A Systematic Review of Advanced Approaches in Wound Healing: Simvastatin Polymeric Nanoparticles and Postbiotics Innovation

Chandrapratap Dhimar [1*], Krishna Sahu [1], Moniza Nurez Khan [1]

Abstract

A wound is a disruption in the continuity of the skin caused by accident, disease, or surgery. Wound treatment is a vital, ongoing biologically and physiologically method that reacts to cell injury. Regarding health, economy, and social aspects, the significant impact of wounds on individuals and society underscores the need for research to identify innovative therapeutic actors that might improve the treatment of wounds. Postbiotics, a recent addition to the biotics category, are bioactive compounds of great value generated by probiotics via metabolic processes. These substances possess various advantageous properties, such as immunomodulatory, antimicrobial, and anti-inflammatory, and promote faster wound healing. The Simvastatin Polymeric Nanoparticles (S-PNP) were synthesized utilizing the nanoprecipitation technique to enhance the solubility of the medicine and its capacity to grow the skin. The drug data, dissolution, particle dimension, charged surface, and broadcasting electron microscope of the produced S-PNP are assessed. S-PNP was applied to the hydrogel, and the physical properties, release behavior in a controlled environment, and penetration across a biological membrane of the hydrogel were assessed. The gel that had been made was administered to the wounds of rats, and a histological examination was conducted. The findings demonstrated notable effectiveness in expediting the rat wound recovery process, resulting in full epithelialization and little invasion of inflammatory cells.

Keywords: Bioactive Compounds, Wound Healing, Nanoparticles, Analysis

Significance | Utilizing innovative postbiotics and Simvastatin Polymeric Nanoparticles, wound research accelerates healing, promising improved treatment with minimal inflammation.

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1. Introduction

A term wound is a disruption in the continuity of the skin caused by a wound, disease, or surgery (Dong, Guo, 2021). Injuries can occur due to a medical condition or as an unintentional or deliberate cause. The skin's main role is to serve as a defensive structure, shielding it from the external conditions Liang et al. (2022). The breakdown of skin integrity creates a suitable environment for different bacteria to infect the wound area. Because intact skin is crucial for shielding the body from its surroundings, activating and advancing regeneration processes (healing) is necessary to repair the current damage Luo et al. (2021). Cutaneous wound healing is an intricate and ever-changing biological process that begins once tissue damage occurs (Grada, Phillips, 2022). The primary objective of wound healing is to prevent infections and restore the functionality and resilience of the skin tissue. A wound, a form of tissue injury, triggers a controlled and organized reaction. The wound healing procedure consists of four main physiological stages: homeostasis, fibrosis,

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proliferating, and remodeling; during the first phase of the healing procedure, known as hemorrhage, platelets start to function and release cytokines, growth factors and other chemicals Cho et al. (2021). This induces the processes responsible for tissue repair, leading to increased cells, angiogenesis, evaporation of extracellular matrix, and tissue remodeling Kant et al. (2021).

Several factors can disrupt the wound healing procedure, resulting in postponed or compromised wound healing. This can have severe consequences for patients, including increased illness, death, and adverse cosmetic outcomes. Wounds' health, economic cost, and social repercussions are significant issues that need careful attention (Farahani, Shafiee, 2021). Damages provide a significant global burden for patients, relatives, healthcare organizations, and caregivers Gaspar-Pintiliescu et al. (2019). In terms of the economy, the United States incurs an annual expenditure of about 1 billion dollars only due to wound-related problems. Therefore, it is imperative to allocate more attention and conduct extensive studies to explore new possible therapeutic substances that can effectively achieve one of the primary objectives of injury therapies: speeding up the healing method Isopencu et al. (2023).

Polymeric nanoparticles have been extensively utilized as carriers in drug delivery structures, particularly for topical wound healing applications, often in hydrogel-loaded gels Zhang et al. (2021). Hydrogels are 3D structures of water-soluble polysaccharides interconnected by cross-linking Bovone et al. (2022). The amount of cross-links inside the gel matrix can impact its permeability, affecting the entry and release of drugs from the matrix's pores. The spontaneous arrangement of various molecular components into separate nanostructures with large aggregates results in a perpendicular self-assembly utilized as a gel for delivering drugs Vendrame et al. (2024). It allows for adjustable release rates after manufacture. Hydrogels, including integrated vascular systems and several compartments, have the potential to facilitate the administration of various medications and combination treatments Andjić et al. (2021).

Simvastatin (SIM) is a compound that inhibits the enzyme 3-hydroxy-2-methyl-glutaryl dehydrogenase Duarte et al. (2021). Tablets are available for reducing blood cholesterol levels. SIM has demonstrated a distinct action in addition to its antihyperlipidemic effects. It has the potential to enhance the process of wound treatment. It improves the creation and discharge of the vein endothelial factors at the injury location, a crucial process for forming fresh blood veins Ahmed et al. (2023). It enhances the epithelialization process and restores the natural epithelial membrane by inhibiting the downstream destinations of mevalonate and farnesyl pyrophosphate by lowering their isoprenylation.

This study aimed to develop Simvastatin Polymeric Nanoparticles (S-PNP) as a potential transdermal application for enhanced solubility and skin permeability in treating skin wounds. Topically applying the anti-microbial substance is highly effective for treating skin and soft tissue infections, offering several advantages over systemic therapy.

This study planned to investigate the effects of postbiotic functions, specifically in cream, on the procedure of wound treatment. Three innovative compositions of cold creams were created to improve the wound treatment processes. The effectiveness of the formulated postbiotics creams was examined using in vivo evaluations, such as measuring wound diameters, calculating wound healing proportions, doing a hydroxyproline content test, and performing histological evaluation in a rat model Sofronaet al. (2020). Mouse evaluations demonstrate that antimicrobial compound foams successfully enhance the healing process of full-thickness skin lesions.

The subsequent sections are organized in the specified sequence: Section 2 comprehensively examines and evaluates various techniques and procedures used to heal wounds. Section 3 presents the proposed approach of using bioactive substances for wound healing and its experimental examination. Section 4 examines and discusses the empirical study and results of the wound healing procedure. Section 5 encompasses the final findings, obstacles, and potential areas for further investigation in the research.

2. Literature review

This section examines the articles about wound healing and explores their progress, concerns, and difficulties. This will facilitate the development of an improved approach to wound treatment.

The proposal suggests creating and producing an adaptable acoustic patch to heal chronic injury Lyu et al. (2021). The piezoelectric ceramic within the patch is divided into many linearly aligned components and then combined onto a flexible circuit substrate. A slim hydrogel patch has the dual purpose of acting as an encapsulating and connection layer. Its function is to prevent wound infection and facilitate the transmission of ultrasonic waves. The therapy outcomes indicate that wounds treated using ultrasonography exhibit a more rapid healing process than wounds not treated with ultrasound. The duration of healing is reduced by approximately 40%.

This research aimed to create a hydrogel by combining cellulose and γ-PGA, employing a double-network approach, and adding ε-PL modification Hu et al. (2023). It was evaluated for its exceptional qualities using a range of experimental paradigms, both in vitro and in vivo. The biological properties and

antibacterial efficacy were thoroughly examined in several preclinical systems.

A novel hydrogel, cross-linked using an enzyme, is introduced for the first period. The hydrogel is made of silk sericin activity Baptista-Silva et al. (2021). According to physiological circumstances, this hydrogel cross-linking process was carried out using peroxidase from horseradish. The gel formation occurred within 3 minutes, as evidenced by its rheological properties. This work proposes a straightforward, efficient, and convenient method to create a sericin-based copolymer to treat persistent low exudative wounds.

To avoid infection and excess inflammatory processes, a proposed technique involves producing a specific type of nanoparticles called reacting Metallic Boride Nanoparticles (MB-NPs) that can trap boron Meng et al. (2022). The findings indicate that the MB-NPs undergo a slow hydrolysis process, forming boron dihydroxy compounds and metallic cations. This process also leads to the creation of a localized alkaline microclimate. This boron-trapping technology offers a method for treating bacterial infections and the associated inflammation.

The research suggests a straightforward single-step process for creating lignin-based polymeric foams Li et al. (2022). This technique partially substitutes conventional petroleum-based ingredients with entirely biodegradable polyether polymers. Mouse evaluations demonstrate that the antimicrobial composite foams successfully enhance the treatment process of the size of skin lesions. This antimicrobial and disposable foam shows considerable promise for practical application in wound care coverings as proof of principle.

The research presented a new approach for creating a macroporous hydrogel that is both bioactive and capable of self-healing Zhang et al. (2021). Using the macroporous polymer as a cell delivery technology has been demonstrated to enhance the survival rate of HUVECs or MAECs. The research developed has a considerably greater pore diameter. This larger hole size promotes cell infiltration, survival, and multiplication. Hence, the combined effect of the hydrogels' bioactivity and macroporous makeup can effectively encourage tissue regeneration.

The main aim of the present research was to analyze the efficacy of Opuntia Ficus-Indica (OFI) and the associated self-nano emulsifying delivering method for the drug in promoting wound healing in a rat scenario with full-thickness epidermal resection Koshak et al. (2021). The injury-healing qualities of OFI are improved by self-emulsification, which results in nano-droplets forming. A raised production of vascular endothelial growth factors shows OFI-enhanced angiogenesis.

A novel hydrogel able to self-heal and exhibit photothermal antimicrobial characteristics was created and utilized for healing wounds Guo et al. (2022). The gel consisted of polyacrylamide and was created using a two-step method: an alkali-induced dopaminergic pre-polymerization and then a reactive polymerization method Geana et al. (2023). The hydrogel has exceptional properties as a wound clothing, including superior tissue association, wound recovery, and antimicrobial capabilities.

The research demonstrates the progress made in the wound-healing process. However, these solutions need better efficiency, highlighting the necessity for a novel approach. This research presents a biocompatible method for facilitating the wound healing process.

3. Proposed Simvastatin Polymeric Nanoparticles

This section proposed Simvastatin Polymeric Nanoparticles (S-PNP) using bioactive components for wound healing. The materials, methods, and the respective experiments with rat samples are expressed in this section.

3.1 Materials

The source of Soy-peptone was Quelab, whereas Merck provided magnesium sulfates, sodium proton phosphates, malt syrups, and sugar. The following chemicals were acquired from Merck: N-chloro-tosylamides, p-dimethyl amino benzenes, purified L-hydroxyprolines, perchloric acids, etc. The substances, chemicals, and salts utilized for buffer solution formulations were of quality for analysis and seemed to be from Merck.

Tween-85 was acquired from Marcel Schuchardt, the deoxycholate of sodium and methylcellulose was obtained from Sigma-Aldrich, and polyvinylpyrrolidone and the cellular acetate membranes were bought from Fisher Sciences. All other substances and scientific substrates were of evaluation standards and utilized without analysis.

3.2 Preparation of Postbiotics

The study employed three specific strains of probiotic microorganisms: subtilis sp. natto, Lactobacillus reuteri strains, and lactic acid bacteria. The L. reuteri and L. fermentum microorganisms were cultivated in MRS broth media at 36°C for 48 hours, under reduced oxygen, until they reached the stationary phase. The B.S. natto strain was developed using a mixture of soy-peptone (12 g), a solution of magnesium sulfate (3 g), sodium phosphate (4 g), malt extract (25 g), sugar (4 g), and extracts of yeast (15 g). The culture was kept at 38°C for 48 hours. The pH was modified to a value of 6.5. The initial concentration of each strain's infection was generated at a density ranging from 2×10^5 to 2×10^6 colony-forming units per milliliter (CFU/mL). Live microbes were quantified by conducting plate counts on MRS agar. The microbes were collected utilizing the Eppendorf 5910R centrifugation at 3500 tests per minute for 25 minutes at 5°C. The waste products were filtered using a 0.4 μm membrane screen to deduce leftover microorganisms and other debris. The resulting liquids were filtrated and freeze-dried using an Alpha 1-2LD Plus

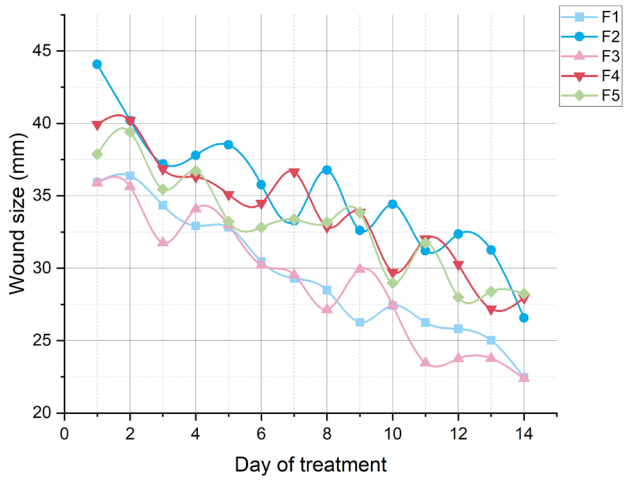

Figure 1. Wound size analysis over days

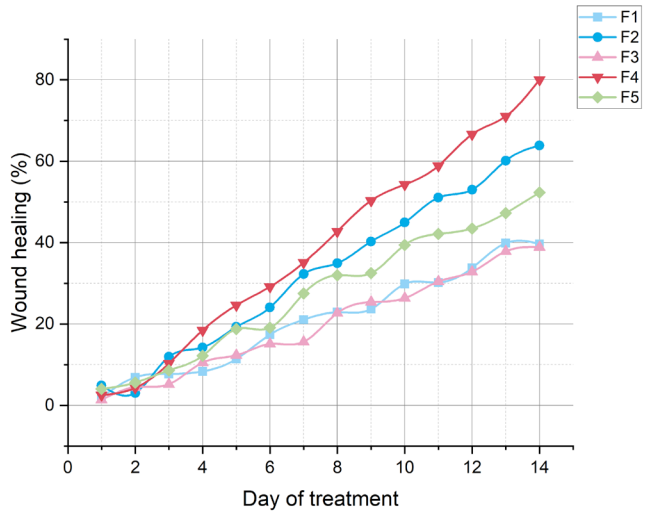

Figure 2. Wound healing analysis over days

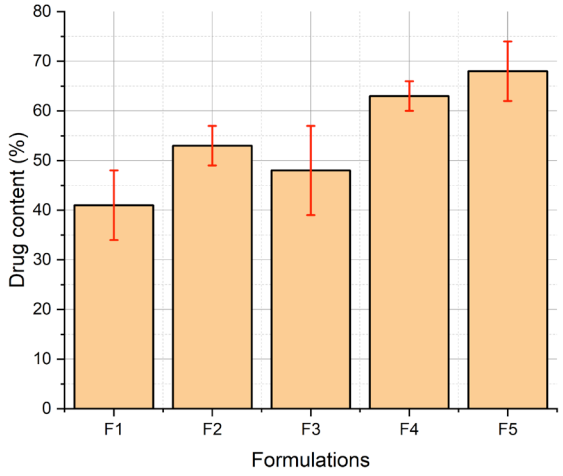

Figure 3. Drug content analysis of formulations

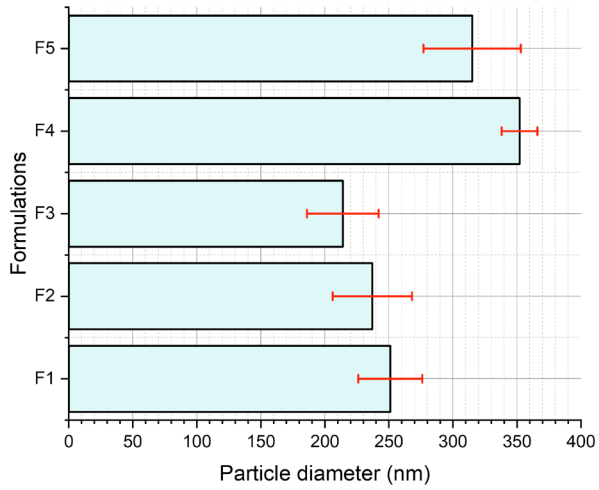

Figure 4. Particle diameter analysis over days

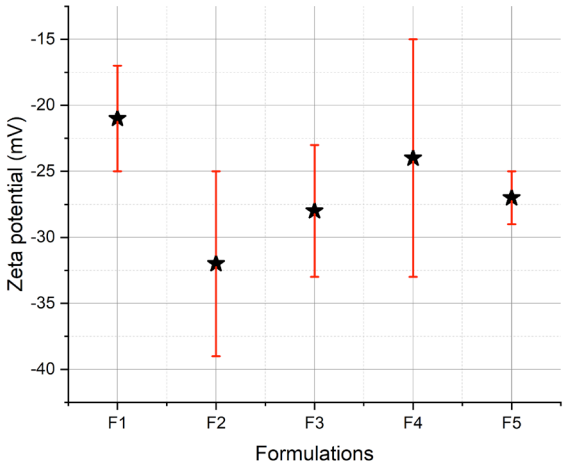

Figure 5. Zeta potential analysis over days

lyophilizer. The freeze-dried samples were then kept at a temperature of -25°C. No lactobacilli development was seen in the microbial enumeration of MRS agar dishes. The presence of endotoxin in L.S. was examined using a test set from Cambrex Company.

3.3 Preparation of S-PNP

The nanoparticles were synthesized using the nano-precipitation technique. Fourteen: SIM was disintegrated in an organic stage at ambient temperature. The natural component was introduced into a 35 mL solution with water-soluble polymers. The organic portion was introduced into the container by a syringe, with the needle inserted immediately, at a frequency of 10 mL every two minutes. The mixture was then agitated on a stirrer with magnets to facilitate the evaporation of the volatile solvents.

Formulas 1 to 2 had 2 mg of methylcellulose as a stabilizer, equal to a concentration of 85.42 µM. Formulas 3 and 4 included a combination of 2 mg of stearic acid (105.47 µM) and 2 mg of sodium deoxycholate (85.21 µM) as the moderator. The remaining formulations used 12 mL of glycerin as the cosolvent, which is equivalent to a concentration of 5.21 µM.

The formed S-PNP was further purified using spinning to isolate them from any large-sized non-reacting components. The samples were centrifugated at 5,000 revolutions per minute for 10 minutes.

3.4 Preparation of Postbiotics Cold Creams

A single milligram of every lyophilized postbiotic was incorporated into ten grams of the manufactured cold cream. The mixture was then stirred for 5 minutes at the ambient temperature to create three distinct compositions of postbiotic cold cream. Three formulations are available with previously produced formulations: Formulation (F) F1 contains lactic acid postbiotic freezing cream, F2 contains Lactobacillus reuteri postbiotic freezing cream, and F3 contains Bacteria subtilis sp. natto postbiotic freezing cream. F4 and F5 show the combinations of previous methods.

3.5 Wound Production

The rat was administered anesthesia using ketamine and xylazine at doses of 80 and 10 mg/kg, accordingly. The required region was then shaved to eliminate hair before removing a layer of skin and making an excision incision measuring 226 mm2 in space and 2 mm in thickness.

3.6 Wound Healing Activity Measurement

Postbiotic compositions, specifically designed for topical use, were developed with a 1% weight/weight postbiotic dosage in freezing cream. These creams were applied to the wounds formed once daily for two weeks. The rats without treatment and those who received the peptide mixture were designated as controlling categories. The measurements of the resected wound sizes were documented for each rat group from day 1 to day 14. Equation (1) computes the percentage of wound healing.

$$WH = \left(1 - \frac{W_{Sp}}{W_{s0}}\right) \quad (1)$$

W_{sp} and W_{s0} represent the dimensions of the injury on a particular day and on day 0, accordingly.

3.7 Drug content

The nanosuspension that had been created underwent centrifugation at a speed of 10,000 revolutions per minute for 10 minutes. 5 mL of the liquid remaining after centrifugation was mixed with 150 mL of a solution of The concentration of the drug that was not bound to anything was determined by computing the absorption coefficient of the diluted liquid at a wavelength of 225 nm employing a double-beam ultraviolet (UV) the spectroscopy with ethanol as a reference. The drug concentration was determined using Equation (2). The study was conducted four times for every group, and the average was computed.

$$DC = \frac{T_d - U_d}{T_d(0)} \quad (2)$$

The overall drug quantity is denoted as T_d, the quantity of drug that is not bound is represented as U_d, and the beginning amount of drug taken is $T_d(0)$.

3.8 Preparation of hydrogel loaded with S-PNP

The formulated S-PNP was explicitly intended for wound healing applications. The formulation was transformed into a gel to facilitate its application and safeguard the produced S-PNP from the outside world. A 2% solution of Carbopol was immersed in 15 mL of fluid for 48 hours. The substance was carefully distributed into the pre-prepared solution of S-PNP while maintaining a consistent stirring motion with a stirrer with a magnet. This was done to avoid the development of clumps or any agglomeration and to achieve a uniform mixture. A solution containing 0.5% NaOH was introduced to the gel as a neutralizer to optimize the expanding properties of Carbopol® monomers by adjusting the pH.

3.9 In vitro analysis

The gel was subjected to in vitro release of SIM using a Franz diffusing tissues, with 36°C±3°C. The medication was inserted into the donor compartment. The dissolution examination was conducted in two distinct solutions: a phosphate buffering with a pH of 6.5, which replicates the pH range of the organic wound surroundings, and an aqueous solution composed of 64% deionized fluid, 22% ethanol, and 3% Tween-80, in a pH of 4.3, resembling the pH of the epidermis. At predetermined periods, 2 mL specimens were taken and promptly changed with new dissolving media. The drug emission was quantified by computing its absorption at 225 nm utilizing a double-beam UV–visible (Vis) spectrometer. The dissolving test was also conducted on raw SIM

distributed in Carbopol gel using a liquid medium to investigate the impact of nanosizing on the speed of medicine delivery.

3.10 Ex vivo permeation study

The study investigated the ability to penetrate SIM from the gel through the abdomen skin of white Wistar rat males. Before the rat's sacrifice, its belly hair was removed. The permeability trials started within a time frame of 2-4 hours following the offering of flesh. The skin was cleansed using Dulbecco's phosphate-buffered saline. The experiment was conducted using the altered Franz cell in the following manner: The epidermis was secured between the donor's and receiver room. The receiver chamber filled with 12 mL of the aqueous medium previously described in the release experiment. At specific times, 2 mL specimens were taken. An equal volume of new dissolving fluid, adjusted to the same climate, was then added to substitute the obtained data. Using UV-Vis spectroscopy, the specimens were appropriately diluted and examined at a wavelength of 225 nm to determine the total quantity of medication released via the skin. Permeation experiments were conducted three times. The diffusion rates were calculated using different theoretical frameworks by employing linear regression testing on the in vitro and ex vivo pemeation graphs. The theoretical framework that most accurately represented the kinetic releasing profile was chosen using the most significant prediction coefficients.

3.11 Gel formulation

The study examined three gel compositions: 1) S-PNP incorporated into a hydrogel, 2) The hydrogel, and 3) a combination of S-PNP and hydrogel in a 1:1 ratio. The selection of hydrogel in this trial was based on its broad-spectrum antibacterial properties and effectiveness in treating skin and soft tissue infections. The solubility of 32 hemihydrate in liquid is elevated, and it is readily distributed into ordinary Carbopol® gel at a dosage of 2%. Following the surgical procedure, the wounds of all the animals were treated daily with topical gel compositions using cotton pads. Each team was administered the medicinal gel for one injury, while the other group's injury was treated with ordinary gel as a control. The therapy was administered to each animal until they were euthanized. The percentage of contracted wounds was determined using Equation (3).

$$W_c = \frac{W_A(0) - W_A(n)}{W_A(0)} \quad (3)$$

The wound area at day 0 and n are denoted $W_A(0)$ and $W_A(n)$.

On days 0, 4, 6, and 12 following the wounds were made, skin slices of about 1 cm^2 were taken and preserved in 4% formaldehyde for histological analysis. The specimens were cryopreserved and sliced perpendicular to their length into sections 7mm thick, taken from the central region of the injuries. These sections were stained with hematoxylin and examined under light microscopy. The specimens were analyzed for the processes of epithelization, inflammation, and the presence of hair shafts. The wound size was measured to assess the healing process quantitatively.

3.12 Histopathological Analysis

The full-size skin cells of the wounds, each measuring 3.5 cm × 1.2 cm, were separated. Following the fabrication of paraffin-embedded groups, each with a depth of 2 mm, they were horizontally sliced to match the breadth of the skin surface. A mixture of two histology staining methods, hematoxylin and eosin, was used for staining. Hematoxylin selectively stains nuclei of cells, whereas eosin marks the matrix of cells and cytoplasmic elements with accuracy. Following that, the histological modifications of skin cells were examined for all the specimens via investigation of distinct stages of epithelialization, inflammation, and granules. The wound healing cycle was assessed by a competent pathologist who unthinkingly evaluated the extent of epithelialization, fibrosis in inflammatory processes, and granules.

3.13 Statistical Analysis

The data evaluation was conducted utilizing GraphPad software version 8. The quantitative parameters represented the mean value plus or minus the Standard Deviations (SD). The contrasts were performed using Analysis Of Variance (ANOVA) for comparability. The statistical significance threshold was considered as having P below 0.04.

4. Experimental Analysis and Outcomes

An injury is a disruption or incision in the skin, and its healing is an ongoing and intricate physiological response that begins after skin damage. The significant physical, social, and economic difficulties linked to wounds need the discovery of innovative medicinal substances that can improve the procedure of healing wounds. Postbiotics, bioactive molecules generated by probiotics, have lately garnered significant attention due to their several advantageous properties. Three novel formulations, known as postbiotics freezing creams, were created to investigate their effectiveness in promoting the healing of wounds. This was accomplished through an in vivo experiment using a model of rats.

The investigation of wound size for five distinct formulations over two weeks is conducted and graphed in Figure 1. As the therapy duration increases, the corresponding wound's size decreases, leading to improved therapeutic efficacy. The suggested S-PNP approach demonstrates favorable outcomes across several wound types, which the provided rat samples have validated. The formulations show reductions in wound size of 38%, 40%, 38%, 30%, and 25%.

An examination of wound healing in rats was conducted over two weeks. The findings of this analysis are graphically shown in Figure 2. With an increase in the duration of therapy, the wound

healing capacity improved for all five formulations. This was achieved by a gradual decrease in the wound's size over 14 days. The data demonstrate mean healing rates of 21.006%, 32.72%, 19.94%, 39.17%, and 27.5% for the five formulations.

Figure 3 displays the results of drug content analysis for five distinct formulations conducted over two weeks. A study is performed on the medication content used in wound therapy to optimize its effectiveness in healing wounds. The proposed S-PNP approach determines the medicine dosage by considering wound size, characteristics, and other pertinent criteria. The utilization of bioactive components leads to an enhanced therapy procedure.

An examination of particle diameter over many days is conducted, and the findings are graphically shown in Figure 4. An analysis is performed on the five distinct formulations, leading to an improved approach to treating the process. The treatment method is intricately linked to the wound-healing process. The bioactive constituents are utilized directly in pharmaceuticals to treat and facilitate the process of healing.

The zeta potential measurement for five compositions across many days is in Figure 5. SIM has low water solubility. The medication that was not administered has a solubility of 1.32±0.21 µg/mL, that matches the information in the literature. The best formulation of S-PNP has a liquidity of 32.64±2.6 µg/mL. This indicates a significant increase in solubility by a factor of around 28.3.

When tested in a phosphate buffer with a pH of 6.5, the SIM hydrogel exhibited a release rate ranging from 1% to 4% during the first 25 minutes. This rate climbed from 20% to 25% after 24 hours, reaching 32% to 48% after twenty-four hours. When placed in a liquid environment, the hydrogel demonstrated a release rate of 2%–9% of SIM during the first 25 minutes. This rate climbed to 45%–52% after twelve hours and reached 61%–75% following 48 hours. The raw SIM Carbopol® gel only released 42% of the substance.

Ex vivo animal skin prototypes can be employed as an alternative to human skin due to ethical, security, and economic considerations. This study presents crucial data on the capacity of the formulated substances to penetrate the layers of skin. Within 25 minutes, 3.17% of SIM could pass using the skin. After 1 day, 42.53% of SIM had permeated via the skin, and after twenty-four hours, the permeation rate increased to 62.42%. The ex vivo skin penetration outcomes were considerably lower than the in vitro dissolution outcomes, which showed that only 10% of SIM disappeared following the initial half an hour and 74% after twenty-four hours. This disparity was substantial, with a p-value of less than 0.12. This might be attributed to the intricate composition of the skin, which significantly diverges from that of a cellophane barrier.

5. Conclusion

Simvastatin Polymeric Nanoparticles (S-PNP) were synthesized using nanoprecipitation technology to improve the medicine's solubility and capacity to permeate the skin. An evaluation was conducted on the drug details, dissolution, particle dimension, charged area, and microscopy of the generated S-PNP. The hydrogel was treated with S-PNP, and its physical characteristics, controlled release performance, and ability to penetrate a biological membrane were evaluated. The findings demonstrated that the use of postbiotics on the cold cream compositions on wounds in a rat model resulted in a quicker pace of wound healing compared to the populations of rats who received no therapy or were treated with freezing cream lacking postbiotics and based on the measurements of wound diameters and the rate of healing wounds, had the highest efficacy. Concerning the hydroxyproline content, B.S. natto exhibited the greatest concentration of hydroxyproline.

Moreover, histological analysis revealed that both L. reuteri and B.S. natto showed superior wound-healing properties. The soluble form of SIM has been enhanced by a factor of 25.3 after being formulated into nanomaterials utilizing the nano-precipitation process. The nanomaterials exhibited better solubility with higher glycerol serving as a natural solvent. The SIM gel formulation indicated extremely encouraging outcomes in the treatment process of the rat injury over 10 days, characterized by full epithelialization, low infiltration of inflamed cells, the creation of mature collagen fibers, and enhanced development of hair follicles. The findings suggest that the newly developed postbiotics formulations might be regarded as an adjunctive treatment for promoting wound repair.

Author contribution

C.D., K.S., M.N.K. wrote, reviewed and edited the article. All authors read and approve for publication.

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Competing financial interests

The authors have no conflict of interest.

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