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PLANT-BASED CREAMS FOR WOUND MANAGEMENT: A COMPREHENSIVE REVIEW OF DEVELOPMENT, QUALITY CONTROL, AND CLINICAL POTENTIAL

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Abstract : Wound healing is a complex biological process that is fundamental to the restoration of tissue integrity. For centuries, traditional medicine has utilized medicinal plants to accelerate this process. Modern pharmacology is increasingly recognizing the potential of these phytomedicines, leading to the development of standardized herbal formulations for wound care. Creams, as semi-solid topical preparations, are an ideal vehicle for delivering herbal extracts to wound sites. This review provides a comprehensive overview of herbal wound healing creams, covering the intricate process of wound healing, the rationale for using herbs, and a detailed discussion of key medicinal plants known for their wound healing properties, such as *Curcuma longa*, *Azadirachta indica*, *Aloe vera*, and *Centella asiatica*. It delves into the critical aspects of formulating a stable and effective herbal cream, including the selection of appropriate bases, emulsifiers, and preservatives. Furthermore, the review outlines the essential parameters for the evaluation of these formulations, encompassing physical, physicochemical, stability, and biological assessments. In vitro and in vivo models for testing efficacy are discussed, emphasizing the importance of scientific validation. The review concludes by highlighting the immense therapeutic potential of herbal creams as a safe, effective, and accessible alternative to conventional wound care agents, while stressing the need for continued research in standardization and clinical validation to integrate them fully into modern healthcare.

INTRODUCTION

A wound is defined as a disruption of the cellular and anatomical continuity of a tissue, which can be caused by physical, chemical, or thermal injury [1]. The process of healing is a natural, dynamic, and intricate biological cascade involving cellular and molecular events that work in concert to repair the damaged tissue. This process is classically divided into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling [2]. While the body has an innate capacity to heal, this process can be impaired by factors such as infection, poor blood supply, malnutrition, and underlying diseases like diabetes, leading to chronic, non-healing wounds that pose a significant clinical challenge [3].

For millennia, civilizations across the globe have relied on nature's pharmacy, utilizing plants and their extracts to manage wounds. This traditional knowledge, passed down through generations, forms the basis of modern ethnopharmacology [4]. Herbal remedies offer a rich source of bioactive compounds that can positively influence the healing process. These compounds can exert multiple

therapeutic effects, including antimicrobial, anti-inflammatory, antioxidant, and astringent actions, while also promoting cell proliferation and collagen synthesis [5].

The development of topical drug delivery systems has allowed for the efficient application of these herbal actives directly to the wound site. Among various topical formulations, creams are particularly advantageous. A cream is a semi-solid emulsion, typically either oil-in-water (O/W) or water-in-oil (W/O), which is cosmetically elegant, easy to apply, and can be formulated to provide a soothing, moisturizing effect on the skin [6]. An herbal wound healing cream combines the therapeutic benefits of medicinal plants with a pharmaceutically optimized vehicle, aiming to protect the wound from infection, reduce inflammation, and accelerate tissue regeneration. This review aims to explore the formulation, evaluation, and therapeutic potential of herbal creams, bridging the gap between traditional wisdom and modern scientific validation.

2. The Rationale for Using Herbs in Wound Healing

The use of conventional treatments, particularly antibiotics, has been revolutionary in managing infected wounds. However, their overuse has led to the emergence of multidrug-resistant bacterial strains, a major global health concern [7]. Furthermore, some synthetic topical agents can cause side effects such as skin irritation, allergic reactions, and cytotoxicity to healthy cells [8]. This has spurred a renewed interest in herbal medicine as a valuable alternative or adjunct therapy.

The rationale for using herbs is rooted in their complex phytochemical composition. Unlike synthetic drugs that often have a single target, a single plant extract contains a multitude of compounds that can act synergistically on various stages of the wound healing process [9].

- **Antimicrobial Activity:** Many plants produce secondary metabolites like tannins, alkaloids, and essential oils that have broad-spectrum antimicrobial activity. These compounds can help prevent or treat wound infections, a critical step for uncomplicated healing [10].
- **Anti-inflammatory Activity:** The initial inflammatory phase is essential for cleaning the wound, but prolonged inflammation can delay healing. Flavonoids and terpenoids found in many herbs are potent anti-inflammatory agents that can modulate this response, reducing pain, swelling, and redness [11].
- **Antioxidant Activity:** Wounded tissues generate reactive oxygen species (ROS), which can cause oxidative damage and impair healing. Phenolic compounds and flavonoids in plants act as powerful antioxidants, neutralizing these free radicals and protecting the newly forming tissue [12].
- **Cell Proliferation and Collagen Synthesis:** Certain phytochemicals, such as the triterpenoids in *Centella asiatica*, have been shown to directly stimulate fibroblast proliferation and collagen synthesis, which are crucial for the formation of the granulation tissue that fills the wound space [13].
- **Astringent Effect:** Tannins have an astringent property, causing the precipitation of proteins on the wound surface. This forms a protective layer that reduces fluid loss and shields the underlying tissue from external irritants [14].

3. Key Medicinal Plants in Wound Healing Formulations

A vast number of plants have been reported to possess wound healing properties. The following are some of the most well-researched and commonly incorporated herbs in topical cream formulations.

Curcuma longa (Turmeric)

Turmeric, a staple in Ayurvedic medicine, contains a group of polyphenolic compounds called curcuminoids, with **curcumin** being the most active [15]. Curcumin accelerates wound healing by modulating multiple biological pathways. It is a potent anti-inflammatory agent that downregulates pro-inflammatory cytokines like TNF-α and IL-1. Its powerful antioxidant properties protect the tissue from oxidative stress. Furthermore, studies have shown that curcumin enhances granulation tissue formation, collagen deposition, and wound contraction [16].

Azadirachta indica (Neem)

Every part of the Neem tree has been used in traditional Indian medicine. For wound healing, its leaves and oil are particularly valuable. Neem contains a complex array of terpenoids, including nimbidin and nimbin, which are responsible for its potent

antibacterial, antifungal, and anti-inflammatory effects [17]. Neem extracts have been shown to be effective against a wide range of skin pathogens, including *Staphylococcus aureus*, making it an excellent agent for preventing wound infections [18].

Aloe vera

The gel from the leaves of *Aloe vera* is renowned for its soothing and healing effects on burns and wounds. Its therapeutic properties are attributed to its rich composition of polysaccharides (e.g., acemannan), anthraquinones, vitamins, and enzymes [19]. Aloe vera promotes healing by keeping the wound moist, stimulating fibroblast activity, and enhancing collagen synthesis. The polysaccharide acemannan is also an immunomodulator that can stimulate macrophage activity, helping to clear wound debris [20].

Calendula officinalis (Marigold)

Calendula officinalis flower extracts are widely used in topical preparations for their anti-inflammatory and wound healing properties. The flowers are rich in flavonoids, triterpenoids, and carotenoids [21]. These compounds have been shown to reduce inflammation, exhibit antimicrobial activity, and promote angiogenesis (the formation of new blood vessels). By stimulating fibroblast metabolism, Calendula enhances collagen production, leading to faster wound closure and increased tissue strength [22].

Centella asiatica (Gotu Kola)

Known as the "herb of longevity," *Centella asiatica* is a revered wound healing agent in Ayurveda. Its primary active constituents are triterpenoid saponins, including asiaticoside, madecassoside, and asiatic acid [23]. These compounds significantly enhance collagen synthesis (particularly type I collagen), promote fibroblast proliferation, and improve the tensile strength of newly healed skin. Asiaticoside has also been shown to stimulate angiogenesis, improving blood circulation to the wounded area and facilitating repair [13, 24].

4. Formulation of Herbal Wound Healing Creams

The formulation of a stable and effective herbal cream is a pharmaceutical science that involves the careful selection of ingredients to create a suitable delivery system. The goal is to produce a semi-solid preparation that is physically and chemically stable, non-irritating, and allows for the efficient release of the herbal active ingredient to the wound site.

Components of a Cream Base

Herbal creams are typically oil-in-water (O/W) emulsions, as they are non-greasy and easily washable with water. The main components include:

1. Aqueous Phase: This is the continuous phase in an O/W cream. It consists of purified water and may include water-soluble components like humectants (e.g., glycerin, propylene glycol) to prevent the cream from drying out and to moisturize the skin [6].
2. Oily Phase: This is the dispersed phase. It is composed of oils, fats, and waxes that provide emollient and occlusive properties. Common ingredients include stearic acid, cetyl alcohol, beeswax, and various vegetable oils (e.g., sesame oil, coconut oil) [25].
3. Emulsifying Agent: This is a critical component that stabilizes the emulsion by preventing the oil and water phases from separating. A combination of emulsifiers is often used. For instance, stearic acid (oily phase) can be saponified with an alkali like triethanolamine or borax (aqueous phase) during the formulation process to form an in-situ emulsifier [26].
4. Herbal Extract: The active ingredient. This can be in the form of a dried powder, a liquid extract (aqueous or alcoholic), or an isolated phytochemical. The method of incorporation depends on its solubility and stability.
5. Preservatives: Since creams contain water, they are susceptible to microbial contamination. Preservatives are essential to prevent the growth of bacteria and fungi. Commonly used synthetic preservatives include methylparaben and propylparaben. There is also growing interest in using natural preservatives like essential oils [27].

General Manufacturing Process

The preparation of an herbal cream generally involves the following steps:

1. Preparation of Phases: The oil-soluble ingredients are mixed and heated in one vessel (Oily Phase), while the water-soluble ingredients and the herbal extract (if water-soluble) are heated in a separate vessel (Aqueous Phase) to approximately 70-75°C.
2. Emulsification: The aqueous phase is slowly added to the oily phase with continuous stirring until a primary emulsion is formed. The temperature is maintained during this process.

3. Homogenization: The mixture is then homogenized to reduce the globule size of the dispersed phase, resulting in a stable and uniform cream.
4. Cooling and Addition of Additives: The emulsion is cooled under slow stirring. Heat-sensitive components like fragrance or specific actives are added when the temperature drops below 40°C.
5. Final Mixing: The cream is mixed until it reaches room temperature and achieves a smooth, homogenous consistency before being filled into suitable containers [25].

5. Evaluation of Herbal Creams

Once formulated, the herbal cream must undergo a series of rigorous tests to ensure its quality, safety, and efficacy.

Physical Evaluation

- Appearance and Color: The cream should be visually inspected for its color and appearance. It should be uniform and free from any lumps or foreign particles.
- Odor: It should have a pleasant or characteristic odor without any signs of rancidity.
- Homogeneity: A small amount of cream is pressed between a thumb and a glass slide to assess its consistency. It should feel smooth and not gritty.
- pH: The pH of the cream is measured using a calibrated pH meter. It should be close to the pH of the skin (approx. 4.5-6.5) to avoid causing irritation [28].
- Spreadability: This parameter indicates how easily the cream spreads on a surface upon application. It is typically measured by placing a known weight on top of a cream sample sandwiched between two glass slides and measuring the diameter of the spread [29].
- Viscosity: The viscosity determines the consistency of the cream. It is measured using a viscometer. The rheological properties are important for the stability and feel of the product.

Physicochemical Evaluation

- Type of Emulsion: The emulsion type (O/W or W/O) is confirmed using tests like the dye solubility test (a water-soluble dye will dissolve in the continuous phase of an O/W emulsion) or the conductivity test (O/W emulsions conduct electricity) [26].
- Globule Size: The size of the oil globules in the emulsion is analyzed using a microscope. A small and uniform globule size generally corresponds to greater stability.
- Drug Content Uniformity: This test ensures that the active herbal ingredient is uniformly distributed throughout the cream. A specific phytochemical marker is quantified from different samples of the batch using techniques like HPLC or HPTLC [30].

Stability Studies

Stability testing is crucial to determine the shelf life of the product. The cream is stored under various conditions of temperature and humidity (as per ICH guidelines) for a defined period. It is periodically evaluated for any changes in its physical and chemical properties, such as phase separation (cracking), liquefaction, color change, or degradation of the active ingredient [31].

Biological and Efficacy Evaluation

- **In Vitro Antimicrobial Activity:** The cream's ability to inhibit microbial growth is tested using methods like the agar well diffusion assay against common wound pathogens (*S. aureus*, *P. aeruginosa*, etc.) [32].
- **In Vivo Wound Healing Studies:** Animal models are used to evaluate the efficacy of the cream in a biological system.
    - Excision Wound Model: A piece of skin is surgically removed, and the cream is applied. The rate of wound contraction and the time taken for complete epithelialization are measured [33].
    - Incision Wound Model: A linear incision is made and sutured. The tensile strength (the force required to reopen the wound) is measured after a healing period, which indicates the quality of collagen formation [33].
    - Histopathological Studies: Tissue samples from the healed wounds are examined under a microscope to assess collagen deposition, cell proliferation, and overall tissue architecture [34].

- Skin Irritation Test: The cream is applied to the skin of animals (e.g., rabbits) to check for any signs of irritation, erythema, or edema, ensuring the formulation is safe for topical use [28].

6. Conclusion and Future Perspectives

Herbal wound healing creams represent a powerful synergy of traditional ethnobotanical knowledge and modern pharmaceutical technology. They offer a promising therapeutic alternative that can address the shortcomings of conventional treatments, such as antibiotic resistance and side effects. The phytochemical richness of plants like turmeric, neem, and *Centella asiatica* provides a multi-targeted approach to healing, effectively managing inflammation, preventing infection, and promoting tissue regeneration.

However, for these formulations to gain wider acceptance in mainstream medicine, rigorous scientific validation is paramount. The future of herbal wound care lies in the standardization of herbal extracts to ensure consistent potency and the use of advanced analytical techniques to quantify marker compounds. More large-scale, randomized controlled clinical trials in humans are needed to definitively establish their efficacy and safety compared to standard treatments.

Furthermore, innovations in drug delivery, such as the development of herbal nanoemulsions or creams loaded with phytosomes, could enhance the bioavailability and penetration of active compounds, further improving therapeutic outcomes. By continuing to explore and scientifically validate these natural remedies, we can unlock their full potential and provide safe, effective, and accessible wound care solutions for a global population.

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