



ISSN: 0976-3031

Available Online at <http://www.recentscientific.com>

International Journal of Recent Scientific Research
Vol. 6, Issue, 5, pp.3916-3920, May, 2015

**International Journal
of Recent Scientific
Research**

RESEARCH ARTICLE

SAFETY AND EFFECTIVENESS OF AMPUCARE IN TREATMENT OF DIABETIC FOOT ULCERS

Ajaz A Rashid Dandekar

Multi-Speciality Clinic, 51/1 Old Bengalipura Street, Near Crawford Market, Mumbai-400003

ARTICLE INFO

Article History:

Received 2nd, April, 2015
Received in revised form 10th,
April, 2015
Accepted 4th, May, 2015
Published online 28th,
May, 2015

Key words:

Ampucare, foot ulcer, diabetes.

ABSTRACT

The aim of this retrospective study is to evaluate the results of healing of diabetic foot ulcers after Ampucare treatment. In this study a total of 100 patients suffering from diabetic foot ulcers were evaluated. Majority of patients were suffering from accidental injury (40%) followed by knee injury (13%), necrotizing fasciitis (10%), leg condition near to amputation (10%), peripheral vascular disease (8%), osteomyelitis (6), cellulitis (5%), abscess (4%) and neuropathy (4%). Most of the patients belonged to the category of irregular and deep floor wound category (28%) followed by irregular wound floor (24%), deep wound floor (19%), irregular and shallow (18%) and deep round (11%). Our results showed that 95% patients were clinically cured after treatment with Ampucare with 96.2 % healing in wound after treatment for 45 days. One important outcome of this study was that use of Ampucare for 45 days prevented amputation in 90 % patients which were near to amputation. In conclusion, Ampucare is a highly effective and safe herbal product for the treatment and management of various type of diabetic wounds.

Copyright © Ajaz A Rashid Dandekar., This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Number of diabetic patients have significantly been increasing in developed and developing countries and has been one of the major causes of morbidity and mortality across the globe (Ghorbani, 2014). As per the report of World Health Organization (October, 2013), 347 million people have diabetes worldwide and it would be the 7th cause of mortality by 2030.

According to a report of Indian Council of Medical Research, there are approximately 35 millions diabetics in India and this would increase to 80 million by 2030 (Chopra and Kuhad, 2008).

It has been reported that diabetic patients have up to 25% lifetime risk of developing a foot ulcer (Singh *et al.*, 2005). Diabetic foot wounds are defined as any break in the cutaneous barrier, usually extending through the full thickness of the dermis (Larijani *et al.*, 2003). The major factors contributing to foot ulcers are peripheral neuropathy and ischemia from peripheral vascular disease (Bowering, 2001).

It is believed, once an ulcer has developed, there is a higher risk of wound progression which may lead to amputation. A report from International Diabetes Federation (IDF) documented that around 40,000 legs are amputated every year in India, most of

them due to diabetic foot ulcer (The Tribune, 2005). Reiber *et al.* (1999) reported amputation up to 85 % of cases with diabetic foot. Approximately, 40% of amputations in diabetic foot ulcer can be prevented with proper clinical management of wound care (Lavery *et al.*, 1995). Diabetic foot ulcers can be divided into types based on their etiologies and clinical characteristics: neuropathic, neuroischemic, and ischemic. (Chao and Cheing, 2009).

Diabetic neuropathy is responsible for 50-75% of non-traumatic amputations (Holzer *et al.*, 1998). Neuropathy is present in more than 80% of patients with foot ulcers and increases the risk of amputation 1.7 fold; 12 fold, if there is deformity, and 36 fold, if there is a history of previous ulceration (Armstrong *et al.*, 1998).

During diabetes, impaired wound healing in patients has been observed which is of great concern (Brem and Tomic-Canic, 2007; Pavlovi *et al.*, 2007). Three aetiologic factors, neuropathy, ischaemia and infection cause impaired wound healing (Papanas N, Maltezos, 2007). Besides these factors, age of patients, nutrition, smoking, diabetes, anemia, obesity, cancer, ischemia, uremia and denervation also affect wound healing process (Atiyeh *et al.*, 2003). The wound healing is a complex process associated with various mechanisms of tissue repairs, including inflammation, granulation tissue formation, reepithelization, angiogenesis and contraction (Yatomi *et al.*,

*Corresponding author: **Ajaz A Rashid Dandekar**

Multi-speciality Clinic, 51/1 old Bengalipura Street, Near Crawford Market, Mumbai-400003

1997). The contribution of each process varies according to the type of wound (Grinnel, 1994).

Table 1 Baseline demographic characteristics of the patients

Characteristic	Ampucare treatment group
Total no. of patients	100
No. of male patients	55
No. of female patients	45
Median age of male patients	54.5± 6.4 years
Median age of female patients	56.7± 7.3 years
No. of male patients suffering from DM1/DM2	25/30
No. of female patients suffering from DM1/DM2	23/22

Table 2 Etiology of wounds.

Cause of infection	Total	Male	Female
Abscess	4	2	2
Cellulitis	5	3	2
Neuropathy	4	1	3
Osteomyelitis	6	3	3
Accidental injury	40	22	18
Knee injury	13	8	5
Necrotizing fasciitis	10	5	5
peripheral vascular disease	8	5	3
leg condition near to amputation	10	6	4
Total	100	55	45

Table 3 Distribution of site of wounds

Site of infections	No. of patients (n=100)
Leg or foot	56
Knee	13
Toe and sole	31

Table 4 Description of wound floor

Score floor	No. of patients
Irregular	24
Deep	19
Irregular and deep	28
Deep round	11
Irregular and shallow	18

However, delay in healing makes diabetic wounds a great problem for health services. In an effort to improve healing rates of diabetic wounds, numerous herbal products and herbs have been reported to be used for treatment (Shukrimi *et al.*, 2008; Udupa *et al.*, 1991; Dahanukar *et al.*, 2000; Ghorbani *et al.*, 2013; Park and Lee, 2013). It is thought that herbal formulations with multiple plants may have greater effects than the same herbs used individually. These synergistic effects enhance the desired action. Based on this belief, Ampucare, a polyherbal formulation for topical application has been evaluated for the control of diabetic foot ulcer.

Table 5 Comparison of reduction in wound surface area.

Days	Wound area (cm ²)	% reduction
On the screening (0 day)	13.3 ±2.1	----
On the 20th day treatment	3.1 ±0.7	76.7
Completion of treatment (after 40 days)	0.5±0.1	96.2

It is an oil based formulation, a ointment, which contains extracts of bark of *Azadirachta indica*, rhizome of *Curcuma longa* and leaves of *Trichosanthes dioica* as active ingredients. The product has been reported to work by multiple modes of action due to herbal synergy and has strong antibacterial coverage,

hence useful for external application for the treatment of wounds including diabetic foot ulcer (Chaudhary *et al.*, 2008). The main objectives of this study was to assess the safety and efficacy of Ampucare in healing diabetic foot ulcers.



Figure 1 Images of selected cases (who gave consent for images) pre & post healing with Ampucare



Figure 2 Image of a patient whose leg was saved from Amputation

MATERIALS AND METHODS

Study Design

This retrospective study was done on 100 patients admitted to Multi Speciality Hospital, Mumbai, India suffering from diabetic foot ulcers during a period of 9 months. Subjects of either sex diagnosed with type 1 or 2 diabetes mellitus, of any age with foot ulceration having the minimum size of 1 cm² which had not healed for at least two weeks.

Active Ingredients of Diabetic Wound Care Oil Based Formulation

The ingredients of Ampucare synergistically act on the wound from the initial stage of wound healing till re-epithelization and wound closure. All these ingredients possess strong antimicrobial activity and synergistically activate fibroblasts, collagen synthesis and promotes effective granulation leading to re-epithelialization (Biswas and Mukherjee, 2003; Kundu *et al.*, 2005; Sidhu *et al.*, 1998; Sidhu *et al.*, 1999).

Curcuma longa

Curcuma longa present in Ampucare acts as a checkpoint to prevent undesirable inflammation, free radical generation and pain that may hamper wound healing. It further enhances transforming growth factor-beta (TGF-β), migration of cells such as myofibroblasts, fibroblasts and macrophages which are essential for wound healing and reepithelialization (new skin formation) (Fabry *et al.*, 1996; Kim *et al.*, 2005; Subapriya *et al.*, 2005).

Azadirachta indica

Azadirachta indica in synergism with curcumin extends antimicrobial activity to Ampucare and helps prevent undue

infection at the wound area (Wuthi-udomlert *et al.*, 2000; Bandyopadhyay *et al.*, 2004; Fabry *et al.*, 1996; Kim *et al.*, 2005; Subapriya *et al.*, 2005).

Trichosanthes dioica

Trichosanthes dioica promotes cellular proliferation and collagen synthesis at the wound site by increase in total protein, total collagen and hydroxyproline contents of granulation tissues (Assesment report on Curcuma longa rhizoma, EMEA).

Other Ingredients

During the initial stage of wound healing, Beta-Sitosterols present in ingredients of Ampucare in combination with tannins extends local immunomodulatory effect by increasing the activity of proinflammatory cytokines and chemokines such as macrophages to site of wound for enhanced phagocytosis of bacterial cells and cellular debris (Mehrotra *et al.*, 2013). It also promotes angiogenesis for faster wound healing as well as maintains an ambient physiological environment for wound healing by retaining moisture (Prakash *et al.*, 2007; Raji *et al.*, 2004). It also improves the local microcirculatory blood flow after tissue trauma to promote wound healing.

Ampucare is a wholesome source of natural nutrients required for tissue regeneration such vitamin C, vitamin E and zinc. Vitamin C maintains membrane integrity and acts as a co-factor in collagen formation, vitamin E acts as a free-radical scavenger which preserves macrophages and polynuclear leukocytes from free radical damage and zinc helps in cell proliferation at the wound area.

RESULTS AND DISCUSSION

Wound healing is the process of repair, that follows injury to the skin and other soft tissues (Bae *et al.*, 2005). There are three stages to the process of wound healing: inflammation, proliferation, and remodeling. The proliferative phase is characterized by angiogenesis, collagen deposition, epithelialisation and wound contraction. Angiogenesis involves new blood vessel growth from endothelial cells. In fibroplasia and granulation tissue formation, fibroblasts exert collagen and fibronectin to form a new, provisional extracellular matrix. Subsequently epithelial cells crawl across the wound bed to cover it and the wound is contracted by myofibroblasts, which grip the wound edges and undergo contraction (Panchatcharam *et al.*, 2006).

In the present study, a total of 100 patients were included of which 45% female and 55% male. Mean age of the male and female patients were 54.5 ± 6.4 and 56.7 ± 7.3 years, respectively. In this study all patients were suffering from diabetes and majority of the patients (52 %) were of diabetes mellitus 2 (DM 2) and rest of the patients were reported with DM 1 (48 %). Of 45 female, 23 patients suffered from DM 1 and 22 were of DM 2. Similarly for male, 25 patients were diagnosed to have DM 1 and 30 diagnosed to be DM 2 (Table 1).

The patients having wound were also suffering from abscess

(4%), cellulitis (5%), neuropathy (4%), osteomyelitis (6), accidental injury (40%), knee injury (13%), necrotizing fasciitis (10%), peripheral vascular disease (8%) and leg condition near to amputation (10%). The details of these infections in male and female is shown in Table 2. The affected part of the majority of the patients was leg or foot (56 %) followed by toe and sole (31 %) and knee (13%) (Table 3). Majority of patients belonged to the category of irregular and deep floor wound category (28%) followed by irregular wound floor (24%), deep wound floor (19%), irregular and shallow (18%) and deep round (11%) (Table 4).

Our results revealed that all the patients showed a good treatment response. 95% patients were clinically cured when treated with Ampucare. The patients who were cured or improved showed a significant reduction in wound area at the completion of the treatment as compare to initial wound area at the time of enrollment.

The average size of ulcer surface area was 13.3 ± 2.1 cm² on the first visit of the subjects prior to start of the therapy which reduced to 3.1 ± 0.7 cm² after 20 days of topical application of Ampucare with the mean improvement percentage 76.7 %. The ulcer surface area was measured after 40 days of the beginning of the study and results showed that the mean ulcer surface area had decreased to 0.5 ± 0.1 cm² with the mean improvement percentage of 96.2% (Table 5, Figure 1). One important outcome of this study was that use of Amucare for 4-5 weeks prevented amputation in 9/10 (90 %) patients which were near to amputation (Figure 2). Wong *et al.* (2001) also reported that amputation could be avoided in 87% of diabetic wound using chinese herbal medicine. The activity of Ampucare against healing of diabetic foot ulcers is due to synergistic activity of herbs as ingredients.

In previous reports, it has been reported that *A. indica* has anti-inflammatory, antihyperglycaemic, antibacterial, antiviral, antioxidant, antimutagenic, wound repair and anticarcinogenic properties. Three tricyclic diterpenoids morganone, margolonone and isomargolonone isolated from neem bark were active against *Klebsiella* species, *Staphylococcus* species and *Serratia* species (Biswas *et al.*, 2002; Prakash *et al.*, 2007). Curcumin increased cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in DNA, total protein and type III collagen content of wound tissues. Curcumin treated wounds were found to heal much faster as indicated by improved rates of epithelialisation, wound contraction and increased tensile strength which were also confirmed by histopathological examinations. Curcumin treatment was shown to decrease the levels of lipid peroxides (LPs), while the levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (Gpx), activities were significantly increased exhibiting the antioxidant properties of curcumin in accelerating wound healing (Fabry *et al.*, 1996; Kim *et al.*, 2005). Better maturation and cross linking of collagen were observed in the curcumin treated rats, by increased stability of acid-soluble collagen, aldehyde content, shrinkage temperature and tensile strength in diabetic wound (Panchatcharam *et al.*, 2006; Biswas and Mukherjee, 2003). In conclusion, Ampucare is a miraculous formulation, better than other products being used, for the treatment of various type of

diabetic wounds and its application right at the beginning of injury / wound can effectively prevent deterioration and amputation like conditions.

References

- Assessment report on curcuma longa rhizoma, EMEA.
- Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system. The contribution of depth, infection, and ischemia to risk of amputation. *Diabetes Care*. 1998;21:855-9.
- Atiyeh BS, Ioannovich I, Magliacani G, Masellis M, Costagliola M, Dham R. The efficacy of moisture retentive ointment in the management of cutaneous wounds and ulcers: A multicenter clinical trial. *Indian J Plastic Surg*, 2003;36:89-98.
- Bae JS, Jang KH, Park SC, Jin HK. Promotion of dermal wound healing by polysaccharides isolated from *Phellinus gilvus* in rats. *J Vet Med Sci*, 2005;67:111-4.
- Bandyopadhyay *et al.* Clinical studies on the effect of Neem (*Azadirachta indica*) bark extract on gastric secretion and gastroduodenal ulcer. *Life Sci*, 2004;75:2867-2878.
- Biswas K, Chattopadhyay I, Banerjee RK, Bandyopadhyay U. *Current Science* 2002, 82, 1336-5.
- Biswas TK, Mukherjee B. Plant medicines of Indian origin for wound healing activity: a review. *Int J Low Extrem Wounds*. 2003;2:25-39.
- Bowering CK. Diabetic foot ulcers: pathophysiology, assessment, and therapy. *Can Fam Phys*. 2001;47:1007-1016.
- Brem H, Tomic-Canic M. Cellular and molecular basis of wound healing in diabetes. *J Clin Invest*. 2007;117:1219-1222.
- Chao CYL, Cheing GLY. Microvascular dysfunction in diabetic foot disease and ulceration. *Diab Metabol Res Rev*. 2009;25: 604-614.
- Chaudhary M, Dwivedi VK, Naithani V. Clinical trial survey report of Ampucare done on patients with different wounds. *J Ecophysiol Occup Health*. 2008;8:89-97.
- Chopra K, Kuhad A. Fight diabetes with physical activity and right diet. *The tribune* January 30, 2008, Chandigarh, India.
- Dahanukar SA, Kulkarni RA, Rege NN. Pharmacology of 11 medicinal plants and natural products. *Indian J Pharmacol* 2000; 32 : S81-118.
- Fabry *et al.* Fungistatic and fungicidal activity of east African medicinal plants. *Mycoses*, 1996;39:67-70.
- Ghorbani A, Shafiee-Nick R, Rakhshandeh H, Borji A. Antihyperlipidemic effect of a polyherbal mixture in streptozotocin-induced diabetic rats. *J Lipids*. 2013;13:675759.
- Ghorbani A. Clinical and experimental studies on polyherbal formulations for diabetes: current status and future prospective. *J Integ Med*, 2014;12:336-345.
- Grinnel F. Fibroblasts, myofibroblasts and wound contraction. *J Cell Biol*, 1994;124:401-4
- Holzer SE, Camerota A, Martens L, Cuedon T, Crystal-Peters J, Zagari M. Costs and duration of care for lower extremity ulcers in patients with diabetes. *Clin Ther*. 1998;20:169-81.
- Kim *et al.* Antibacterial activity of *Curcuma longa* L. against methicillin-resistant *Staphylococcus aureus*. *Phytother Res*, 2004;19:599-604.
- Kundu *et al.* Turmeric (*Curcuma longa*) rhizome paste and honey show similar wound healing potential: a preclinical study in rabbits. *Int J Low Extrem Wounds*, 2005;4:205-213.
- Larijani B, Forouzandeh F. Diabetic foot disorders. *Iran J Diab Lipid Disord*. 2003;2:103-93.
- Lavery LA, Lavery DC, *et al.* Increased foot pressures after great toe amputation in diabetes. *Diab Care*. 1995;18:1460-2.
- Mehrotra S, Agnihotri G, Singh, F. Immunomodulatory potential of *Curcuma longa*: a review. *South Asian J Exp Biol*. 2013;6:299-307.
- Panchatcharam M, Miriyala S, Gayathri VS, Suguna L. *Mol Cell Biochem*. 2006;290:87-6.
- Papanas N, Maltezos E. The diabetic foot: established and emerging treatments. *Acta Clin Belg*. 2007; 62: 230-8.
- Park C, Lee JS. Natural ingredients for diabetes which are approved by Korean FDA. *Biomed Res*. 2013;24:164-169.
- Pavlovi MD, Milenkovi T, Dini M, *et al.* The prevalence of cutaneous manifestations in young patients with type 1 diabetes. *Diabetes Care*. 2007;30:1964-1967.
- Prakash *et al.* Total phenol, antioxidant and free radical scavenging activities of some medicinal plants. *Int J Food Sci Nutr*. 2007;58:18-28.
- Raji *et al.*, Effects of *Azadirachta indica* extract on gastric ulceration and acid secretion in rats. *J Ethnopharmacol*, 2004;90:167-170.
- Reiber GE, Vileikyte L, Boyko EJ, del Aguila M, Smith DG, Lavery LA, Boulton AJ. Causal pathways for incident lower extremity ulcers in patients with diabetes from two settings. *Diab Care*, 1999;22:157-162.
- Shukrimi A, Sulaiman AR, Halim AY, Azril A. A comparative study between honey and povidone iodine as dressing solution for Wagner type II diabetic foot ulcers. *Med J Malaysia*. 2008;63:44-46.
- Sidhu *et al.* Curcumin enhances wound healing in Streptozotocin induced diabetic rats and genetically diabetic mice. *Wound Repair Regen.*, 1999;7:362-374.
- Sidhu *et al.*, Enhancement of wound healing by curcumin in animals. *Wound Repair Regen*. 1998;6: 167-177.
- Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA* 293:217-228, 2005.
- Subapriya *et al.* Medicinal properties of neem leaves: a review. *Curr Med Chem Anticancer Agents*. 2005;5:149-156.
- The Tribune. Diabetes claims a leg every 30 second . The tribune November 23, 2005, Chandigarh, India.
- Udapa SL, Shaila HP, Udapan AL, Ramesh KV, Kulkarni DR.
- Wound healing properties of some medicinal plants. *Biochem Arch*. 1991;7:207-12.
- Wong MWN, Leung PC, Wong WC. Limb salvage in extensive diabetic foot ulceration – a preliminary clinical study using simple debridement and herbal drinks. *Hong Kong Med J*. 2001;7: 403-407.

Wuthi-udomlert *et al.* Antifungal activity of *Curcuma longa* Grown in Thailand. *Southeast Asian J Trop Med Public Health*, 2000;31 Suppl 1:178-182.

Yatomi Y, Igarashi Y, Yang L *et al.* Sphingosine 1-phosphate, a bioactive sphingolipid abundantly stored in platelets, is a normal constituent of human plasma and serum. *J Biochem.* 1997;121:969-973.

How to cite this article:

Ajaz A Rashid Dandekar, Safety And Effectiveness of Ampucare In Treatment of Diabetic Foot Ulcers. *International Journal of Recent Scientific Research Vol. 6, Issue, 5, pp.3916-3920, May, 2015*
