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# THE EFFECT OF HEMP ROOT HAIR ON DIABETIC FOOT ULCER

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### ABSTRACT

A wound is a condition in which the continuity of body tissue is disrupted, either by blunt or sharp trauma, causing tissue damage. The wound healing process involves three phases: the inflammatory phase, the proliferation phase, and the remodeling phase. Although the healing time of a wound can be predicted, prolonged conditions that do not match predictions result in a long wound care period and chronic wounds. Several factors can help accelerate the wound healing process, such as the use of cannabis root extract. To determine the effect of hemp root hair on the diabetic foot ulcer. This study used a literature review approach. Articles were searched using two databases, Google Scholar and PubMed, with the keywords "hemp root hair" and "diabetic foot ulcer." The criteria for articles were original articles published between 2018 and 2025. Of the 8 articles reviewed, all articles showed that cannabis extract can accelerate the wound healing process due to its antibacterial, anti-inflammatory, and anti-cancer properties. In addition to these properties, it can also stimulate tissue granulation, maintain skin hydration balance, and promote new tissue re-epithelialization. The review of the 8 articles concluded that hemp root hair extract can accelerate the wound healing process, whether derived from flowers, leaves, or roots. However, among these three components, cannabis root extract has higher antibacterial and anti-inflammatory properties and produces higher levels of cannabinoids.

**Keywords**: Hemp root hair, diabetic foot ulcer

## INTRODUCTION

A wound is a condition in which the continuity of body tissue is disrupted, either due to blunt trauma or sharp trauma resulting from surgical procedures that cause tissue damage (1). Wound healing is a dynamic process involving highly specialized cellular, humoral, and molecular mechanisms (2). The wound healing process takes 4 to 12 weeks. If the wound does not heal within this period, even with proper care, it is considered chronic. Wound healing occurs either primarily or secondarily; primary wound healing refers to healing without infection, without excessive fluid discharge, and with the edges of the wound coming together, such as in post-surgical wounds. If wound healing is disrupted by infection, dehiscence (separation of the wound edges), hypoxia, or immune dysfunction, this marks the beginning of the secondary wound healing process. This process is characterized by the formation of granulation tissue and epithelialization over new tissue. Wounds that heal secondarily are more susceptible to infection, closure is not cosmetically pleasing, and tissue strength is less than optimal (3).

Chronic wounds require longer healing times, can have a significant physical, mental, economic, and social impact on patients, and contribute to lost productivity, resulting in higher treatment costs. Chronic wounds impose a significant economic burden, affecting the entire healthcare system. Certain medical conditions can slow or prevent wound healing, such as: obesity, certain health conditions such as heart failure, lung disease, anemia, varicose veins, or a history of deep vein thrombosis (DVT), immune deficiency, uncontrolled diabetes, and cancer, as well as certain skin problems such as excessively dry skin, use of radiotherapy, peripheral neuropathy, and peripheral edema. The most common wound condition among the population today is diabetic foot ulcers.

Diabetic foot ulcers are open wounds that occur on the feet of people with diabetes due to nerve and blood vessel damage, as well as biomechanical factors resulting from high and uncontrolled blood sugar levels. Furthermore, it is estimated that approximately 50% to 60% of ulcers are mildly infected, and approximately 20% of moderate to severe infections result in lower limb amputation. The 5-year mortality rate for individuals with diabetic foot ulcers is approximately 30%, exceeding 70% for those who undergo major amputation. The mortality rate for patients with diabetic foot ulcers is 231 deaths per 1000 people per year, compared to 182 deaths per 1000 people per year in people with diabetes without foot ulcers. Black, Hispanic, or Native American individuals and those with low socioeconomic status have higher rates of diabetic foot ulcers and subsequent amputations compared to white individuals. Classifying ulcers based on the degree of tissue loss, ischemia, and infection is crucial in identifying the risk of disease that threatens lower limb amputation. The initial treatment step is to correct ischemia and infection **(4)**.

According the International Diabetes Federation to (IDF). approximately 18.6 million people worldwide suffer from diabetic foot ulcers each year, and 80% of these cases result in amputation (4). This condition is very concerning given the high rate of amputations, so several researchers have conducted studies related to the wound healing process using cannabis sativa oil extract, which functions to help transport or regulate oxygen to the wound area (5). According to a study conducted by Atalay et al. in 2020 on the antioxidant and anti-inflammatory properties of cannabis in white rats with burns, cannabidiol (CBD) extract provided protection against oxidative stress and had the potential to reduce inflammation and cell damage in the microenvironment and surrounding tissue. Additionally, repeated administration of CBD in inflammatory conditions can increase glutathione peroxidase and reductase activity, resulting in a six-fold decrease in malondialdehyde (MDA) levels compared to untreated controls (7).

#### **METHODS**

The research design used in this study is a literature review, which is an activity that discusses information published in a specific subject area and within a specific time period (8). The identification and analysis of the effects of cannabis extract (cannabis root) on the wound healing process were obtained from several accredited journals from 2015 to 2025, using search methods through open access channels such as Google Scholar and PubMed. In searching for journals, researchers used the keywords cannabis root and wound healing, obtaining 24,600 full-text articles, then selected 8 studies according to the inclusion criteria.

### RESULTS AND DISCUSSION

The search yielded 24,600 articles, of which 8 articles met the inclusion criteria. The results of the analysis are shown in the following table:

Table 1. Characteristics of the Articles Analyzed

| Researcher               | Year | Country  | Research<br>Objective                                       | Participa<br>nts                     | Data Collection<br>Design and<br>Methods  | Findings  | Implications  |
|--------------------------|------|----------|---|--------------------------------------|---|---|---|
| Kongkadee K<br>et al (9) | 2022 | Thailand | wound<br>healing<br>process<br>using<br>cannabis<br>extract | Humans<br>with<br>abrasions<br>wound | Control group<br>without cannabis<br>extract,<br>intervention group<br>with cannabis<br>extract, and<br>comparison group<br>with hemp extract | The average percentage of wound closure was 27.92 ± 1.21% when exposed to 5 µg/mL hemp extract and 33.49 ± 1.67% when | Cannabis extract may help accelerate the wound healing process by inhibiting TNF-α and IL- 1β in inflammation |

| Researcher                        | Year | Country  | Research<br>Objective   | Participa<br>nts | Data Collection<br>Design and<br>Methods  | Findings   | Implications  |
|-----------------------------------|------|----------|---|------------------|---|--|---|
|                                   |      |          |   |                  |   | exposed to $0.5 \mu g/mL$ CBD, compared to $24.34 \pm 2.29\%$ for the untreated control.   |   |
| Akarsu and<br>Akarsu (10)         | 2024 | Croatia  | Evaluatin g the wound healing process with Cannabis sativa L. plant extract and cannabidi ol on incision wounds   | Mice             | The intervention group of mice was given incision wounds under anesthesia, then the wounds were sutured and healed using cannabidiol extract and hemp extract with low TetraHydroCannabidiol (THC) content, while the control group used povidone iodine. | Hemp extract<br>has greater<br>potential<br>benefits for<br>wound<br>healing<br>compared to<br>CBD and is<br>lower than<br>povidone<br>iodine.   | Hemp extract is more effective for wound healing than cannabidiol and povidone iodine   |
| Khlongkhlae<br>o A, et al<br>(11) | 2024 | Thailand | Compara tive evaluation of the antibacte rial properties and wound healing activity of ethanol extracts from C. sativa leaves and ethanol extracts from flowers | Human            | Disk diffusion test, a qualitative method used to determine bacterial sensitivity to an antibiotic.     Microorganism sensitivity test on human fibroblasts     Human scratch wounds  | Leaf extract is superior to flower extract in promoting fibroblast proliferation and migration and wound healing properties and can be developed as a new therapeutic agent to promote efficient wound repair and manage chronic wounds that do not heal | Cannabis leaf extract is better for wound healing, including chronic wounds, because it has antibacterial properties against S. Aureus, Pseudomonas aeruginosa, Klebsiela, Bacillus cereus, and is able to promote cell proliferation and fibroblast migration. |
| Shah P, et al (12)                | 2024 | USA      | The effect of cannabid iol on the healing of diabetes mellitus wounds   | Rats             | Circular wound incisions of 6 mm on the dorsal side of wild mice, which healed without therapy (control group), and on type 2 diabetic mice using cannabidiol   | Circular wound incisions of 6 mm on the dorsal side of wild mice, which healed without therapy (control  | Cannabidiol<br>can aid the<br>diabetic wound<br>healing process<br>(Diabetic<br>ulcers)   |

| Researcher          | Year | Country | Research<br>Objective  | Participa<br>nts | Data Collection<br>Design and<br>Methods   | Findings  | Implications  |
|---------------------|------|---------|--|------------------|--|---|---|
| Suman S, et al (13) | 2022 | India   | Evaluati<br>ng<br>cannabis<br>sativa<br>root<br>extract<br>for<br>antibacte<br>rial and<br>antioxida<br>nt<br>propertie<br>s | Cell culture     | Using 1. MIC (Minimum Inhibitory Concentration) test to test the effectiveness of cannabis root extract against antimicrobials 2. DPPH (2,2- Diphenyl-1- picrylhydrazyl) test: a test used to measure the antioxidant activity of a compound or extract 1. 3. MTT (3- (4,5- Dimethylthiazol-2- yl)-2,5- diphenyltetrazoliu m bromide) test: used to measure cell viability or proliferation, especially in cytotoxicity studies (e.g., against cancer cells) | group), and on type 2 diabetic mice using cannabidiol (experimenta 1 group) Diabetic mice administered cannabidiol were able to increase Connective Tissue Growth Factor (CTGF), which functions to enhance diabetic wound healing Cannabis root extract has been used for the biosynthesis of Sylver Nanoparticle s (AgNPs), which are significantly effective against Staphylococc us aureus (Grampositive), an extraordinary antioxidant where 58.01 ± 0.09% free radical scavenging was observed at a concentration of 100 µg/ml, with very low toxicity observed in red blood cells, namely 6.47 ± 0.04% at a high | Cannabis extract is effective as an antibacterial, antioxidant, and cancer prevention agent |

| Researcher                | Year | Country  | Research<br>Objective  | Participa<br>nts  | Data Collection<br>Design and<br>Methods  | Findings  | Implications  |
|---------------------------|------|----------|--|-------------------|---|---|---|
|                           |      |          |  |                   |   | concentration<br>of 200 µg/ml   |   |
| Dziok MZ et<br>al (14)    | 2021 | Polandia | Evaluati ng the impact of two types of Cannabis sativa L. herb extracts on keratinoc ytes and fibroblas ts   | In Vitro          | The cytotoxicity of cannabis extracts was determined using the Alamar Blue, Neutral Red, and LDH assays. The ability of the extract to inhibit matrix metalloproteinase, collagenase, and elastase activity was assessed. A hydrogel model preparation was also prepared, and its effects on transepidermal water loss and skin hydration were measured | Cannabis extract is a valuable source of biologically active substances that reduce oxidative stress, inhibit skin aging processes, and have a positive impact on skin cell survival and skin hydration   | Cannabis<br>extract<br>functions as an<br>anti-stress agent<br>that accelerates<br>wound healing,<br>inhibits skin<br>aging, and<br>maintains skin<br>freshness.  |
| Kaminsky,<br>et al (15)   | 2024 | France   | Determin<br>ing the<br>compositi<br>on of<br>cannabis<br>root hair<br>extract<br>for<br>antimicro<br>bial, anti-<br>inflamma<br>tory, and<br>antioxida<br>nt | In Vitro          | Biotechnology: cannabis root hair culture, accumulation of cannabinoids and triterpenes in hemp root hair and aeroponic hemp roots.   | Soil-grown roots produce 12 times more cannabinoids and 6 times more triterpenes than aeroponic roots, in addition to producing 3 times more biomass in bioreactors. Preliminary bioassays also indicate stronger antioxidant and antifungal properties | Cannabis root hairs are more effective in preventing inflammation and as antimicrobials and antioxidants than aeroponic root hairs. This means that root hairs are also highly effective in the wound healing process due to the elements contained in the root hairs |
| Ghacham SE,<br>et al (16) | 2023 | Morocco  | Evaluatin g the efficacy of essential oil newly extracted from Cannabis Sativa L. hydrodist  | The incised mouse | Cannabis Sativa Essential Oil (CSEO) was analyzed using gas chromatography- mass spectrometry. Neurobehavioral, histological, and biochemical analyses were performed to test   | CSEO has<br>higher<br>antibacterial<br>content,<br>accelerates<br>re-<br>epithelializati<br>on and<br>granulation<br>tissue<br>formation. In  | CSEO is very<br>effective for<br>chronic wound<br>healing<br>because, in<br>addition to<br>being<br>antibacterial, it<br>also accelerates<br>re-<br>epithelialization   |

| Researcher | Year | Country | Research<br>Objective                | Participa<br>nts | Data Collection<br>Design and<br>Methods                              | Findings  | Implications   |
|------------|------|---------|--------------------------------------|------------------|---|---|--|
|            |      |         | illed<br>from<br>plant<br>leaves for |                  | the effects of<br>CSEO application<br>on an incisional<br>wound model | addition,<br>CSEO<br>reduces<br>cortisol levels | and granulation,<br>resulting in<br>shorter wound<br>healing times |
|            |      |         | wound<br>healing                     |                  |   | involved in inhibiting the healing              | <b>3</b>   |
|            |      |         |                                      |                  |   | process and<br>has an<br>anxiolytic<br>effect   |  |

### **CONCLUSION**

Cortisol regulates sugar, fat, and protein metabolism, controls stress responses, suppresses inflammation and immune reactions, and regulates blood pressure. However, cortisol also has the opposite effect, as shown in a study conducted by Ahmed et al. (2022) on the reduction of cortisol effects, which can reduce the effects of bradycardia (17). Bradycardia is a condition where the heart beats slower than normal, meaning less oxygen is supplied because the heart pump is inadequate. This hinders the wound healing process due to insufficient oxygen supply.

Cannabis extract contains biologically active compounds: cannabinoids, terpenes, and flavonoids, which function as antibacterial, anti-inflammatory, and reduce oxidative stress, inhibit the skin aging process, and have a positive impact on skin cell survival and skin hydration (14).

The wound healing process is a physiological process that is important for maintaining skin integrity after trauma, whether accidental or intentional. healing involves Normal wound three consecutive hemostasis/inflammation phase, the proliferation phase, and the remodeling phase. After skin injury, the exposed subendothelium, collagen, and tissue factors activate platelet aggregation, resulting in degranulation and the release of chemotactic factors (chemokines) and growth factors (GF) to form a blood clot and achieve hemostasis. Neutrophils, the first cells to appear at the injury site, clear debris and bacteria to provide a favorable environment for wound healing. Next, macrophages accumulate and facilitate bacterial phagocytosis and tissue destruction. The hemostasis and inflammation phase typically takes 72 hours. The subsequent proliferation phase is characterized by the accumulation of numerous cells and connective tissue, including fibroblasts, keratinocytes, and endothelial cells. The extracellular matrix (ECM), including proteoglycans, hyaluronic acid, collagen, and elastin, forms granulation tissue to replace the clot formation. Many types of cytokines and growth factors participate in this phase, such as Transforming Growth Factorβ (TGF-β, including TGF-β1, TGF-β2, and TGF-β3), Interleukin (IL), and

angiogenesis factors (i.e., vascular endothelial growth factor). This phase continues for days and weeks. The final phase of wound healing is the remodeling phase, which requires a precise balance between apoptosis of existing cells and the production of new cells. The gradual degradation of abundant ECM and immature type III collagen and the formation of mature type I collagen are crucial in this phase, which continues for several months and years. Any deviation in this phase can lead to excessive wound healing or chronic wounds (18)

Acute wounds are at risk of becoming chronic wounds if the elements necessary for the wound healing process are not met. Chronic wounds are wounds with a longer healing time than predicted. In addition, several factors can inhibit the wound healing process. Several factors can inhibit the wound healing process, including infection, nutritional problems, certain medical conditions, and systemic factors such as age and smoking. These factors can interfere with various stages of healing, such as new tissue formation and vascular repair. However, research conducted by Khlongkhlaeo et al. (2024) states that Cannabidiol (CBD) and Tetrahydrocannabinol (THC) contained in Cannabis sativa can enhance cell viability in fibroblasts, which are the primary cells in connective tissue responsible for producing collagen and extracellular fibers. These are crucial for wound healing and maintaining tissue structure, thereby helping to shorten the healing time for chronic wounds (11).

Cannabis extract has various important properties that aid in the wound healing process, including increasing Connective Tissue Growth Factor (CTGF), which functions to improve the healing of diabetic wounds, the biosynthesis of Sylver Nanoparticles (AgNPs), which is significantly effective against Staphylococcus aureus (Gram-positive), antioxidants, skin hydration balance, anti-inflammatories, antioxidants, and anti-cancer properties. Cannabis root hair extract can produce higher levels of cannabinoid extract than leaves and flowers, meaning that the highest concentration of cannabidiol is found in the root hair.

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