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Comparative efficacy of two polyherbal creams with framycetin sulfate on diabetic wound model in rats

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ABSTRACT

Background: Diabetes mellitus is one of the metabolic disorders that impede normal steps of wound healing process. Worldwide, 15% of the 200 million diabetics suffer from diabetic wounds. Diabetic complications, such as foot ulcer, impose major public health burdens worldwide.
Objective: The present study was carried out to evaluate comparative efficacy of polyherbal creams with framycetin sulfate cream on diabetic rats using incision and excision wound models.
Materials and methods: Alloxan (120 mg/kg, intraperitoneal) induced diabetic rat models (incision and excision models) were used to evaluate wound healing effect of cream A, B, and framycetin sulfate. Cream A and B were applied for a period of 10 and 20 days for incision and excision wound models, respectively. Incision wound model was used to assess the effect on breaking strength. Wound contraction and epithelialization period were measured using excision wound model. The data were analyzed by one-way ANOVA followed by Bonferroni post-test.
Results: Tensile strength of the animals treated with cream B (941.66 ± 15.36) was found to be significantly greater ($P < 0.001$) as compared to tensile strength of the animals treated with cream A (825 ± 22.36). Wound treated with cream B was found to heal significantly ($P < 0.001$) faster (day 17) as compared to wounds treated with framycetin sulfate (day 21).
Conclusions: Cream B was found to be more effective wound healing agent than cream A and framycetin sulfate cream in treating diabetic wounds.

1. Introduction

A wound is defined as loss or breaking of cellular, anatomical, or functional continuity of living tissues [1]. It is a clinical entity, is as old as human, and is often considered as major problem in clinical practice. Healing of wounds involve the activity of an intricate network of blood cells, cytokines, and growth factors which ultimately leads to the restoration of the injured skin or tissue to normal condition. The classic model of wound healing is divided into three sequential phases: Inflammatory phase (consisting of hemostasis and inflammation), proliferative phase (consisting of granulation, contraction, and epithelialization), and remodeling phase, which organizes structure with increased tensile strength [2]. Though healing process takes place by itself and does not require much help, various physiologic and mechanical factors, such as poor nutrition, insufficient oxygenation, infection, prolonged inflammation, age, diabetes and other diseases, drugs, smoking, alcoholism, depression, and other factors [3] may impair the healing response, resulting in a chronic wound that fails to proceed through the usual stepwise progression.

Diabetes mellitus constitutes one of the most important public health problems due to its high prevalence and enormous social and economic consequences [4]. Delayed cutaneous wound healing is a chronic complication in diabetic patients and is caused primarily by hyperglycemia, prolonged inflammatory phase, defected angiogenesis, diminished expression of cytokines, oxidative stress, vascular insufficiency, and microbial infections [5–8]. Several

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other diabetic complications such as neuropathy, nephropathy, atherosclerosis, and foot deformities contribute to the severity of the disease and in the development of chronic wounds in diabetic patients that might be complicated leading to ulceration, necrosis, and amputation [5,7]. Diabetes mellitus is life-threatening and becomes the third largest killer of humans after cancer and cardiovascular diseases, even with the use of several recent synthetic drugs for effective treatment options [9].

Healing impairment of diabetic patients is still a serious clinical problem for physicians worldwide due to unclear etiology Hence, impaired wound healing in diabetics has caught the attention of the world to help promote healing process and prevent the rising complications. A new era in wound healing research is required, involving new treatment strategies to deal with this emerging issue. One of these is the use of medicinal plants as a source for natural products to explore new therapeutic agents/tools intended for diabetic wound management and treatment.

India has a rich tradition of plant-based knowledge on healthcare. Many Ayurvedic plants have a very important role in the process of wound healing. A large number of plants, plant extracts, decoctions, or pastes are equally used by tribals and folklore traditions in India for the treatment of cuts, wounds, and burns [10]. Plants are potent healers because they promote the repair mechanisms in a natural way [11]. The phytomedicines are safe, effective, and relatively cheap options for wound healing [12]. These natural agents induce healing and regeneration of the lost tissue by multiple mechanisms such as coagulation, disinfections, debridement, antioxidant, and provide suitable environment for natural healing process [3].

Literature survey revealed that many plants are known to have antioxidant, antimicrobial, anti-inflammatory, and wound healing properties for example, *Aloe vera*, turmeric, and neem [13]. We searched for such medicinal plants from Ayurvedic literature and followed the reverse pharmacology path. This led us to the short-listing of plant materials from almost 200 different options.

The present study was carried out to evaluate comparative efficacy viz., cream A (Ari's Wound Healing Cream) and cream B (Amarantha Wound Healing Cream) with framycetin sulfate cream in diabetic wounds. Cream A was prepared using extracts of eight herbs viz., *Glycyrrhiza glabra, Ficus infectoria, Shorea robusta, Curcuma longa, Berberis aristata, Rubia cordifolia, Azadirachta indica*, *Pongamia glabra,* and Yashad Bhasma as classical Ayurvedic preparation. Cream B was prepared using Jatyadi Oil and classical Ayurvedic preparation, Yashad Bhasma and extracts of seven herbs viz., *Ficus religiosa, Ficus bengalensis, Centella asiatica, S. robusta, G. glabra, A. indica,* and *P. glabra*. Cream A differs from cream B in the form of quantity and types of ingredients used in the formulations. The major differentiating factors between the two creams are the presence of Jatyadi Oil and Mandukparni extract in cream B. Furthermore, the percentage of Yashad Bhasma in cream B is more than cream A. Both the creams have *Vranaropak* properties.

The selected ingredients of both formulations were reported to have significant antimicrobial, antioxidant, wound healing, and anti-inflammatory properties. The literature survey scientifically revealed the use of *Jatyadi* Oil in the management of wounds [14]. Yashad Bhasma is a classical Ayurvedic formulation which plays a significant role in protein synthesis, cell division, wound healing. It is known to have antiseptic and astringent properties [15]. The plant ingredients such as *C. longa*, *B. aristata*, *A. indica*, *P. Glabra,* and *S. robusta* possess antimicrobial and wound healing properties [16]. The plant ingredients such as *F. religiosa* and *F. bengalensis* help to constrict and heal the wounds due to their astringent property [17,18]. Few herbs such as *C. asiatica* have ability to heal the wounds by increasing synthesis of collagen and intracellular fibronectin content [19]. *G. glabra* has also been used in the treatment of wounds, ulcers, and burns [20].

The growing popularity of natural and herbal medications, easy availability of raw materials, cost-effectiveness, and paucity of reported adverse reaction, prompted us to assess wound healing efficacy of two Ayurvedic topical creams in comparison with framycetin sulfate cream.

2. Materials and methods

2.1. Materials

Cream A and B were developed and supplied by Ari Healthcare Pvt. Ltd., Pune.

Composition of cream A (Ari's Wound Healing Cream):

Ingredients	Botanical name	Part of plant	Types of extract	Quantity (%)
Yashtimadhuka extract	*Glycyrrhiza glabra*	Stem	Hydroalcohol	4
Plaksha extract	*Ficus infectoria*	Leaf and bark	Hydroalcohol	3
Shala extract	*Shorea robusta*	Bark	Hydroalcohol	3
Haridra extract	*Curcuma longa*	Rhizome	Alcohol	2
Daruharidra extract	*Berberis aristata*	Stem	Hydroalcohol	2
Manjishtha extract	*Rubia cordifolia*	Stem	Hydroalcohol	2
Nimba extract	*Azadirachta indica*	Leaf	Hydroalcohol	2
Karanja extract	*Pongamia glabra*	Bark	Hydroalcohol	1
Yashad Bhasma	Ayurvedic classical formulation	Powder	Powder formulation	0.3
		Cream base: QS to make		100

Composition of cream B (Amarantha Wound Healing Cream): Each gram of cream contains percent of ingredients (w/w).

Ingredients	Botanical name	Part of plant	Types of extract	Quantity (%)
Jatyadi Oil	Ayurvedic classical formulation	Oil	Medicated oil	4
Ashvattha extract	*Ficus religiosa*	Stem	Hydroalcohol	3
Nyagrodha extract	*Ficus bengalensis*	Root	Hydroalcohol	2
Mandukaparni extract	*Centella asiatica*	Whole plant	Alcohol	3
Shala extract	*Shorea robusta*	Bark	Hydroalcohol	3
Yashtimadhuka extract	*Glycyrrhiza glabra*	Stem	Hydroalcohol	2
Nimba extract	*Azadirachta indica*	Leaf	Hydroalcohol	1
Karanja extract	*Pongamia glabra*	Bark	Hydroalcohol	1
Yashad Bhasma	Ayurvedic classical formulation	Powder	Powder formulation	1.5
		Cream base: QS to make		100

2.2. Experimental animals

Albino Wistar rats of both sexes weighing 180–200 g were used for the study. The animals were procured from Haffkine Biopharmaceuticals, Mumbai. All animals were housed in polypropylene cages under standard experimental conditions with 26 ± 2 °C ambient temperature and 12 h light–dark cycle. The animals were fed standard pellet diet and were provided water *ad libitum*. All experimental protocols were approved by the Institutional Animal Ethics Committee (CUSCP/IAEC/27/2011-12) of C.U. Shah College of Pharmacy, Santacruz (W), Mumbai, India.