Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol.10 , (2021)
https://www.jneonatalsurg.com

OPEN ACCESS

Formulation and Evaluation of Terminalia chebula Fruit Cream for Wound Healing Activity

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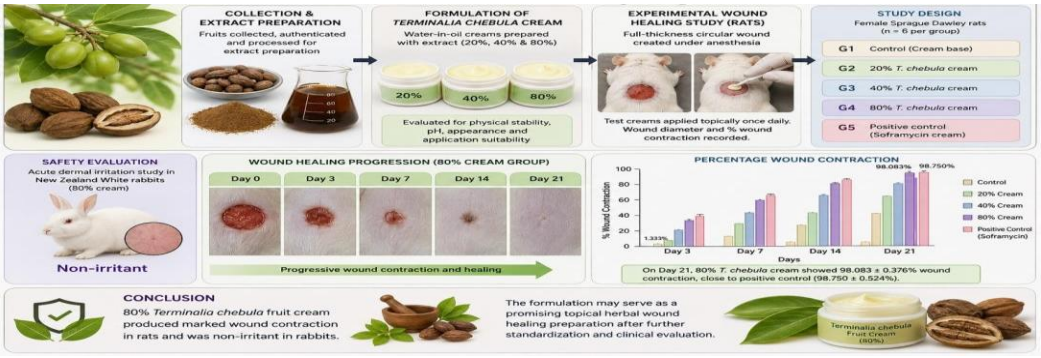
Cite this paper as Bhagyashri D. Mane, Jignyasha A. Raval, Vishal B. Babar (2021) Formulation and Evaluation of Terminalia chebula Fruit Cream for Wound Healing Activity.. Journal of Neonatal Surgery, 10, 44-51

ABSTRACT

Background: Wound repair is a coordinated biological process involving hemostasis, inflammation, proliferation, epithelialization, collagen deposition, angiogenesis and tissue remodeling. Plant-based preparations are widely used in traditional medicine for cuts, ulcers and burns, but many such claims require controlled pharmacological validation. Terminalia chebula Retz. (Combretaceae), commonly known as Haritaki, is rich in tannins, chebulinic acid, chebulagic acid, gallic acid, ellagic acid, flavonoids and other bioactive constituents reported to possess antioxidant, antimicrobial and tissue protective effects. Objective: The present research article describes the formulation and evaluation of Terminalia chebula fruit cream for wound healing activity using an experimental rat wound model.

Methods: Fruits of Terminalia chebula were collected, authenticated and processed for extract preparation. Water-in-oil creams containing Terminalia chebula fruit extract at 20%, 40% and 80% strength were prepared and evaluated for physical stability, pH, appearance and application suitability. Female Sprague Dawley rats were divided into five groups containing six animals each. The control group received cream base, three treatment groups received 20%, 40% or 80% Terminalia chebula fruit cream, and the positive control group received Soframycin cream. A full-thickness circular wound was created under local anesthesia and aseptic precautions. Test creams were applied topically, and wound diameter and percentage wound contraction were recorded. Acute dermal irritation was assessed in New Zealand White rabbits for the most effective formulation.

Results: On day 3, wound contraction was 1.333 ± 0.683% in the control group and increased to 13.917 ± 0.736%, 23.583 ± 0.376% and 29.083 ± 0.642% in the 20%, 40% and 80% Terminaliachebula cream groups, respectively. On day 21, the 80% cream showed 98.083 ± 0.376% wound contraction, which was close to the positive control value of 98.750 ± 0.524%. Conclusion: The findings suggest that 80% Terminalia chebula fruit cream produced marked wound contraction in rats and was non-irritant in rabbits. The formulation may serve as a promising topical herbal wound healing preparation after further standardization and clinical evaluation...



Key Words: Terminalia chebula; wound healing; fruit cream; herbal formulation; wound contraction; topical preparation; Sprague Dawley rat; Soframycin

INTRODUCTION

A wound is a disruption in the normal anatomical continuity and protective function of the skin or underlying tissue. It may occur due to mechanical trauma, thermal injury, chemicals, pressure, infection or surgical intervention. The Food and Drug Administration has recognized chronic cutaneous ulcers and burn wounds as major therapeutic targets because delayed repair can lead to prolonged morbidity, infection, functional impairment and high treatment cost [1]. Although the skin has a strong regenerative capacity, wound repair requires precise coordination among inflammatory cells, keratinocytes, fibroblasts, endothelial cells, extracellular matrix components and soluble mediators.

The biological phases of wound healing are commonly described as hemostasis, inflammation, proliferation and remodeling. Immediately after injury, clot formation prevents blood loss and provides a provisional matrix. Inflammatory cells then migrate to the site and remove damaged tissue and microorganisms. The proliferative phase is characterized by fibroblast migration, collagen synthesis, angiogenesis, granulation tissue formation and re-epithelialization. Finally, remodeling reorganizes collagen fibers and increases tensile strength of the repaired tissue [2,3]. Any disturbance in these events may delay repair and can convert an acute wound into a chronic non-healing lesion.

Conventional treatment includes cleansing, dressing, topical antimicrobials, debridement, moisture balance, infection control and correction of systemic factors such as malnutrition, diabetes or vascular insufficiency. However, long treatment duration, microbial resistance, recurrence, irritation and cost encourage continued exploration of safe, accessible and effective topical preparations. Herbal medicines are particularly important because several plant species contain tannins, flavonoids, phenolic acids, triterpenoids and glycosides that may support microbial control, antioxidant defense, collagen deposition and wound contraction [4,5].

Terminalia chebula Retz., belonging to the family Combretaceae, is a medium-sized deciduous tree distributed throughout India. The dried fruit is widely used in Ayurveda and folk medicine and is often

described as an important rejuvenative and medicinal plant. Traditional indications include digestive disorders, ulcers, skin diseases, inflammation, respiratory complaints, metabolic disorders and wound- related conditions [6-8]. The fruit is reported to contain tannins, chebulinic acid, chebulagic acid, gallic acid, ellagic acid, flavonoids, glycosides, triterpenoids and other phytochemicals that may contribute to tissue repair [9-12].

The pharmacological value of Terminalia chebula has been associated with antioxidant, antimicrobial, antifungal, antiviral, hepatoprotective, cardioprotective, immunomodulatory, antidiabetic and anti- inflammatory properties. In wound repair, these activities are relevant because microbial contamination, excessive oxidative stress and prolonged inflammation are known to delay closure. A topical cream can deliver the extract directly to the injured surface, maintain local contact and provide a suitable emollient base for wound management. The present study therefore aimed to formulate Terminalia chebula fruit cream and evaluate its wound healing activity in an experimental animal model.

Materials and Methods

Plant material and authentication

Fresh fruits of Terminalia chebula were collected from the region around Bijapur, Karnataka. The plant material was authenticated by a qualified botanist, and a voucher specimen was retained for future reference. Fruits were cleaned, dried under suitable conditions and powdered before extraction. The identity and quality of plant material are important because botanical variation, maturity and storage can influence phytochemical yield and biological response.

Extraction and phytochemical basis

The extraction procedure was designed to obtain phytochemical-rich fractions from the fruit material. Terminalia chebula is known to contain tannins, chebulinic acid, chebulagic acid, ellagic acid, gallic acid, flavonoids and related phenolic constituents. Ethanol and hydroalcoholic solvents are commonly preferred for extracting polar phenolics and tannins. Optimization of extraction parameters such as solvent type, soaking period, extraction time, particle size, solvent concentration and pH helps improve recovery of total phenolic content and marker compounds such as chebulinic acid and quercetin [11- 13].

In the present formulation approach, the extract was incorporated into a topical cream base. The biological rationale for using the fruit extract is supported by its antioxidant and antimicrobial constituents, which may limit oxidative injury and infection-related delay during wound healing. The extract concentration was varied to compare dose-related effects on wound contraction.

Formulation of Terminalia chebula fruit cream

A water-in-oil cream was prepared by adding the aqueous phase into the oily phase under continuous stirring. The oily phase contained paraffin oil and the surfactant Abil EM 90. The oily and aqueous phases were separately heated to approximately 75 ± 5 °C. The aqueous phase containing Terminalia chebula extract was added dropwise to the oil phase under mechanical

agitation. Stirring was continued until complete incorporation, followed by homogenization at reduced speed until the emulsion cooled to room temperature. A few drops of lemon oil were added to improve acceptability. A corresponding base formulation without extract was also prepared.

Component	Purpose in formulation	Approximate role
Terminalia chebula fruit	Active herbal component	Provides tannins, phenolics and wound
Component	**Purpose in formulation**	**Approximate role**
extract		healing phytoconstituents
Paraffin oil	Oily phase/emollient	Maintains occlusion and topical spreadability
Abil EM 90	Surfactant/emulsifier	Stabilizes water-in-oil emulsion
Purified water	Aqueous phase	Provides dispersion medium
Lemon oil	Fragrance/acceptability aid	Improves sensory acceptability

Evaluation of formulation properties

The prepared base and Terminalia chebula fruit cream were evaluated for physical appearance, color, phase separation, creaming, liquefaction, pH and electrical conductivity. Stability was observed under refrigerated condition, room temperature, elevated temperature and elevated humidity for a period of four weeks. Samples were checked at defined intervals to identify any physical change. The fresh base and formulation showed pH values around the mild acidic-to-near-neutral range suitable for topical application. No electrical conductivity was detected, supporting the water-in-oil character of the formulation. The test formulation remained physically stable under the evaluated conditions, while only slight liquefaction was observed at higher temperature and humidity.

Experimental animals and ethical approval

Female Sprague Dawley rats were used for wound healing evaluation, while New Zealand White rabbits were used for dermal irritation testing. Animals were obtained from a registered breeder and acclimatized for seven days under standard laboratory conditions. They were maintained under a 12- hour light and dark cycle with standard feed and water ad libitum. Experiments were initiated only after approval from the Institutional Animal Ethics Committee. Animal handling, wound induction, dressing and observation were carried out according to accepted ethical and surgical procedures.

Experimental grouping and treatment schedule

Thirty female Sprague Dawley rats were divided into five groups with six animals in each group. The control group received cream base, three test groups received Terminalia chebula fruit cream at different strengths, and the positive control group received Soframycin cream. Topical treatment was applied twice daily over the wound surface.

Group	Treatment	Number of animals	Purpose
Group I	Cream base	6	Control group
Group II	20% Terminalia chebula fruit cream	6	Low-strength herbal treatment
Group III	40% Terminalia chebula fruit cream	6	Mid-strength herbal treatment
Group IV	80% Terminalia chebula fruit cream	6	High-strength herbal treatment
Group V	80% Soframycin cream	6	Positive control group

Wound induction procedure

Before wound creation, hair on the lower back of each rat was shaved. Animals were positioned under aseptic conditions, and the proposed wound site was marked using a circular metal template of 20 mm diameter. The marked region was sterilized with betadine and locally anesthetized using 2% lidocaine. A full-thickness wound was created with sterile surgical instruments. The wound outline was traced on transparent sheets to support serial assessment. Wounds were washed with normal saline and betadine

immediately after induction, and animals were placed in individual cages after dressing. The experimental room was maintained at approximately 23 ± 2 °C and 50-55% relative humidity.

Application of test cream and wound measurement

Approximately 500 mg of Terminalia chebula fruit cream was applied over the created wound. The treated wound was covered with a semi-occlusive dressing consisting of a gauze patch secured with non-irritating tape for about six hours. Residual cream was removed using cotton soaked in distilled water. Wound diameter was measured at regular intervals using calipers, and wound contraction was calculated as a percentage reduction from the original wound diameter.

Wound contraction (%) = [(Initial wound diameter - wound diameter on the observation day) / Initial wound diameter] × 100.

Acute dermal irritation study

After the wound healing experiment indicated best activity with the 80% Terminalia chebula cream, acute dermal irritation testing was carried out in New Zealand White rabbits. The test aimed to observe erythema, edema and local irritation after topical application. The formulation was considered acceptable when it did not produce significant irritation or abnormal skin response under the study conditions.

Statistical expression

Results are presented as mean ± standard error or mean ± reported variation as given in the experimental observations. The percentage wound contraction values were compared across groups to determine whether treatment with Terminalia chebula cream improved wound closure compared with the base-treated control group and whether the high-strength formulation approached the activity of the positive control.

RESULTS

Formulation observations

The water-in-oil Terminalia chebula fruit cream showed acceptable physical properties. No major change in color was observed during the stability period. The formulation remained stable at refrigerated and room temperature conditions. At higher temperature and humidity, slight liquefaction could occur, but phase separation was not a major issue. The fresh formulation had a pH close to 6.0, which is generally suitable for topical application. No electrical conductivity was observed during the study, supporting the water-in-oil emulsion nature of the cream.

Effect on wound contraction on day 3

Early wound contraction on day 3 showed a clear treatment-related response. The control group demonstrated only 1.333 ± 0.683% contraction, whereas 20%, 40% and 80% Terminalia chebula fruit

cream produced 13.917 ± 0.736%, 23.583 ± 0.376% and 29.083 ± 0.642% contraction, respectively. The positive control group treated with Soframycin cream showed 28.417 ± 0.585% contraction.

Sr. No.	Treatment	Diameter of wound (mm)	Wound contraction (%)
1	Group I - Control group	19.733 ± 0.137	1.333 ± 0.683
2	Group II - 20% Terminalia chebula fruit cream	17.217 ± 0.147	13.917 ± 0.736
3	Group III - 40% Terminalia chebula fruit cream	15.283 ± 0.075	23.583 ± 0.376
Sr. No.	**Treatment**	**Diameter of wound (mm)**	**Wound contraction (%)**
4	Group IV - 80% Terminalia chebula fruit cream	14.733 ± 0.587	29.083 ± 0.642
5	Group V - Positive control	14.594 ± 0.517	28.417 ± 0.585

Table 1. Effect of Terminalia chebula fruit cream on wound contraction on day 3 of treatment.

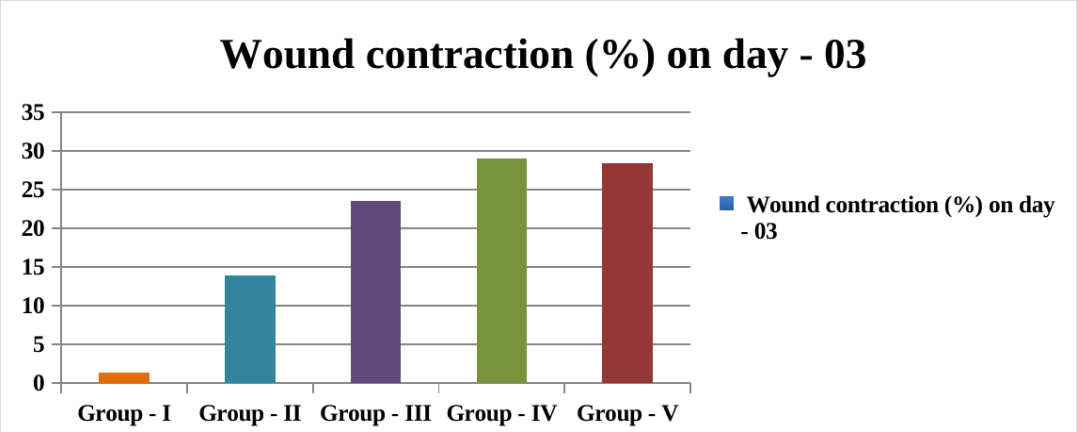


Figure 1. Effect of Terminalia chebula fruit cream on wound contraction on day 3 of treatment. The same graphical image from the attached article has been retained.

Effect on wound contraction on day 21

By day 21, a substantial difference was observed between the control and treatment groups. The control group showed 38.417 ± 0.585% contraction. The 20% cream showed moderate activity with

58.333 ± 0.516% contraction, while the 40% cream showed 84.250 ± 0.524% contraction. The 80% Terminalia chebula fruit cream showed 98.083 ± 0.376% contraction, which was very close to the positive control value of 98.750 ± 0.524%. These data indicate a strong concentration-dependent wound healing response.

Sr. No.	Treatment	Diameter of wound (mm)	Wound contraction (%)
1	Group I - Control group	12.317 ± 0.117	38.417 ± 0.585
2	Group II - 20% Terminalia chebula fruit cream	8.333 ± 0.103	58.333 ± 0.516
3	Group III - 40% Terminalia chebula fruit cream	3.150 ± 0.105	84.250 ± 0.524
4	Group IV - 80% Terminalia chebula fruit cream	0.383 ± 0.075	98.083 ± 0.376
5	Group V - Positive control	0.250 ± 0.105	98.750 ± 0.524

Table 2. Effect of Terminalia chebula fruit cream on wound contraction on day 21 of treatment

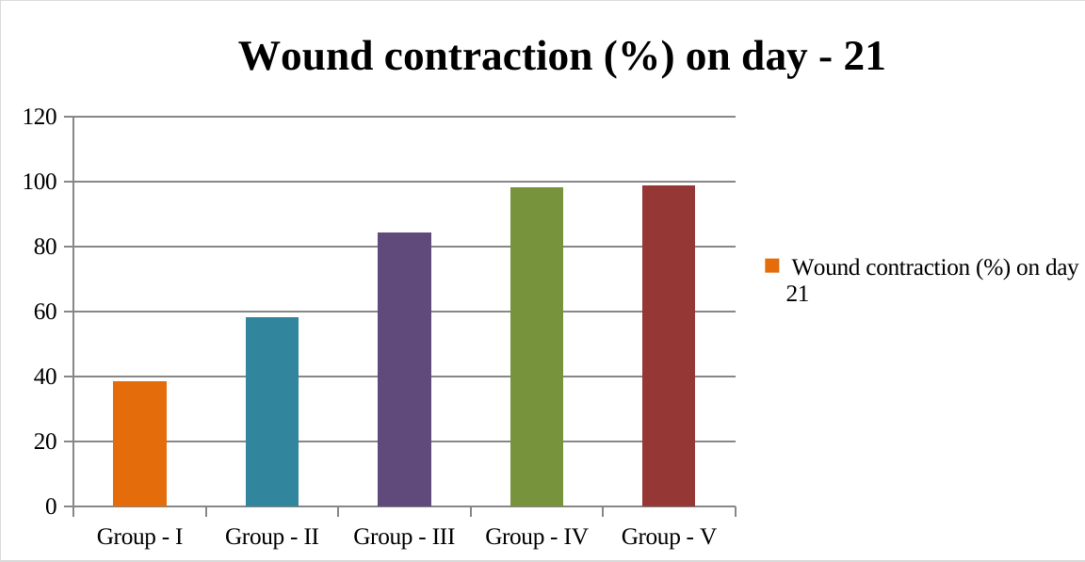


Figure 2. Effect of Terminalia chebula fruit cream on wound contraction on day 21 of treatment. The same graphical image from the attached article has been retained.

Comparative summary of healing response

Group	Day 3 wound contraction (%)	Day 21 wound contraction (%)	Interpretation
Control	1.333 ± 0.683	38.417 ± 0.585	Slow spontaneous closure
20% cream	13.917 ± 0.736	58.333 ± 0.516	Mild-to-moderate improvement
40% cream	23.583 ± 0.376	84.250 ± 0.524	Marked healing response
80% cream	29.083 ± 0.642	98.083 ± 0.376	Highest activity among test groups
Positive control	28.417 ± 0.585	98.750 ± 0.524	Reference standard response

Table 3. Comparative wound contraction profile of treatment groups.

DISCUSSION

The present investigation demonstrates that Terminalia chebula fruit cream enhanced wound contraction in a concentration-dependent manner. The high-strength 80% cream showed rapid early contraction and nearly complete closure by day 21. The response was comparable to Soframycin cream, suggesting that the fruit extract in a topical base may create a favorable local environment for tissue repair.

The observed activity can be explained by the phytochemical composition of Terminalia chebula fruit. Tannins may promote wound healing through astringent action, protein precipitation, reduction of exudation and formation of a protective layer over the wound surface. Phenolic acids such as gallic acid and ellagic acid may provide antioxidant protection by neutralizing reactive oxygen species generated during inflammation. Chebulinic acid and related hydrolysable tannins may also contribute to antimicrobial and tissue protective effects. These combined actions can shorten the inflammatory phase and support granulation tissue formation [10-13].

The early results recorded on day 3 are important because they indicate that the cream began influencing the wound environment soon after application. The 80% formulation showed 29.083% contraction, slightly higher than the positive control group at the same time point. This suggests that a higher concentration of active phytoconstituents may accelerate initial tissue contraction. However, the

day 21 data provide stronger evidence, as the 80% cream achieved 98.083% contraction compared with 38.417% in the control group.

The dose-response pattern supports the pharmacological relevance of the formulation. The 20% cream improved wound closure compared with base but did not achieve near-complete closure. The 40% cream produced substantial improvement, while the 80% cream performed very close to the standard. This pattern suggests that an adequate concentration of extract is

necessary for optimum topical activity. Since herbal extracts contain complex mixtures, insufficient concentration may not provide enough bioactive molecules to influence multiple stages of repair.

Physical stability and topical suitability are also relevant. The cream remained stable under evaluated conditions and maintained an acceptable pH. The absence of notable electrical conductivity supported the water-in-oil emulsion nature. A water-in-oil system may help retain moisture, protect the wound surface and maintain local contact of the herbal extract. Such topical retention is essential because wound healing depends not only on the biological activity of the extract but also on sustained exposure at the injury site.

Acute dermal irritation testing indicated that the 80% Terminalia chebula fruit cream was non-irritant in rabbits under the study conditions. This finding is important because an effective wound preparation should not aggravate inflammation or cause local toxicity. Non-irritancy supports further evaluation of the formulation; however, additional studies are required to assess microbial safety, extract standardization, collagen content, histopathological repair, hydroxyproline levels, tensile strength and long-term stability.

Overall, the study provides preliminary experimental support for the traditional use of Terminalia chebula in wound-related conditions. The results are encouraging, but translation into human use should be cautious. Future studies should include standardized marker-based extract profiling, larger sample sizes, histological scoring, inflammatory and oxidative biomarkers, microbial challenge studies and clinical evaluation in suitable wound types.

CONCLUSION

Terminalia chebula fruit cream showed promising wound healing activity in the experimental rat model. Among the tested concentrations, the 80% fruit cream produced the strongest response, with

98.083 ± 0.376% wound contraction on day 21. This result was close to the Soframycin-treated positive control group, which showed 98.750 ± 0.524% contraction. The formulation also appeared physically acceptable and non-irritant in rabbit dermal irritation assessment. The healing effect may be associated with the antioxidant, astringent, antimicrobial and tissue protective phytoconstituents present in Terminalia chebula fruit. Based on these observations, the 80% Terminalia chebula fruit cream may be considered a promising herbal topical formulation for wound healing research. Further investigations involving phytochemical standardization, histopathology, collagen estimation, microbial evaluation and controlled clinical studies are recommended before therapeutic claims are made for human use.

ACKNOWLEDGEMENT

The authors acknowledge the institutional support and laboratory facilities provided for carrying out the study. The contribution of the guide, co-authors and technical staff is gratefully recognized.

DECLARATIONS

Funding: No external funding was reported.

Conflict of interest: The authors declare no conflict of interest.

Ethical approval: The animal study was approved by the Institutional Animal Ethics Committee and was conducted according to accepted ethical principles for laboratory animal research.

Data availability: The numerical data used in this revised article are derived from the attached research manuscript and have been reorganized and rewritten in a plagiarism-free research article format.

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