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Management of a diabetic foot ulcer with a Myrtle (*M. communis*) gel based on Persian medicine: A case report

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) are one of the most important medical issues facing patient with diabetes. Neurological, vascular and immune factors may lead to delayed wound healing in diabetics. Current treatments for DFUs are often expensive, show variable efficacy and are not available to all patients. Pharmacological evaluation highlights several herbal and traditional medicines offer potential treatment candidates that can be considered for development of new therapeutics against various diseases. According to Persian Medicine (PM) literature, Myrtle (*Myrtus communis*) fruits and leaves, when applied topically, may be 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 woman 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 a gel containing Myrtle (*M. communis*), implied potential beneficial effect of Myrtle gel on DFUs. Myrtle gel (*M. communis*) used in combination with conventional diabetic medicines may offer an effective too for management of DFUs.

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1. Introduction

Long-term hyperglycemia associated with diabetes leads to peripheral limb damage. Foot ulceration is the most common complication in diabetic patients [1], with vasculopathy and neuropathy are two major etiologies of delayed diabetic wound healing [2,3]. Effective care for Diabetic Foot Ulcers (DFU) currently include comprehensive and includes blood sugar level control, locally effective wound care, infection control, pressure relieving and blood flow improvement [4].

Most current treatments applied for DFUs are ineffective, can cause complications and show prolonged healing times. As such,

DFUs are considered an increasing public-health problem associated with increasing diabetes prevalence 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 DFUs [9]. Treatment of DFUs and other associated wounds requires more efficient therapeutics, with several herbal and traditional medicines demonstrating some potential [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 TM/CAM 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) is a traditional medicine system backed by several thousands of historical written and evidence in different languages [14], with

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numerous remedies are mentioned in PM for wound healing [15]. So far, the effectiveness of only some traditional PM medicines has been proven [16]. In a study that ranked effective remedies suggested by PM for treatment of DFUs, based on their efficacy, Myrtle (*Myrtus communis* L) was considered to be the most likely traditional PM medicine to be an effective DFU treatment [17]. *M. communis* is a medicinal plant that is widely used in PM. Medieval Persian scholars believed that Myrtle possesses astringent, hemostatic and wound healing effects, and [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.

2. Ethical issues

The study was approved by the local medical ethics committee of Shahed University (ID number: IR.Shahed.REC.1394.97). Also, informed consent was provided by the patient following consultation with the patient and her family to use Myrtle gel topically to treat DFU.

3. Presenting concerns

A 66 year old female patient presented with a deep necrotic wound on tip of the first digit of the right foot. The patient attended the outpatient department on 25 February 2017. The patient had a history of diabetes for over 12 years but no previous foot ulceration. The patient was being treated with insulin 7 months prior to admission for treatment of the wound, and 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. Fig. 1 shows a timeline of the relevant history of and interventions used for the case.

4. Clinical findings

Based on physical examination, the patient 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 patient's 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.

5. Diagnostic focus and assessment

Blood tests revealed the following data: hemoglobin, 127 g/l; total white blood cell count, 10.9 × 10⁹; 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).

6. 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 prescription (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 existing antibiotic regimen, which had already begun at the hospital, was continued [oral clindamycin (300 mg q8h) and ciprofloxacin (500 mg q12 h)]. 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.

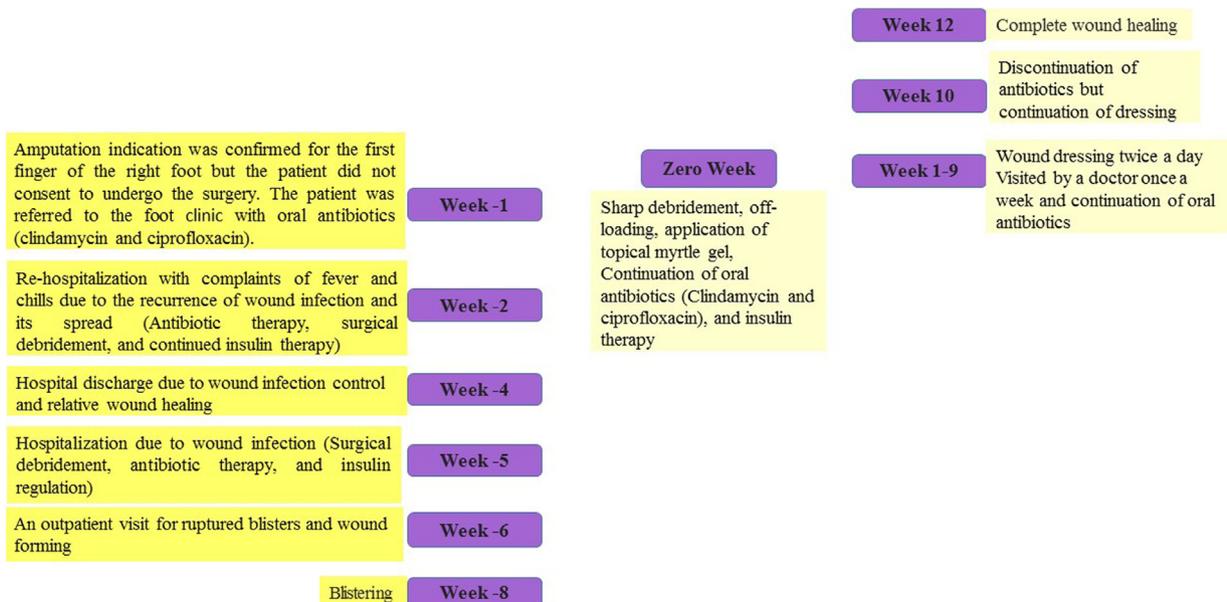


Fig. 1. Timeline showing relevant history and interventions considered for the patient.



Fig. 2. 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.

For preparation of the Myrtle gel, 100 g of washed myrtle fruits (*M. communis*) 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 AlCl_3 reagent and expressed as 10.93 mg galic acid equivalent /mL and 50 μg rutin equivalent /mL, respectively.

7. Follow-up and outcomes

The patient 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 (Fig. 2B, C). Finally, the wound was completely closed in the 12th week.

8. Discussion

DFUs are one of the most costly complications of diabetes [21]. Most DFUs are unresponsive to different therapies currently available [22], and many current therapies remain unaffordable to patients. Untreated DFUs have significant disease burden, with lower limb amputation being 15 times more common in diabetic people than in non-diabetics [23]. As such, more effective drugs with lower cost are highly required for effective treatment and management of DFUs. TM/CAM has been increasingly used globally for the promotion of health and treatment of numerous diseases [24]. Although medicinal plants introduced by TM/CAM systems such as PM have been used as drugs among different nations since ancient times, research needs to be done to evaluate claims of efficacy and determine phytochemical components of traditional medicines [25]. PM has recommended numerous remedies for wound healing [14]. Myrtle (*M. communis*) is one of the medicinal plants mentioned in traditional PM information sources for the healing of burns, wounds and foot ulcers [26,27]. Animal studies appear to support its use, with low-dose Myrtle extract showing wound healing effects in rats [28], and healing effects on burn wounds [29]. In vitro studies suggest Myrtle extract could improve wound healing via a mechanism of action of inhibition of inflammatory responses, decreasing oxidative stress, induction of angiogenesis and prevention of skin infections [30]. The bioactive compounds found in *M. communis* such as flavonoids, tannins, alkaloids and essential oils are known to be responsible for most of these effects [20]. However, to date no research on the

effect of *M. communis* on DFUs, was found. In this case report, the foot ulcer was healed by using a Myrtle product, which in addition to supportive traditional, animal and in vitro evidence highlights the need to conduct further trials on this treatment. Validation of a PM intervention in a contemporary clinical setting also suggests that 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.

CRediT authorship contribution statement

Seyed-Ali Khodaie: Performed experiments, Original draft preparation. **Saeidhossein Khalilzadeh:** Methodology. **Fatemeh Emadi:** Supervision, Conceptualization. **Mohammad Kamalinejad:** Conceptualization, Investigation. **Razieh Jafrai Hajati:** Writing - review and editing. **Mohsen Naseri:** Supervision, Conceptualization, Methodology.

Declaration of Competing Interest

The authors report no declarations of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.aimed.2020.08.008>.

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