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Assessment of the Efficacy of Aloe Vera Resin Extract as an Anti-Diabetic Foot Ulceration Agent

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ABSTRACT
A diabetic foot ulcer is one of the most significant and devastating complications of diabetes. DFU is considered a major source of morbidity and mortality in patients with diabetes. Therefore, this study aimed to test the possibility of using Aloe Vera resin extract as an antibacterial agent (Libyan remedy) against isolated bacteria from a patient's foot. This study was concerned with the determination of the possible microbial cause of the diabetic foot ulcer; therefore, its design included microorganism isolation, identification, and finally, testing of the antibacterial activity of Aloe Vera resin against bacteria isolated from diabetic foot ulcers. Curiously, the results demonstrated that every antibiotic used in this experiment created inhibition zones against the bacteria that were isolated from patients' feet and had a pronounced resistance to the extract from aloe vera resin. In contrast, aloe vera resin extract created inhibition zones against bacteria isolated from healthy feet in comparison to the other widely used, well-known broad-spectrum antibiotics. The pathogen that was isolated from the patient's feet, according to our lab results, was Staphylococcus bacteria. Aloe Vera resin extract had no inhibition zones against Staphylococcus species bacteria that were collected from patient feet, which contradicted the hypothesis that Aloe Vera is a good antibacterial agent that could be used to prevent diabetic foot ulcers. Nonetheless, it demonstrated a slight antibacterial effect on normal flora foot bacteria. Bacterial resistance due to possible mutations could be the cause of this. It is also important to take into account the anti-inflammatory properties of aloe Vera resin extract.

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INTRODUCTION

Diabetic foot is one of the most significant and devastating complications of diabetes, and is defined as a foot affected by ulceration that is associated with neuropathy and/or peripheral arterial disease of the lower limb in a patient with diabetes [1]. The development of a foot ulcer usually involves several mechanisms, such as neuropathy, increased biomechanical stress, external trauma, and peripheral arterial disease (PAD) [2]. Loss of sensation in the feet of patients with peripheral diabetic neuropathy causes recurrent minor injuries from external (shoes, burns, foreign bodies) or internal (calluses, nails, foot deformities) sources that go unnoticed at the time and can eventually result in foot ulcers. Especially in patients with peripheral arterial disease, this may be followed by ulcer infection, which could ultimately result in foot amputation [1].

DFU is considered a major source of morbidity and a leading cause of hospitalization in patients with diabetes. It is estimated that approximately 20% of hospital admissions among patients with DM are the result of DFU [3]. In fact, approximately 15% of people with diabetes will develop a foot ulcer at some point in their lives. Amputation is the biggest risk for these patients. Many studies have shown that between 25 and 50 percent of diabetic patients have their limbs amputated right away at their initial visit because of an infection. It is estimated that diabetes accounts for between 50 and 70 percent of all lower limb amputations [4].

Patients with peripheral neuropathy frequently develop diabetic foot ulcers as a result of repetitive stress over an area that experiences high vertical or shear stress. Foot ulcer development is also influenced by peripheral artery disease (PAD), if it exists [5]. PAD is a clinical condition characterized by occlusion or stenosis of the arteries in the lower limbs. For those over forty, atherosclerosis is the primary cause of PAD. When compared to people without diabetes, the incidence of PAD is two to four times higher in those with diabetes. In adults aged 40 and over, the prevalence of PAD is 9 percent in diabetic subjects, which is twice as high as the prevalence of 4 percent in non-diabetics[6]. Wound healing in these patients is not only influenced by the presence of PAD but also by factors such as infection, edema, and the presence of co-morbidities [7].

Diabetes mellitus impairs the biological process of wound healing by influencing one or more of the biological mechanisms involved. This results in chronic non-healing wounds, like diabetic foot

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ulcers (DFA). In addition to diabetes, other risk factors for DFU include peripheral arterial disease (PAD), immune system factors, sensory, motor, and autonomous neuropathy, and, in certain situations, repetitive external or minor trauma (which causes skin breakdown and ultimately infection). Also regarded as risk factors are bony foot abnormalities like hammertoes and bunions, which can produce pressure points that could develop into ulcers [8, 9].

The primary management goals for DFU are to obtain wound closure as expeditiously as possible [3]. Diabetic foot ulcers can be managed according to three main principles: minimizing pressure on the affected area, controlling infection, and promptly and appropriately removing calluses. Both medical and surgical management are part of the management of diabetic foot. When the ulcer is small, recent, and in patients who are not suitable candidates for reconstructive surgery, medical management is recommended. Arterial reconstruction, sympathectomy, and amputation are all included in surgical care. It is always important to take adequate arterial perfusion for healing into account when evaluating the indications for diabetic foot surgery [10, 11].

In Libyan society today, using medicinal plants is regarded as one of the most significant ways to treat diabetic foot. Utilizing medicinal plants for wound care and management entails debridement, disinfection, and creating a suitable environment for the body's natural healing process. The increased and renewed interest in the use and application of medicinal plants in the wound healing process, both in diabetic and non-diabetic conditions, is thought to be due to the assumption that their ingredients are less toxic and have fewer side effects than therapeutic agents[12]. The production of some medicinal products, such as bromelain, a herbal protease currently used for enzymatic debridement of wounds, has demonstrated that medicinal plants may also be a source of wound healing agents. As a supplement to conventional wound care, herbal medicines have been utilized as systemic or topical preparations, such as oils, gels, and creams [12].

According to one study, Aloe vera extract improved wound healing in diabetics and recommends using it as a treatment. In comparison to an untreated animal, Aloe. vera may have positive effects on the different stages of wound healing, including fibroplasia, collagen formation, and contraction, which would result in faster healing [13, 14] .

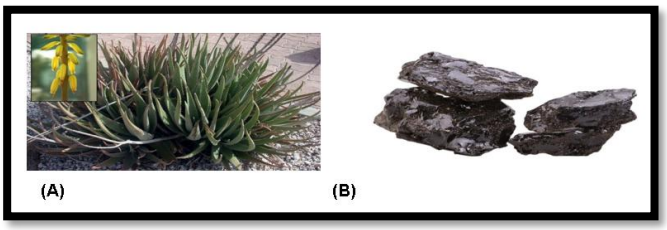

Figure 1. (A) Aloe vera, which is the primary source of aloe resin. (B) Aloe Vera resin

The resin of Aloe ferox Mill, which belongs to the *Xanthorrhoeaceae* family, is obtained by evaporating the latex that drains from the leaves, transversely cut. Aloe ferox has been used in traditional medicine as an anti-inflammatory, immunostimulant, antibacterial, antifungal, antitumor, laxative, and for the treatment of wounds and burns[15]. Aloe leaves contain many classes of bioactive compounds, including chromones, flavonoids, anthraquinones, anthrones, amino acids, lipids, carbohydrates, vitamins, and minerals [16]. Furthermore, the unique compound of Aloe, which has not been found in any other plant, is C-glycosylated chromones, which are considered as a phenolic compound that possesses antioxidant, antimicrobial, anticancer, and anti-inflammatory activities[17]. Topical products of Aloe are used for their anti-inflammatory and wound healing properties for acne, abrasions, sunburn, minor burns, diabetic ulcers, and stomatitis. It works by inactivation bradykinin to inhibit PGA2, arachidonic acid oxidation, and thromboxane A2 blocking [18].

Aloe activity may result from its ability to increase blood flow in the affected area[19]. In one study, results indicated that the wound closure rate in animal models demonstrated that the whole-leaf juice assisted the healing process and inhibited microbial growth with no visible side effects[18]. Another published paper is focused on the application of modern delivery techniques to natural bioactive products to improve their permeability, bioavailability, and therapeutic efficacy. Many natural products have desirable biological properties applicable to wound healing, but are limited by their inability to cross the stratum corneum to access the wound[20].

Accordingly, medicinal plants can be considered as promising adjuvant therapies to conventional wound care for the treatment of diabetic foot ulcers, to accelerate the process of wound healing in affected patients. This highlights the important role of natural products derived from plants in the development of wound healing agents[12]. Therefore, this study aims to test the possibility of

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using Aloe Vera resin as an antibacterial agent in diabetic foot ulcers against isolated bacteria from patients.

METHODS AND MATERIALS

Study design

This study was concerned with the determination of the possible microbial cause of the diabetic foot ulcer; therefore, its design included microorganism isolation, identification, and finally, testing of the Libyan traditional remedy that claimed that Aloe Vera resin might be used as a good treatment for a diabetic foot ulceration. It is worth noting that the samples were collected from diabetic foot patients at Soaq Al-khamees Diabetic center (Alkhoms city-Libya)

Microbiological testing

Preparation of Aloe vera resin extract

The Aloe Vera resin (from traditional plant shopping center (Attar), Msallata City-Libya) was dissolved in distilled water to make 10% (w/v) dispersion. Aloe vera supernatant was diluted to make 1% (v/v) dispersion to mimic traditional medicinal use concentrations. In some pilot studies, Aloe Vera resin was used as a row material.

Agar disk-diffusion method

The Kirby-Bauer test, also known as the disk-diffusion agar method test, measures how sensitive bacteria are to antibiotics. Antibiotic discs are used to test how much the antibiotics affect the bacteria. In short, the procedure involves spreading bacteria on an agar plate first, followed by the addition of an antibiotic disk or aloe extract (3 mg/ml). For a liquid substance, agar can have a hole bored through the middle of it. After a full day of bacterial growth on the agar medium, the bacteria are examined. The lethality of each antibiotic on the particular bacteria is indicated by the amount of space surrounding each plate. Whereas an ineffective antibiotic will not alter the surrounding bacterial concentration at all, a highly effective antibiotic will create a broad ring of no bacterial growth. The zone of inhibition of intermediate antibiotics can be used to gauge how effective they are. The best antibiotic to use against a novel or drug-resistant pathogen is determined using this method [21, 22, 23]. In this part of the current study, we have compared the efficacy of 3mg/ml Aloe vera resin against different well-known antibiotics (Co-trimoxazol 25 µg (SXT), Augmentin 30µg (AUG), Meropenem 10µg (MEM), and Ciprofloxacin 5µg (CIP); Lioflchem-Italy). The zones of inhibition of Aloe vera resin and the other antibiotics were captured using a smartphone, and the images were treated using the following command: (ImageJ ----->straight tool ----> Analyze ----> Measure ----> repeat the same process for each inhibition zone), and then the collected data were transferred to an excel sheet and the bar charts were generated (figure 3).

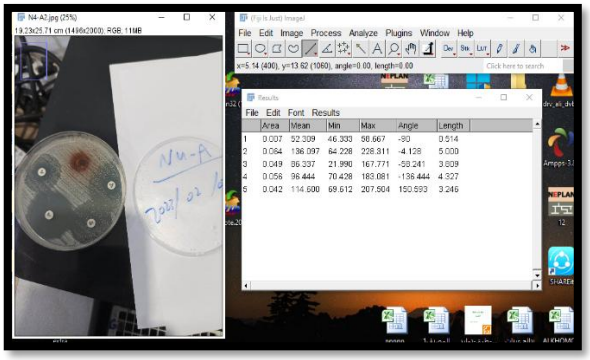

Figure 3. Using ImageJ to calculate the zones of inhibition of different antibacterial agents

Microscope examination

This stage includes a Gram stain of isolated bacteria from normal volunteers and DFU patients. The slides were then examined under the microscope (Hamilton Microscope) to determine the type of bacteria.

Statistical analysis

Data were analyzed using GraphPad Prism 6. Variables were expressed as numbers, percentages, means, and standard error of means as appropriate. Differences between the variables were explored using the Mann-Whitney U test, and a significant two-sided p value was set at 0.05 or less.

RESULTS

The Libyan traditional remedy that says (aloe resin might be used to control diabetic foot ulcerations) was tested. Therefore, we have compared the efficacy of 3mg/ml aloe V. extract against different well-known antibiotics (Co-trimoxazol 25 µg (SXT), Augmentin 30µg (AUG), Meropenem 10µg (MEM), and Ciprofloxacin 5µg (CIP); Lioflchem-Italy). Zones of inhibition of Aloe vera extract and the other antibiotics were captured using a smartphone, and the images were treated using FIJI software (Figure 4). The bar chart in (Figure 5) shows the percentage of the inhibition zone of Aloe Vera extract against the other different antibiotics in plates cultured from swabs collected from a normal foot (non-diabetic and non-ulcerated foot) bacteria (as a reference). Aloe, in addition to the entire antibiotics that were used in that test, had made inhibition zones against

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normal foot (non-diabetic and non-ulcerated foot) bacteria ($p<0.05$).

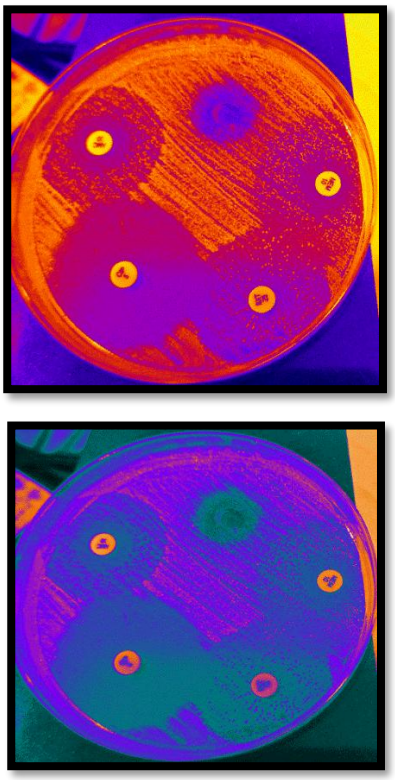

Figure 4.Bacterial culture visualization using Image j, treated images of bacterial culture shows clear inhibition zones in nutrient agar cultures of bacteria collected from normal non-diabetic foot (standard) that made by Aloe Resin extract and antibiotics used in this test

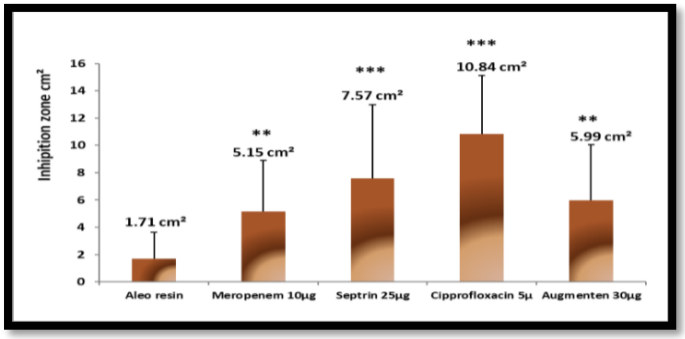

Figure 5.Aloe resin Anti Anti-bacterial effect on non diabetic foot volunteers

Previous results encouraged us to test Aloe Resin on bacteria collected from diabetic foot patients. The Images and bar chart in figures 6&7 show the percentage of the inhibition zone of Aloe extract against other different antibiotics in plates cultured from swabs collected from diabetic foot patients. Interestingly, only Ciprofloxacin 5µg, Co-trimoxazol 25 µg, Meropenem 10 µg, and Augmenten 30 µg made inhibition zones against bacteria collected from the feet of patients with a clear resistance to aloe resin extract ($p<0.05$).

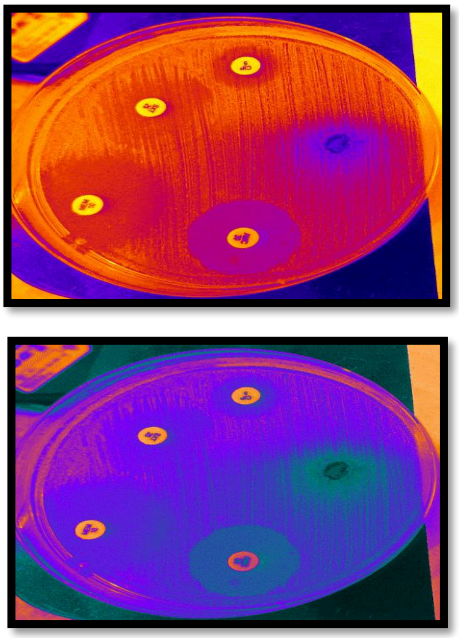

Figure 5. Bacterial culture visualization using ImageJ j, treated images of bacterial culture show no inhibition zone in the nutrient agar culture of bacteria collected from a diabetic syndrome patient, that made by aloe resin, but other antibiotics used show clear inhibition zones

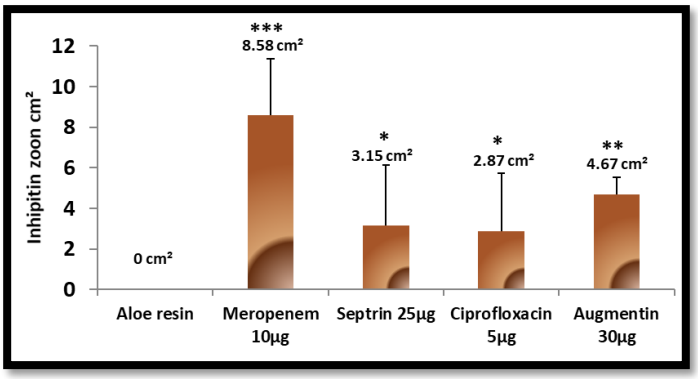

Figure 7. Aloe resin Anti Anti-bacterial effects on diabetic foot syndrome volunteers

To identify the type of bacteria that cause diabetic foot ulceration, we have Gram-stained cultivated bacteria under the microscope as shown in (Figure 8). Results indicate the presence of staph. Aureus bacteria that were isolated from diabetic foot patients.

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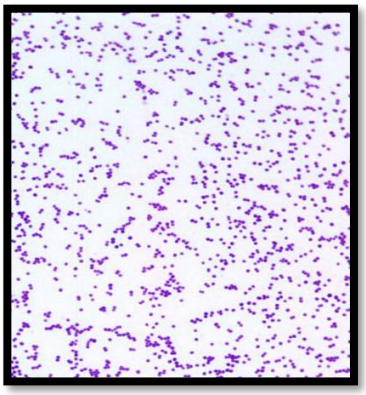

Figure 8-Staphylococcus aureus morphology visualised using Gram staining (10× magnification)

DISCUSSION

One of the most dangerous side effects of diabetes mellitus is diabetic foot disease. In addition to causing the patient great pain and financial hardship, it also has a significant negative impact on the patient's family, medical staff and facilities, and society in general [24]. According to the International Diabetes Federation, 9.1 million - 26.1 million people will develop DUFs every year[5]. DFI affects one in 10 patients with DM during their lifetime. They have an increased risk of lower extremity amputations, and the main cause is diabetic peripheral arterial disease, accelerated by the direct damage to the nerves and blood vessels by high blood glucose levels. Smokers, older patients with a longer history of uncontrolled diabetes, and those with gangrenous infections and large ulcers have poorer outcomes with amputations [25]. When amputation happens, it is usually associated with significant morbidity and mortality in addition to immense social, psychological, and financial consequences [26]. Therefore, the current study aimed to test the possibility of using Aloe resin as an antibacterial agent (Libyan remedy) against isolated bacteria from patients' feet and to determine the main causative bacteria of diabetic foot ulcerations.

Interestingly, results showed that all antibiotics had made inhibition zones against the bacteria collected from the feet of patients with a clear resistance to Aloe. On the other hand, aloe Vera extract had made inhibition zones against bacteria isolated from normal feet compared with the other well-known broad-spectrum antibiotics. Our laboratory results showed that the pathogen isolated from the patient's feet was Staphylococcus bacteria.

One might ask, why aloe resin? To answer this question, you have to be aware of the importance of herbal medicines. Traditional medicines derived from medicinal plants are used by about 60% of the world's population[27]. Professionals tend to deal with DFD as a local problem and therefore focus on using local topical agents, which may prevent infection or promote healing, such as honey[26]. Although it has been used in medicine for upwards of two thousand years, the knowledge of the chemistry of this drug is still imperfect[28]. On the therapeutic level, many recent studies reported the activity of aloe in the treatment of eye[27], constipation, malaria[29]antioxidant, antidiabetic, anti-tumor, anti-inflammatory, wound-healing properties, and antimicrobial activity [16]. Aloe's anti-inflammatory activity remains poorly investigated. Until present, there have been few to no reported studies that have assessed the anti-inflammatory properties of Aloe resins[18].

Historically, Aloe species were used as a topical treatment to treat the skin as a wound-healing plant to reduce the inflamed skin in traditional medicine[30]. The anti-inflammatory properties could be due to the availability of different forms of polysaccharides in Aloe species, with quantity dependent on the plant's age. Additionally, Aloe products could help in the production of more collagen when applied topically on the skin [31]. However, our results are inconsistent with the postulated hypothesis that introduces aloe as a good antibacterial agent that might be used as a diabetic foot anti-ulceration. The possible mechanism of Action of aloe on wound healing, studied by various researchers, reported that the effective components for wound healing may be tannic acid [32], and a type of polysaccharide [33]. According to other researchers, after topical and oral Aloe vera, glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interact with fibroblast growth factor receptors to stimulate the fibroblast's activity and proliferation, which in turn greatly increases collagen synthesis [34]. Aloe gel not only increased collagen content of the wound but also changed collagen composition and increased the degree of collagen cross-linking. Due to this, it accelerated wound contraction and increased the breaking strength of the resulting scar tissue [35]. An increased synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound following oral or topical treatment has been reported [34, 36] showed that A. Vera stimulated fibroblast proliferation and migration, and that these properties of A. Vera could help with wound healing. The results of the one study indicated that aloe is a potential wound-healing and anti-inflammatory agent in rat models of wound and inflammation. Further studies are

needed to elucidate the mechanism of action and the nature of the chemically active constituents responsible for the wound healing and anti-inflammatory activities of aloe mucilage [37]. Aloe is used for their anti-inflammatory and wound healing properties for acne, abrasions, sunburn, minor burns, diabetic ulcers, and stomatitis. It works by inactivation bradykinin to inhibit PGA2, arachidonic acid oxidation, and thromboxane A blocking[18].

CONCLUSION

We conclude that our results are inconsistent with the postulated hypothesis that introduces A. Vera as a good antibacterial agent that might be used as a diabetic foot anti-ulceration. Where A. Vera had no inhibition zones against Staph. species of bacteria that were collected from the feet of patients. However, it shows a slight antibacterial activity against bacteria isolated from normal feet. Further research is required to clearly determine the various properties of A. Vera, their optimal doses, forms, and their adverse effects and toxicity. Other factors should also be considered, such as the type, size, and location of the wound, as well as vascular supply, infection, and other conditions that might complicate the healing process.

Conflict of interest. Nil

REFERENCES

1. Alexiadou K, Doupis J. Management of diabetic foot ulcers. Diabetes Ther. 2012;3:1-15.
2. Al-Fatimi M, Wurster M, Schröder G, Lindequist U. Antioxidant, antimicrobial and cytotoxic activities of selected medicinal plants from Yemen. J Ethnopharmacol. 2007;111(3):657-66.
3. Ahmadian R, Bahramsoltani R, Marques AM, Rahimi R, Farzaei MH. Medicinal plants as efficacious agents for diabetic foot ulcers: a systematic review of clinical studies. Wounds. 2021;33(8):207-18.
4. Aldayel TS, Grace MH, Lila MA, Yahya MA, Omar UM, Alshammary G. LC-MS characterization of bioactive metabolites from two Yemeni Aloe spp. with antioxidant and antidiabetic properties. Arab J Chem. 2020;13(4):5040-9.
5. Alavi A, Sibbald RG, Mayer D, Goodman L, Botros M, Armstrong DG, et al. Diabetic foot ulcers: part II. Management. J Am Acad Dermatol. 2014;70(1):21.e1-24.
6. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367-75.
7. Bakhotmah BA, Alzahrani HA. Self-reported use of complementary and alternative medicine (CAM) products in topical treatment of diabetic foot disorders by diabetic patients in Jeddah, Western Saudi Arabia. BMC Res Notes. 2010;3:254.
8. Balouiri M, Sadiki M, Ibnsouda SK. Methods for in vitro evaluating antimicrobial activity: A review. J Pharm Anal. 2016;6(2):71-9.
9. Baltzis D, Eleftheriadou I, Veves A. Pathogenesis and treatment of impaired wound healing in diabetes mellitus: new insights. Adv Ther. 2014;31(8):817-36.
10. Brown DF, Kothari D. Comparison of antibiotic discs from different sources. J Clin Pathol. 1975;28(10):779-83.
11. Celestino VRL, Maranhão HML, Vasconcelos CFB, Lima CR, Medeiros GCR, Araújo AV, et al. Acute toxicity and laxative activity of Aloe ferox resin. Rev Bras Farmacogn. 2013;23(2):279-83.
12. Craig W. On the therapeutics of aloin. Edinb Med J. 1877;22(10):911.
13. Freytag A. Suggested role of traumatic acid in Aloe wound healing. Pharmazie. 1954;9(11):705.
14. Grace OM, Simmonds MSJ, Smith GF, van Wyk AE. Documented utility and biocultural value of Aloe L. (Asphodelaceae): a review. Econ Bot. 2009;63(2):167-78.
15. Hajhashemi V, Ghannadi A, Heidari A. Anti-inflammatory and wound healing activities of Aloe littoralis in rats. Res Pharm Sci. 2012;7(2):73-8.
16. Heatley NG. A method for the assay of penicillin. Biochem J. 1944;38(1):61-5.
17. Heggers JP, Kucukcelebi A, Listengarten D, Stabenau J, Ko F, Broemeling LD, et al. Beneficial effect of Aloe on wound healing in an excisional wound model. J Altern Complement Med. 1996;2(2):271-7.
18. Hęś M, Dziedzic K, Górecka D, Jędrusek-Golińska A, Gujska E. Aloe vera (L.) Webb.: natural sources of antioxidants - a review. Plant Foods Hum Nutr. 2019;74(3):255-65.
19. Hitam SAS, Hassan S, Maning N. The significant association between polymicrobial diabetic foot infection and its severity and outcomes. Malays J Med Sci. 2019;26(1):107-14.
20. Kameyama S, Shinho M. Wound healing compositions from Aloe arborescens extracts. Jpn Kokai Tokkyo Koho. 1979. Patent 79,151,113.
21. Kania A, Kałużyński G, Pełka M, Fijałkowska J, Ciulkiewicz Ł. An overview of Aloe vera impact on the healing process of Diabetic Foot Ulcer. J Educ Health Sport. 2024;54:67-82.
22. Kumar MS, Datta P, Dutta Gupta S. In vitro evaluation of UV opacity potential of Aloe vera L. gel from different germplasms. J Nat Med. 2009;63(2):195-9.
23. Leone S, Pascale R, Vitale M, Esposito S. Epidemiology of diabetic foot. Infez Med. 2012;20 Suppl 1:8-13.
24. Mothana RA, Al-Musayeib NM, Matheeussen A, Cos P, Maes L. Assessment of the in vitro

antiprotozoal and cytotoxic potential of 20 selected medicinal plants from the island of Soqotra. Molecules. 2012;17(12):14349-60.
25. Oguntibeju OO. Medicinal plants and their effects on diabetic wound healing. Vet World. 2019;12(5):653-63.
26. Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggesi A, Bakker K, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. Diabetologia. 2007;50(1):18-25.
27. Ramirez-Acuña JM, Cardenas-Cadena SA, Marquez-Salas PA, Garza-Veloz I, Perez-Favila A, Cid-Baez MA, et al. Diabetic foot ulcers: current advances in antimicrobial therapies and emerging treatments. Antibiotics (Basel). 2019;8(4):193.
28. Ryall C, Duarah S, Chen S, Yu H, Wen J. Advancements in skin delivery of natural bioactive products for wound management: A brief review of two decades. Pharmaceutics. 2022;14(5):1072.
29. Schaper NC, Andros G, Apelqvist J, Bakker K, Lammer J, Lepantalo M, et al. Diagnosis and treatment of peripheral arterial disease in diabetic patients with a foot ulcer. A progress report of the International Working Group on the Diabetic Foot. Diabetes Metab Res Rev. 2012;28 Suppl 1:218-24.
30. Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchliffe RJ, Lipsky BA, et al. Practical guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36 Suppl 1:e3266.
31. Semwal RB, Semwal DK, Combrinck S, Viljoen A. Health benefits of chromones: common ingredients of our daily diet. Phytochem Rev. 2020;19(4):761-85.
32. Sharrif Moghaddasi M, Verma SK. Aloe vera their chemicals composition and applications: a review. Int J Biol Med Res. 2011;2(1):466-71.
33. Sinwar PD. The diabetic foot management - Recent advance. Int J Surg. 2015;15:27-30.
34. Skidmore-Roth L. Mosby's handbook of herbs & natural supplements. 4th ed. St. Louis, Mo.: Elsevier/Mosby; 2009.
35. Suliman RS, Alghamdi SS, Ali R, Aljatli DA, Huwaizi S, Suliman R, et al. Metabolites profiling, in vitro, in vivo, computational pharmacokinetics and biological predictions of Aloe perryi resins methanolic extract. Plants (Basel). 2021;10(6):1106.
36. Tresierra-Ayala M, Rojas AG. Association between peripheral arterial disease and diabetic foot ulcers in patients with diabetes mellitus type 2. Med Univ. 2017;19(76):123-6.
37. Yazdanpanah L, Nasiri M, Adarvishi S. Literature review on the management of diabetic foot ulcer. World J Diabetes. 2015;6(1):37-54.