



Herbal Diabetic Foot Ulcer And Wound Healing Cream

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1] **ABSTRACT**

Diabetic foot is a severe public health issue, yet rare studies investigated its global epidemiology. Here we performed a systematic review and meta-analysis through searching PubMed, EMBASE, ISI Web of science, and Cochrane database. We found that that global diabetic foot ulcer prevalence was 6.3% (95%CI: 5.4–7.3%), which was higher in males (4.5%, 95%CI: 3.7–5.2%) than in females (3.5%, 95%CI: 2.8–4.2%), and higher in type 2 diabetic patients (6.4%, 95%CI: 4.6–8.1%) than in type 1 diabetics (5.5%, 95%CI: 3.2–7.7%). North America had the highest prevalence (13.0%, 95%CI: 10.0–15.9%), Oceania had the lowest (3.0%, 95%CI: 0.9–5.0%), and the prevalence in Asia, Europe, and Africa were 5.5% (95%CI: 4.6–6.4%), 5.1% (95%CI: 4.1–6.0%), and 7.2% (95%CI: 5.1–9.3%), respectively. Australia has the lowest (1.5%, 95%CI: 0.7–2.4%) and Belgium has the highest prevalence (16.6%, 95%CI: 10.7–22.4%), followed by Canada (14.8%, 95%CI: 9.4–20.1%) and USA (13.0%, 95%CI: 8.3–17.7%). The patients with diabetic foot ulcer were older, had a lower body mass index, longer diabetic duration, and had more hypertension, diabetic retinopathy, and smoking history than patients without diabetic foot ulceration. Our results provide suggestions for policy makers in deciding preventing strategy of diabetic foot ulceration in the future.

Diabetic foot ulcers are a serious and common complication of diabetes, resulting from a combination of factors including peripheral neuropathy, peripheral vascular disease, and often unperceived trauma. They are open sores that don't heal, often affecting the bottom of the foot, and are a major cause of hospitalization, amputation, and reduced quality of life for individuals with diabetes.

PATHOPHYSIOLOGY :-

Diabetic Neuropathy:

High blood sugar levels damage nerves, particularly in the feet, leading to a loss of sensation (peripheral neuropathy). This can make it difficult to feel pain or pressure, increasing the risk of unnoticed injuries.

Peripheral Vascular Disease (PAD):

Diabetes can also damage blood vessels, leading to reduced blood flow to the feet. This can hinder healing and increase the risk of infection.

Unperceived Trauma:

Due to neuropathy, individuals may not feel minor injuries, like cuts or blisters, leading to untreated wounds that can develop into ulcers.

Ischemia:

Poor blood flow (ischemia) can also contribute to tissue damage and ulcer formation, especially if combined with neuropathy.

2] KEYWORDS

Natural products, topical herbal cream ,plant based treatment, Antibacterial plant extract .

3] DIABETIC WOUNDS

Diabetic wounds, characterized by impaired healing and increased risk of complications like infection and amputation, arise from a complex interplay of factors, including hyperglycemia, neuropathy, and compromised immune function. These wounds are often slow-healing due to disruptions in various stages of the normal wound healing process, such as inflammation, proliferation, and remodeling. Understanding the pathophysiology of diabetic wounds is crucial for developing effective treatment strategies.

PATHOPHYSIOLOGY :-

Hyperglycemia:

Elevated blood sugar levels disrupt the normal inflammatory response, leading to increased production of inflammatory cytokines and matrix metalloproteinases (MMPs). This can cause excessive degradation of the extracellular matrix (ECM), impairing wound healing.

Neuropathy:

Diabetic neuropathy, especially peripheral neuropathy, can lead to loss of sensation in the feet, making individuals less aware of minor injuries or pressure points. This can result in unnoticed wounds that become infected and difficult to heal.

Micro- and Macrovascular Dysfunction:

Diabetes can cause damage to small and large blood vessels, leading to reduced blood flow (ischemia) to the affected tissues. This impaired blood supply further hinders wound healing and increases the risk of infection.

Compromised Immune Response:

Diabetic individuals often have a weakened immune system, making them more susceptible to infections. This impaired immune function can further complicate the healing process.

Extracellular Matrix (ECM) Alterations:

Diabetes can cause changes in the composition and structure of the ECM, which is crucial for wound healing. These changes can lead to impaired collagen synthesis and reduced wound tensile strength.

Infection:

Diabetic wounds are more prone to infection due to impaired immune function and compromised blood supply. Infections can further delay healing and increase the risk of complications like osteomyelitis and amputation.

Other Factors:

Age, smoking, obesity, and other comorbidities can also contribute to the development and impaired healing of diabetic wounds.

Implications for Wound Healing:**Delayed Healing:**

Diabetic wounds are often slow to heal, taking significantly longer than non-diabetic wounds.

Increased Risk of Infection:

The combination of impaired immune function and compromised blood supply makes diabetic wounds highly susceptible to infection.

Increased Risk of Amputation:

In severe cases, diabetic foot ulcers can lead to limb amputation due to persistent infection and lack of healing.

Impact on Quality of Life:

Diabetic wounds can cause pain, discomfort, and functional limitations, significantly impacting the quality of life of individuals with diabetes.

CAUSE :-

Assessment of the cause of an ulcer helps clinicians in determining the most appropriate treatment. Many clinicians classify foot ulcers in people with diabetes as neuropathic, ischaemic, or neuroischaemic, depending on the relative contributions of the late diabetic complications of peripheral neuropathy and arterial disease to the ulcer's cause.⁹ Motor¹⁰ and autonomic¹¹ deficits could also contribute to the risk of ulceration. Neuropathic ulcers, the most common type, result from

4] AIM:-

The main aim of making a herbal cream for diabetic foot ulcers and wound healing is to provide an

alternative or adjunct treatment that can help accelerate wound healing, reduce infection risk, and improve the overall healing process for individuals with diabetes. This is achieved by utilizing the natural healing and antimicrobial properties of certain herbs.

Here's a more detailed breakdown of the aims:

Accelerate Wound Healing:

Herbal creams often contain ingredients that stimulate tissue regeneration, promote granulation tissue formation, and increase the production of collagen, all of which are crucial for wound closure.

Reduce Infection Risk:

Many herbs possess potent antibacterial and anti-inflammatory properties, which help to prevent or control infections in diabetic foot ulcers, a common and serious complication.

Improve Overall Healing Process:

Herbal creams can address various aspects of wound healing, including angiogenesis (formation of new blood vessels), epithelialization (formation of new skin cells), and pain relief, leading to a more efficient and comfortable healing process.

Alternative or Adjunct Treatment:

Herbal creams can be used as an alternative to or alongside conventional treatments, offering a natural and potentially safer option for managing diabetic foot ulcers, especially in cases where antibiotic resistance or other factors make conventional treatments less effective.

Address Complications:

Diabetic foot ulcers can lead to serious complications like infections, amputations, and decreased quality of life. Herbal creams aim to prevent or reduce these complications by promoting faster and more effective healing.

5] OBJECTIVES :-

The main objectives of making a herbal cream for diabetic foot ulcers and wound healing are to promote faster healing, prevent infection, and reduce complications associated with the condition. Herbal remedies can help control infection, stimulate tissue growth, and improve blood circulation, which are crucial for healing diabetic wounds.

Here's a more detailed breakdown of the objectives:

Faster Wound Healing:-

Diabetic foot ulcers are slow to heal due to impaired blood flow and nerve damage caused by diabetes.

Herbal remedies can stimulate the growth of new tissue (granulation tissue) and promote collagen deposition, which are essential for wound closure.

Some herbs have been shown to increase blood flow to the wound area, further enhancing the

healing process.

2. Preventing and Treating Infections:

Diabetic foot ulcers are highly susceptible to infection due to impaired immune function in individuals with diabetes.

Many herbal plants possess antimicrobial and anti-inflammatory properties that help fight bacteria and reduce inflammation at the wound site.

This can prevent the progression of infection, which can lead to complications like sepsis and even amputation.

3. Reducing Complications:

Diabetic foot ulcers can lead to serious complications, including infections, gangrene, and amputation.

By promoting faster healing and preventing infections, herbal creams can help minimize the risk of these complications.

This can improve the quality of life for individuals with diabetes and reduce healthcare costs associated with managing diabetic foot ulcers.

4. Other Objectives:

Pain Relief:

Some herbs have analgesic properties that can help relieve pain associated with diabetic foot ulcers.

Improved Circulation:

Certain herbs can improve blood circulation, which is crucial for healing and preventing further damage to the feet.

Cost-Effectiveness:

Herbal remedies can be a more affordable alternative to traditional treatments, making them accessible to a wider range of individuals.

Examples of Herbal Ingredients:

Neem (Azadirachta indica):

Known for its antimicrobial, anti-inflammatory, and wound-healing properties.

Aloe vera:

Helps to soothe the skin, promote wound healing, and reduce inflammation.

Safety and Efficacy:

While herbal remedies show promise, more research is needed to determine their safety and effectiveness for all individuals with diabetic foot ulcers.

Individual Variation:

The response to herbal remedies can vary depending on individual factors, such as the severity of the

ulcer and the individual's overall health.

Consultation with a Healthcare Professional:

It's essential to consult with a healthcare professional remedies, especially if you have other health conditions or are taking medications

Diabetic neuropathy :-

More than 60% of diabetic neuropathy and 50–75% of non-traumatic amputations are caused by DFUs [19,20]. In this clinical situation, the creation of a few enzymes, such as aldose reductase and sorbitol dehydrogenase, is decreased, limiting the activity of glucose-6-phosphate dehydrogenase and hence constraining nicotinamide adenine dinucleotide phosphate (NADPH) synthesis from nicotinamide adenine dinucleotide (NAD). As a result, sorbitol and fructose gets converted from glucose, which reduces myoinositol production in nerve cells even further. The foot may have diminished peripheral sensibility and epidermal cracks as a result of nerve cell damage [21,3].

6] LITERATURE REVIEW :-

Herbal remedies, particularly in the form of creams, show promise as adjunct treatments for diabetic foot ulcers, offering potential benefits in wound healing and infection control. While research on herbal creams for diabetic foot ulcers is ongoing, studies suggest that certain herbal formulations and active compounds can promote angiogenesis, reduce inflammation, and combat bacterial infections, contributing to faster wound healing.

Mechanisms of Action and Key Herbal Compounds:-

Anti-inflammatory and Antimicrobial Properties:

Many herbal extracts, such as those from Phellodendri Cortex (Huangbai) and A. catechu, exhibit potent anti-inflammatory and antibacterial effects, which are crucial for managing the inflammatory response and infection that often accompany diabetic foot ulcers.

Angiogenesis and Wound Healing:

Some herbal compounds, like those found in A. deliciosa, have been shown to promote angiogenesis (the formation of new blood vessels) and improve tissue regeneration, which is vital for wound healing.

Cell Migration and Proliferation:

Certain herbal formulations can stimulate cell migration and proliferation, contributing to the formation of new tissue and the closure of the wound.

Specific Herbal Formulations and Their Potential Benefits:

Polyherbal Formulations:

Combinations of different herbs can offer synergistic effects, potentially enhancing the efficacy of the treatment. For example, one study found that a polyherbal formulation containing A. catechu showed

a high capacity to promote cell movement and modulate enzymes involved in wound healing.

Individual Herbal Extracts:

Extracts from specific herbs, such as Phellodendri Cortex, *A. deliciosa*, and *Azadirachta indica* (Neem), have shown promising results in animal models and clinical studies, supporting their potential as wound-healing agents.

Considerations and Future Research:

Standardization and Safety:

While promising, further research is needed to standardize herbal formulations and ensure their safety and efficacy in clinical settings.

Clinical Trials:

More rigorous clinical trials are required to evaluate the effectiveness of herbal creams for diabetic foot ulcers compared to conventional treatments.

Mechanism of Action:

A deeper understanding of the mechanisms by which herbal compounds promote wound healing is essential for developing more effective and targeted treatments.

7] REPORTED ACTIVITY FROM MODERN LITERATURE :-

Modern literature indicates that herbal formulations, including creams and ointments, show promise in promoting wound healing in diabetic foot ulcers, particularly in preventing amputations and accelerating healing. While some studies have shown positive effects of specific herbs and herbal combinations, more robust clinical trials are needed to confirm their efficacy and safety.

Elaboration:

Herbal Creams and Ointments:

Studies have explored the use of creams and ointments derived from medicinal plants for diabetic foot ulcer treatment.

Positive Effects:

Some studies have reported that herbal formulations can prevent amputations in infected diabetic wounds and accelerate wound healing.

Need for More Research:

Despite promising results, more well-designed clinical trials are needed to confirm the effectiveness and safety of specific herbal products and their mechanisms of action on diabetic wound healing.

Integration of Traditional and Modern Medicine:

Combining traditional herbal remedies with modern wound care practices may offer a more holistic and effective approach to treating diabetic foot ulcers.

Limitations:

Many studies on herbal products in diabetic wound healing are animal-based or lack robust

clinical trials in humans.

Safety and Regulatory Considerations:

Clinical trials for herbal products require special regulatory pathways and permission.

In summary, while herbal products show potential for improving wound healing in diabetic foot ulcers, more rigorous research is needed to establish their efficacy and safety for clinical use.

PLAN OF WORK

A work plan for developing an herbal diabetic foot ulcer and wound healing cream should encompass research, formulation, testing, and clinical evaluation. This plan should involve identifying suitable herbal ingredients with wound-healing and antimicrobial properties, formulating a stable and effective cream, conducting in vitro and in vivo tests to assess its efficacy and safety, and potentially a pilot clinical study to evaluate its effectiveness in patients.

Research and Ingredient Selection:

Literature Review:

Conduct a thorough review of existing literature on herbal remedies for wound healing and diabetic foot ulcers, focusing on plants with documented anti-inflammatory, antimicrobial, and wound-healing properties.

Phytochemical Analysis:

Analyze the chemical composition of potential herbal ingredients, identifying bioactive compounds responsible for their therapeutic effects.

In vitro Studies:

Evaluate the antimicrobial activity of selected herbal extracts against common pathogens associated with diabetic foot ulcers, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Cell Culture Studies:

Assess the wound healing potential of herbal extracts by examining their effects on cell proliferation, migration, and collagen synthesis in relevant cell lines.

2. Cream Formulation:

Base Selection:

Choose a suitable cream base that is stable, compatible with the herbal extracts, and suitable for topical application.

Herbal Extract Incorporation:

Determine the optimal concentration of herbal extracts in the cream to achieve desired therapeutic effects without compromising stability or causing adverse reactions.

Preservatives and Stabilizers:

Incorporate appropriate preservatives and stabilizers to prevent microbial growth and maintain the cream's stability during storage.

Physicochemical Properties:

Evaluate the cream's viscosity, spreadability, and pH to ensure optimal application and efficacy.

3. Testing and Validation:

In vivo Animal Studies:

Conduct animal studies using a diabetic foot ulcer model to evaluate the cream's efficacy and safety.

Histological Analysis:

Examine tissue samples from the ulcer sites in the animal studies to assess the cream's effects on wound healing, inflammation, and tissue regeneration.

Clinical Evaluation:

Conduct a pilot clinical study in patients with diabetic foot ulcers to assess the cream's effectiveness, safety, and tolerability.

Safety Testing:

Perform toxicity tests on the cream to ensure its safety for human use.

4. Manufacturing and Packaging:

Scale-up Production: Develop a scalable manufacturing process for the herbal cream.

Quality Control: Implement rigorous quality control measures throughout the manufacturing process to ensure the product's purity, potency, and safety.

Packaging: Select appropriate packaging material that protects the cream from degradation and contamination.

5. Regulatory Compliance:

Regulatory Guidelines:

Adhere to relevant regulatory guidelines for herbal products and wound healing creams.

Clinical Trial Registration:

Register any clinical trials conducted with the cream with appropriate regulatory authorities.

6. Dissemination and Commercialization:

Publication of Findings:

Publish research findings in peer-reviewed journals to contribute to the scientific knowledge base.

Commercialization Strategy:

Develop a marketing strategy to promote the herbal cream to healthcare professionals and patients.

Distribution Network:

Establish a distribution network to make the cream available to patients in need.

This plan provides a framework for developing a herbal diabetic foot ulcer and wound healing cream. The specific steps and timelines may need to be adjusted based on the availability of resources, the complexity of the formulation, and the regulatory requirements of the target market.

8] METHODOLOGY:-

A typical methodology for developing an herbal diabetic foot ulcer and wound healing cream involves several key steps: herbal formulation, extraction, preparation, and testing. Herbal ingredients are identified for their wound-healing, anti-inflammatory, and antimicrobial properties. These herbs are then extracted using appropriate methods, often involving solvents or water, to isolate the active compounds. The extracts are then combined into a cream base, and the final product undergoes in vitro and in vivo testing to evaluate its efficacy and safety.

ELOBORATION:-

Herbal Selection and Formulation:

Researchers identify and select herbs known for their wound-healing, anti-inflammatory, and antimicrobial properties.

Examples of herbs used in such formulations include:

Radix Rehmanniae: Promotes healing and tissue regeneration.

Radix Astragali: Enhances fibroblast proliferation.

Pelargonium graveolens and Oliveria decombens: Show good tissue repair in diabetic foot ulcers.

Aloe vera: Known for its anti-inflammatory and wound-healing properties.

Calendula: Used in traditional medicine for wound healing and skin damage.

A polyherbal formulation, combining multiple herbs, may be developed to target various aspects of wound healing.

2. Herbal Extraction:

Herbs are extracted using various methods to isolate their active compounds. methods include BY ME:

Ethanol Extraction:

Efficiency:

Ethanol is a polar solvent that can extract a variety of compounds with high efficiency.

Applications:

Ethanol is used to extract a wide range of compounds, including tannins, polyphenols, flavonoids, terpenoids, and sterols.

Tinctures:

Ethanol is a common solvent for making tinctures, which are extracts of plant or animal material dissolved in alcohol.

Stability:

Ethanol can help stabilize herbal extracts and is a component of many herbal fluid preparations.

Boiling Point:

Ethanol has a boiling point of 78.4 °C. Methanol Extraction:

Polar Compound Extraction:

Methanol is particularly good at extracting polar and moderately polar compounds.

Efficiency:

Methanol generally provides higher extraction yields compared to ethanol.

Boiling Point:

Methanol has a lower boiling point (64.7 °C) than ethanol, making it easier to evaporate after extraction.

Artifacts:

Some studies suggest that methanol can generate artifacts during extraction, so caution should be exercised when using it.

Factors to Consider:

Target Compounds:

The specific compounds you are trying to extract will influence the choice of solvent.

Polarity:

Polar solvents like ethanol and methanol are suitable for extracting polar compounds.

Thermo ability:

If the target compounds are heat-sensitive, techniques like Soxhlet extraction with high temperatures may not be suitable.

Extraction Time:

Increasing extraction time can increase the yield of extracts.

Solvent Concentration:

The concentration of the solvent (e.g., 80% methanol) can also affect extraction efficiency.

3. Cream Preparation:

The herbal extracts are combined with a suitable cream base.

The cream base should be compatible with the herbal extracts and provide a suitable vehicle for topical application.

The cream is formulated to ensure proper consistency, stability, and shelf-life.

4. In Vitro Testing:

In vitro testing:

Antibacterial activity: Evaluated using methods like the agar well diffusion test, where the herbal cream is tested against common wound pathogens.

Wound healing activity: Cell culture models may be used to assess the effects of the cream on cell migration, proliferation, and collagen production.

Histological analysis: Examined to assess the quality of tissue regeneration and the presence of inflammation.

Clinical trials: If the in vitro and in vivo results are promising, the cream may be further

developed and tested in clinical trials with diabetic patients.

9] MATERIAL:-

1] NEEM :-

Neem (*Azadirachta indica*), a tree native to the Indian subcontinent, is renowned for its diverse medicinal properties and has been used in traditional Ayurvedic medicine for centuries. Neem exhibits antimicrobial, anti-inflammatory, antipyretic, and antioxidant effects, making it valuable for various health conditions. Its active compounds, like azadirachtin, are responsible for its insecticidal and antifungal properties.

Key Properties and Uses:

Antimicrobial: Neem has antibacterial, antifungal, and antiviral properties, helping to fight infections.

Anti-inflammatory: It can reduce swelling and pain, making it useful for conditions like arthritis and muscle soreness.

Antipyretic: Neem helps manage fever symptoms and prevent extreme temperature spikes.

Antioxidant: It protects the body from damage caused by free radicals.

Insecticidal: Neem is effective against a wide range of insects, including mosquitoes, flies, and mites.

Antidiabetic: Neem may help manage blood sugar levels and potentially encourage insulin production.

Anti-dermatic: Neem can be used to treat various skin conditions like ringworm, eczema, and scabies.

Other Uses: Neem has also been used for traditional purposes, such as in oral hygiene, as a contraceptive, and as a remedy for digestive issues.

Active Compounds:

Azadirachtin:

A key compound in neem, responsible for its insecticidal, antifeedant, and other pharmacological properties.

Nimbin:

A triterpene compound with antipyretic, fungicidal, antihistamine, and antiseptic properties.

Traditional Uses:

Ayurvedic Medicine:

Neem has been used in traditional Ayurvedic systems to treat various ailments, including leprosy, intestinal helminthiasis, respiratory disorders, and skin conditions.

Folk Medicine:

Neem has been used as a general folk medicine for treating infections, skin diseases, and other

conditions.

Modern Research:

Cancer Research:

Neem compounds have shown potential in cancer research, with studies indicating their ability to modulate cell signaling pathways and influence the activity of tumor suppressor genes.

Liver and Kidney Health:

Neem's antioxidant and anti-inflammatory properties may help protect the liver and kidneys from damage caused by oxidative stress.

Diabetes Management:

Neem may help improve blood sugar levels and reduce inflammation in people with diabetes.

2] AEGLE MEMELOS :-

Aegle marmelos, commonly known as Bael or Bilva, is a medicinal tree with a range of properties, including antimicrobial, anti-inflammatory, and antioxidant activities. It's traditionally used in Ayurveda and folk medicine to treat various ailments. The plant's bioactive compounds, such as coumarins and alkaloids, contribute to its medicinal potential.

Here's a more detailed look at its properties and uses:

Medicinal Properties:

Antimicrobial:

marmelos has shown antibacterial and antifungal activity against various pathogens.

Anti-inflammatory:

The plant's extracts and essential oils have demonstrated anti-inflammatory effects.

Antioxidant:

marmelos contains antioxidants that help protect the body from oxidative stress and damage.

Antidiabetic:

Some studies suggest that A. marmelos may help regulate blood sugar levels.

Antidiarrheal:

The fruit and extracts are used in traditional medicine to treat diarrhea and dysentery.

Anticancer:

Research indicates that certain compounds in A. marmelos may have anticancer properties.

Hepatoprotective:

Some studies suggest that it may protect the liver from damage.

Radioprotective:

It has shown potential in protecting against radiation damage.

2. Uses in Traditional Medicine:

Gastrointestinal Issues:

A. marmelos fruit and leaves are used to treat diarrhea, dysentery, and other gastrointestinal problems.

Respiratory Infections: The plant is used to treat colds, coughs, and other respiratory ailments.

Diabetes: Traditional uses include the management of diabetes.

Other Uses: A. marmelos is also used for wound healing, as a diuretic, and to address other health concerns.

3. Phytochemical Composition:

Coumarins:

marmelos fruits contain coumarins like imperatorin, which have various pharmacological effects.

Alkaloids:

The plant contains alkaloids, which contribute to its medicinal properties.

Essential Oils:

Leaves and flowers contain essential oils with aromatic properties and potential medicinal effects.

4. Nutritional Value:

Vitamins and Minerals:

Bael fruit is a good source of vitamins (A, C, B-complex) and minerals (calcium, potassium).

Dietary Fiber:

It's a good source of dietary fiber, which aids in digestion and bowel regularity.

3] BERBERIES ARISTATA :-

Berberis aristata, also known as Daruharidra or Indian barberry, possesses a wide range of medicinal properties, including anti-inflammatory, antioxidant, and anti-microbial effects. It is a valuable plant in traditional medicine, used to treat various ailments, including eye disorders, skin problems, and metabolic disorders.

Key Properties and Uses:

Anti-inflammatory:

Berberine, a key compound in Berberis aristata, has demonstrated anti-inflammatory activity, potentially helpful in managing conditions like arthritis and other inflammatory diseases.

Antioxidant:

The plant is rich in antioxidants, which can help protect the body against damage from free radicals and reduce the risk of chronic diseases.

Anti-microbial:

Berberis aristata exhibits antimicrobial properties, making it effective in treating various

infections, including bacterial and fungal infections.

Other Traditional Uses:

Eye disorders: Used to treat various eye problems, including conjunctivitis. Skin diseases: Used to treat conditions like eczema and skin infections.

Metabolic disorders: May help manage conditions like diabetes and high cholesterol. Wound healing:

Traditional applications include wound healing and the treatment of ulcers. Digestive issues: Used to treat diarrhea, dysentery, and other digestive ailments.

4] ALOE-VERA :-

Aloe vera is renowned for its diverse therapeutic properties, including antioxidant, anti-inflammatory, and antibacterial effects. It is also known for its wound-healing, skin-soothing, and blood sugar-regulating properties.

Key Properties and Benefits:

Antioxidant:

Aloe vera contains antioxidants that protect against free radical damage, potentially reducing inflammation and preventing cell damage.

Anti-inflammatory:

It can help reduce swelling and inflammation, making it beneficial for skin irritations and potentially aiding in the treatment of inflammatory conditions.

Antibacterial:

Aloe vera has antibacterial properties that can help prevent infection, especially in wounds and burns.

Wound Healing:

It promotes the growth of new skin cells, stimulates collagen production, and accelerates the healing process.

Sunburn Relief:

Aloe vera is a popular remedy for soothing sunburns due to its cooling and moisturizing effects.

Blood Sugar Regulation:

Some studies suggest that aloe vera may help regulate blood sugar levels, potentially aiding in diabetes management.

Digestive Health:

Aloe vera may improve digestive health by soothing the gut and promoting regular bowel movements.

Hydration:

Aloe vera is primarily composed of water, making it a natural source of hydration for the body. Other

Notable Properties:

Immune System Support:

Aloe vera may help boost the immune system by stimulating immune cells and producing substances that protect against disease.

Anti-ageing:

Some research suggests that aloe vera can help reduce the signs of aging by protecting against oxidative stress and promoting skin elasticity.

Anticancer:

Some studies indicate that aloe vera may have anticancer properties, though more research is needed to confirm these effects.

5] SESAME OIL :-

Sesame oil is known for its high concentration of antioxidants, anti-inflammatory, and antibacterial properties. It also has a high percentage of unsaturated fatty acids, including oleic and linoleic acids. Furthermore, sesame oil can be used to help lower blood pressure, potentially improve skin health, and may even act as a natural sunscreen.

Here's a more detailed look at the properties of sesame oil:

Nutritional Value:

Rich in Unsaturated Fats: Sesame oil is high in monounsaturated and polyunsaturated fats, including omega-3, omega-6, and omega-9 fatty acids.

High in Antioxidants: Contains lignans like sesamin, sesamol, and sesaminol, which are powerful antioxidants.

Contains Vitamins and Minerals: Includes Vitamin E, calcium, magnesium, iron, phosphorus, and zinc.

Potential Health Benefits:

Antioxidant Properties: Helps protect cells from damage caused by free radicals.

Anti-inflammatory Properties: May help reduce inflammation and pain, potentially beneficial for conditions like arthritis.

Heart Health: May help lower LDL cholesterol and triglycerides, potentially reducing the risk of heart disease.

Blood Pressure: Some research suggests it may help lower blood pressure.

Skin Health: May improve skin elasticity, promote collagen production, and potentially protect against sun damage.

Bone Health: Rich in calcium, zinc, and copper, which are important for bone density and strength.

Digestive Health: May help promote smoother digestion and relieve constipation.

Anemia: High in iron, potentially beneficial for individuals with anemia.

Other Potential Benefits: May also have anti-aging, anticancer, and immunoregulatory properties.

Uses:

Culinary: Used for cooking, frying, and as a flavoring enhancer in various cuisines, particularly in Asia.

Skincare: May be used topically to moisturize, heal wounds, and protect the skin from sun damage.

Haircare: May be used to moisturize and nourish the hair.

6] VITAMIN-E CAPSULE :-

Vitamin E capsules are supplements containing a fat-soluble antioxidant, vitamin E, which protects cells from damage caused by free radicals. They offer various benefits, including boosting immune function, promoting skin and hair health, and potentially supporting cardiovascular health.

days after the wounds were created for the determination of malondialdehyde levels and red cell superoxide dismutase, catalase and glutathione peroxidase activities. The results showed that α -tocopherol reduced plasma malondialdehyde levels, increased glutathione peroxidase activity and accelerated the rate of wound closure in treated rats. mg/kg bodyweight α -tocopherols daily by oral gavage. All rats were fed standard food and water ad libitum. Blood samples were taken at 0, 5 and 10 g) was monitored by measuring the length of the wounds daily. The rats were divided into two categories; normal and streptozotocin-induced diabetic rats. For each category, the animals were further divided into two groups; those untreated and those receiving 200 cm linear incisions created on the back of each male Sprague–Dawley rat (250–300 Vitamin E is composed of various subfamilies that include tocopherols and tocotrienols. These compounds have antioxidant properties but differ in structure, dietary source and potency. In this study we evaluated the efficacy of α -tocopherol as an antioxidant and its role in wound closure in normal and streptozotocin-induced diabetic rats. The healing of 6

Key Properties of Vitamin E Capsules:

Antioxidant:

Vitamin E neutralizes free radicals, protecting cells from damage that can lead to various health problems, including aging, heart disease, and cancer.

Immune Support:

Vitamin E helps maintain a healthy immune system by supporting the function of immune cells and potentially reducing the risk of infections.

Skin and Hair Health:

Vitamin E can help moisturize and protect skin, reducing signs of aging and UV damage. It can also promote hair growth, reduce breakage, and improve shine.

Cardiovascular Health:

Vitamin E's antioxidant properties may help protect the cardiovascular system from damage

caused by free radicals, potentially reducing the risk of heart disease.

Other Potential Benefits:

Vitamin E may also play a role in maintaining healthy blood cells, improving eyesight, and supporting overall well-being.

Forms of Vitamin E in Capsules:

Natural vs. Synthetic:

Natural vitamin E, often found in plant-based capsules, is more readily absorbed by the body and has higher biological activity compared to synthetic vitamin E.

7] **BEESWAX :-**

Beeswax is a natural, solid wax produced by honeybees. It's a non-toxic, anti-corrosive, and edible substance with a range of properties including being malleable, water-insoluble, and flammable. It has a melting point between 62-65°C, a relative density of 0.958-0.970 at 15°C, and various acid and saponification numbers. Beeswax is also known for its antibacterial and antifungal properties, making it useful in skincare and other applications.

Here's a more detailed look at beeswax properties:

Physical Properties:

Malleability: Beeswax can be molded into various shapes, earning it the nickname "the world's first plastic".

Solubility: It is insoluble in water but soluble in most organic solvents.

Melting Point: 62-65°C (144-147°F).

Density: 0.958-0.970 g/cm³ at 15°C.

Color: Can range from light yellow to dark brown and white.

Smell: A sweet, honey-like aroma.

Texture: Brittle when cold, tenacious at room temperature, and softens at body temperature. Chemical Properties:

Composition: Primarily made up of esters, fatty acids, propolis, and hydrocarbons.

Saponification Number: 85-100 mg KOH/g.

Acid Number: 17-24 mg KOH/g.

Antimicrobial Properties: Beeswax has antibacterial and antifungal properties.

Antioxidant Properties: Contains antioxidants.

Anti-inflammatory Properties: Can help reduce inflammation. Other Notable Properties:

Edible: Beeswax is safe to consume in small quantities.

Non-Toxic: It's a non-toxic material.

Anti-Corrosive: Resistant to corrosion.

Humectant: Helps retain moisture in the skin.

Low Comedogenic: Generally considered low-comedogenic, meaning it's less likely to clog pores.

8] BORAX :-

Borax is a white, crystalline compound that is stable at room temperature and highly soluble in water, forming alkaline solutions. It is known for its ability to form complex structures with various organic and inorganic substances, making it a versatile chemical agent.

Physical Properties:

Appearance: White, crystalline solid.

Molar Mass: 201.22 g/mol (anhydrous), 381.38 g/mol (decahydrate).

Density: 2.4 g/cm³ (anhydrous), 1.73 g/cm³ (decahydrate).

Melting Point: 743°C (anhydrous), 75°C (decahydrate).

Solubility: Soluble in water.

Boiling Point: 1575°C (anhydrous).

Bulk Density: 48 lb/ft³ (769 kg/m³). Chemical Properties:

Stability: Chemically stable under normal conditions.

Reaction with Acids: Forms boric acids.

Flammability: Yellow-green flame.

Other Solvents:

High solubility in ethylene glycol, low solubility in acetone. Honey:

Diabetic wounds are unlike typical wounds in that they are slower to heal, making treatment with conventional topical medications an uphill process. Among several different alternative therapies, honey is an effective choice because it provides comparatively rapid wound healing. Although honey has been used as an alternative medicine for wound healing since ancient times, the application of honey to diabetic wounds has only recently been revived. Because honey has some unique natural features as a wound healer, it works even more effectively on diabetic wounds than on normal wounds. In addition, honey is known as an “all in one” remedy for diabetic wound healing because it can combat many microorganisms that are involved in the wound process and because it possesses antioxidant activity and controls inflammation. In this review, the potential role of honey’s antibacterial activity on diabetic wound-related microorganisms and honey’s clinical effectiveness in treating diabetic wounds based on the most recent studies is described. Additionally, ways in which honey can be used as a safer, faster, and effective healing agent for diabetic wounds in comparison with other synthetic medications in terms of microbial resistance and treatment costs are also described to support its traditional claims.

CAUSES :-

Diabetic neuropathy:

Nerve damage, especially in the feet, reduces sensation to pain, pressure, and temperature, making individuals unaware of minor injuries that can develop into ulcers.

Poor blood circulation:

Diabetes can damage blood vessels, reducing blood flow to the feet and making it difficult for wounds to heal.

Other risk factors:

Smoking, obesity, high blood pressure, and inflammation can also increase the risk of diabetic foot ulcers.

Symptoms:

Early symptoms:

Redness, swelling, a small sore or blister that doesn't heal, changes in skin texture or temperature.

As the ulcer progresses:

Pain (can be absent due to neuropathy), pus or drainage, a foul odor, skin discoloration, and hardening of the skin.

Advanced stages:

Black tissue (eschar) surrounding the ulcer, potential signs of infection like fever or chills. Diagnosis:

Physical exam

: A doctor will examine the feet for signs of injury, ulceration, and signs of infection.

Neuropathy assessment:

Tests may be performed to assess nerve function and sensation.

Imaging studies:

X-rays or MRIs may be used to check for bone involvement or the extent of infection. Treatment:

Blood sugar control:

Tight control of blood sugar is crucial for wound healing and preventing further complications.

Offloading:

Reducing pressure on the ulcer to promote healing, often through special shoes or casts.

Debridement:

Removal of dead or infected tissue to prevent infection and promote healing.

Antibiotics:

Prescribed for infection, potentially including oral or IV antibiotics.

Wound care:

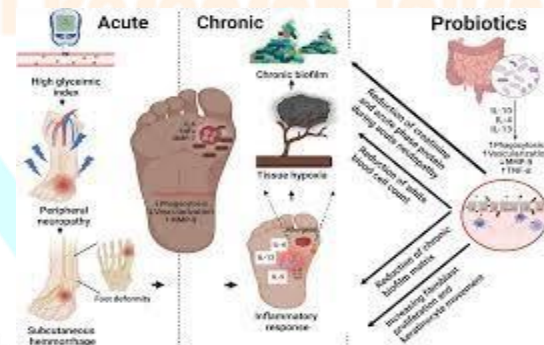
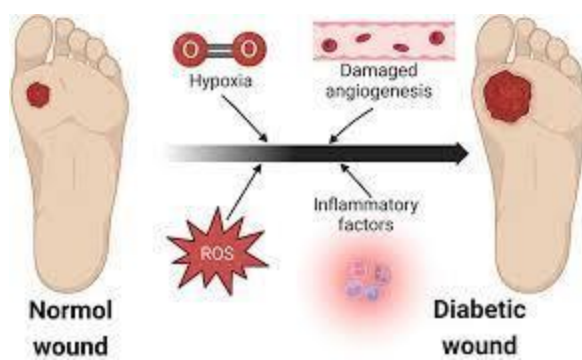
Cleaning the wound, applying bandages, and monitoring for signs of infection.

Surgical intervention:

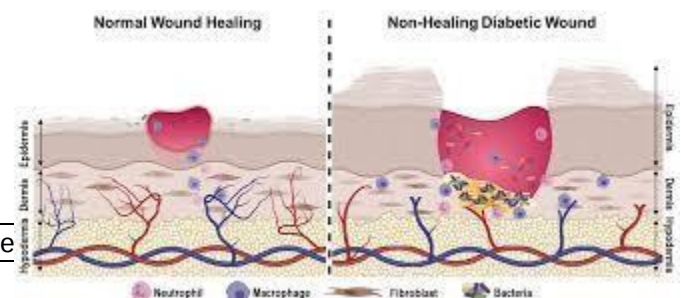
May be needed to remove infected tissue, repair blood vessels, or in some cases, amputation to save the limb.

Patient education:

Learning about foot care, including daily inspection, proper footwear, and avoiding smoking.

10] DIAGRAM :-**DIABETIC FOOT ULCER :-****DIABETIC FOOT****DIABETIC WOUND :-**

Novel Rese





11] HERBL DIABEIC FOOT ULCER AND WOUND HEALING CREAM PREPARATION :-

EXTRACTION PROCESS REAL IMAGES :-



12] RESULTS AND FINDINGS :-

Approximately 20% of hospital admissions among diabetic patients are the result of foot problems. Diabetic foot assessment should include dermatological, vascular, neurological and musculoskeletal systems. There are three basic treatments for management of DFU: (i) debridement; (ii) antibiotics and (iii) revascularization. The cost to treat one simple ulcer is \$5000 to \$8000.

12] CLINICAL TRIALS :-

1]Effect of neem leaves extract irrigation on the wound healing outcome in nurse managed diabetic foot ulcers

M Jayalakshmi

Nat J Physiol Pharm Pharmacol, 2020•njppp.com

Background

Foot ulcer is a common and massive complication of Diabetes that the economic, social, and public health workers tackled throughout the world.

Aim and Objective

This study aimed to compare and evaluate the effect of neem extract irrigation with normal saline on the wound healing outcome among diabetic foot ulcer patients.

Materials and Methods

The present single-blind experimental design study was conducted on 160 diabetic Foot ulcer patients who attended a diabetic foot clinic center during the period February 2019–February 2020. Patients were allocated in two groups, by simple random assignment. Intervention group received Neem extract irrigation and control group received Normal saline irrigation weekly twice. In both groups, wound assessment was done using PUSH tool at baseline and then at the end of each week till 4 weeks are completed. Data were analyzed in SPSS20 software, and $P < 0.05$ was considered statistically significant.

Results

The total pre intervention means and standard deviation of the Wound surface area in the intervention and control groups were respectively 17.13 ± 21.46 and 19.84 ± 23.98 , and the post intervention mean and standard deviation of the Wound surface area at the end of 4 weeks of

study period was respectively 6.92 ± 16.62 and 14.04 ± 21.32 . The difference between the two groups at the end of 3rd and 4th week were statistically significant ($P = 0.018$ and $P = 0.047$).

Conclusion

Neem leave extracts irrigation promotes wound healing activity and is preferred being natural and safe without producing any adverse effect.

2]The wound healing effect of various extracts from *Onosma microcarpum* root in a diabetic animal model

N Mohammadi, G Bahrami, N Ghiasvand, S Miraghaei, SH Madani, I Karimi, Y Shokoohinia

Journal of Reports in Pharmaceutical Sciences, 2017 • journals.lww.com

Abstract

Onosma microcarpum (Boraginaceae) locally known as “Tashnedary” is considered as one of important medicinal plants in west of Iran. Its roots have been used by the rural healers to treat the burns and wound healing. In this study, different extracts of roots were used for the evaluation of its healing effect in diabetic wound model in rats. Diabetes was induced in Wistar rats, then wound incised on the back of rat, and subsequently they were divided into nine groups which eight of them contain eucerin with four concentrations of hexane extract (20%, 30%, 40%, 60%) and three other extract as acetone 30%, ethanol 30% and hydroethanol 30%, and one base eucerin without extract. Other formula was traditional formula and phenytoin. A photograph of the dorsum of the rat was taken from a standard height in days 0, 3, 6, 9, 15 and 20. Then, samples were processed in the pathologic surveys. Our study showed that the best result was demonstrated by Phenytoin cream treated group. Our results indicated that like the general belief in west of Iran population, the ointment with n-Hex 30% extracts of *O. microcarpum* could promote healing in described animal model, diabetic foot ulcer, compared to control

3] An in vivo and in vitro investigation of the effect of Aloe vera gel ethanolic extract using animal model with diabetic foot ulcer

M Daburkar, V Lohar, AS Rathore, P Bhutada, S Tangadpaliwar Journal of Pharmacy and Bioallied Sciences,

2014 • journals.lww.com

Aim:

To examine the preventive effect of Aloe vera gel ethanolic extract using diabetic foot ulcer (DFUs) protocol in Wistar rats.

Materials and Methods:

Male Wistar rats were divided into untreated control (Group I), untreated DFUs (Group II), DFUs treated with A. vera gel ethanolic extract (Group III), DFUs treated with topical A. vera gel (Group IV), DFUs treated with A. vera gel ethanolic extract and topical A. vera gel (Group V). The rats in the treatment groups were daily administered the A. vera gel and ethanolic extract for 9 days. Fasting blood glucose levels and percentage of wound ulcer contraction were measured on day 3, 6, and 9.

Statistical Analysis used:

The results are expressed as a mean±Standard Error Mean (SEM). Data were analyzed using one-way analysis of variance (ANOVA) after Newman–Keuls test. $P < 0.05$ were considered statistically significant in all cases.

Results:

Oral administration of A. vera gel ethanolic extract at a dose of 300 mg/kg body weight per day to diabetic rats for a period of 9 days resulted in a significant reduction in fasting blood glucose and a significant improvement in plasma insulin. Topical application of A. vera gel at a dose 30 mg/kg body weight per day to streptozotocin (STZ)-induced diabetic rats for a period of 9 days resulted in no change in blood glucose and plasma insulin. Oral administration as well as topical application of A. vera gel ethanolic extract and gel significantly reduced the blood glucose, improved the plasma insulin, and significantly increased DNA and glycosaminoglycans (GAGs) to improve the wound ulcer healing as well as the breaking strength on day 9.

Conclusions:

Present findings provide a scientific rationale for the use of A. vera gel ethanolic extract, and showed that the gel attenuated the diabetic foot wound in rats.

4] The use of herbal medicine in diabetic foot complications: A case report from a Saudi Arabian Bedouin

M Malone, A Al Gannass

Wound Practice & Research: Journal of the Australian Wound ..., 2012•search.informit.org

The flora of plant life within Saudi Arabia has one of the richest biodiversity systems in the Arabian Peninsula and encompasses a mass of important medicinal herbs, shrubs and plants. According to Al-Yahya, the Arabian Peninsula is the birthplace of herbal drugs and the use of folk medicine still plays an important role within Saudi Arabian culture. Many patients in Saudi Arabia still seek out alternative forms of therapy such as the use of honey, black seeds, myrrh, fenugreek, kawajawa and other herbs, roots and shrubs, as this rich family tradition and culture is passed down from generation to generation. The use of such alternative forms of medicine, however, can often result in problems with compliance to the modern management of medical conditions such as diabetic foot ulceration, and can expose patients unwittingly to the hazards of traditional remedies and to the hazards of non-adherence to modern medical management.

5] Assessment of maximum tolerated dose of a new herbal drug, Semelil (ANGIPARSTM) in patients with diabetic foot ulcer: A Phase I clinical trial

R HESHMAT, K Mohammad, TMR Mohajeri, AA Keshtkar, DF GHARIB 2008•sid.ir

Abstract

Background and the purpose of the study: In many cases of diabetic foot ulcer (DFU) management, wound healing is incomplete, and wound closure and epithelial junctional integrity are rarely achieved. Our aim was to evaluate the maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of Semelil (ANGIPARSTM), a new herbal compound for wound treatment in a Phase I clinical trial.

Methods: In this open label study, six male diabetic patients with a mean age of 57 ± 7.6 years were treated with escalating intravenous doses of Semelil, which started at 2 cc/day to 13.5 cc/day for 28 days. Patients were assessed with a full physical exam; variables which analyzed included age, past history of diabetes and its duration, blood pressure, body temperature, weight, characteristics of DFU, Na, K, liver function test, Complete Blood Count and Differential (CBC & diff), serum amylase, HbA1c, PT, PTT, proteinuria, hematuria, and side effects were recorded. All the measurements were taken at the beginning of treatment, the end of week 2 and week 4. We also evaluated Semelil's side effects at the end of weeks 4 and 8 after ending therapy. [PDF]

6] Effects of intravenous Semelil (ANGIPARSTM) on diabetic foot ulcers healing: A multicenter clinical trial

R HESHMAT, A BAHRAMI, H DELSHAD, OG RANJBAR, K Mohammad, R HEYDARPOUR...

2008•sid.ir

Abstract

Some diabetic FOOT ULCER s, which are notoriously difficult to cure, are one of the most common health problems in diabetic patients. There are several surgical and medical options which already have been introduced for TREATMENT of diabetic FOOT ULCER s, so some patient will require amputation. The purpose of this study was to evaluate the efficacy of intravenous SEMELIL (ANGIPARSTM), a naive herbal extract to accelerate healing of diabetic FOOT ULCER s. A multi- centric randomized controlled trial was conducted to evaluate intravenous SEMELIL for healing of diabetic FOOT ULCER s. Sixteen diabetic patients were treated with intravenous SEMELIL, and nine other patients were treated with placebo as control group. Both groups were otherwise treated by wound debridement and irrigation with normal saline solution, systemic antibiotic therapy and daily wound dressing. Before and after intervention, the FOOT ULCER surface area was measured, by digital photography, mapping and planimetry. After 4 weeks, the mean FOOT ULCER surface area decreased from 479.93 ± 379.75 mm² to 198.93 ± 143.75 mm² in the intervention group ($p = 0.000$) and from 766.22 ± 960.50 mm² to 689.11 ± 846.74 mm² in the control group ($p = 0.076$). Average wound closure in the TREATMENT group was significantly greater than placebo group (64% vs. 25%, $p = 0.015$). This herbal extract by intravenous rout in combination with conventional therapy is more effective than conventional therapy by itself probably without side effect. However, further studies are required in the future to confirm these results in larger population

13] CONCLUSION :-

According to the current review's findings, the major risk of increasing foot ulceration is caused by nerve cell damage, ischemia, hypoxia, decreased angiogenesis, lack of vasodilator production, and, most likely, infection from bacteria. Furthermore, many molecular factors, including receptors,

proteolytic enzymes, and neuropeptides, have been altered in this pathological condition, potentially leading to prolonged wound healing due to down-regulation of KGF, IL-10, PDGF, IGF-1, EGF, and HIF and up-regulation of TNF- α , IL-6, and TGF- β 2. All of these elements and molecular markers play an important role in extending the healing of diabetic ulcerated wounds and can be used as diagnostic tools by researchers to detect patients suffering from DFU. Furthermore, the primary goal of this study is to compile all available information on *in vitro*, *in vivo*, case reports, and clinical symptoms utilizing natural substances to treat and manage DFU. The current review's findings provide information on the use of natural products for the management of DFU, including the utility of 18 medicinal plants with 01 isolated components, 07 polyherbal formulations such as herbal lotions, 03 insect products, and a few micronutrients such as vitamins and minerals. Despite the limited information available on the natural substance used for the management of DFU, some medicinal plants with promising pre-clinical and clinical effects reported in this article involve *Actinidia deliciosa*, *Ageratina pichinchensis*, *Aloe barbadensis*, *Astragalus membranaceus* var. *mongholicus*, *Azadirachta indica*, *Coffea canephora*, *Melilotus officinalis*, *Myrtus communis*, *Onosma microcarpum*, *Quercus infectoria*, *Teucrium polium*, and *Tinospora cordifolia*.

This review identified many research gaps, which may theoretically be considered legitimate information for further exploration by researchers worldwide. To begin with, although the plant extracts employed in clinical studies have significant advantages, the specific mechanism of action at the biochemical and molecular levels has less been researched, indicating research gaps.

Secondly, it was discovered that relatively little research had been conducted on isolated and purified chemicals from natural sources. As a result, this remains a study gap for scientists to investigate more on the active phytoconstituents and to come up with novel molecules for the treatment of DFU. Thirdly, even though a few polyherbal formulations were documented in this study, there are relatively few marketed treatments available from alternative medicines to treat DFU. As a result, extensive clinical trials on DFU are required, taking into account the therapeutic properties of plants, animals, insects, and their active compounds. Hence, this research concludes that natural therapy can be explored further to treat and manage DFU in an efficient, cost-effective, and reproducible manner.

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