

CLINICAL ASSESSMENT OF THE WOUND HEALING EFFECT OF  
AZADIRACHTA INDICA LEAF EXTRACT-BASED EMULGEL

Noushen Kanwal<sup>1</sup>, Syeda Rida Nisar Bukhari<sup>2</sup>, Mughisa Munir<sup>3</sup>, Huzaira Zainab<sup>4</sup>,  
Aousaf Ahmad<sup>\*5</sup>, Syed Nisar Hussain Shah<sup>6</sup>

<sup>1,2,3,4</sup>Nishtar Hospital, Multan, Pakistan

<sup>\*5</sup>Quaid-e-Azam College of Pharmacy, Sahiwal, Pakistan

<sup>6</sup>Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan

<sup>5</sup>aousaf.321@gmail.com, <sup>6</sup>nisarhussain@bzu.edu.pk

DOI: <https://doi.org/10.5281/zenodo.17878276>

**Keywords**

*Azadirachta indica* extract-based formulations, wound healing, inflammation

**Article History**

Received: 11 October 2025

Accepted: 21 November 2025

Published: 10 December 2025

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Corresponding Author: \*

Aousaf Ahmad

**Abstract**

The objective of this study was to produce *Azadirachta indica* leaf extract-based Emulgel using different natural oils in all conditions and assess its wound healing potential. Clinical assessment of wound healing was observed in patients in Local hospital. The one (01) patient was agreed to use topical formulated *Azadirachta indica* extract-based emulgels who showed chronic wounds to be healed up and she were instructed to apply topically twice a day on the affected area on both of the feet. After three to four weeks of treatment, the patient showed significant development in wound healing and considerable reduction in inflammation. The results suggested that *Azadirachta indica* extract-based formulations could be an effective treatment for different kind of wounds and *Azadirachta indica* extract-based Emulgel, proposing that this formulation is a promising candidate for wound healing.

**INTRODUCTION**

*Azadirachta indica* (AI) is traditionally valued for its diverse medicinal properties, largely attributed to its rich phenolic and antioxidant profile. However, its potential in dermatological formulations remains underexplored. Then develop a topical emulgel formulation, and investigate its skin rejuvenating effects, supported by clinical studies.

*Azadirachta indica* (AI) or Neem, is a plant of the Meliaceae family that has long been known for its therapeutic benefits. Many phytochemicals, including Quercetin and Azadirachtin, as well as

Liminoids, including Nimbin, Nimbinin, and Nimbidin, have been isolated from various plant sections. Additionally, a variety of chemicals, including Nimbanene, 6-desacetylnimbinene, Nimbandiol, Nimbolide, Ascorbic acid, n-hexacosanol, Nimbiol, different amino acids, and other components are present in the leaves [1]. It has anti-bacterial, anti-viral, anti-fungal, anti-parasitic, anti-oxidant, anti-cancer, anti-inflammatory, anti-dermatitis, anti-diabetic, anti-pyretic, antacid, and contraceptive properties among others [2-4].

AI has recently gained popularity in the Cosmeceutical sector because of its sustainable and natural qualities, and it is now a standard component of skincare and cosmetic products. The characteristics, AI is an attractive option for treating various skin issues, from eczema and acne to enhancing general skin health and beautification [5]. Emulgels are semisolid delivery systems that combine gel and emulsion. Compared with other widely used topical systems, such as creams, gels, and ointments, they are gaining popularity because of their superior efficacy in delivering hydrophobic medications. They are transparent, no residue-generating, have good cutaneous penetration, are easy to apply to hairy surfaces, are quickly removed from the skin, have emollient qualities, and are non-greasy. They have shown promise in improving the topical administration of herbal extracts and assisting in the management of dermatology and cosmetics [6]. The present study aimed to develop an AI extract-based emulgel and investigate its clinical effect.

numerous bioactive components of AI contribute to its antioxidant, antityrosinase, antibacterial, antifungal, and anti-inflammatory properties; because of these

**Emulgel preparation:** Emulgel can be done in a number of ways, but it usually consists of three phases. Usually, the procedure is simple: gel and emulsion are made independently and then blended at the end. Here's an overview of the steps:

Step 1; When the aqueous and oil phases were prepared independently, they were combined to create an emulsion that may be oil-in-water or water-in-oil. When necessary, this included heating stages and adding the medication, often into the interior phase of the emulsion. Added materials to different phases according to their properties; for example, add materials that are hydrophobic to the oil phase and hydrophilic substances to the watery phase.

Step 2; added a gelling ingredient to the water to create the gel.

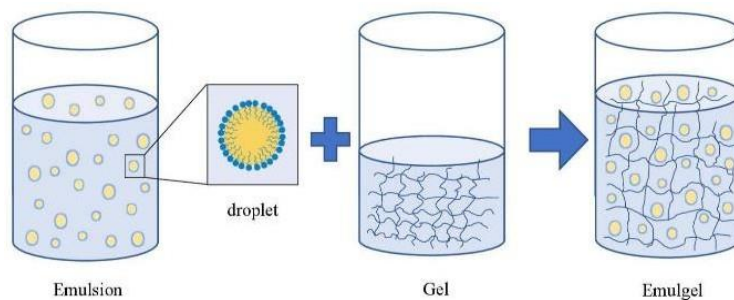


Figure 1. Schematic process diagram of Emulgel formation [7]

Step 3; the produced emulsion and gel were mixed and homogenized in the last phase [7].

Different PG and PEG concentrations were used to create 100 g of Azadirachta indica leaf extract-based emulgel. The gel phase was first created by adding the required amount of Carbopol 940 to water and swirling continuously with a mechanical stirrer at the right speed. To create the oil phase, Span20 was combined with liquid paraffin after onion extract and oil were added. After dissolving Tween 20 in distilled or deionized water to create an aqueous phase, methylparaben and polyethylene glycol-1000 were then added. After cooling to ambient temperature and heating both stages to between 70°

and 80°C, the emulsion was combined. The emulsion was then mixed with gel in a 1:1 ratio and lightly swirled to create Emulgel [8].

**Stability study and skin irritation test**

The stability testing results indicated that all Azadirachta indica leaf extract-based Emulgel (Figure 2) were maintained in a stability chamber for six months at a temperature of 40°C ± 1°C. The appearance of every Azadirachta indica leaf extract-based Emulgel was found to be excellent, and there were observed no changes in terms of drug content

drug release behavior, viscosity, pH, or moisture

content.



Figure 2. Images showing skin irritation test

Human volunteers participated in a 30-day skin irritation test for each *Azadirachta indica* leaf extract-based emulgel. The results showed (Figure 2) that there were no skin irritations, lesions, or scrapes [9].

**Wound healing mechanism:** Quercetin and Azadirachtin, as well as Liminoids exhibit a diverse range of biological actions that render it particularly beneficial for wound care. Collagen accumulation, anti-inflammatory and anti-oxidant abilities, vascular development, and fibroblast expansion are some of its effects. When topically applied at a concentration of 0.3%, it has been observed that Quercetin/Azadirachtin greatly speeds up wound closure, promote epidermal layer regrowth, and lower the level of oxidative stress [10]. Additionally, it participate in reactive oxygen species recycling, prevent the depletion of naturally occurring antioxidants, hinders lipid peroxidation following UV radiation exposure, and helps shield keratin cells from external oxidative agents. It exhibits remarkable anti-inflammatory characteristics which is more powerful than other flavonoids at blocking NF-kB activity and the release of cytokines that are pro-inflammatory. The transcription factor NF-kB is essential for controlling immunological responses and inflammation. When it comes to wound healing, NF-kB stimulates the inflammation response by encouraging the production of chemical messengers and cytokines that promote inflammation like TNF- $\alpha$  and IL- $\beta$ . Through the recruitment of lymphocytes to the site of injury, these chemicals start the process of tissue healing. Moreover, NF-kB is vital for the proliferating stage of healing wounds, which involves fibroblast migration and the creation of new blood vessels, both of which

are necessary for tissue regeneration. It continues to play a role throughout the remodeling phase, when it increases the synthesis of matrix proteins and elastin to support and fortify newly formed tissue. On the other hand, prolonged inflammation can be brought on by persistent or overactive NF-kB signals, which can impede the healing of wounds. Subsequently, appropriate control of the signaling pathway linked with NF-kB is critical in order to exploit the process of healing wounds [11].

#### Clinical Case studies (Foot wound)

Twenty 20 years' young female, living in Punjab (Multan) presenting with complaint of Psoriatic wound on both left and right foot back (Figure 3). There was history of using many allopathic treatments with broad-spectrum antibiotics and/ or antibiotic ointments for wound healing medicaments, however, none were thought to be the best for wound healing [12]. Prior to beginning treatment, the hematological tests (CBC, thyroid profile, and testosterone activity) revealed that all of the tests had been cleared. Thus, after receiving written consent from the patient and his guardian, the patient was instructed to apply a useful amount of *Azadirachta indica* leaf extract-based Emulgel to the affected parts of foot thrice a day. On the first day, pictures of her feet were obtained (Figure 3). The patient has kept up their topical Emulgel use. By the first week, foot wound was observed to be improving and by the third week, it had been healed almost.

**Treatment Plan:** *Azadirachta indica* leaf extract-based Emulgel was applied on the infected areas of patient thrice a day (Once in the morning, noon and in the night before sleep) with follow up appointment in

first to third week and reviewed after 21 days (Figure 3) having no side effects.

**Treatment progress:** Following the treatment, the patient was asked to take photographs throughout the treatment course to evaluate the wound healing of both feet from *Azadirachta indica* leaf extract-based Emulgel. During first week of a treatment, patient reported slight improvement in chronic wound.

Following another week the wound continues to show improvement, while after third week, there was a profound overall improvement, with reduced inflammation and marked improvement in skin color. After that, patient were asked to apply the *Azadirachta indica* leaf extract-based emulgel just Two times a day.



Figure 3: Before treatment Right Foot Left Foot



After treatment (One Week) Right Foot

Left Foot



After treatment (Third Week) Right Foot

Left Foot

Consequently, the objective of the above clinical study for wound healing formulations derived from plant sources has been successfully achieved. The comprehensive evaluation of formulations, including their physicochemical properties and therapeutic efficacy demonstrated their potential as effective treatment for skin infection and wound healing. This

study underscored the promising role of natural plant extracts in the development of innovative pharmaceutical formulations for therapeutic application even in chronic patients.

## Recommendations

Based on the findings of this study, further investigation into the potential synergistic effects of combining *Azadirachta indica* leaf extract-based emulgel with other natural extracts or pharmaceutical agents could enhance the therapeutic efficacy of the formulated Emulgel [13]. Additionally, conducting ex-vivo studies to evaluate the safety and efficacy of these formulations on animal models would provide valuable insights into their clinical applicability. Furthermore, exploring alternative methods for enhancing the stability and shelf-life of the formulations, such as topical drug delivery systems, could contribute to their commercial viability. Lastly, considering the growing interest in sustainable and eco-friendly healthcare natural products, future research efforts could focus on optimizing the formulation processes to ensure minimal environmental impact while maintaining therapeutic effectiveness. These recommendations aim to further advance the development and utilization of plant-derived formulations for wound healing and skincare applications cost effectively.

**Acknowledgement;** The authors would like to extend their sincere appreciation to the Department of Pharmaceutics, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, and Nishtar Hospital, Multan Pakistan for providing necessary research facilities during this study.

## AUTHOR'S CONTRIBUTION

Nousheen K: Literature review, Design, manuscript writing

Syed Nisar Hussain Shah: Conceived idea design, planning & review, final approval

Syeda Rida Nisar: Manuscript writing and reading, clinical approach & patient adherence

Mughisa Munir: Literature search and manuscript review

Aousaf Ahmad: Manuscript writing and review

**Disclaimer:** None.

**Conflict of Interest:** None.

**Source of Funding:** None.

**Data Availability:** All data generated or analyzed during this study are included in this published article.

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