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Case Report

Topically Applied Glycerol-Based Turmeric Extract Formulation Ameliorates Diabetic Foot Ulcer: A Case Report

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Abstract

Diabetic foot ulcers (D-FUs) are a severe complication that affects up to 34% of diabetic individuals. Approximately 20% of cases result in amputation and a doubled 10-year mortality risk. Although sophisticated therapies have achieved some success, there is a need for effective alternatives. The active compound curcumin of turmeric (*Curcuma longa*) possesses antimicrobial, antioxidant, and anti-inflammatory properties that may facilitate wound healing. A 41-year-old male presented with a two-month duration of antibiotic-resistant D-FU and had an inadequately controlled 12-year history of type 2 diabetes. The ulcer remained unresponsive despite conventional interventions, such as antibiotics. After saline cleansing, a topical turmeric extract glycerol-based formulation was applied to the wound daily. The formulation was freshly prepared by combining 1:1 g/ml of turmeric extract powder with glycerol. The turmeric extract treatment resulted in a substantial improvement in the condition of the lesion over 35 days. Exudate and erythema decreased within seven days, the infection had resolved, and the lesion had significantly healed by day 35. This case report indicates that turmeric extract has the potential to serve as a cost-effective adjunctive therapy for chronic D-FUs. However, additional research is necessary to optimize curcumin formulation to enhance its pharmacokinetics and to elucidate curcumin wound-healing mechanisms to promote diabetic wound healing and reduce related complications.

Keywords: Amputation, Curcumin, Diabetic complications, Ulcer, Wound healing.

تركيبة مستخلص الكركم القائمة على الجليسيرين المستخدمة موضعيا موضعيا تحسن قرحة القدم السكرية: تقرير حالة

الخلاصة

تقرحات القدم السكرية (D-FUs) من المضاعفات الشديدة التي تؤثر على ما يصل إلى 34٪ من مرضى السكري. ويؤدي ما يقرب من 20٪ من الحالات إلى بتر الأطراف ومضاعفة خطر الوفاة بعد 10 سنوات. على الرغم من أن العلاجات المتطورة قد حققت بعض النجاح، إلا أن هناك حاجة إلى بدائل فعالة. يمتلك مركب الكركمين النشط من الكركم (*Curcuma longa*) خصائص مضادة للميكروبات ومضادة للأكسدة ومضادة للالتهابات قد تسهل التئام الجروح. تمثل الحالة رجل يبلغ من العمر 41 عاما يعاني من D-FU المقاوم للمضادات الحيوية لمدة شهرين تاريخ غير كاف لمدة 12 عاما من مرض السكري من النوع 2. ظلت القرحة غير مستجيبة على الرغم من التدخلات التقليدية، مثل المضادات الحيوية. بعد التطهير الملحي، تم وضع تركيبة موضعية من مستخلص الكركم القائم على الجلسرين على الجرح يوميا. تم تحضير التركيبة حديثا عن طريق الجمع بين 1: 1 جم / مل من مسحوق مستخلص الكركم مع الجلسرين. أدى العلاج بمستخلص الكركم إلى تحسن كبير في حالة المريض على مدى 35 يوما. انخفضت الإفرازات والحمامي في غضون سبعة أيام ، واختفت العدوى، وشفيت الآلتهابات بشكل ملحوظ بحلول اليوم 35. يشير تقرير الحالة هذا إلى أن مستخلص الكركم لديه القدرة على أن يكون بمثابة علاج مساعد فعال من حيث التكلفة لأمراض D-FUs المزمنة. ومع ذلك ، من الضروري إجراء مزيد من الأبحاث لتحسين تركيبة الكركمين لتعزيز الحركية الدوائية وتوضيح آليات التئام الجروح و لتعزيز التئام جروح التقرح السكري وتقليل المضاعفات ذات الصلة.

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INTRODUCTION

Diabetic foot ulcer (D-FU) is one of the most serious and disabling complications of diabetes, contributing significantly to mortality among diabetic patients [1]. They are affecting up to 34% of individuals with diabetes at some point in their lives [2], and approximately 20% of moderate to severe cases result in amputation [3]. The mortality risk in diabetic patients with D-FUs is twice as high over a 10-year period due to complications like infection or sepsis, compared to those without D-FUs [1]. Several emerging therapies showed promise in treating these difficult-to-heal wounds. For instance, platelet-rich plasma (PRP) gel, which is rich in growth factors, has also shown success in treating non-responsive D-FUs [4]. Negative pressure wound therapy combined with debridement and antibiotics has proven effective in reducing wound size and promoting healing [5]. In some

cases, a combination of maggot therapy, negative pressure wound therapy, and silver foam dressing has resulted in the complete healing of refractory D-FUs [6]. These advanced therapies offer new hope for patients with chronic, non-healing D-FUs and may help reduce the need for amputation when conventional treatments are inadequate. Despite advancements in medical and surgical interventions, the treatment of D-FUs is often insufficient, and diabetic foot complications are still common that necessitate the search for alternative approaches. Turmeric (*Curcuma longa*), a spice from the Zingiberaceae family, has been widely studied for its medicinal properties, primarily due to its active compound, curcumin. Research highlights turmeric's therapeutic potential for conditions such as cancer, diabetes, cardiovascular diseases, arthritis, Alzheimer's disease, and various inflammatory disorders. Traditionally, turmeric powder has been utilized in Eastern herbal medicine for centuries. Curcumin, a polyphenol derived from turmeric, has gained attention for its potential in treating D-FUs, owing to its anti-inflammatory, antioxidant, and antimicrobial properties [7]. A previous study revealed that the topical application of turmeric extract enhances and accelerates the healing of cutaneous wounds in rats. This reduction in wound-healing time highlights curcumin's potential as a safe and effective agent for improving postoperative care, particularly in surgeries involving flaps and skin grafts [8]. These properties make curcumin a promising agent for promoting wound healing in diabetic patients. Curcumin has demonstrated potential in managing diabetic foot complications through stimulation of fibroblast proliferation, enhancing collagen synthesis, and supporting re-epithelialization. It also accelerated D-FU wound healing through rejuvenation and restoration of the FBN1/TGF-β pathway [6,7,9]. This case report describes the complete recovery of a patient with a D-FUs following topically applied turmeric extract formulation for one month.

Case Presentation

The patient was a 41-year-old male with a 12-year history of type 2 diabetes who has had left D-FUs for two months. The patient also has a family history of diabetes. He showed poor glycemic control and had a history of hyperlipidemia. He has been hospitalized many times for the routine treatment of D-FU, such as cleaning with normal saline, wound dressing, and antibiotic interventions. The glucose level was not controlled despite using the oral hypoglycemic agent glimepiride 6 mg tablet once daily before meals and metformin 850 mg three times daily after meals. For treatment of high cholesterol and triglycerides, he was taking 10 mg simvastatin after meals at night. The patient had a frequent visit to his diabetologist; he was admitted with a chief complaint of the left foot little toe ulceration. In history-taking and physical examination, it was found that the patient had antibiotic-resistant D-FUs. The patient had a history of intermittent fever; there was no prior history of trauma before the development of the ulcer. Treatment was initially started by a local physician, which provided minimal relief. The wound was unopened in the dorsal aspect, while there was a small-sized punctuated wound (1.5 cm diameter) on the plantar aspects of the foot. The wound on the dorsal aspect was characterized by erythema, swelling, and the presence of a significant amount of exudate, with a gangrenous appearance (Figure 1, Day 1). Some of the patient's laboratory data on admission are shown in Table 1. The patient had abnormal lipid levels and elevation of liver enzymes consistent with fatty liver changes on ultrasound.

Table 1: Lab investigation of the patient on admission

Test	Results
Blood sugar	438 mg/dl
HBA1c	12.1%
S. Creatinine	0.9 mg/dl
S. Uric acid	4.61mg/dl
S. Cholesterol	234 mg/dl
S. Triglyceride	327 mg/dl
S. LDL	93 mg/dl
S. HDL	38 mg/dl
Hemoglobin	16.2 g/dl
WBC	10.3 *109 /L
T. S. Bilirubin	0.7 mg/dl
S. GPT	70 IU
S. GOT	43 IU
S. Alkaline phosphate	99 IU

GOT: glutamic oxaloacetic transaminase, GPT: glutamic pyruvic transaminase, HbA1c: glycated hemoglobin, HDL: High density lipoprotein, LDL: low density lipoprotein, S: serum, T.S: total serum, WBC: White blood cells.

Turmeric extract formulation and application

A glycerol-based turmeric extract formulation was prepared by mixing 15 g of turmeric powder (purchased from the local market) with 15 ml of glycerol (pharmaceutical grade 98% from Avonchem Limited, Macclesfield, Cheshire, UK). A homogenizer was utilized in the formulation process to guarantee uniformity and complete dispersion of the turmeric extract within the formulation vehicle. This process ensures that any large particles of the extract are broken down, allowing for an even distribution throughout the mixture. The semisolid preparation was applied topically once daily for one month after cleaning the wound with normal saline.

DISCUSSION

The response of applying the turmeric extract formulation is depicted in Figure 1. On day 1, no treatment was given. In the first week, applying the formulation to the wound led to a slight disappearance of the exudate and erythema and mild amelioration of the severity of the little toe swelling. At the follow-up visit, the wound size became smaller in size and depth, and the infection had cleared. Diabetic foot ulcers are a serious diabetic complication with considerable medical and socioeconomic consequences, contributing significantly to patient morbidity, mortality, and reduced quality of life. Research has demonstrated that D-FUs adversely impact patients' social, physical, and psychological well-being [10]. In this case report, the patient had a long history of poor glycemic control, resulting in diabetic neuropathy and eventually a D-FU, which is resistant to antibiotic treatment. The study investigated the effect of a semisolid topical preparation of turmeric powder combined with glycerol on D-FU healing.

Figure 1: Stagewise photos of the wound during glycerol-based turmeric extract formulation treatment.

The formulation was applied once daily after cleansing the wound with normal saline, and the progress of wound healing was monitored through weekly photographing. Remarkable improvements and complete wound healing were observed after one month of the treatment, independent of fasting blood glucose and HbA1c levels. The use of turmeric topical application has been investigated in several studies beyond D-FUs, as researchers have developed topical turmeric gels using carboxymethylcellulose, triethanolamine, glycerin, and rose water [11]. Additionally, turmeric-based peel-off face masks have been formulated with polyvinyl alcohol, glycerin, and gelatin, offering benefits such as skin tightening, moisturizing, and tan removal [12]. Recent studies have further investigated turmeric-based semisolid preparations for topical use. Turmeric extract, composed of curcumin, demethoxycurcumin, and bisdemethoxycurcumin, has been successfully integrated into cream formulations, resulting in yellow-orange, homogeneous products with good dispersibility and pH levels [13]. These findings emphasize turmeric's versatility in various semisolid formulations, providing easily applicable and practical formulas in the treatment of D-FUs. The pathophysiology of D-FU is multifactorial and includes metabolic dysfunction, neuropathy, angiopathy, and immunopathy. Hyperglycemia is central to this process, causing peripheral nerve damage through oxidative stress and inflammation. Neuropathy, vascular insufficiency, and infections are key factors contributing to D-FU development [14]. Cellular involvement includes immune, endothelial, keratinocyte, and fibroblast activity, while molecular factors involve disrupted signalling pathways, high matrix metalloproteinase levels, and excessive advanced glycation end-products (AGEs). Epigenetic factors and hyperglycemia-induced metabolic and immunological changes also complicate wound healing [15]. Curcumin, the main polyphenol in turmeric, shows potential in treating D-FUs due to its anti-inflammatory, antioxidant, and anti-infective properties [16]. Preclinical studies suggest that curcumin enhances wound healing by improving blood vessel density, collagen production, and cell proliferation, although its anti-inflammatory effects remain under investigation [17]. A clinical trial demonstrated that topical turmeric ointment significantly reduced D-FU size compared to placebo, independent of glycemic control, highlighting its therapeutic potential. The finding of this case report is consistent with the results indicated by Agharazi *et al.*, in which the topically applied curcumin resulted in a profound improvement and reduced the size of the ulcers accompanied by diabetic complications [18]. Molecular pathways such as Notch, Wnt/β-catenin, and HIF-1, which are critical to cell proliferation, migration, and hypoxia response, are disrupted in D-FUs [19]. Curcumin has shown promise in modulating these pathways, including inhibiting miR-152-3p and activating the FBN1/TGF-β pathway to enhance fibroblast activity and angiogenesis [9]. Moreover, excessive expression of nuclear factor-kappa B (NF-κB) in diabetic wounds resulted in an elevation of inflammatory cytokines that foster inflammation and oxidative stress [20], prolong inflammation, and inhibit angiogenesis, consequently hindering diabetic wound healing. A recent review reported that naturally occurring phytoconstituents, including curcumin, are well-known inhibitors of NF-κB pathways and are now recognized as safe, effective, and affordable remedies for the treatment of D-FUs [21]. The positive outcome of turmeric formulation in healing the wounds demonstrated in the current case report might be related to hampering these pathways. Although the current report focuses on the therapeutic outcomes of herbal medicine in treating a serious complication of diabetes mellitus, some limitations should be mentioned. First, in the macroscopical assessment of the wound, the study did not utilize image software like ImageJ or Imitowound to assess wound improvement pre- and post-intervention. Additionally, the formulation was not validated, and no histopathological analysis was performed to quantify the structural remodeling of the wound before and after treatment. Photographs were taken, but no quantification of ulcer progression was conducted. In conclusion, the report highlighted the significance of a topically applied turmeric extract, an easily prepared, affordable, and cost-effective therapeutic

approach, as a homemade remedy in the treatment of non-healing diabetic foot wounds. However, additional research is necessary to optimize curcumin formulation to enhance its pharmacokinetics and to elucidate its wound-healing mechanisms to promote diabetic wound healing and reduce related complications.

Conclusion

Topically applied turmeric extract treatment resulted in a substantial improvement in the condition of the diabetic foot ulcer lesion over 35 days.

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Conflict of interests

No conflict of interest was declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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