biomaterials Applications*. 2021; 35(9):1096-11086. <https://doi.org/10.1177/0885328221995920>
9. Christie J, Liu Z, Westby MJ, Jefferies JM, Hudson T, Edwards J, Mohapatra DP, Hassan IA, Dumville JC, Normal G. Antiseptics for burns. The Cochrane database of systematic review. 2017; 7:31-32.
10. Zhang H, Peng M, et al. Silver nanoparticles-doped collagen-alginate antimicrobial biocomposite as potential wound dressing. *Journal of materials science*. 2018; 53(21):14944-14952. <https://doi.org/10.1007/s10853-018-2710-9>
11. Hebeish A, et al. Antimicrobial wound dressing and anti-inflammatory efficacy of silver nanoparticles. *International journal of biological macromolecules*. 2014; 65:509-515. <https://doi.org/10.1016/j.ijbiomac.2014.01.071>
12. Saghazadeh S, Rinoldi C, Schot M, Kashaf S,S, Sharifi F, Yue K, Khademhosseini A. Drug delivery systems and materials for wound healing applications. *Adv Drug Deliv Rev*. 2018; 127:138-166. <https://doi.org/10.1016/j.addr.2018.04.008>
13. Shah S.A, Sohail M, Khan S, Minhas M.U, Matas M.D, Kousar M. Biopolymer-based biomaterials for accelerated diabetic wound healing. A critical review. *Int J Biol Macromol*. 2019; 139:975-993. <https://doi.org/10.1016/j.ijbiomac.2019.08.007>
14. Lvov Y and Abdullayev E. Functional polymer-clay nanotube composites with sustained release of chemical agents. *Prog Polym Sci* 2013; 38:1690-1719. <https://doi.org/10.1016/j.progpolymsci.2013.05.009>
15. Malakinezhad H, Kalaee M, Abdouss M, et al. Fabrication and characterization of biodegradable Ph Responsive halloysite poly(lactic-co-glycolic acid)micro-sphere for controlled released of phenytoin sodium. *J Inorg Organomet Polym Mater*. 2020; 30:722-730. <https://doi.org/10.1007/s10904-019-01263-4>
16. Arroyo AG, Iruela-Arispe ML (2010) Extracellular matrix, inflammation, and the angiogenic response. *Cardiovascular Research*. 2010; 86:226-235. <https://doi.org/10.1093/cvr/cvq049>
17. Eldad A, Ickeson M, Zur T, et al. Silver-sulphadiazine eschar pigmentationa mimics invasive wound infection. *J Burn Care Rehabil*. 2003; 24:154-7. <https://doi.org/10.1097/01.BCR.0000069440.78932.70>
18. Tsai TC, Peng SK, Shih YR, Luk HN. Sulfadiazine-induced methemoglobinemia in a boy with thalassemia. *Can J Anesth*. 2005; 52:1002-3. <https://doi.org/10.1007/BF03022075>
19. Starodub ME, Trevors JT. Silver accumulation and resistance in *E. coli*. *J Inorganic Biochem*. 1990; 39(4):3017-25. [https://doi.org/10.1016/0162-0134\(90\)80030-2](https://doi.org/10.1016/0162-0134(90)80030-2)
20. Gupta A, Maynes M, Silver S. Effects of halides on plasmid-mediated silver resistance in *Escherichia coli*. *Appl Environ Microbiol*. 1998; 64(12):5042-45. <https://doi.org/10.1128/AEM.64.12.5042-5045.1998>
21. Lansdown A B G, Sampson B, et al. Silver aids healing in the sterile skin wound: experimental studies in the laboratory rat. *Br J Dermatol*. 1997; 137:728-35. <https://doi.org/10.1111/j.1365-2133.1997.tb01109.x>
22. Demling RH, DeSanti L. The role of silver in wound healing. Part 1: Effects of Silver on Wound Management. *Wounds*. 2001; 13(1):A3-A15.
23. Kirsner RS, Orsted H, Wright JB (2002) Matrix metalloproteinases in normal and impaired wound healing. A potential role of nanocrystalline silver. *Wounds*. 2002; 13(3):C5-12.
24. Bult A, Klasen HB. *Archiv der Pharmazie* (Weinheim). 1980; 313:1016. <https://doi.org/10.1002/ardp.19803131208>
25. Nesbitt R.U, Sandmann BJ. *Journal of Pharmaceutical Sciences*. 1977; 66:519. <https://doi.org/10.1002/jps.2600660414>
26. Boelema GJ, Bult A, Metting HJ, Bajema BL, Doornbos DA. *Pharm Weekblad* Scientific edition. 1982; 4(38). <https://doi.org/10.1007/BF01963659>
27. Khan M.Q, Kharaghani D, Shahzad A, Saito Y, Yamamoto T, Ogasawara H, et al. Fabrication of antibacterial electrospun cellulose acetate/silver-sulfadiazine nanofibers composites for wound dressings applications. *Polym. Test*. 2019; 74:39-44. <https://doi.org/10.1016/j.polymertesting.2018.12.015>
28. Hangyi Lu, Wang Q, et al. Electrospun water-stable zein/ethyl cellulose composite nanofiber and its drug release properties. *Mater. Sci. Eng. C*. 2017; 74:86-93. <https://doi.org/10.1016/j.msec.2017.02.004>
29. Li H, Zhang Z, Godakanda V.U, Patel K, et al. The effect of collection substrate on electrospun ciprofloxacin-loaded poly(vinylpyrrolidone) and ethyl cellulose nanofibers as potential wound dressing materials. *Mater Biol Appl*. 2019 Nov; 104:109917. <https://doi.org/10.1016/j.msec.2019.109917>
30. Godakanda V.U, Li H, Alquezar L, Zhao L, et al. Tunable drug release from blend poly (vinyl pyrrolidone)-ethyl cellulose nanofibers. *Int. J. Pharm*. 2019; 562:172-179. <https://doi.org/10.1016/j.ijipharm.2019.03.035>
31. Malakinezhad H, Kalaee M, Abdouss M, et al. Fabrication and characterization of biodegradable pH Responsive halloysite poly(lactic-co-glycolic acid)micro-sphere for controlled released of phenytoin sodium. *J Inorg Organomet Polym Mater*. 2020; 30:722-730. <https://doi.org/10.1007/s10904-019-01263-4>
32. Starodub ME, Trevors JT. Silver accumulation and resistance in *E. coli*. *The Journal of Biochemistry*. 1990; 39(4):3017-25. [https://doi.org/10.1016/0162-0134\(90\)80030-2](https://doi.org/10.1016/0162-0134(90)80030-2)
33. Ali I.H, Khalil I.A, El-Sherbiny I.M. Collagen nanofiber containing silver nanoparticles for improved wound-healing applications. *ACS Appl. Mater. Interfaces*. 2016; 8:14453-14469. <https://doi.org/10.1021/acsami.6b04369>
34. Nezhad-Mokhtari P, Ghorbani M, Roshangar L, Soleimani Rad J. Chemical gelling of hydrogels-based biological macromolecules for tissue engineering: photo- and enzymatic-crosslinking methods. *Int. J. Biol. Macromol*. 2019; 139:760-772. <https://doi.org/10.1016/j.ijbiomac.2019.08.047>
35. Aghaei A, Soori H, Mehrabi Y, Ramezankhani A. Factors related to pediatric unintentional burns: the comparison of logistic

regression and data mining algorithms J Burn Care Res 2019; 40(5):606-612. <https://doi.org/10.1093/jbcr/irz066>

36. Hosseini SM, Fekrazad R, Malekzadeh H, Farzadinia P, Hajiani M. Evaluation and comparison of the effect of honey, milk, and combination of honey-milk on experimental induced second-degree burns of Rabbit. J Family Med Prim Care. 2020; 9(2):915-920. [https://doi.org/10.4103/jfmpc.jfmpc\\_801\\_19](https://doi.org/10.4103/jfmpc.jfmpc_801_19)

37. Aghaei A, Soori H, Mehrabi Y, Ramezankhani A. Factors related to pediatric unintentional burns: the comparison of logistic regression and data mining algorithms. J Inj Violence Res. 2019; 11(4 Suppl. 2):35.

38. Castellano JJ, Shafii SM, Ko F, et al. Comparative evaluation of silver-containing antimicrobial dressings and drugs. Int Wound J 2007; 4:114-22. <https://doi.org/10.1111/j.1742-481X.2007.00316.x>

39 31. Glat P.M, MD, Kubat W.D, Glat DO, et al. Randomized Clinical Study of SilvaSorb® Gel in Comparison to Silvadene® Silver Sulfadiazine Cream in the Management of Partial-Thickness Burns. Journal of Burn Care. 2009; Mar; 30(2):262-7. <https://doi.org/10.1097/BCR.0b013e318198a2e8>

40. Duhn LJ, Medves JM. A systematic integrative review of infant pain assessment tools. Adva Neonatal Care. 2004; 4:126-40. <https://doi.org/10.1016/j.adnc.2004.04.005>

41. Akbari H, Fatemi MJ, Iranpour M, et al. The healing effect of nettle extracts on second degree burn wounds. World J Plast Surg. 2015; 4:23-8.

42. Mohseni, M., et al., Antimicrobial wound dressing containing silver sulfadiazine with high biocompatibility: in vitro study. Artificial organs. 2016; 40(8):765-773. <https://doi.org/10.1111/aor.12682>

43. Shamloo A, Sarmadi M, et al, Accelerated full-thickness wound healing via sustained bFGF delivery based on a PVA/chitosan/gelatin hydrogel incorporating PCL microspheres. 2018; 537(1-2):278-289. <https://doi.org/10.1016/j.ijpharm.2017.12.045>

44. Rasha AA, Rasha EE and Galal HE: Design and synthesis of a new class of pyridine-based n-sulfonamides exhibiting antiviral, antimicrobial, and enzyme inhibition characteristics. CS Omega 2020; 5(18):10401-414