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Pharmacological Evaluation of the Wound Healing Potential of Rubus paniculatus in Preclinical Models

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ABSTRACT

Rubus paniculatus, a wild Himalayan raspberry traditionally used in Indian ethnomedicine, was evaluated for its wound healing efficacy using preclinical burn models. Hydroalcoholic extracts of the plant were formulated into topical creams (1% and 2.5%) and tested against silver sulfadiazine (1%) in Wistar rats with thermally induced partial-thickness burns. Phytochemical screening confirmed the presence of flavonoids, tannins, phenolics, saponins, and glycosides—compounds known for their antioxidant and anti-inflammatory properties. Over a 21-day treatment period, the 2.5% extract formulation significantly accelerated wound contraction, epithelialization, and skin restoration compared to controls and standard treatment ($p < 0.0001$). Histological and physical observations supported enhanced tissue regeneration and cosmetic recovery. These findings validate the traditional use of R. paniculatus in wound care and highlight its potential as a plant-based therapeutic for burn management

Keywords: *Rubus paniculatus, wound healing, burn model, phytotherapy, silver sulfadiazine, topical formulation, preclinical pharmacology.*

1. INTRODUCTION

Wound healing is a complex, multistage biological process involving haemostasis, inflammation, proliferation, and remodelling. It is essential for restoring the skin's barrier function and maintaining homeostasis after injury. Disruption of this process, particularly in chronic wounds, can lead to delayed healing, infection, and scarring, posing a significant clinical burden worldwide [1,2].

The skin's regenerative capacity is orchestrated by a dynamic interplay of immune cells, growth factors, and extracellular matrix components. These elements coordinate to clear pathogens, stimulate angiogenesis, and promote re-epithelialization [1,3]. However, conventional wound therapies often fall short in addressing chronic or infected wounds, prompting interest in plant-based alternatives with anti-inflammatory, antioxidant, and antimicrobial properties [4,5].

Rubus paniculatus, a wild Himalayan raspberry, has been traditionally used in Indian medicine for treating skin injuries and infections. Its phytochemical profile includes flavonoids, tannins, phenolics, and saponins—compounds known to support tissue regeneration [2,6]. Despite its ethnomedicinal relevance, scientific validation of its wound healing potential remains limited.

This study aims to evaluate the pharmacological efficacy of *R. paniculatus* extract in a preclinical burn model, comparing its performance to silver sulfadiazine—a standard topical antimicrobial agent widely used in burn care [7]. The investigation includes phytochemical screening, topical formulation development, and in vivo assessment of wound contraction, epithelialization, and skin restoration

2. MATERIALS AND METHOD

2.1 Plant Collection and Extraction

Leaves of *R. paniculatus* were collected from Uttarakhand, India, authenticated, and subjected to hydroalcoholic extraction using Soxhlet apparatus (ethanol: water, 70:30 v/v). The extract was concentrated under reduced pressure to yield a semi-solid crude extract [2].

2.2 Phytochemical Screening

Qualitative analysis confirmed the presence of flavonoids, tannins, phenolics, saponins, glycosides, and proteins—compounds associated with wound healing activity.

2.3 Formulation of Topical Cream

Two concentrations (1% and 2.5% w/w) of *R. paniculatus* extract were incorporated into an oil-in-water emulsion base. The

final pH was adjusted to 5.5 ± 0.2, and the creams were stored in sterile containers.

2.4 Experimental Animals and Burn Induction

Healthy adult male Wistar rats (150–200 g) were used. Partial-thickness burns were induced using a heated cylindrical metal rod under thiopental anesthesia. Animals were divided into five groups (n=6): untreated control, cream base, silver sulfadiazine (1%), *R. paniculatus* 1%, and *R. paniculatus* 2.5%. Treatments were applied topically once daily for 21 days.

Group I: Negative control (no treatment)

Group II: Positive control (cream base)

Group III: Standard (silver sulfadiazine 1%)

Group IV: Test A (*R. paniculatus* cream 1%)

Group V: Test B (*R. paniculatus* cream 2.5%)

Topical treatments (100 mg/rat) were applied once daily for 21 days.

2.5 Evaluation Parameters

Wound diameter was measured on Days 0, 7, 14, and 21

Epithelialization time was recorded

Skin restoration was scored visually

Data were analyzed using one-way ANOVA followed by Tukey's post hoc test ($p < 0.05$)

3. RESULT

3.1 Phytochemical Profile

The extract tested positive for flavonoids, tannins, phenolics, saponins, glycosides, and proteins. Alkaloids were absent. These constituents are known to modulate inflammation, promote collagen synthesis, and support angiogenesis [4,6].

3.2 Wound Contraction

By Day 21, the 2.5% *R. paniculatus* group showed the greatest reduction in wound diameter (3.35 ± 0.19 mm), significantly outperforming silver sulfadiazine (5.10 ± 0.14 mm) and controls ($p < 0.0001$).

See Table 1-4 for detailed wound diameter measurements and statistical comparisons.

3.3 Epithelialization and Skin Restoration

The 2.5% extract group exhibited the shortest epithelialization time (12.5 ± 0.55 days) and the highest skin restoration score (4.67 ± 0.52), indicating near-complete recovery with minimal scarring.

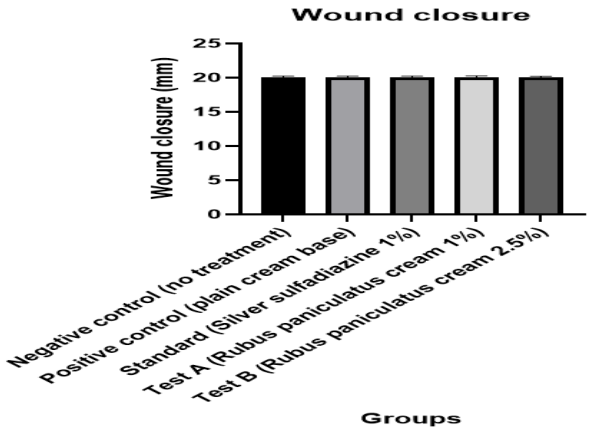
Refer to Table 5-6.

WOUND CONTRACTIONS- At Day 0: Table 1

S. No	Group Name	Total diameter
1	Negative control (no treatment)	20.05 ± 0.1871
2	Positive control (plain cream base)	20.05 ± 0.1871
3	Standard (Silver sulfadiazine 1%)	20.03 ± 0.2160
4	Test A (*Rubus paniculatus* cream 1%)	20.03 ± 0.2582
5	Test B (*Rubus paniculatus* cream 2.5%)	20.03 ± 0.1862

S.no	Tukey's multiple comparison tests	Mean Difference	95.00% CI of diff.	Significant?	Adjusted P Value
1	Negative vs Positive group	0.000	-0.3541 to 0.3541	no	>.999
2	Positive vs. Standard group	0.01667	-0.3374 to 0.3707	no	>.999
3	Positive vs Test A group	0.01667	-0.3374 to 0.3707	no	>.999
4	Positive vs Test B group	0.01667	-0.3374 to 0.3707	no	>.999
5	Standard vs Test B group	0.000	-0.3541 to 0.3541	no	>.999
6	Test A vs Test B	0.000	-0.3541 to 0.3541	no	>.999

Graph 1.

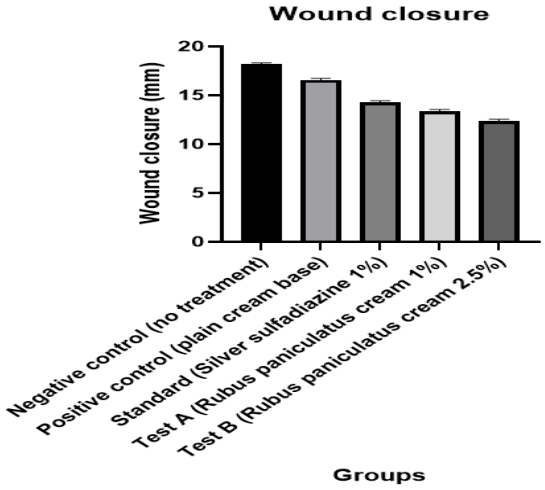


At Day 7: Table 2

S. No	Group Name	Total diameter
1	Negative control (no treatment)	18.8 ± 0.1472
2	Positive control (plain cream base)	16.55 ± 0.1871
3	Standard (Silver sulfadiazine 1%)	14.25 ± 0.1871
4	Test A (*Rubus paniculatus* cream 1%)	13.35± 0.1871
5	Test B (*Rubus paniculatus* cream 2.5%)	12.35 ± 0.1871

S.no	Tukey's multiple comparison tests	Mean Difference	95.00% CI of diff.	Significant?	Adjusted P Value
1	Negative vs Positive group	1.633	1.328 to 1.938	yes	<.001
2	Positive vs. Standard group	2.300	1.995 to 2.605	yes	<.001
3	Positive vs Test A group	3.200	2.895 to 3.505	yes	<.001
4	Positive vs Test B group	4.200	3.895 to 4.505	yes	<.001
5	Standard vs Test B group	1.900	1.595 to 2.205	yes	<.001
6	Test A vs Test B	1.000	0.6951 to 1.305	yes	<.001

Graph 2.

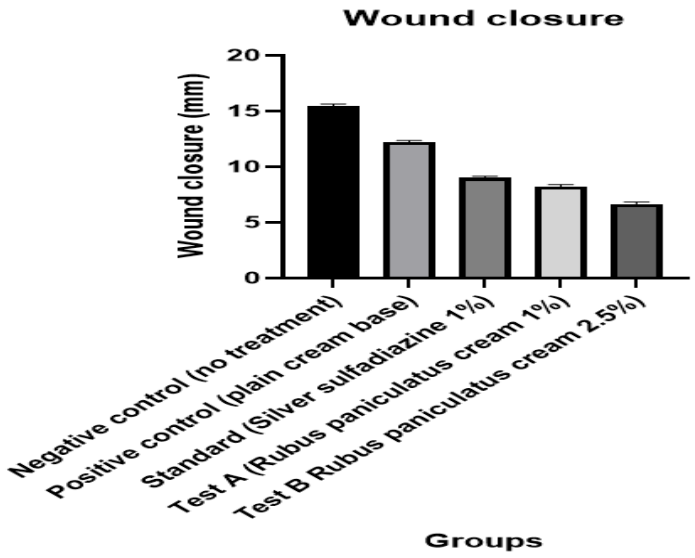


At Day 14: Table 3

S. No	Group Name	Total diameter
1	Negative control (no treatment)	15.45 ± 0.1871
2	Positive control (plain cream base)	12.22 ± 0.1472
3	Standard (Silver sulfadiazine 1%)	9.017 ± 0.1472
4	Test A (*Rubus paniculatus* cream 1%)	8.233 ± 0.1633
5	Test B (*Rubus paniculatus* cream 2.5%)	6.650 ± 0.1871

S.no	Tukey's multiple comparison tests	Mean Difference	95.00% CI of diff.	Significant?	Adjusted P Value
1	Negative vs Positive group	3.233	2.950 to 3.517	yes	<0.0001
2	Positive vs. Standard group	3.200	2.916 to 3.484	yes	<0.0001
3	Positive vs Test A group	3.983	3.700 to 4.267	yes	<0.0001
4	Positive vs Test B group	5.567	5.283 to 5.850	yes	<0.0001
5	Standard vs Test B group	2.367	2.083 to 2.650	yes	<0.0001
6	Test A vs Test B	1.583	1.300 to 1.867	yes	<0.0001

Graph 3



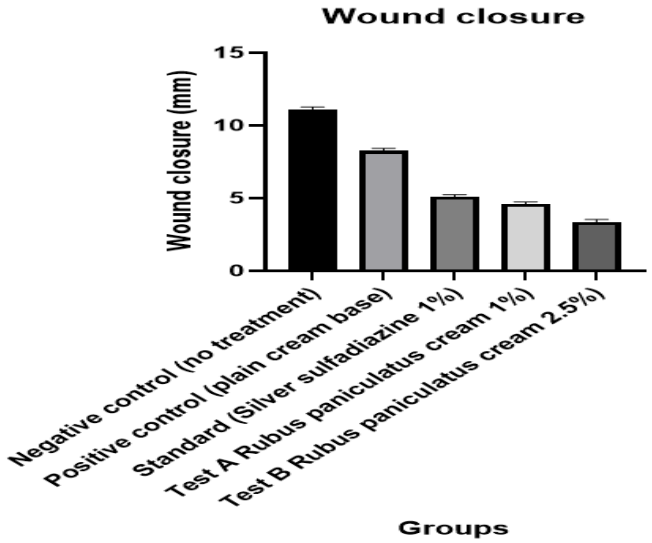
At Day 21: Table 4

S. No	Group Name	Total diameter
1	Negative control (no treatment)	11.12 ± 0.1472
2	Positive control (plain cream base)	8.250 ± 0.1871
3	Standard (Silver sulfadiazine 1%)	5.100 ± 0.1414
4	Test A (*Rubus paniculatus* cream 1%)	4.600 ± 0.1414

5	Test B (*Rubus paniculatus* cream 2.5%)	3.350 ± 0.1871

S.no	Tukey's multiple comparison tests	Mean Difference	95.00% CI of diff.	Significant?	Adjusted P Value
1	Negative vs Positive group	2.867	2.592 to 3.142	yes	<0.0001
2	Positive vs. Standard group	3.150	2.875 to 3.425	yes	<0.0001
3	Positive vs Test A group	3.650	3.375 to 3.925	yes	<0.0001
4	Positive vs Test B group	4.900	4.625 to 5.175	yes	<0.0001
5	Standard vs Test B group	1.750	1.475 to 2.025	yes	<0.0001
6	Test A vs Test B	1.250	0.9748 to 1.525	yes	<0.0001

Graph 4.

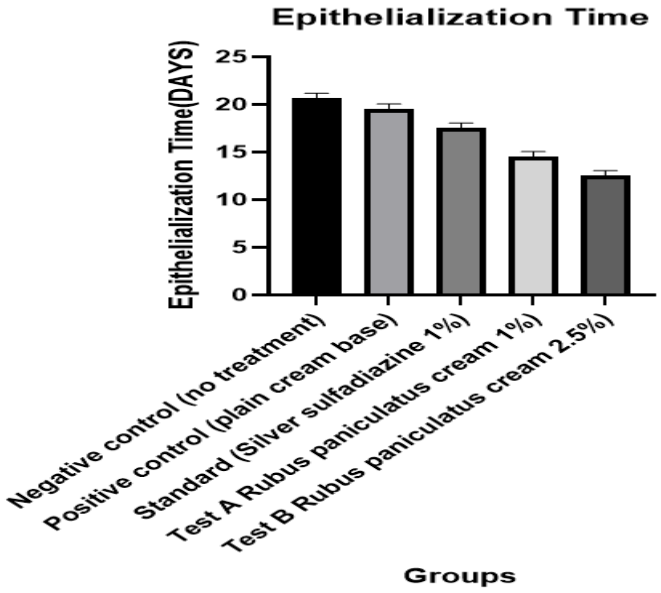


EPITHELIAZATION TIME: 21-DAY OBSERVATION PERIOD

Table 5

S. No	Group Name	Total diameter
1	Negative control (no treatment)	20.67 ± 0.5164
2	Positive control (plain cream base)	19.50 ±0.5477
3	Standard (Silver sulfadiazine 1%)	17.50 ± 0.5477
4	Test A (*Rubus paniculatus* cream 1%)	14.50 ± 0.5477
5	Test B (*Rubus paniculatus* cream 2.5%)	12.50 ± 0.5477

Graph 5.



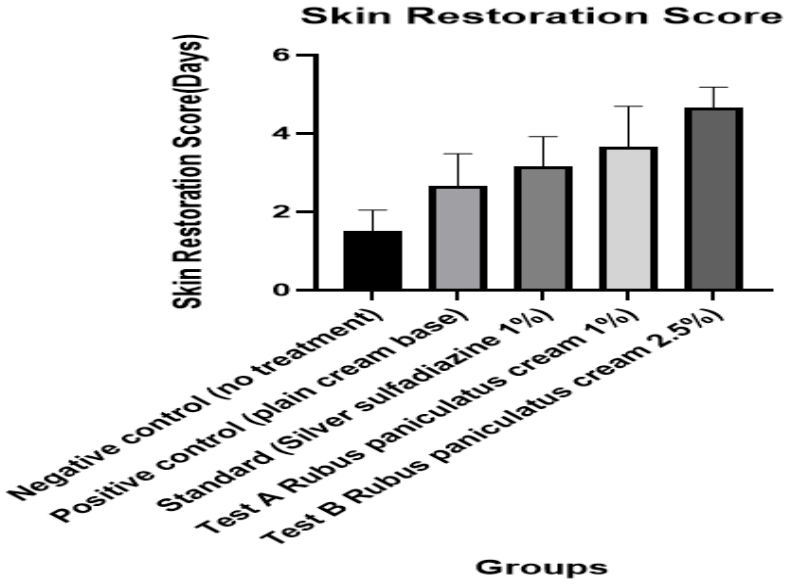
5.2.3 SKIN RESTORATION DAY (21 DAYS)

Table 6

S. No	Group Name	Total diameter
1	Negative control (no treatment)	1.500 ± 0.5477
2	Positive control (plain cream base)	2.667 ± 0.8165
3	Standard (Silver sulfadiazine 1%)	3.167 ± 0.7528

4	Test A (*Rubus paniculatus* cream 1%)	3.667 ± 1.033
5	Test B (*Rubus paniculatus* cream 2.5%)	4.667 ± 0.5164

Graph 6.



4. DISCUSSION

The findings demonstrate that *R. paniculatus* extract significantly enhances wound healing in a dose-dependent manner. The 2.5% formulation outperformed silver sulfadiazine in wound contraction, epithelialization, and cosmetic restoration. These effects are likely mediated by the extract's phytochemicals, which modulate oxidative stress, inflammation, and fibroblast activity [2,4,6].

Silver sulfadiazine, while effective against burn-related infections, has limitations such as delayed epithelialization and potential cytotoxicity [7]. In contrast, plant-based therapies offer a safer, multi-targeted approach to wound repair [5,8].

The results align with previous studies on Rubus species, which have shown antimicrobial, antioxidant, and anti-inflammatory properties relevant to skin regeneration [4,6]. Importantly, no adverse effects were observed, supporting the extract's safety for topical use.

5. CONCLUSION

This study provides compelling preclinical evidence supporting the wound healing efficacy of *Rubus paniculatus* extract when formulated into a topical cream. The 2.5% extract formulation demonstrated superior performance across all evaluated parameters—including wound contraction, epithelialization time, and skin restoration score—compared to both the untreated controls and the standard silver sulfadiazine treatment. These outcomes were statistically significant and biologically relevant, indicating that *R. paniculatus* not only accelerates wound closure but also enhances the quality of tissue regeneration. The observed therapeutic effects are likely attributable to the extract's rich phytochemical composition, particularly flavonoids, phenolics, and saponins, which are known to modulate oxidative stress, inflammation, and fibroblast activity. Unlike silver sulfadiazine, which is associated with delayed epithelialization and potential cytotoxicity, the plant-based formulation was well tolerated and showed no signs of irritation or adverse effects throughout the study period. Importantly, this research bridges traditional ethnomedicinal knowledge with modern pharmacological validation. It positions *R. paniculatus* as a promising candidate for the development of safe, effective, and affordable botanical wound care products—especially in resource-limited settings where access to conventional therapies may be restricted.

Future studies should focus on elucidating the molecular mechanisms underlying its regenerative effects, optimizing formulation stability, and conducting clinical trials to confirm its efficacy in human subjects. Additionally, standardization

of extract composition and quality control parameters will be essential for regulatory approval and therapeutic translation.

In conclusion, *Rubus paniculatus* represents a scientifically validated, phytochemically rich, and clinically relevant plant species with significant potential to enhance wound healing outcomes. Its integration into modern wound care protocols could offer a valuable alternative or adjunct to conventional treatments, particularly in the management of superficial burns and chronic skin injuries.

6. LIST OF ABBREVIATIONS

ANOVA – Analysis of Variance

CD – Cluster of Differentiation

ECM – Extracellular Matrix

EGF – Epidermal Growth Factor

EGFR – Epidermal Growth Factor Receptor

FGF – Fibroblast Growth Factor

HIF – Hypoxia-Inducible Factor

IAEC – Institutional Animal Ethics Committee

IL – Interleukin

MMP – Matrix Metalloproteinase

NF-κB – Nuclear Factor kappa-light-chain-enhancer of activated B cells

PDGF – Platelet-Derived Growth Factor

ROS – Reactive Oxygen Species

SEM – Standard Error of Mean

TGF-β – Transforming Growth Factor Beta

TNF-α – Tumor Necrosis Factor Alpha

VEGF – Vascular Endothelial Growth Factor

WIHN – Wound-Induced Hair Neogenesis

WHO – World Health Organization

Conflict of Interest: The author has no conflict of interest.

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Author Contribution

VS- Writing original

Draft WK- Original concept

SS- Supervision

Ethical Approval: The research study was conducted at Siddhartha institute of pharmacy, Near IT park, Dehradun 248001. The animal house is CPCSEA approval. And the registration no. of the animal house – 1435/PO/RE/S/11/CPCSEA..

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