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Formulation and evaluation of Silver sulphadiazine loaded nanosponge based emulgel for topical delivery in wound healing

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ABSTRACT

Objective: The aim of present research work is formulation & evaluation of silver sulfadiazine nanosponges using emulsion solvent evaporation techniquefor topical delivery in wound healing. **Methods:** The optimised nanosponges were characterized by using zeta potential, particle size analysis, PDI analysis, and drug entrapment efficiency tests. The effectiveness of the gel was assessed using the partial thickness burn wound model in wistar albino rat. Burn wound model includesthe study of skin irritation, hydroxyproline concentration, histopathological analysis, and wound contraction.**Results:** Further, it was observed from the results zeta potential was -14.8 to -53.4, particle size range 132-782.4, and particle density 0.201 to 1.000. Three-day skin irritation research results show that gel I and II's wound contraction rates are 89.0% and 91.9%, respectively. Improved wound contraction, no skin irritation, low toxicity on dermal cell lines, and less application requirement were all displayed by the optimised gel**. Conclusion:** Formulated silver sulfadiazine nanosponges used in wound healing exhibits marked effect.

Keywords: Silver sulfadiazine, nanosponges, Burn, Wounds, Healing, Formulation

1. Introduction

The skin functions as a defensive shield, safeguarding the body from both deliberate and unintentional harm. Burn injuries are major contributors to both death and illness, and the treatment of burns often necessitates extended stays in the hospital and subsequent rehabilitation, resulting in higher healthcare expenses. Burn injuries result in poor wound healing and prolonged healing time owing to vascular blockage [(1)]. Topical administration of antibacterial drugs is necessary for burn wound care because vascular blockage prevents routinely given antibiotics from reaching the burnt region. Topical treatment enables the direct administration of the active component to the specific region of interest [(2)].

The primary objective of wound treatment is to efficiently avoid infection and facilitate the healing process. Topical use of antibacterial drugs is necessary to prevent infection, minimize the development of wound eschar, and facilitate the healing process of burn wounds. Partial thickness wounds primarily impact the epidermis and hypodermis, making them more vulnerable to infection [(3)]. Pseudomonas aeruginosa and Staphylococcus aureus are the predominant opportunistic bacteria often linked to burn wound infections. In addition, if a wound is not treated, it may slow down the healing process, promote the formation of scars, and perhaps lead to the presence of bacteria in the bloodstream, sepsis, or multiple-organ dysfunction syndrome. This condition occurs when organs from different systems in the body are unable to maintain their normal balance, necessitating urgent medical intervention [(4)].

Silver sulfadiazine (SSD) is often used as an antibacterial treatment to treat burn injuries locally. The SSD products now on the market are often offered as a cream with a concentration of 1% weight/weight. The current SSD commercial products possess many limitations. These factors encompass the swift delivery of the medication to specific regions, the requirement for frequent administration (usually two to four times per day), heightened inflammation due to the substances used in the product, harm to keratinocytes and fibroblasts, the development of false scabs, and the potential for heavy metal poisoning with prolonged usage [(5)]. The abrupt and quick release of SSD has increased the skin's vulnerability to sunlight, leading to blistering, peeling, or loosening of the skin, skin lesions, intense itching of burn wounds, skin rashes, allergic reactions, and cytotoxicity. These variables hinder the healing process [(6)]. Therefore, it is essential to use an alternative method to control the rate at which the medicine SSD is discharged and improve its effectiveness. Lately, there has been an increasing fascination in utilizing nanosponge-based gels to accomplish the precise and regulated dispensation of active pharmaceutical ingredients (APIs).

The nanosponge drug delivery system is an advanced method of delivering drugs that may function as a localized and time-delayed drug reservoir. Nanosponges are polymeric microspheres that have pores and typically range in diameter from 5 to 300 μm. Nanosponges are spherical particles that include several lacunae and have the ability to encapsulate a broad range of active pharmaceutical ingredients (APIs) [(7)]. At present, there is no product available for purchase that has a sustained release topical formulation of SSD. A recent article by Boateng et al. (2015) discussed the use of bio-polymeric wafers to give sustained amounts of SSD for treating infected chronic wounds. The findings confirmed the need of using a topical dosage form of SSD that provides prolonged release. Hence, the aim of this work was to develop a durable extended-release topical formulation of SSD by incorporating SSD into

nanosponges and dispersing the drug-loaded nanosponges into carbopol gel as a carrier. SSD is a highly ionizable drug. The formulator has a big hurdle while trying to incorporate an ionizable medicine into nanosponges using the w/o/w emulsion solvent evaporation technique. Thus far, only a restricted quantity of studies has shown the confinement of ionisable medicines inside nanosponges or microspheres [(8)]. If the drug undergoes ionization during the formulation process, it has a significant impact on the drug's entrapment, since a majority of the drug is released into the external aqueous phase. Therefore, it is necessary to develop a method to keep the medicine in its non-ionized condition throughout the formulation process and prevent it from seeping into the surrounding aqueous phase.

2. Materials and Methods

2.1. Materials

The sample of Silver sulfadiazine (SSD) was procured from SPA Corporation, Udaipur, Rajasthan, India. The Ethyl cellulose (EC) with a viscosity grade of 18-22 cps was procured from Hi-Media Laboratories Pvt. Ltd. in Mumbai, India. All remaining reagents were procured from Loba Chemie Pvt. Ltd., located in Mumbai, India. The commercially purchased substances were of analytical quality and utilised without any modifications.

2.2. Methods

2.2.1. Preparation of nanosponges

To generate a water-based phase, the user weighed out 400 mg of SSD accurately and combined it with a 0.1% w/v xanthan gum solution. A polymer solution was created by dissolving ethyl cellulose (400, 800, and 1200 mg) in a mixture of 25% ammonia and methanol, resulting in the formation of an organic phase. The aqueous phase was gradually added to the organic phase while continually spinning to form a primary water-in-oil emulsion. An aqueous solution was prepared by dissolving 1 gm of PVA in 100 ml of water, serving as the exterior phase. The PVA was dissolved by swirling it continuously at a temperature of 60°C to generate the solution. The pH of the external aqueous solution was altered by the addition of 1 N hydrochloric acid (HCl). The first emulsion was introduced into the outer aqueous phase, comprising a 1% weight/volume solution of polyvinyl alcohol (PVA) in water. The mixture was agitated continuously at a rate of 500 revolutions per minute to form a water-in-oil-in-water emulsion. Following a 2-hour stirring period, the mixture underwent filtration to isolate the nanosponges (NSPs). The NSPs underwent dehydration in a convection oven set at a temperature of 40 °C for a period of 12 hours.

2.2.2. Drug entrapment efficiency

A solution was made by dissolving 20 ml of drug-loaded ethyl cellulose nanosponge in a mixture of 2 ml of dichloromethane and methanol. Subsequently, 48 ml of a 0.05% v/v aqueous ammonia solution was introduced into the mixture. The liquid obtained was subjected to heating at a temperature range of 50-55°C for duration of 30 minutes. The final volume was adjusted to 50 ml by adding the same aqueous ammonia solution. An evident phase emerged after the chilling and filtration operation. The sample underwent analysis by spectrophotometer at a specific wavelength of 262 nm, utilizing a UV-1800 spectrophotometer manufactured by Shimadzu, a company based in Japan. Before doing the analysis, the sample was diluted accordingly using an aqueous ammonia solution. The drug content and drug entrapment efficiency of NSPs were assessed. The tests were repeated three

times and the findings were reported as the average value plus or minus the standard deviation. The drug entrapment efficiency was calculated

% Drug entrapment efficiency = Actual Drug Content in nanosponges / Theoretical Drug Content × 100

2.2.3. Measurement of particle size

The particle size distribution of SSD nanosponges was assessed using the laser diffraction technique, namely the Malvern Mastersizer or Mastersizer 2000 from Malvern Instruments in the UK. The dispersion used water as the medium, and the measurement of particle size distribution was conducted.

2.2.4. Preparation of nanosponges loaded gel

A 1%w/v Carbopol gel base was prepared by dispersing 1 gm of carbopol 934 in a solution containing 95 ml of water and 5 gm of glycerin. The mixture was thereafter allowed to rest overnight. The dispersed mixture was equilibrated to a pH of 7.0 using triethanolamine to establish a gel matrix. A dose of 40 mg of a medication equal to NSPs was ingested and evenly distributed inside a gel basis weighing 4 g, resulting in a gel containing 4 g of silver sulphadiazine NSPs [(9)].

2.2.5. Study of acute skin irritation

Skin irritation toxicity was conducted in New Zealand White (NZW) Rabbits. On back surface of New Zealand White (NZW) Rabbits, hairs were removed then optimized formulation was applied topically. This study was conducted as per the OECD guidelines for Acute Dermal Irritation in rabbits (OECD 404). Animals were observed once a day for 72 hours aftertopical application of the formulation.

2.2.6. Burn Wound Model

The Wistar albino rats were administered pentobarbitone (30mg/kg, ip) to induce anesthesia, after which the hair in the back area was removed. The shaved region was sterilized using 70% v/v isopropyl alcohol. A partial thickness burn wound was then formed by using a 100 g cylindrical stainless-steel rod with a diameter of about 300 mm^2. The rod had an insulated rubber handle and was used to inflict the burns. The rod was submerged in a flask containing water that was brought to its boiling point of 100°C. Prior to each application of the burn, the level of sedation was evaluated by conducting two consecutive toe-pinch tests on two separate limbs. The transfer of the rod from the boiling water to the skin was completed within a time frame of 3 seconds, with a margin of error of ±1 second, in order to minimize heat loss. The hot rod was pressed on the skin for duration of 10 seconds. The characteristics for healing burn wounds, namely the rate of wound contraction and the duration of epithelialization [(10, 11)].

2.2.7.1. Area of wound healing assessment

The evaluation of wound healing will be conducted based on the percentage of wound contraction and the duration of epithelization. The percentage of wound contraction will be determined by using the following formula, where the starting size of the wound is taken as 100%.

%wound contraction = (Initial wound area − Specific day wound area)/Initial day wound area × 100

2.2.7.2. Determination of Hydroxyproline

A quantity of about 250 mg of moist tissue was subjected to a drying process at a temperature of 50 degrees Celsius for duration of 24 hours. The object was measured and stored in test tubes with glass stoppers. 1 mL of 6N HCl was added to each tube holding 40 mg of the dried granulation tissue. The tubes were then placed in a boiling water bath for duration of 24 hours, with 12 hours allotted to each day over a span of two days, in order to facilitate hydrolysis. The hydrolysate was then cooled, and an excessive amount of acid was neutralized using a 10N solution of NaOH with phenolphthalein as an indicator. The neutral hydrolysate was diluted with distilled water to achieve a concentration of 20 mg/ml. The ultimate hydrolysate was used to determine the hydroxyproline content. 0.3 mL of hydrolysate, 2.5N NaOH, 0.01M CuSO4, and 6% H_2O_2 were added to each tube. The tubes were aggressively agitated and promptly put in a water bath at a temperature of 80 ˚C. After duration of 15 minutes, the tubes were extracted and then chilled for a period of 5 minutes in cold water. 0.6 ml of a recently made 5% solution of Para dimethyl amino-benzaldehyde in n-Propanol, together with 1.2 ml of 3N H_2SO_4, was added. The test tubes were once again immersed in a hot water bath at a temperature of 75˚C for duration of 15 minutes, followed by a cooling period of 5 minutes under a flowing stream of water. The colour intensity was quantified at a wavelength of 540nm relative to the blank sample. The hydroxyproline concentration in the tissue was determined using a standard curve established using a 4-Hydroxy-L-proline standard from HI Media Laboratories Pvt. Ltd., Mumbai, India. The standard curve ranged from 75 to 900 µg/0.3ml using a 3mg/ml working solution.**[12,13].**

2.2.7.3. Histopathological study

Biopsy samples were collected from the rats in both the control and treatment groups to obtain healed skin tissue. The excised tissues were immersed in a solution containing 10% formalin for fixation. The tissues underwent typical histochemical methods, where they were treated with paraffin wax, sectioned into 5µm thicknesses, placed on glass slides, deparaffinized, and stained with Hematoxylin–Eosin. The investigation was conducted to validate the experimental findings regarding the levels of inflammatory cells, collagen fibres, fibroblasts, and angiogenesis in the tissue **[14].**

2.2.7.4 Statistical analysis

The experimental results were presented as the mean ± SEM. The statistical data were examined using one-way analysis of variance (ANOVA) using Graph prism Software (version 5.0). A significance level of $P<0.05$ was used, indicating a 95% confidence interval.

3. RESULTS AND DISCUSSION

3.1. Evaluation of nanosponges and nanosponges loaded gel

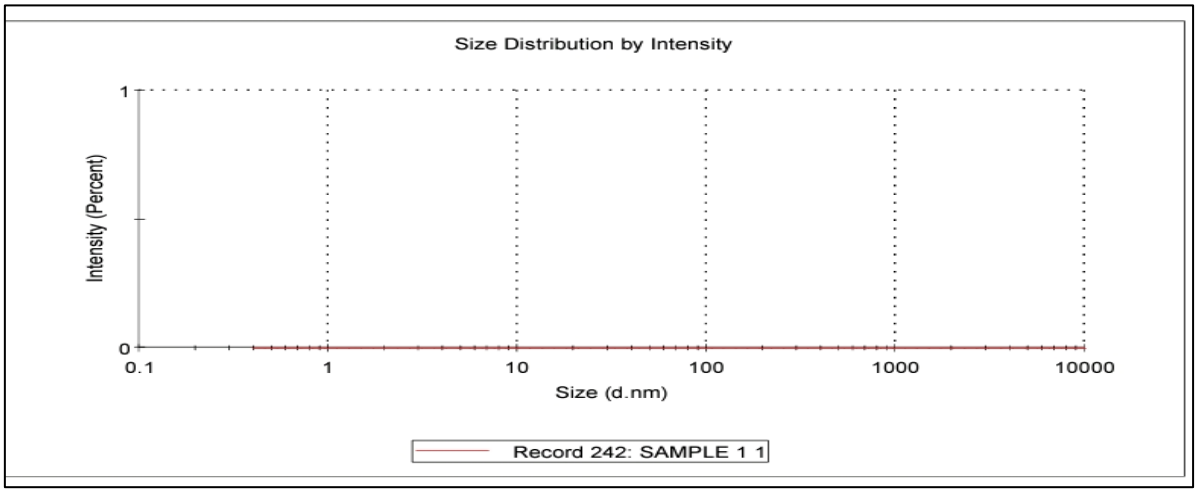
3.1.1. Drug entrapment efficiency

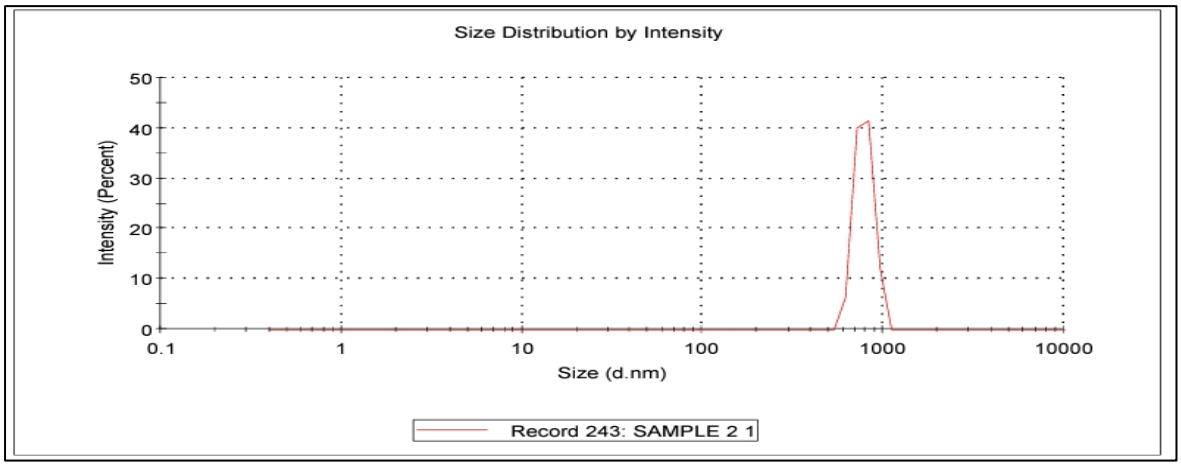
In the early studies, nanosponges leaked a lot of medicine when exposed to neutral and alkaline chemicals. Multiple researches have shown that changing the external aqueous phase pH improves highly ionizable drug entrapment. This study found the same thing. Table 1 showed that two factors greatly affected drug entrapment. The exterior aqueous phase pH comes first, followed by the main emulsion stability. The primary emulsion must be stable for ionizable medicine entrapment to be effective. The external aqueous phase pH affects medicinal material ionization and solubility SSD may produce ions indicated that it is ionic at higher pH. The ionic form is more soluble than the molecular form and rapidly passes to the aqueous phase. To collect ionizable drugs, utilize an external aqueous phase with a pH that

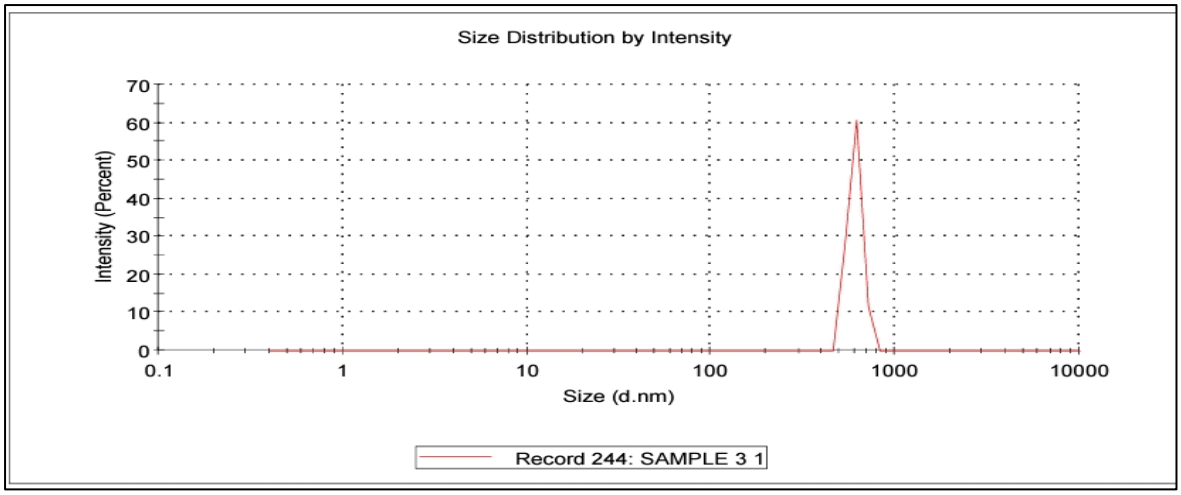
encourages a high log D value. Use a pH where the medicine is not charged and has the lowest water solubility. Polymer drastically reduced primary emulsion stability. Drug molecules migrate from the inner to outer aqueous phases, reducing drug entrapment. This migration is thermodynamically advantageous because the outer aqueous phase is more polar than the inner. The external aqueous phase's low pH increases protons and reduces SSD's ionization, which slows drug outflow. These findings confirm the importance of external aqueous phase ionization and pH in trapping ionized medications.

3.1.2. Particle size analysis, Zeta Potential and PDI

The particle size ranged from 603.3 to 782.4 d. nm, PDI ranged from0.201 to 1.000, Zeta potential value from -14.8 to 53.04 mV.(Sample 1 to 4)







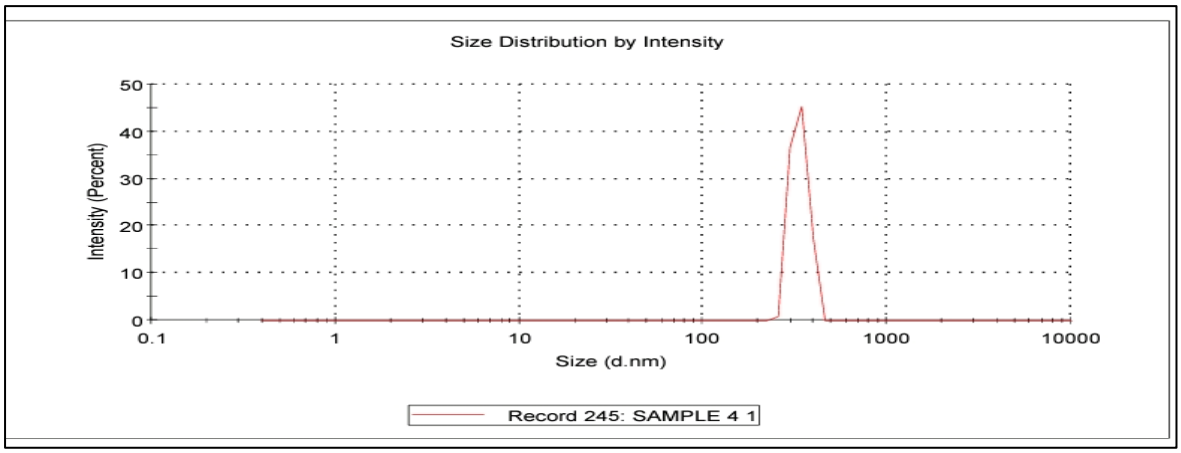
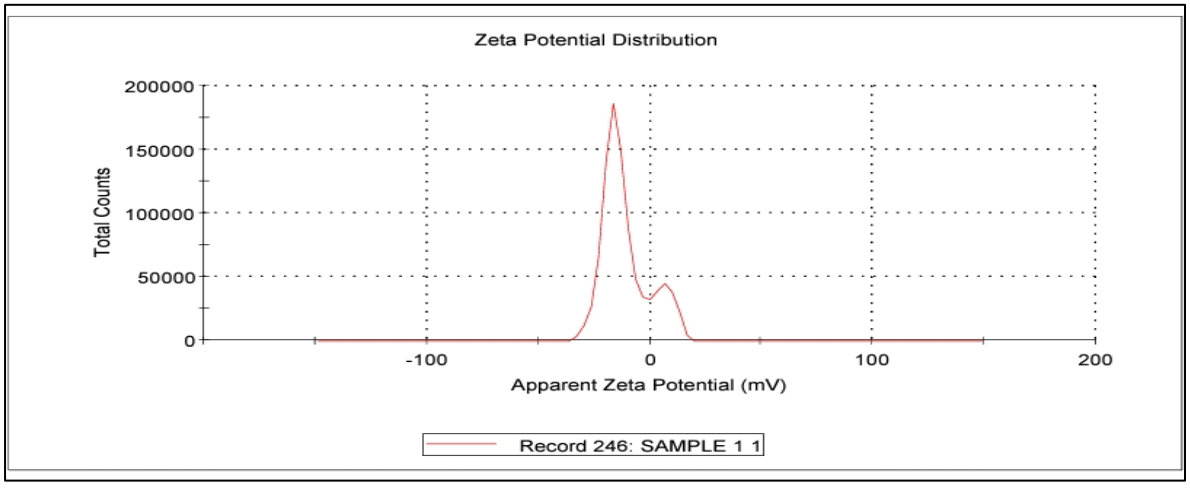


Figure no.1: -Particle size distribution



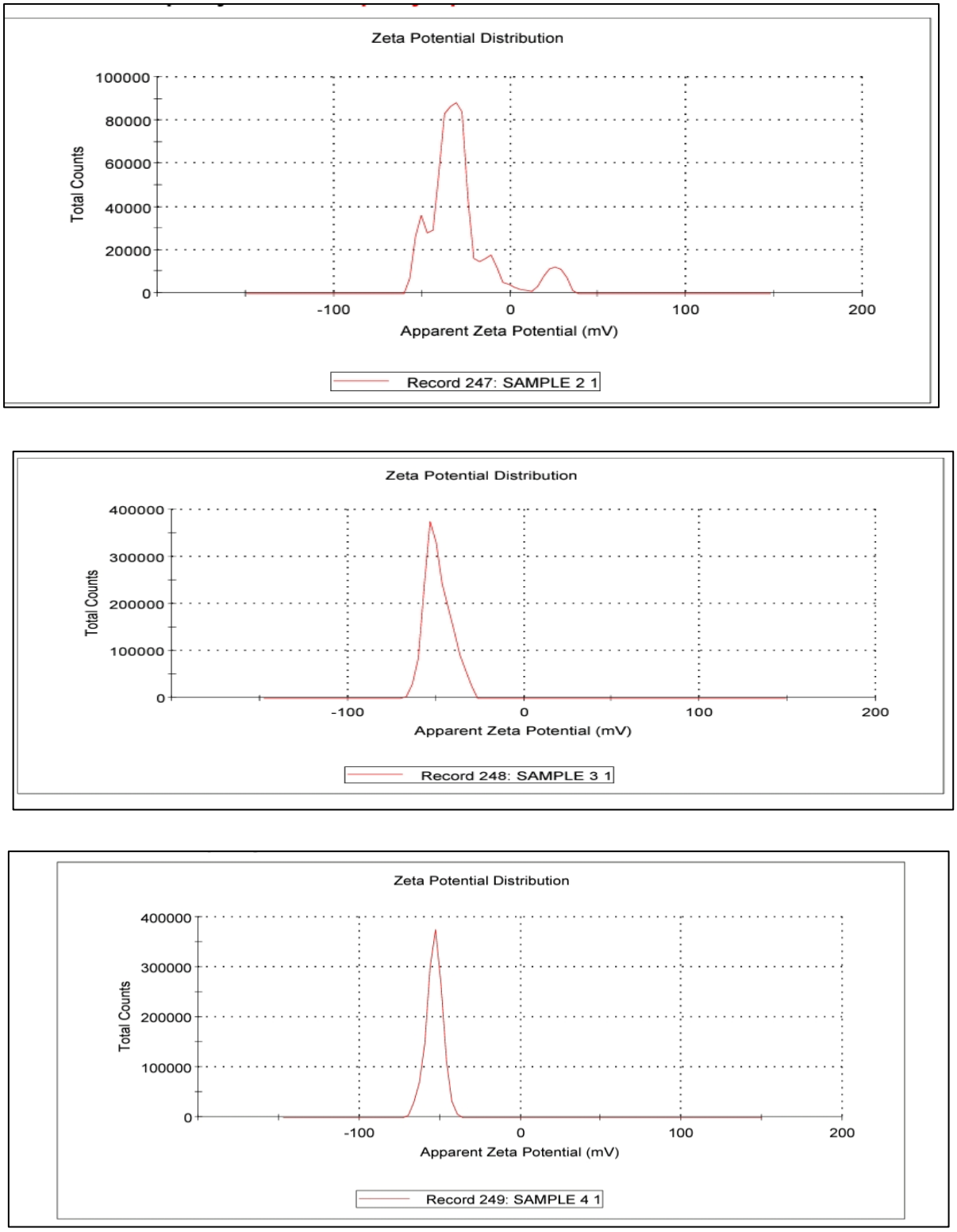


Figure no.2: - Zeta Potential (Sample 1-4)

Table 1: Particle size, PDI and zeta potential of silver sulfadiazine nanosponges prepared with xanthan gum and ethyl cellulose.

Formulation Code	Particle size	PDI	Zeta Potential
F-1	132	0.279	-14.8
F-2	782.4	0.201	-33.0

F-3	603.3	1.000	-48.6
F-4	333.4	1.000	-53.4

3.4. Burn wound model

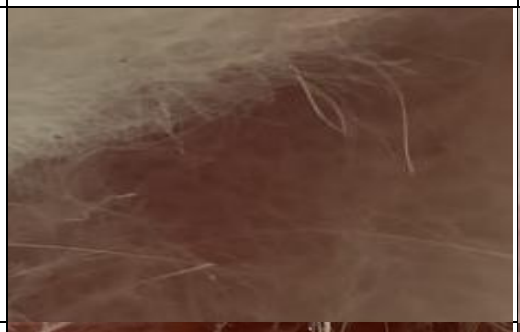
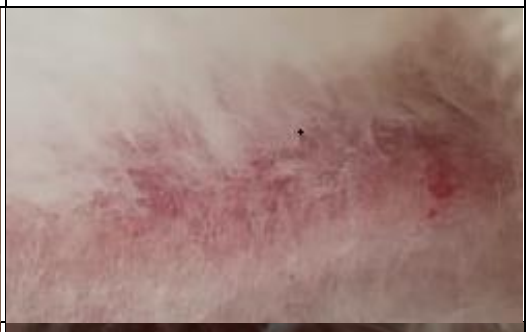
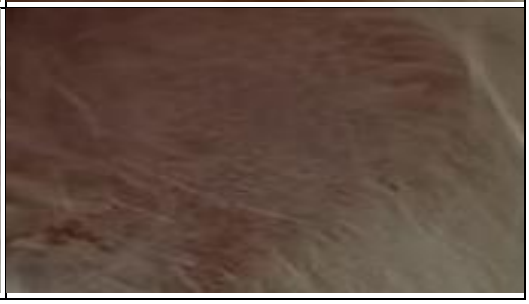
3.4.1. Acute skin irritation study

Skin irritation toxicity was conducted in New Zealand White (NZW) Rabbits. On back surface of New Zealand White (NZW) Rabbits, hairs were removed then optimized formulation was applied topically. This study was conducted as per the OECD guidelines for Acute Dermal Irritation in rabbits (OECD 404). Animals were observed once a day for 72 hours after topical application of the formulation. The degrading or score of erythema, eschar, and edema formation was performed as per the below table

Table.2: Evaluation of skin irritation toxicity

Skin reaction	Observation time	Optimized Formulation I (Score)	Optimized Formulation II (Score)
Erythema/Eschar formation	24 h	0	0
	72 h	0	0
Edema formation	24 h	0	0
	72 h	0	0

h- hours, 0-No erythema/edema at all

	Optimized Formulation I	**Optimized Formulation II**
Before application of Formulation		
Application of Formulation		
After 24 H		

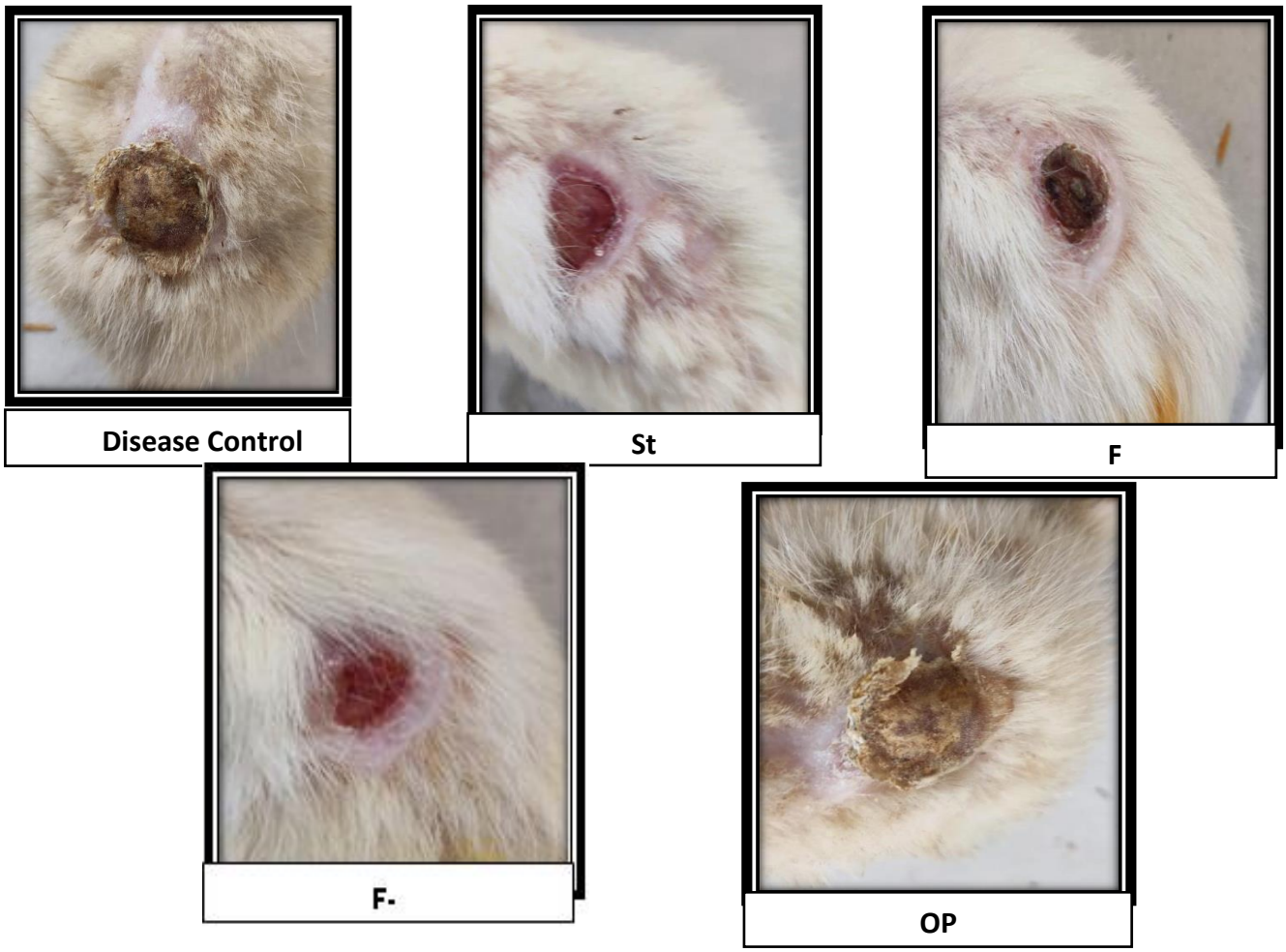
After 72 H		

3.4.2. Burn wound model in Wistar albino rat

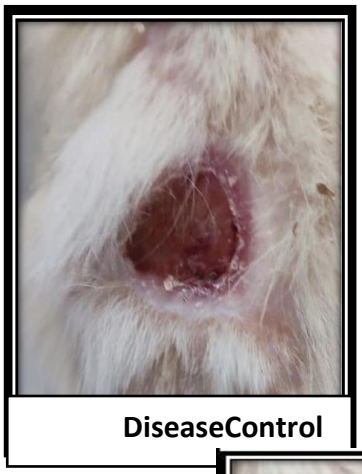
3.4.2.1. Wound contraction

Given images were representative of partial thickness burn wounds in wistar albino rat. Table displays the proportion of wound contraction for various treatment groups.

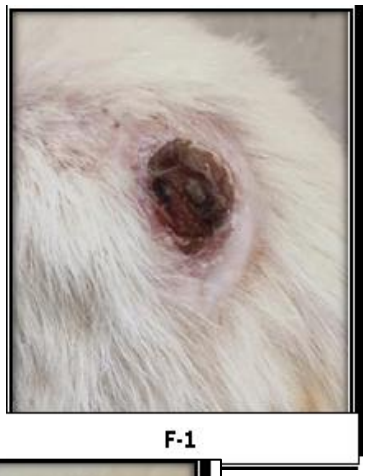
Day5

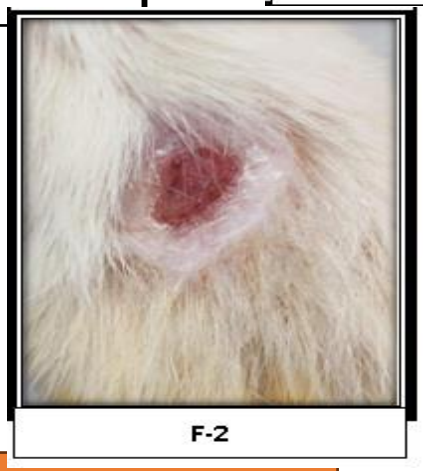


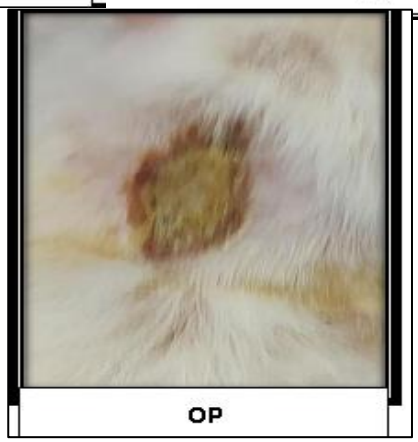
Day10


DiseaseControl

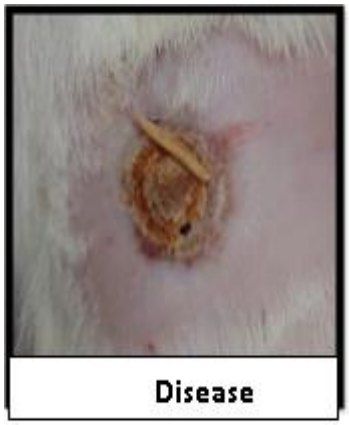

Standard

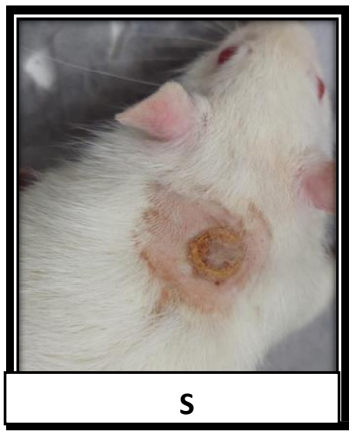

F-1


F-2


OP

Day15


Disease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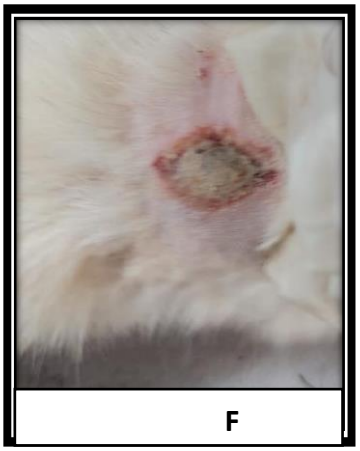
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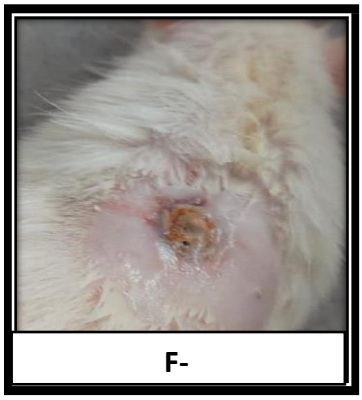
F-

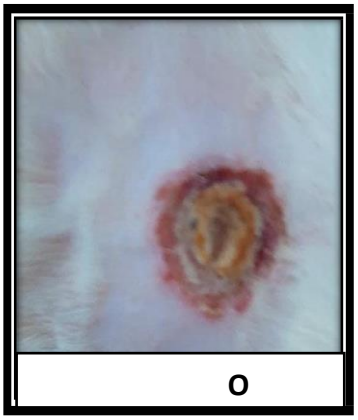
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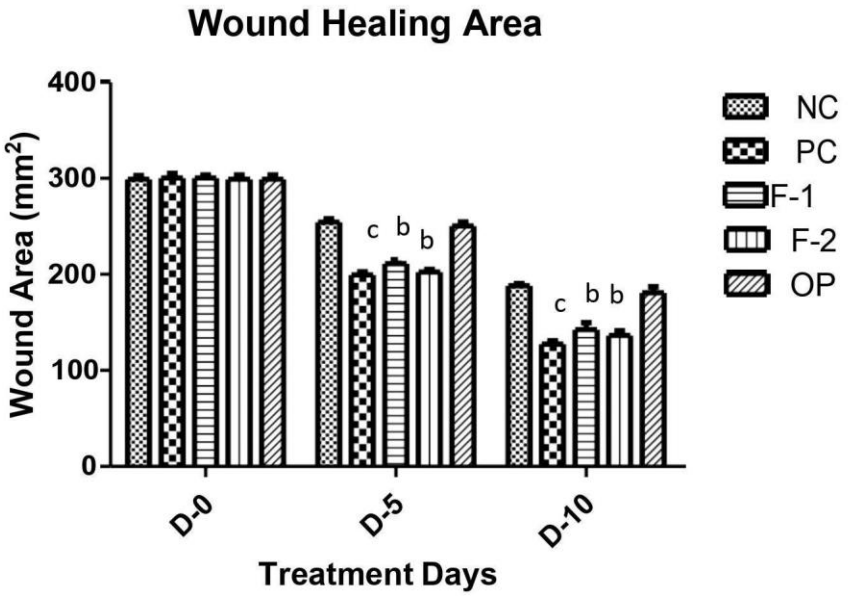
Figure no.3: Healing Pattern in burn wound At Day 0, Day 5, Day 10, Day 15

Graph-1: Effect of Formulation-1 and 2 on wound area (mm^2) in burn wound model.



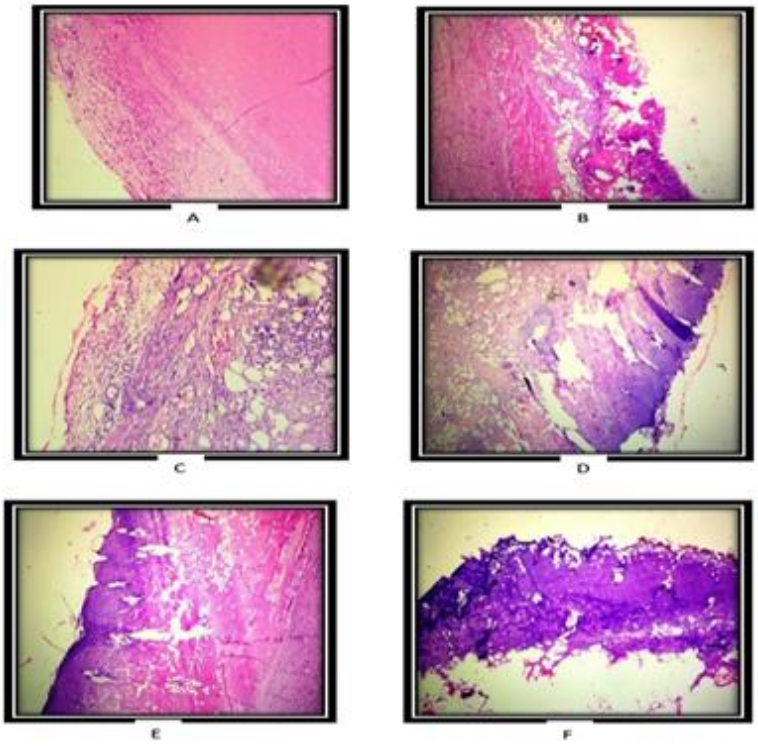
*Values expressed in Mean ± SEM; n = 6; [a] P<0.05, [b] P<0.01, [c] P<0.001 when compared withnegative control.

Table 3: Effect of Formulation-1 and 2 on rate of epithelialization in burn wound model

Treatment	**Epithelialization Period (mean ±SEM)**
NC	24.42±0.40
PC	13.14±0.79
OptimizedFormulation-1	18.68±0.74
Optimized Formulation-2	15.4±0.94
Only Polymer	20.92±0.81

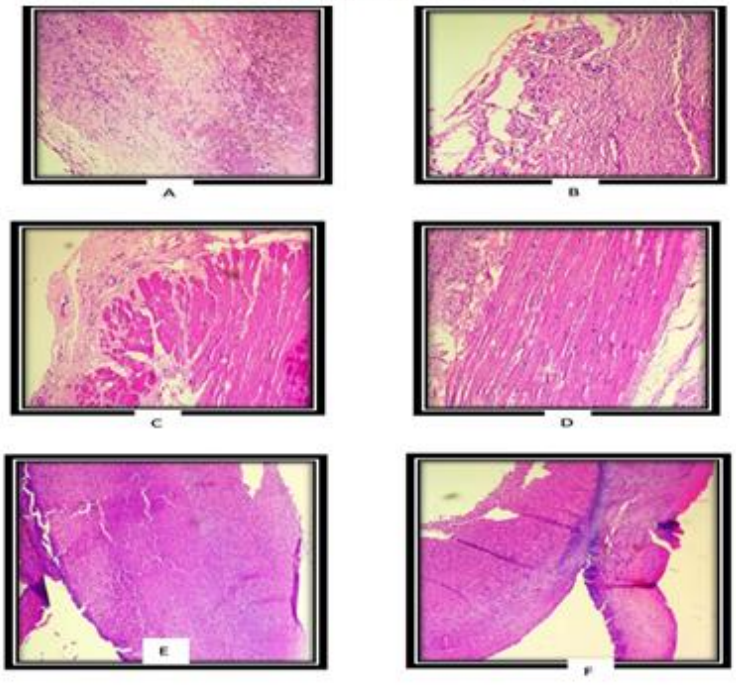
3.4.2.2. Histopathological observations

The histopathology of several treatment groups is shown in Figure. The histological study of the stained samples indicated that the approach used to create burn wounds consistently resulted in the formation of partial thickness burn wounds.



Histopathology of skin treated with Formulation-1 and 2 on day 10 stained with H&E (X100): A) Normal; B) Disease Control; C) Standard (Silver Sulfadiazine); D) Formulation-1; E) Formulation-2; F) Only Polymer

Histopathological Study on Day 10



Histopathology of skin treated with Formulation-1 and 2 on day 15 stained with H&E (X100): A) Normal; B) Disease Control; C) Standard (Silver Sulfadiazine); D) Formulation-1; E) Formulation-2; F) Only Polymer

Histopathological Study on Day 15

Figure no.4: Histopathological observations

3.4.2.3. Hydroxyproline content

Hydroxyproline was significantly (P<0.001) reduced in negative control group as compared to normal control group. The hydroxyproline was significantly (P<0.001) elevated in rats treated with optimized formulations and standard drug i.e. silver sulfadiazine, as compared with negative control group.

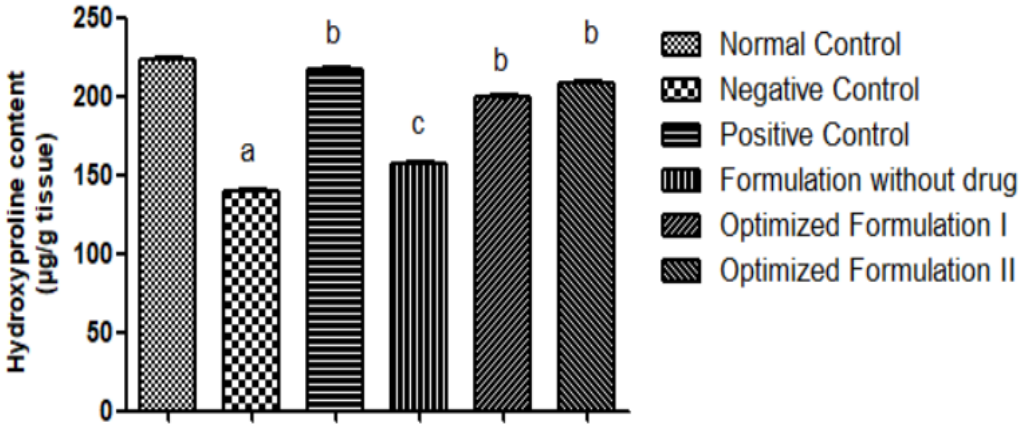


Figure no.5: Effect of formulation on hydroxyproline

*Results are expressed as mean ± SEM, (n=6); [a]P<0.001 vs normal control group; [b]P<0.001 vs negative control group; [c]P<0.05 vs negative control group.

4. Conclusion

Using ethyl cellulose & Xanthan Gum Nanosponges was formulated by emulsion solvent evaporation method. Based on its particles size & entrapment efficiency, optimized batch I, II used to prepared a nanosponge loaded gels using polymers like ethyl cellulose, Xanthan gum and polyvinyl alcohol. Optimised nanosponges formulation characterization using drug entrapment efficiency, Zeta Potential, particle size analysis, and PDI analysis tests. Particle size range from 132-782.4, Zeta potential -14.8 to -53.4 and PDI 0.201 to 1. 000. Skin irritation study shows no irritation shown in both formulations when applied on rabbit. Wistar albino rat used in burn model shows results on day 5,10,15 days 89.0%,91.9% respectively.The optimised gel exhibited a decreased need for application, absence of skin irritation, little toxicity on dermal cell lines, and improved wound contraction.

Abbreviations

SSD	Silver Sulphadiazine
PDI	Polydispersity Index
APIs	Active Pharmaceutical Ingredients
EC	Ethyl Cellulose
PVA	Polyvinyl Alcohol
NSPs	Nanosponges
HCL	Hydrochloride
NAOH	SodiumHydroxide
H_2O_2	HydrogenPeroxide
$CUSO_4$	CopperSulphate

H_2SO_4	SulphuricAcid
OECD	Organization for Economic Cooperation and Development
gm	Gram
mg	Miligram
ml	Mililiter
nm	Nanometer
mm^2	Milimeter square
ANOVA	Analysis of Variance
SEM	Standard Error of Mean
NC	Normal Control
PC	Positive Control
Fig	Figure

Conflict of Interest: None

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References

1. Sangnim T, Puri V, Dheer D, Venkatesh DN, Huanbutta K, Sharma A. Nanomaterials in the Wound Healing Process: New Insights and Advancements. Pharmaceutics. 2024;16(3):300.
2. Sangha MS, Deroide F, Meys R. Wound healing, scarring and management. Clinical and Experimental Dermatology. 2024;49(4):325-36.
3. Moreira TD, Martins VB, da Silva Júnior AH, Sayer C, de Araújo PH, Immich AP. New insights into biomaterials for wound dressings and care: Challenges and trends. Progress in Organic Coatings. 2024; 187:108118.
4. 4.Goh M, Du M, Peng WR, Saw PE, Chen Z. Advancing burn wound treatment: exploring hydrogel as a transdermal drug delivery system. Drug Delivery. 2024;31(1):2300945.
5. 5.Huang Y, Kang H, Wang Y, Liu K, Wei W, Dai H. One Stone Three Birds: Silver Sulfadiazine Modulates the Stability and Dynamics of Hydrogels for Infected Wound Healing. Advanced Healthcare Materials. 2024:2400242.
6. 6.Nunes JH, Nakahata DH, Corbi PP, de Paiva RE. Beyond silver sulfadiazine: A dive into more than 50 years of research and development on metal complexes of sulfonamides in medicinal inorganic chemistry. Coordination Chemistry Reviews. 2023; 490:215228.
7. 7.Mandal S, Bhumika K, Kumar M, Hak J, Vishvakarma P, Sharma UK. A Novel Approach on Micro Sponges Drug Delivery System: Method of Preparations, Application, and its Future Prospective. Indian Journal of Pharmaceutical Education and Research. 2024;58(1):45-63.

8. 8.Boateng J, Burgos-Amador R, Okeke O, Pawar H. Composite alginate and gelatin-based bio-polymeric wafers containing silver sulfadiazine for wound healing. International Journal of Biological Macromolecules.2015; 79:63-71.
9. 9.Kumar PM, Ghosh A. Development and evaluation of silver sulfadiazine loaded microsponge based gel for partial thickness (second degree) burn wounds. European Journal of Pharmaceutical Sciences.2017; 96:243-54.
10. 10.Cai EZ, Ang CH, Raju A, Tan KB, Hing EC, Loo Y, Wong YC, Lee H, Lim J, Moochhala SM, Hauser CA, Lim TC. Creation of consistent burn wounds: a rat model. Arch Plast Surg. 2014 Jul;41(4):317-24. doi: 10.5999/aps.2014.41.4.317.
11. 11.Lambebo MK, Kifle ZD, Gurji TB, Yesuf JS. Evaluation of Wound Healing Activity of Methanolic Crude Extract and Solvent Fractions of the Leaves of Vernonia auriculifera Hiern (Asteraceae) in Mice.J ExpPharmacol.2021 Jul 23; 13:677-692.doi: 10.2147/JEP.S308303.
12. 12.Murthy S, Gautam MK, Goel S, Purohit V, Sharma H, Goel RK. Evaluation of in vivo wound healing activity of Bacopamonniera on different wound model in rats. Biomed Res Int. 2013; 2013:972028. doi: 10.1155/2013/972028.
13. 13.Newman RE, LoganMA.The determination of hydroxyproline.The Journal of Biological Chemistry, 1950; 184(1):299–306.
14. 14.R. Gangadhara*, K. P. Satheesh1, N. Devanna, L. Sasikala and Vandavasi Koteswara Rao. Formulation and invitro characterization of ketorolac loaded nanosponges, international journal of research in pharmacy and chemistry.,IJRPC 2021, 11(3), 99-103.
15. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier. Indian J of Pharmaceutical Education and Research. 2023;57(3s):s481-s498.
16. Mandal S, Jaiswal DV, Shiva K. A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. International Journal of Pharmaceutical Research. 2020 Jul;12(3).
17. Mandal S, Bhumika K, Kumar M, Hak J, Vishvakarma P, Sharma UK. A Novel Approach on Micro Sponges Drug Delivery System: Method of Preparations, Application, and its Future Prospective. Indian J of Pharmaceutical Education and Research. 2024;58(1):45-63.
18. Mishra, N., Alagusundaram, M., Sinha, A., Jain, A. V., Kenia, H., Mandal, S., & Sharma, M. (2024). Analytical Method, Development and Validation for Evaluating Repaglinide Efficacy in Type Ii Diabetes Mellitus Management: a Pharmaceutical Perspective. *Community Practitioner*, *21*(2), 29–37. https://doi.org/10.5281/zenodo.10642768
19. Singh, M., Aparna, T. N., Vasanthi, S., Mandal, S., Nemade, L. S., Bali, S., & Kar, N. R. (2024). Enhancement and Evaluation of Soursop (Annona Muricata L.) Leaf Extract in Nanoemulgel: a Comprehensive Study Investigating Its Optimized Formulation and Anti-Acne Potential Against Propionibacterium Acnes, Staphylococcus Aureus, and Staphylococcus Epidermidis Bacteria. *Community Practitioner*, *21*(1), 102–115. https://doi.org/10.5281/zenodo.10570746
20. Khalilullah, H., Balan, P., Jain, A. V., & Mandal, S. (n.d.). *EUPATORIUM*

REBAUDIANUM BERTONI (STEVIA): INVESTIGATING ITS ANTI-INFLAMMATORY POTENTIAL VIA CYCLOOXYGENASE AND LIPOOXYGENASE ENZYME INHIBITION - A COMPREHENSIVE MOLECULAR DOCKING AND ADMET. *Community Practitioner*, *21*(03), 118–128. https://doi.org/10.5281/zenodo.10811642

21. Mandal, S. (n.d.). *GENTAMICIN SULPHATE BASED OPHTHALMIC NANOEMULGEL : FORMULATION AND EVALUATION , UNRAVELLING A PARADIGM SHIFT IN NOVEL PHARMACEUTICAL DELIVERY SYSTEMS*. *Community Practitioner*, *21*(03). https://doi.org/10.5281/zenodo.10811540
22. Mandal, S., Tyagi, P., Jain, A. V., & Yadav, P. (n.d.). *Advanced Formulation and Comprehensive Pharmacological Evaluation of a Novel Topical Drug Delivery System for the Management and Therapeutic Intervention of Tinea Cruris (Jock Itch)*. Journal of Nursing, *71*(03). https://doi.org/10.5281/zenodo.10811676
23. Pal N, Mandal S, Shiva K, Kumar B. Pharmacognostical, Phytochemical and Pharmacological Evaluation of Mallotus philippensis. Journal of Drug Delivery and Therapeutics. 2022 Sep 20;12(5):175-81.
24. Singh A, Mandal S. Ajwain (Trachyspermum ammi Linn): A review on Tremendous Herbal Plant with Various Pharmacological Activity. International Journal of Recent Advances in Multidisciplinary Topics. 2021 Jun 9;2(6):36-8.
25. Mandal S, Jaiswal V, Sagar MK, Kumar S. Formulation and evaluation of carica papaya nanoemulsion for treatment of dengue and thrombocytopenia. Plant Arch. 2021;21:1345-54.
26. Mandal S, Shiva K, Kumar KP, Goel S, Patel RK, Sharma S, Chaudhary R, Bhati A, Pal N, Dixit AK. Ocular drug delivery system (ODDS): Exploration the challenges and approaches to improve ODDS. Journal of Pharmaceutical and Biological Sciences. 2021 Jul 1;9(2):88-94.
27. Shiva K, Mandal S, Kumar S. Formulation and evaluation of topical antifungal gel of fluconazole using aloe vera gel. Int J Sci Res Develop. 2021;1:187-93.
28. Ali S, Farooqui NA, Ahmad S, Salman M, Mandal S. Catharanthus roseus (sadabahar): a brief study on medicinal plant having different pharmacological activities. Plant Archives. 2021;21(2):556-9.
29. Mandal S, Vishvakarma P, Verma M, Alam MS, Agrawal A, Mishra A. Solanum Nigrum Linn: An Analysis Of The Medicinal Properties Of The Plant. Journal of Pharmaceutical Negative Results. 2023 Jan 1:1595-600.
30. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis Of The Most Recent Trends In Flavoring Herbal Medicines In Today's Market. Journal of Pharmaceutical Negative Results. 2022 Dec 31:9189-98.
31. Mandal S, Vishvakarma P, Mandal S. Future Aspects And Applications Of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. European Journal of Molecular & Clinical Medicine.;10(01):2023.
32. Chawla A, Mandal S, Vishvakarma P, Nile NP, Lokhande VN, Kakad VK, Chawla A. Ultra-Performance Liquid Chromatography (Uplc).

33. Mandal S, Raju D, Namdeo P, Patel A, Bhatt AK, Gupta JK, Haneef M, Vishvakarma P, Sharma UK. Development, characterization, and evaluation of rosa alba l extract-loaded phytosomes.
34. Mandal S, Goel S, Saxena M, Gupta P, Kumari J, Kumar P, Kumar M, Kumar R, Shiva K. Screening of catharanthus roseus stem extract for anti-ulcer potential in wistar rat.
35. Shiva K, Kaushik A, Irshad M, Sharma G, Mandal S. Evaluation and preparation: herbal gel containing thuja occidentalis and curcuma longa extracts.
36. Vishvakarma P, Kumari R, Vanmathi SM, Korni RD, Bhattacharya V, Jesudasan RE, Mandal S. Oral Delivery of Peptide and Protein Therapeutics: Challenges And Strategies. Journal of Experimental Zoology India. 2023 Jul 1;26(2).
37. Mishra, N., Alagusundaram, M., Sinha, A., Jain, A. V., Kenia, H., Mandal, S., & Sharma, M. (2024). Analytical Method, Development and Validation for Evaluating Repaglinide Efficacy in Type Ii Diabetes Mellitus Management: a Pharmaceutical Perspective. *Community Practitioner*, *21*(2), 29–37. https://doi.org/10.5281/zenodo.10642768
38. Singh, M., Aparna, T. N., Vasanthi, S., Mandal, S., Nemade, L. S., Bali, S., & Kar, N. R. (2024). Enhancement and Evaluation of Soursop (Annona Muricata L.) Leaf Extract in Nanoemulgel: a Comprehensive Study Investigating Its Optimized Formulation and Anti-Acne Potential Against Propionibacterium Acnes, Staphylococcus Aureus, and Staphylococcus Epidermidis Bacteria. *Community Practitioner*, *21*(1), 102–115. https://doi.org/10.5281/zenodo.10570746