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Seyed-Ali Khodaie (Investigation), Saeidhossein Khalilzadeh (Methodology), Fatemeh Emadi (Supervision) (Conceptualization), Mohammad Kamalinejad (Conceptualization) (Investigation), Raziieh Jafrai Hajati (Investigation), Mohsen Naseri (Supervision) (Conceptualization) (Methodology)



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## Management of a diabetic foot ulcer based on the Persian medicine: A case report

Seyed-Ali Khodaie<sup>1,2</sup>, Saeidhossein Khalilzadeh<sup>2</sup>, Fatemeh Emadi<sup>1,3</sup>, Mohammad Kamalinejad<sup>4</sup>,  
Razieh Jafrai Hajati<sup>3</sup>, Mohsen Naseri<sup>3\*</sup>

<sup>1</sup>Department of Traditional Persian Medicine, Faculty of Medicine, Shahed University, Tehran, Iran

<sup>2</sup>Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>3</sup>Traditional Medicine Clinical Trial Research Center, Shahed University, Tehran, Iran

<sup>4</sup> School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* Corresponding author: Traditional Medicine Clinical Trial Research Center, Shahed University, Tehran, Iran. Tel.: +9866464320; fax: +9866464322.

E-mail address: naseri@shahed.ac.ir, naserishahed@yahoo.com

### Highlights

- Myrtle gel (a pharmaceutical produced based on the Persian medicine) was used to treat foot ulcer topically. After twelve weeks of treatment, the wound completely was closed.

### Abstract

**Background:** Diabetic foot ulcers (DFUs) are one of the most important medical issues. Neurological, vascular, immune complications beside other factors in diabetic patients, may lead to delayed wound healing. Most current treatments are expensive, show variable efficacy and they are not available to all patients. Herbal and traditional medicines are potential candidates that, following pharmacological evaluations, can be considered for development of new therapeutics against various diseases. According

to Persian Medicine (PM) literatures, Myrtle (*Myrtus communis*) fruits and leaves, when applied topically, are able to repair wounds and foot ulcers. Polyphenols and anthocyanins are the most important bioactive compounds found in *M. communis* which exert wound healing properties.

**Case summary:** The case was a diabetic 66 year old women who had complaints related to a necrotic wound at the distal tip of the first digit of the right foot. She was treated with a surgical debridement and antibiotic regime and had an erythematous margin, no malodor and minimal discharge. An excisional debridement showed that the skin, subcutaneous tissue and periosteum were involved. Also, there was no evidence of osteomyelitis in radiographs.

**Intervention:** After sharp debridement, the wound area was washed with sterile normal saline and dried. Then, the wound was dressed with a myrtle gel 6%. The dressing was changed twice a day for 12 weeks and diabetes medications and antibiotic regime were continued.

**Conclusion:** Promising results obtained following application of myrtle gel, implied potential beneficial effect of the product on DFUs. On the basis of the results, it appears that currently used medicines in combination with topical myrtle gel as a PM remedy, can be more effective in DFUs.

Keywords: Diabetes, Foot ulcer, Persian Medicine, *Myrtus communis*, Case report

## Introduction

Long-term hyperglycemia leads to end-organ damages. Foot ulceration is the most common complication in diabetic patients [1]. Vasculopathy and neuropathy are two major etiologies of delayed diabetic wound healing [2, 3]. Effective care for Diabetic Foot Ulcers (DFU) should be comprehensive and include proper diabetes control, locally effective wound care, infection control, pressure relieving and blood flow improvement [4].

Sadly, most of current treatments applied for foot ulcers are insufficient, cause complications and show prolonged healing times. Therefore, foot ulcers are considered an increasing public-health problem due to substantial morbidity, lowered quality of life, high cost of treatment, poor long-term outcome and being a cause for lower limb amputation [5-8]. Every minute, two lower limbs are amputated in the world due to

DFU [9]. Treatment of DFU and wound still requires more efficient therapeutics [10]. Recently, interest in application of traditional, complementary and alternative medicine (TM/CAM) for the treatment of numerous diseases has grown [11-12]. The combination of traditional medicine and Western medicine has been shown to be cost-effective compared with Western medicine alone, in the treatment of chronic diseases [13]. Persian Medicine (PM) backed by several thousands of historical written and evidence in different languages, and famous scientists is one of the old and comprehensive traditional systems of medicine [14]. Numerous remedies are mentioned in PM for wound healing [15]. So far, the effectiveness of some of them has been proven [16]. In a study that ranked effective *materia medica* as remedies suggested by PM for treatment of DFUs, based on their efficiency, According to this research, *Myrtus communis* L. (Myrtle) had highest score [17]. . *M. communis* belonging to the family Myrtaceae, is a medicinal plant that is widely used in PM. The medieval Persian scholars believed that it possesses astringent, hemostatic and wound healing effects (18). All parts of this plant are utilized for various medical purposes [19, 20]. The main phytochemicals present in myrtle berries include essential oil and phenolic compounds such as flavonoids, gallic acid and anthocyanins. Polyphenols and anthocyanins have antioxidant effects [18]. In this paper, a case with DFU who was treated by the myrtle gel is presented.

### **Ethical issues**

The study was approved by the local medical ethics committee of Shahed University (ID number: IR.Shahed.REC.1394.97). Also, following consultation with the patient and her family, they agreed to use myrtle gel topically to treat foot ulcer.

### **Presenting concerns**

A 66 year old female patient presented with a deep necrotic wound on tip of the first digit of the right foot. She attended our outpatient department on 25 February 2017. The patient had a history of diabetes for over 12 years but no previous foot ulceration. She was being treated with insulin 7 months prior to admission for treatment of the wound. Also, she was admitted with complaint of inflamed and infected

foot ulcer twice in the last two months. Ulcer was developed at the first phalanx of the first digit of the right foot. In addition to controlling the patient's blood sugar and wound infection, surgical debridement was performed in the hospital. The foot ulcer had not responded to these treatments, and the patient was referred for other treatments to foot clinic. Figure1 shows a timeline of the relevant history of and interventions used for the case.

### **Clinical findings**

Based on physical examination, she was 170 cm tall and weighed 65 kg. Blood pressure was in normal range. The dorsalis pedis and posterior tibial arteries were palpable, but with feeble pulses. Also, the feet had neuropathy. A necrotic wound located at the first fingertip of the right foot was approximately 2.8×2×0.4 cm in size (Fig. 2A) and had a marginal erythema and minimal discharge but without malodor.

### **Diagnostic focus and assessment**

Blood tests revealed the following data: hemoglobin, 127 g/l; total white blood cell count,  $10.9 \times 10^9$ ; fasting glucose, 9.2 mmol/l; postprandial glucose, 12.8 mmol/l; and HbA1c 9.3%. Also, the wounded digit was warmer than other parts of the foot and the first fingernail had nail dystrophy. An excisional debridement revealed that the skin, subcutaneous tissue and periosteum were involved. However, there was no evidence of osteomyelitis in radiographs. Furthermore, inspection of the bone digit showed hard bone with no evidence suggestive of osteomyelitis. The main diagnoses included type 2 diabetes mellitus with a necrotic wound of the first digit on the right foot (Wagner classification II).

### **Therapeutic focus and assessment**

Health education related to diabetes and foot ulcer such as offloading, avoiding pressure on the wounded limb was taught to the patient and her family. The patient was not following an appropriate diet for diabetes. Diabetes drugs continued according to previous Diabetologist order (10 U of fast-acting insulin aspart was taken subcutaneously before breakfast, lunch and evening meal along with 30 U of long-acting insulin glargine once a day at night). Furthermore, the antibiotic regimen, which had already begun at the hospital, was continued [oral clindamycin (300 mg q8h) and ciprofloxacin (500 mg q12h)]. Sharp

debridement was done to remove necrotic tissue and its dystrophic nail was removed. The wound area was washed with sterile normal saline and then dried using a sterile gauze. Finally, the wound was dressed with a thin layer of myrtle gel 6%. The patient's family was taught how to change the dressing twice a day.

For preparation of the myrtle gel, 100 g of washed myrtle fruits was boiled in 1 L of distilled water for 15 min in a beaker. After cooling, the extract was filtered using Whatman 1 filter paper and then, condensed using a rotary evaporator. Finally, 15 g of dried extracts was prepared. In order to prepare myrtle gel (6%), the gel base containing polymer carbopol 934, was added to the resulting extract. The total phenol and flavonoid contents were detected using spectrophotometry method by Folin-Ciocalteu reagent and  $\text{AlCl}_3$  reagent and expressed as 10.93 mg galic acid equivalent /ml and 50  $\mu\text{g}$  rutin equivalent /ml, respectively.

#### **Follow-up and outcomes:**

She was visited every week in our clinic by the physician and a trained nurse. At each visit, necrotic tissues were removed if necessary, and wound size was measured and assessed for signs of infection. During the first week, only wound length decreased by 0.2 mm, and there was no new necrotic tissue. Two weeks later, the wound size was  $2.5 \times 2 \times 0.3$  cm. At the third, fifth and seventh week, the wound was measured  $2.4 \times 1.8 \times 0.3$  cm,  $2.3 \times 1.5 \times 0.2$  cm, and  $2.0 \times 1.3 \times 0.1$  cm, respectively. On 14 May 2017 (the tenth week), the size of the wound was measured  $1.0 \times 0.3 \times 0.0$  cm and there was no infection (Fig2. B, C). Finally, the wound was completely closed in the 12th week.

#### **Discussion**

DFUs are one of the most costly complications of diabetes [21]. Most of the ulcers are unresponsive to different therapies currently available for management of DFUs [22]. Furthermore, many of such patients cannot afford current therapies. It should also be noted that lower limb amputation is 15 times more common in diabetic people [23]. So, more effective drugs with lower cost are highly required. Lately, traditional medicine and herbs has been increasingly used around the world for the promotion of health

and treatment of numerous diseases [24]. Medicinal plants introduced by traditional medicine have been used as feed and drug among different nations since ancient times. Nevertheless, research should be done to approve efficacy and determine phytochemical components of traditional medicines [25]. PM has recommended numerous remedies for wound healing [14]. Myrtle is one of the plants mentioned in the sources of PM for the healing of burns, wounds and foot ulcers [26, 27]. In a study, low-dose Myrtle extract (ME) had wound healing effects in rats [28]. Also, myrtle extract had healing effect on burn wound [29]. A previous study also showed that ME could improve wound healing via inhibition of inflammatory responses, decreasing oxidative stress, induction of angiogenesis and prevention of skin infections [30]. The bioactive compounds such as flavonoids, tannins, alkaloids and essential oils are known to be responsible for most of these effects [20]. However, no research on the effect of *M. communis* on DFUs, was found. Fortunately, in this case, the foot ulcer was healed by using a myrtle product. It seems Persian medicine-inspired approaches formulated by modern technology called reverse pharmacology, can be helpful in treating various diseases, including DFUs [31].

#### **Author Disclosures**

None reported

#### **Author statement**

**Seyed-Ali Khodaie:** Performed experiments, Original draft preparation, Investigation;

**Saeidhossein Khalilzadeh:** Methodology; **Fatemeh Emadi:** Supervisor, Conceptualization;

**Mohammad Kamalinejad:** Conceptualization, Investigation; **Jafari Hajati Raziieh:** Draft preparation; Investigation; **Naseri Mohsen:** Supervision, Conceptualization, Methodology

#### **Disclosure Statement**

The authors have declared that there is no conflict of interest.

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Figure 1: Timeline showing relevant history and interventions considered for the patient.

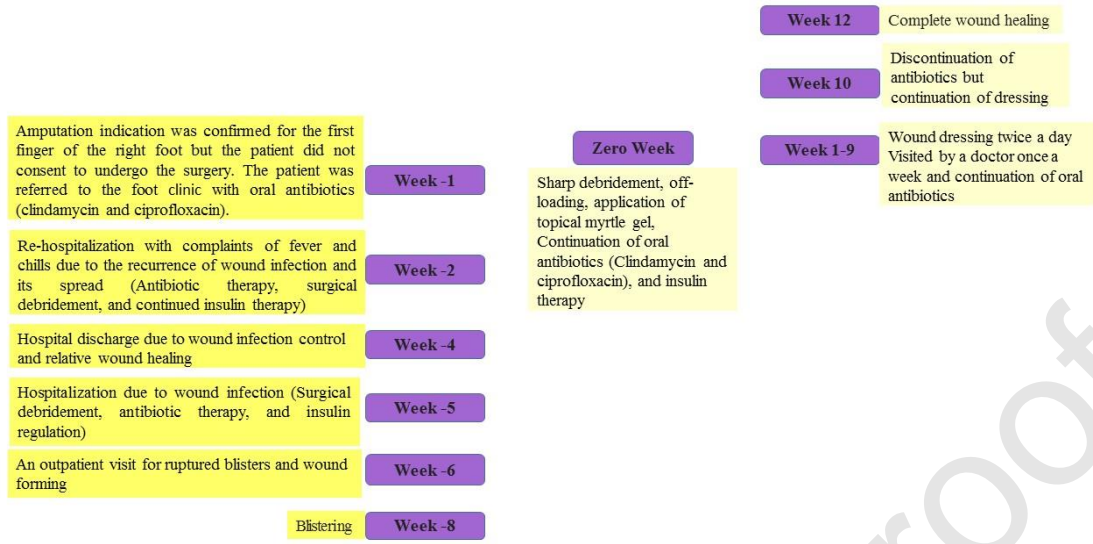


Figure 1: Timeline showing relevant history and interventions considered for the patient



Figure2: Changes in the wound appearance over the 10-week period:

A. Wound appearance at the first visit; B. Wound at week 5; and C. Wound at week 10