

Supportive Care and Various Methods for Managing and Stimulation of Granular Tissue in Diabetic Foot Ulcer

Dr.P.Praveen Kumar¹, R.Malavikka², S.Manibharathi², M.Parkavi², U.Ramya²,
K.Roshni²

¹Assistant Professor, Department of Pharmacy practice, Arunai College of Pharmacy, Velu Nagar, Thenmathur, Thiruvannamalai-606 603.

²B.Pharmacy, Arunai College of Pharmacy, Velu Nagar, Thenmathur, Thiruvannamalai-606 603.

Date of Submission: 01-09-2024

Date of Acceptance: 10-09-2024

ABSTRACT:

Diabetic foot ulcers are associated with significant morbidity and mortality and can subsequently lead to hospitalization and lower limb amputation if not recognized and treated in a timely manner. Diabetic foot ulcers affect about 18.6 million people worldwide and 1.6 million in the US annually. Approximately half of diabetic foot ulcers become infected, and about 20% of these infections result in amputation of part of the foot or the whole foot. In this article, we focused on various methods for managing and stimulation of granular tissue in diabetic foot ulcers (DFUs) to rectify the drawbacks which helpful to prevent amputation.

KEYWORDS:

Diabetic mellitus, Stimulate cells to grow, Reactive oxygen species(ROS), Stimulation methods, Diabetic foot ulcer, Cell migration, Angiogenesis, Hyperbaric oxygen therapy (HOT), Vascular endothelial growth factor, Platelet rich plasma, Wireless micro current stimulation.

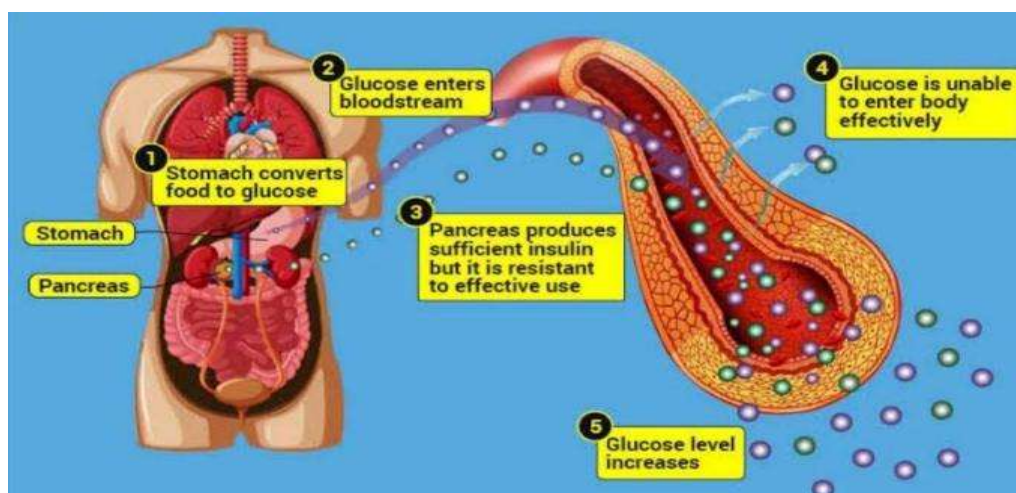
I. INTRODUCTION:

DIABETES:

Diabetes Mellitus, often known as Diabetes, is a common endocrine disease characterized by sustained high blood sugar level. Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body becoming unresponsive to the hormones effects. It is a group of disease that result in too much of sugar in the blood (high blood glucose). Diabetes also known as hyperglycemia.

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar); which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. Diabetes is a common condition that affects people of all ages.

As per the study in 2021 there were 101 million people in India with diabetes .In TamilNadu 16.4% were affected with diabetes .In Goa most of people affected for diabetes.



TYPES:



TYPE 1 DIABETES:



In type 1 diabetes, the body does not produce any insulin. Normally the body breaks down the carbohydrates you eat into blood sugar, which it uses for energy. Insulin is a hormone that the body needs to get sugar from the blood stream into the blood cell of the body in the absence of insulin blood sugar can become very high, resulting in vomiting, dehydration and acidotic blood. The treatment for the diabetes is insulin.

TYPE 2 DIABETES:



In type 2 diabetes, the body makes insulin but is unable to use it properly due to insulin resistance in the cells. Type 2 is typically treated through lifestyle changes, medication and sometimes insulin as the disease progresses.

GESTATIONAL DIABETES:



Gestational diabetes starts when the body is not able to make and use all the insulin it needs for pregnancy. Without enough insulin, sugar cannot leave the body and be used by cells as a source of energy. If not properly treated, gestational diabetes can cause complications in both the mother and the infant.

SYMPTOMS:

- Increased thirst & dry mouth.
- Frequent urination.
- Fatigue.
- Blurred vision.
- Slow healing sores or cuts.
- Numbness.
- Weight loss.
- Glycosuria.

CAUSES:

- Family history.
- Obesity.
- Drinking alcohol.
- Age.
- Insulin resistance.
- Heart disease.
- Autoimmune disease.
- Hormonal imbalance.
- Pancreatic damage.
- Genetic mutations.
- Acromegaly increases
- Long time use of HIV/AIDS medication and corticosteroids.

RISK FACTORS:

- Cardiovascular disorder
- Eye infection.
- Kidney infection.

ULCER:

An ulcer is a sore that heals slowly and reoccurs if they are not treated. Ulcers can appear both on the internal and external body membranes. It can occur on any body part, from the eye to foot.



TYPES OF ULCER:

- Peptic ulcer
- Arterial ulcer
- Esophageal ulcer
- Diabetic foot ulcer
- Mouth ulcer
- Gastric ulcer
- Duodenal ulcer

SYMPTOMS OF ULCER:

- Nausea
- Bloating
- Pain
- Bleaching
- Weight loss
- Fatigue
- Stomach burn
- Vomiting

CAUSES:

- Stress
- Smoking
- Drinking too much of alcohol
- Chewing tobacco
- Regular use of non steroidal anti-inflammatory drugs

TREATMENT :

- Antibiotic
- Proton pump inhibitor
- Antacid
- Anti diarrhoeal

DIABETIC FOOT ULCER (DFU):



A diabetic foot ulcer is an open sore or wound that occurs in patients with diabetes, and is commonly located on the bottom of the foot.

Diabetic foot ulcers commonly occur on the pressure points of the foot: the ball, heel, the tips of the toes, and side of the foot if a person's shoes are too tight. Diabetic foot ulcers are also most common in older people. DFU is approximately 15% of patients with diabetes, and commonly located on the bottom of the foot. Foot problems are common in people with diabetes. They can happen overtime when high blood sugar damages the nerves and blood vessels in the feet. The nerve damage, called diabetic neuropathy. For patient with diabetes, this often results in numbness in the feet and a loss of pain sensation, which can make it difficult for them to notice when they have cuts, blisters, or sores on their feet. So, the diabetic foot ulcer is a complication to diabetic patient. Because wound healing process is taken longer time for diabetic patient.

Reason for delayed of wound healing in diabetic foot ulcer:

Uncontrolled diabetes may also affect circulation, causing blood to move more slowly, which makes it more difficult for the body to deliver nutrients to wounds. It results, injuries heal slowly or may not heal at all.

SIGN AND SYMPTOMS:

- The ulcers are surrounded by a thick callus and may have a gray or black base.
- There may also be surrounding swelling and redness.
- Splinters
- Scrapes
- Pus
- Odour
- Pain

CAUSES:

Ulcers in people with diabetes are most commonly caused by:

- Poor circulation
- High blood sugar (Hyperglycemia)
- Irritated or wound and feet
- Nerve damage
- Infection
- Immune system issues

RISK FACTORS:

Some factors can increase the risk of foot ulcer including

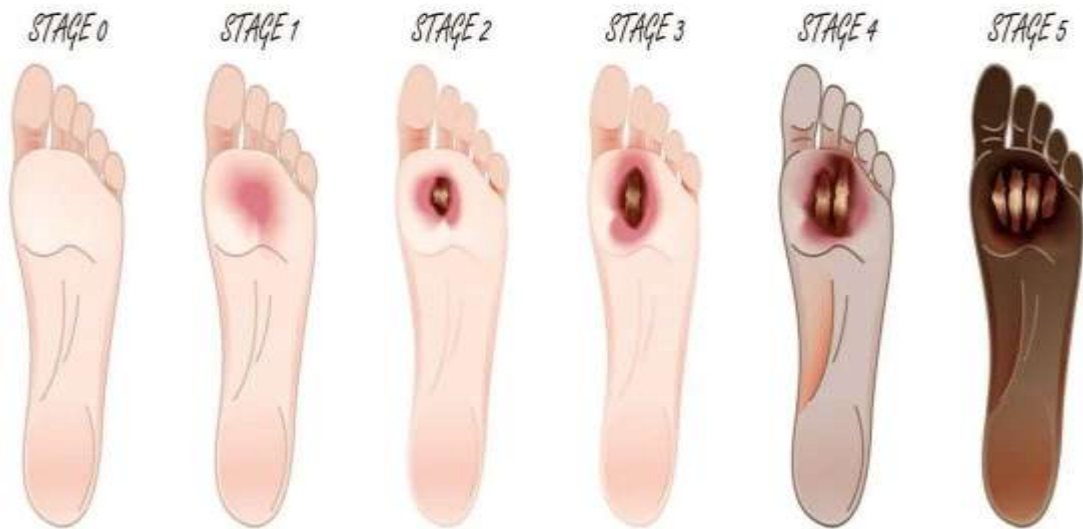
- Poorly fitted or poor quality.
- Poor hygiene(not washing regularly or thoroughly or not drying the feet well after washing).
- Improper trimming of toenails.
- Alcohol consumption.
- Eye disease from diabetes.
- Heart disease.
- Kidney disease.
- Obesity

- Tobacco use .

STAGES OF DIABETIC FOOT ULCER:

There are 6 stages of diabetic foot ulcer.They are

- Stage 0
- Stage 1
- Stage 2
- Stage 3
- Stage 4
- Stage 5



STAGE 0:
 Undamaged or intact skin.In this stage foot symptoms like pain, only.
 No open lesions; just deformity.

STAGE 1:
 Superficial wound ulcer involved in skin.

STAGE 2:
 Deep ulcers involving ligaments, muscles, tendons, etc..

STAGE 3:
 Ulcer with bone involvement. It developed into deep ulcer and part of the bone in your foot is visible.

STAGE 4:
 Gangrene localized to forefoot .

STAGE 5:
 Extensive gangreneous on the entire foot.

BASIC PREVENTION OF DIABETIC FOOT ULCER:



TREATMENT OF DIABETIC FOOT ULCER:

Many treatment is use to treat the diabetic foot ulcer. But the best treatment for diabetic foot ulcer is to stimulate the granular tissue. Many methods are used to stimulate the granular tissue for diabetic foot ulcer. They are

- Wireless Micro Current Stimulation
- Vascular endothelial growth factor stimulation
- Glycemic control
- Platelet derived growth factor
- Electrical stimulation skin fibroblast growth factor of secretion of cytokines
- Honey a potential therapeutic agent for managing diabetic foot ulcer
- Hyperbaric oxygen therapy
- Negative pressure wound therapy
- Anti-platelet rich plasma
- Therapeutic magnetic resonance

II. REVIEW OF LITERATURE:

1) **Peter G Wirsing Alexander D Habrom ES** in the form of WMCS is an excellent method to significantly accelerate the process of wound healing. WMCS has a huge potential to treat hard-to-heal wounds as well as to heal chronic wounds in general. Therefore, we see the use of WMCS in pressure ulcers, venous-, arterial- and mixed-leg ulcers and diabetic foot ulcers, especially in cases of existing severe accompanying diseases. An extra ordinary inflammation and infection of the wound should be treated by fully tested antibiotics before starting the WMCS treatment. Necrotic tissue and coverings must be re- moved before WMCS is started.

2) **Frederik S. Bang BSc. Med, Veronica Leeberg MD** In conclusion, this review finds that the usage of VEGF for DFU is still in progress, and all articles included in our study have led to the same positive direction. From our study it should be considered that only one of the four studies included was performed in humans, however, the tendency towards using VEGF seems to be positive in all models. There is a trend toward faster healing and it's safe when used topically on humans. Furthermore, the viral particles of VEGF seem to have a systematic effect when a dose exceeding 5.0×10^9 vp pr wound in animal models. This review inspires further research on VEGF stimuli. It is suggested that future research should focus on VEGF's relevant dosage and release rate, such that progress in

the area will make the results become more homogenous and comparable.

3) **Jiali Xiang, Shumin Wang** , In summary, there was no difference in wound Healing rate among groups of different baseline HbA1c levels, but good control of blood glucose at baseline would be beneficial if future HbA1c could be controlled reasonably. Slightly higher levels of HbA1c within 7.0-8.0% during treatment were associated with higher ulcer healing rate in patients with DFU, particularly for those with better glycemic control at baseline. Besides, in contrast to HbA1c less than 7.0%, the wound healing rate under the condition of HbA1c higher than 8.0% during DFU treatment was almost the same or a little better. These results suggested that HbA1c should be maintained higher than 7.0% for the glycemic control of DFU patients, and the best range for HbA1c should be within 7.0-8.0%. Meanwhile, we did not observe elevated mortality among lower or higher glycemic level groups. These results about the influence of reasonable blood.

4) **Jayalal. J. A., Edwin Kin Raj. S²** The wounds in the study group treated with rh- PDGF dressing showed more granulation tissue and contraction in the wound surface area than the wounds in the control group (80% versus 48%; 7sq.cm vs 12sq.cm: $P < 0.01$ - statistically significant) which indicates rh-PDGF dressing is an effective modality to facilitate wound granulation and wound contraction in patients suffering from diabetes. Rh- PDGF dressing is found to be a more effective, safe promoter of wound healing and can be used as an adjunct to saline dressing for healing diabetic wounds. Healing of ulcers receiving PDGF was significantly faster as compared to ulcer receiving saline dressing.

5) **Fahmida Alam, Md. Asiful Islam**, Honey is an alternative medicine that is considered to be a suitable therapy with improved outcomes. It is a cost-effective and safe natural agent with rapid diabetic wound healing capacity. However, additional successful clinical evidence is required with validated laboratory findings to establish honey as one of the most effective alternative topical medicines for treating diabetic wounds.

- 6) **Tieh Abedin-Do, Ze Zhang, Yvan Douville**, Diabetic human skin fibroblasts were successfully extracted, cultured and sub-cultured. The exposure to ES at 20 or 40 mV/mm for 6 and 24 h increased diabetic fibroblast adhesion and proliferation, as well as the secretion of cytokines and FGF-7. This study also demonstrates that the effects of ES on DHSF were maintained for at least 5 days post-exposure to ES. Our overall results therefore suggest that ES could be used to activate diabetic fibroblasts and show potential as a tool to improve the healing of diabetic ulcers.
- 7) **Miguel A. Ortega, Oscar Fraile-Martinez**, Hyperbaric oxygen therapy (HBOT) consists of using of pure oxygen at increased pressure (in general, 2-3 atmospheres) leading to augmented oxygen levels in the blood (Hyperoxemia) and tissue (Hyperoxia). The increased pressure and oxygen bioavailability might be related to a plethora of applications, particularly in hypoxic regions, also exerting antimicrobial, immuno modulatory and angiogenic properties, among others. In this review, we will discuss in detail the physiological relevance of oxygen and the therapeutical basis of HBOT, collecting Furthermore, potential areas of re- search will also be examined, including inflammatory and systemic maladies, COVID-19 and cancer. Finally, the ad- verse effects and contraindications associated with this therapy and future directions of research will be considered. Overall, we encourage further research in this field to extend the possible uses of this procedure. The inclusion of HBOT in future clinical research could be an additional support in the clinical management of multiple pathologies.
- 8) **Gill Norman Chunhu Shi, En Lin Goh**, Indications for the use of negative pressure wound therapy (NPWT) are broad and include prophylaxis for surgical site infections (SSIs). Existing evidence for the effectiveness of NPWT on postoperative wounds healing by primary closure remains uncertain .
- 9) **Peter Everts, Kentaro Onishi**, Antiplatelet-rich plasma represents a promising advancement in the treatment of diabetic foot ulcers, offering enhanced healing through its rich concentration of growth factors and

regenerative properties. While more research is needed to standardize protocols and optimize patient selection, current evidence supports the integration of PRP into comprehensive wound care strategies for DFUs. By leveraging the body's natural healing mechanisms, PRP therapy holds the potential to improve outcomes and quality of life for patients suffering from this challenging complication of diabetes.

- 10) **Letizia Ferroni et al. Eur J Histochem. 2017.** Therapeutic magnetic resonance offers a novel and promising approach to the treatment of diabetic foot ulcers. By leveraging low-frequency electromagnetic fields, TMR enhances cellular functions, improves blood flow, reduces inflammation, and alleviates pain, thus promoting more effective wound healing. Although further research and standardization are needed, TMR represents a valuable addition to the therapeutic arsenal against DFUs, potentially improving outcomes and quality of life for patients suffering from this challenging diabetic complication.

III. METHODOLOGY METHODS TO STIMULATE THE GRANULAR TISSUE IN DIABETIC FOOT ULCER:

There are 10 basic methods is used to stimulate the granular tissue in diabetic foot ulcer. They are

- METHOD 1:** Wireless Micro Current Stimulation
METHOD 2: Vascular endothelial growth factor stimulation
METHOD 3: Glycemic control
METHOD 4: Platelet derived growth factor
METHOD 5: Electrical stimulation skin fibroblast growth factor of secretion of cytokines
METHOD 6: Honey a potential therapeutic agent for managing diabetic foot ulcer
METHOD 7: Hyperbaric oxygen therapy
METHOD 8: Negative pressure wound therapy
METHOD 9: Anti-platelet rich plasma
METHOD 10: Therapeutic magnetic resonance

METHOD 1: WIRELESS MICRO CURRENT STIMULATION FOR THE TREATMENT DIABETIC FOOT ULCER

INTRODUCTION:

Chronic diabetic foot ulcers are very hard to recover that cause the death of patients. Wireless micro current stimulation (WMCS) is one of the treatments in diabetic foot ulcer, it is moreover similar to electrode based electrical stimulation. Wireless micro current stimulation (WMCS) is a new method and an innovative technique.

Micro current is used to reduce pain, increase the rate of tissue synthesis. The wireless micro current stimulation (WMCS) device utilizes current & carry capacity of air gases such as the ability of oxygen & nitrogen to accept or donate electrons. Oxygen is very helpful in growing the skin. Nitrogen (nitric oxide) helps to heal chronic wound healing. Wound healing incase of artificial skin stimulated with electric current was 3 times faster than the natural healing process.

Wireless micro current stimulation (WMCS) current type is direct current (DC) of very low intensity. In this method no physical contact rather undergoes spray effect.

This method works by transferring distantly low-intensity electric current to the patients. The patient has to be part of an electrical circuit and, for this reason, has to be connected with the device through a wrist strap wire as shown in Figure given below



A control box permits the adjustment of the current (1.5-4.0 μ A). Intensity was set to 1.5 μ A for all therapies distance from the head of the device was 12-15cm. The treatment surfare covered is about 400cm²

Time taken for this treatment is 45 to 60 minutes, so it is important that the patient lies or sits comfortably because the wound position relative to the wireless micro current stimulation (WMCS) device should remain steady throughout the treatment.

Before the treatment starts fibrin or other coverings are removed. Twice or thrice per week this treatment should be given to the patients.

47 patients with hard to heal wounds were treated by this method. Patient's age ranged 39-91 years & 22 were men and 25 were women. The patients chosen for this technique should undergo venous, arterial and mixed leg ulcers, diabetic foot lesions.

Clear progress of wound healing even after 2 weeks was observed in all cases. The mean reduction of the wound surface after wireless micro current stimulation (WMCS) treatment was 95% in 8 weeks. Complete healing was achieved within 3 months. This method is very easy to use and there are no side effects in this method when compared to other Electrical stimulation methods.

Reduction of wound size (%) in all patients under wireless micro current stimulation(WMCS) graph representation given below



METHOD 2:

VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) STIMULATION IN DIABETIC FOOT ULCERS

INTRODUCTION:

Diabetic foot ulcers are a common and severe complication of diabetes mellitus (DM).

Vascular endothelial growth factor (VEGF) commonly known as vascular permeability factor (VPF).

It is produced by many cells such as endothelial cells, fibroblasts, smooth muscle cells, platelets, keratinocyte, neutrophiles & macrophages.

Vascular endothelial growth factor plays a role in normal physiological function such as bone formation and wound healing.

Vascular permeability factor is a signal protein, it stimulates the formation of blood vessels. VEGF'S normal function is to create new blood vessels after injury.

VEGF is classified into 5 members,

- > VEGF-A
- > VEGF-B
- > VEGF-C
- > VEGF-D
- > PGF (Placental growth factor).

These are acts through the receptors,

- > VEGFR-1, VEGFR-2 and VEGFR-3

By stimulating the angiogenesis, vascular endothelial growth factor stimulates wound healing.

Angiogenesis occurs with increased expression of proangiogenic & decreased expression of antiangiogenic mediators.

Hypoxia is the primary stimulator of VEGF through hypoxia- inducible factor (HIF-1), which is also known in bone healing. Recombinant human VEGF (rhVEGF) used to treat diabetic ulcer. Telbermin, a rhVEGF, has shown a tendency to increase complete ulcer healing.

Telbermin tested as a topical agent applied to diabetic foot ulcer (DFU). It was found to be well tolerated in doses up to 72µg/cm² three times a week for up to 6 weeks.

Therefore, VEGF may prove to be an effective treatment for diabetic ulcer.

METHOD 3:

GLYCEMIC CONTROL WOULD HELP TO WOUND HEALING IN DIABETIC PATIENTS.

INTRODUCTION:

The effect of glycemic control on wound healing in patients with diabetic foot Ulcers (DFUs) is inconsistent among different Studies. This study was performed to investigate the association between level of hemoglobin A1c(HbA1c) at baseline as well as during treatment & wound healing and mortality in patients with DFU.

Blood glucose management is considered a basic component of the treatment of wound healing in DFU patients. previous clinical studies showed no Significant association between baseline HbA1c and wound healing. However, Recent research detected that, for those patients with baseline HbA1c < 7.5% a risk in HbA1c during treatment

was associated with an increased chance of wound Healing.

METHODS:

1. Study population

Hospitalized patients with DFU were consecutively recruited for the study.

- I. Grade 5 wounds according to the Wagner ulcer classification system which required major Amputation.
- II. patients with type-1 diabetes.
- III. Non-compliant patients.

2.Clinical characteristics Collection

All the enrolled patients were interviewed on admission for medical History Collection including,

- > Type & duration of diabetes mellitus
- > Duration of DFU
- > Smoking status
- > Therapeutic regimen for diabetes
- > Previous history of foot ulcer & amputation
- > Presence of comorbidities.

The first HbA1c value after admission was defined as baseline HbA1c. It was measured every 3 months according to standard care of glycemic management and HbA1c measurement was repeated at the endpoint.

3.Wound severity assessment and intervention

All ulcers were assessed on admission

❖ Based on Wagner's classification characterized as

- > Local swelling or induration
- > Erythema
- > Local tenderness or pain
- ❖ American classification system
- > Mild
- > Moderate
- > Severe

4.Out comes and follow-up

It includes ulcer healing and death. The whole observation period lasted for 1 year.

5.Statistical Analysis

The data were analyzed using SAS 9.3 statistical software.

Discussion

Level of HbA1c that ranged from 7.0% to 8.0% during treatment would be more helpful for wound

healing in diabetic foot ulcer patients than other levels.

**METHOD 4:
THE EFFECT OF PLATELET DERIVED
GROWTH FACTOR ON DIABETIC FOOT
ULCERS.**

INTRODUCTION:

Type two Diabetic mellitus is a type of metabolic disorder characterized by hyperglycemia, Such as Diabetic neuropathies, diabetic foot, diabetic retinopathy.

“Platelet derived growth factor (PDGF) is one of the growth factors important in angiogenesis & regeneration that is used in treating chronic ulcers. PDGF-regulate cell growth & division, it help to heal wounds and to repair damaged blood vessel walls.

A recombinant human (rh)- PDGF dressing is an effective modality for facilitating wound healing in patients suffering patients.

MATERIALS AND METHODS:

- I. 50 patients with diabetic foot ulcers were admitted.
- II. 25 patients were included in the Study/ treatment group. 25 patients were in the control group.
- III. For rh-PDGF dressing, the infected ulcer was cleaned with normal saline.
- IV. The dressings were changed daily in both groups & the appearance of healthy granulation tissue is observed.
- V. The intended period of treatment was 8 weeks & visit at an interval of 1 week for 8 weeks.



Ulcer at Day 0 and end of week 2



Ulcer at end of week 4 and week 8

**METHOD 5:
 EFFECT OF ELECTRICAL STIMULATION
 ON DIABETIC HUMAN SKIN FIBROBLAST
 HEALING. GROWTH OF WOUND HEALING**

INTRODUCTION:

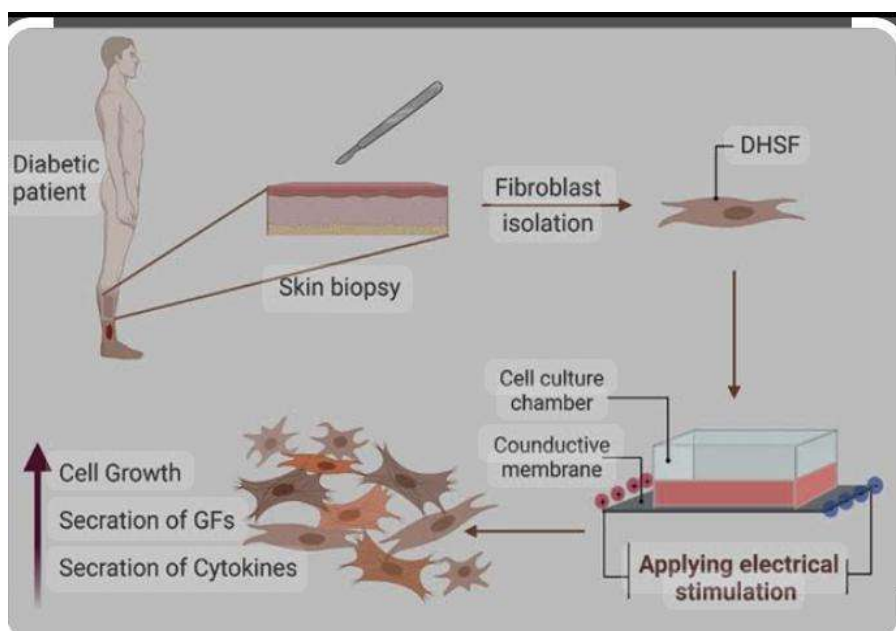
Electrical stimulation (ES) is a physical-based therapy able to increase cell activity and migration into wounds, as well as inhibiting bacterial activity.

The exposure to electrical stimulation at 20 or 40 mV/mm for 6 and 24 hours increased diabetic fibroblast adhesion and proliferation, as well as secretion of cytokines and FGF-7.

They are maintained at least 5 days. Safe electrical stimulation, intensities DHSF.

Diabetic human skin Fibroblast (DHSF) were seeded (5×10^4 cells/cm²) on the membrane in electrical cell culture.

Device and cultured for 24h at 5% Carbon dioxide, humid atmosphere. ES at various (100, 80, 60, 40 and 20 mV/mm) were then applied or not to the cells for 6 or 24h. Following each stimulation period, the culture medium was refreshed and the cells were cultured for an additional 48h.



ADVANTAGES:-

Although there are many benefits of ES, the ones most relevant for diabetic ulcer and peripheral neuropathy are the ability to manage pain, aid circulation, combat neuropath and even to antibacterial effect.

Clinical evidence:-

They are using local heat and electrical stimulation for 30 min three times per week.

**METHOD 6:
 HONEY:- A POTENTIAL THERAPEUTIC
 AGENT FOR MANAGING DIABETIC
 WOUNDS.**

INTRODUCTION:

In diabetic patient, honey compared with dextrose caused a significantly lower rise of plasma glucose level (PGL). It has reduced for blood lipids, homocysteine.

METHOD:

Honey contains various substances such as glucose, fructose, sucrose, minerals, vitamins, antioxidants, amino acid and other products.

The presence of large quantities of Assimilable sugars, vitamins, amino acid, and trace element honey contributes to Potential in stimulating tissue growth.

Application of nutrition of wounds and increased growth of granulation tissue.

Honey helps to stimulate angiogenesis and increase oxygen and nutrients to wound area for better wound Healing. During debridement, old, dead cells or tissue are Removed by mechanical, chemicals surgical, or autolytic means.

Honey contain protease enzyme .

First,

The antioxidants fight against microorganism and decrease infection site of the wound.

Second,

The antioxidants reduce reactive oxygen species (ROS) and inflammation caused by the wounds aid the healing process.

Honey's physical chemical characteristics, such as presence of hydrogen peroxide it low PH level and its high sugar and phenolic content, promote anti-inflammatory and anti oxidative activities, improving wound healing.

ADVANTAGES:

- Reduce odors and pus.
- Help clean the wound.
- Reduce infection.
- Reduce pain.
- Decrease time to healing .

- This is the process by which new blood vessels formed from pre existing vessels, which increase the amount of oxygen nutrient in wound area.

CLINICAL EVIDENCE:-

Even though 47 of the patient had previously been treated with conventional treatment by commercial wound dressing or antibiotics.

The dressing can be left on longer periods (4-7 days).

Applying honey from 1 to 4 times daily.

METHOD 7: HYPERBARIC OXYGEN THERAPY

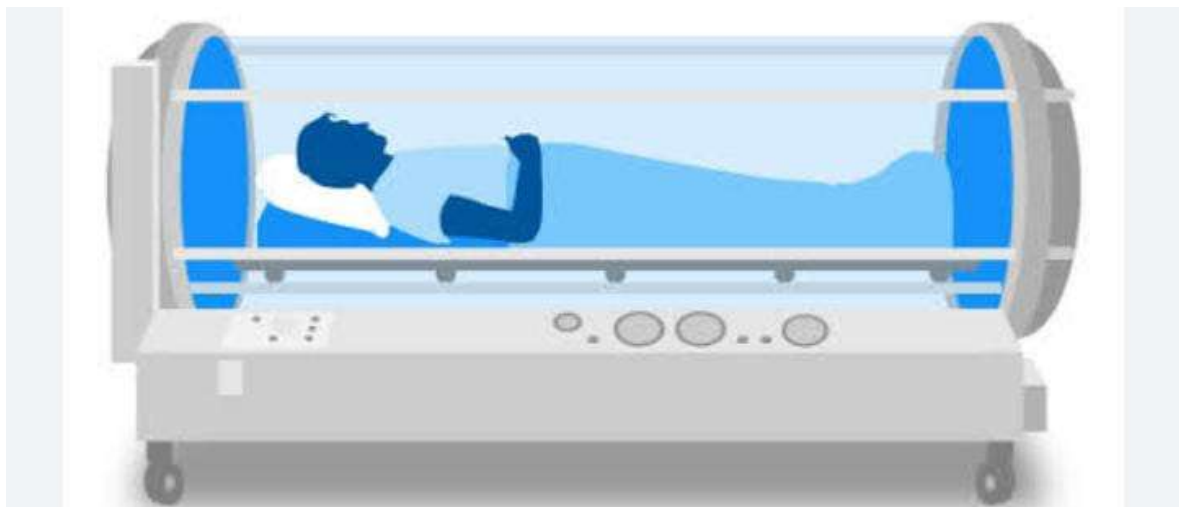
INTRODUCTION:

Hyperbaric oxygen therapy is a therapeutic approach that treats the chronic wounds and other medical condition by supplying you with 100% oxygen inside a special chamber.

It heals damaged tissue by helping your body grow new skin, blood vessels & connective tissue. Room air contains 21% oxygen, while hyperbaric oxygen therapy provides you with air that contains 100% oxygen.

A pressurized chamber delivers oxygen that two to three times higher than normal air pressure, which helps your lungs gather & absorb more oxygen.

Oxygen helps the tissue in your body heal & withstand infection. The first documented use of hyperbaric medical therapy was in 1662 by Henshaw, a British physician. Other names for hyperbaric oxygen therapy include HBO Therapy or HBOT.



HYPERBARIC OXYGEN THERAPY

PROCEDURE : BEFORE USING HYPERBARIC OXYGEN THERAPY:

Before receiving hyperbaric oxygen therapy, your healthcare provider will assess many factors, including your age & overall health. These assessments will help them to determine how long your therapy should last & how many session you need.

Health condition is very important for this therapy. Before entering this therapy the person do not smoke and avoid alcohol and carbonated beverages. The person should avoid all perfumes and any body lotions.

You will change into a hospital gown & remove any metal objects or electronic device outside the chamber. These items could create sparks, cause a fire in high oxygen treatment.



DURING HYPERBARIC OXYGEN THERAPY:

During hyperbaric oxygen therapy, once the door chamber has closed, you might hear a slight hissing sound as a oxygen fills the chambers & the pressure inside slowly grows. A healthcare provider will be in the room throughout the procedure to answer any questions & monitor your condition & overall health.

They may have you take short breaks during the treatments to breath normal air. The chamber will provide the oxygen to stimulate the granular tissue for fast wound healing.

During this therapy people can relax, sit or lie comfortably in these chambers and take deep breaths. Session can last from 45 minutes to 300 minutes.

AFTER HYPERBARIC OXYGEN THERAPY:

Toward the end of the hyperbaric oxygen therapy health provider will gradually decreases the pressure inside your chamber so your body can adjust to the pressure outside of the chamber.

Your healthcare provider will remove you from the chamber or help you remove your mask or hood. Then they will examine some of your vital sign, including your blood pressure and pulse, & check your ears. They will test your blood sugar level.

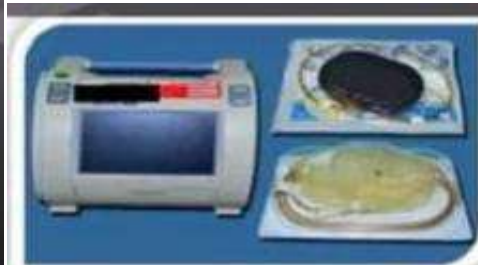
BENEFITS:

- Increase blood and circulation.
- Improve immune system.
- Reduce inflammation.
- Reduce chronic pain.
- Accelerate wound healing.
- Stimulate the granular tissue.
- Promote new blood vessel growth.

RECOVERY TIME:

- You can return to your usual daily activities immediately following a hyperbaric oxygen therapy session.
- Most people see benefits from hyperbaric oxygen therapy after several session.
- Healing success rate -85percent.

**METHOD 8:
 NEGATIVE PRESSURE WOUND THERAPY
 INTRODUCTION:**



Negative Pressure Wound Therapy (NPWT) aims to optimize the wound healing by applying sub-atmospheric pressure to help reduce inflammatory exudates and promote granular tissue.

It primarily utilized to treat complex wounds are non-healing or at risk of non-healing, such as diabetic foot ulcer.

NPWT is first described by Fleischmann et al in 1993. It promotes wound healing by applying a vacuum drainage through a special sealed dressing.

This therapy also known as Vacuum Assisted Closure (VAC). Therapeutic technique using suction pump, tubing, remove excess exudates and promote the granular tissue growth in acute or chronic wound healing.

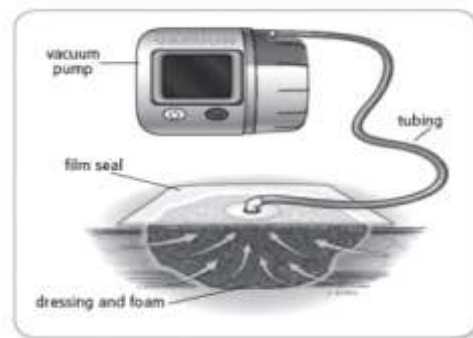
EQUIPMENT:

- Sterile open cell wound interface of small, medium & large sites.
- Flexible vacuum tubing.
- Occlusive adhesive transparent dressing.
- Canister (collection chamber with connecting tubing).
- Vacuum pump.
- Sterile gauze.
- Non paraffinized, coated polyester net.
- NPWT pack
- Specialized negative pressure adhesive dressing (closed wounds).
- Specialized pre cut or unprepared foam dressing (open wounds).
- Transparent adhesive sealant tape.
- NPWT suction device.

WORKING OF NPWT:

This therapy involves a special dressing (bandage), tubing, a negative pressure device, and canister to collect fluids.

- Your healthcare providers will fit layers of foam dressing to the shape of the wound. The dressing will then be sealed with a film.
- The film has an opening where a tube is attached. The tube leads to a vacuum pump can be set so that it is ongoing, or so it starts and stops intermittently.
- The vacuum pump pulls fluid and infection from the wound. This helps pull the edges of the wound together. It also helps the wound heal by promoting the growth of new tissue.
- ABS plastic vacuum assisted closure device is used for NPWT.
- Device produces the pressure over the area of the wound. Device set up 40mmHg to 200mmHg. The device is used to decrease the exudate air pressure.



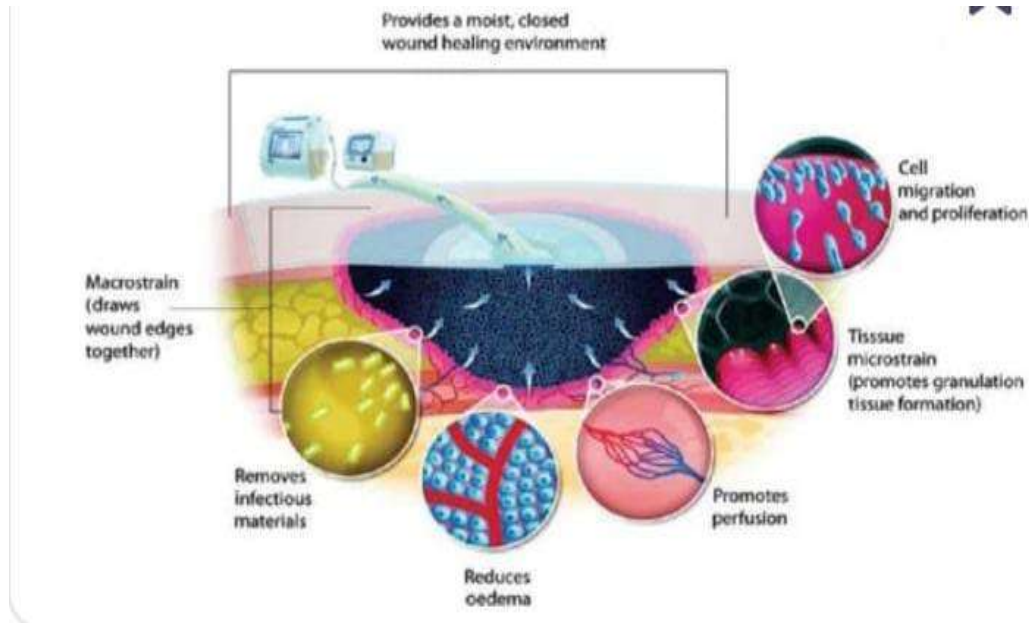
- The NPWT taken for several weeks or month based on the wound characteristics. During this therapy, you will need to carry the device everywhere you go. During the therapy time, make sure you have good nutrition and get enough rest.

MECHANISM OF ACTION:

System consists of a sponge a semi occlusive barrier, & fluid collection system. Its effectiveness is explained by 4 mechanisms.

- Macrodeformation of tissues.

- Drainage of extracellular inflammatory fluids.
- Stabilization of environment of wound.
- Microdeformation.



BENEFITS OF NPWT:

- ✓ Gradually drains excess fluid (exudate) from wound bed.
- ✓ Stimulates antibacterial action to prevent wound infection.
- ✓ Reduces swelling(edema)
- ✓ Improves blood circulation in the wound bed.
- ✓ Promotes a moist wound healing environment.
- ✓ Minimizes inflammation (redness and swelling).

- ✓ Facilitates the growth of new tissue (Granulation).

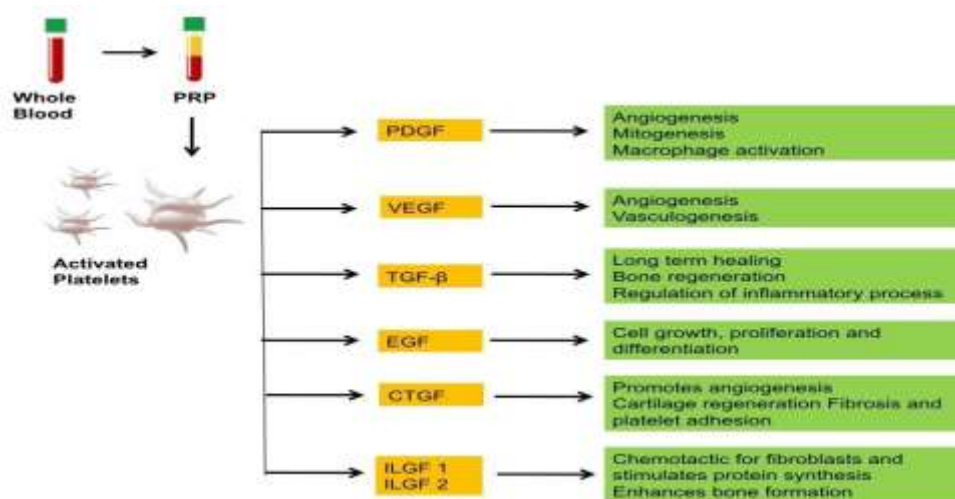
RECOVERY TIME :

- By using this method the rate of wound healing is increases.
- Most of the peoples see the benefits by using this methods.

METHOD 9:

PLATELET RICH PLASMA IN THE TREATMENT OF DIABETIC FOOT ULCERS

INTRODUCTION :



PLATELET-RICH PLASMA (PRP):

PRP is derived from the patient’s own blood and is rich in platelets, growth factors, and cytokines. These components play crucial roles in wound healing by promoting cell proliferation, angiogenesis, and tissue regeneration. PRP is prepared by centrifuging blood to concentrate the platelets and then activating them to release growth factors.

MECHANISM OF ACTION:

Growth Factors:

PRP contains a high concentration of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF). These factors stimulate cellular processes essential for wound healing.

ANGIOGENESIS:

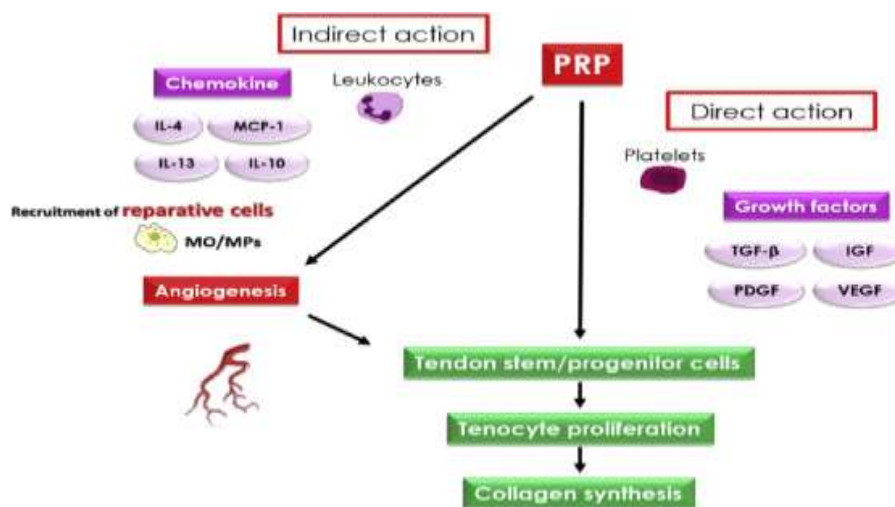
VEGF and other angiogenic factors in PRP promote the formation of new blood vessels, enhancing blood supply to the wound area and supporting tissue repair.

COLLAGEN PRODUCTION:

PRP enhances the synthesis of collagen, a fundamental component of wound healing that provides structural integrity to the newly formed tissue.

INFLAMMATION MODULATION:

PRP can modulate the inflammatory response, reducing excessive inflammation and promoting a balanced environment conducive to healing.



CLINICAL APPLICATION IN DFUS:

Preparation and Application: PRP is prepared by drawing blood from the patient, centrifuging it to separate the platelet-rich fraction, and then activating it. The activated PRP is applied directly to the ulcer or injected around the wound margins.

Combination with Conventional Treatments: PRP therapy is often used alongside standard wound care practices, including debridement and infection control, to enhance healing outcomes.

EFFICACY AND EVIDENCE:

Healing Rates: Studies have shown that PRP significantly accelerates healing rates in DFUs compared to standard care alone. Patients receiving

PRP treatment often experience faster reduction in ulcer size and increased rates of complete wound closure.

Reduced Amputation Rates: PRP therapy has been associated with lower rates of amputation in patients with severe DFUs, likely due to its ability to promote rapid and effective wound healing.

Pain Reduction: Patients undergoing PRP treatment often report reduced pain, which can improve their overall quality of life and adherence to treatment protocols.

ADVANTAGES OF PRP THERAPY:

Autologous Source: PRP is derived from the patient’s own blood, minimizing the risk of allergic reactions or disease transmission.

Minimally Invasive:The procedure to prepare and apply PRP is relatively simple and minimally invasive, making it suitable for outpatient settings.

Reduced Need for Surgery:By promoting effective healing, PRP can reduce the need for surgical interventions and lower healthcare costs associated with long-term wound management.

CHALLENGES AND CONSIDERATIONS:

Standardization:Variability in PRP preparation methods and concentrations can affect clinical outcomes. Standardized protocols are needed to ensure consistency and reproducibility.

Cost and Accessibility:PRP preparation can be expensive, and not all healthcare facilities may have the necessary equipment or trained personnel to perform the procedure.

Patient Selection:Identifying patients who will benefit most from PRP therapy is crucial. Factors such as ulcer size, duration, and presence of infection can influence treatment efficacy.

METHOD 10:

THERAPEUTIC MAGNETIC RESONANCE IN THE TREATMENT OF DIABETIC FOOT ULCERS

INTRODUCTION :

THERAPEUTIC MAGNETIC RESONANCE (TMR):

Therapeutic magnetic resonance involves the use of low-frequency electromagnetic fields to stimulate biological processes that promote healing. TMR devices emit electromagnetic fields that interact with tissues at a cellular level, influencing cellular functions and promoting tissue repair and regeneration.

MECHANISM OF ACTION:

Cellular Stimulation:

TMR stimulates cellular activities such as cell proliferation and differentiation. The electromagnetic fields can enhance the function of fibroblasts, keratinocytes, and endothelial cells, which are crucial for wound healing.

Improved Blood Flow:

TMR can enhance microcirculation and improve blood flow to the wound area. Better perfusion facilitates the delivery of oxygen and nutrients necessary for tissue repair.

Anti-inflammatory Effects:

TMR has been shown to modulate inflammatory responses, reducing excessive

inflammation that can wound healing. This balanced inflammatory response creates a conducive environment for healing.

Pain Reduction:

The application of TMR can reduce pain in the wound area, which not only improves patient comfort but also supports better adherence to treatment protocols.

CLINICAL APPLICATION IN DFUS:

Device and Protocol:

TMR treatment involves placing a TMR device near the ulcer. The device generates low-frequency electromagnetic fields that penetrate the tissue. Treatment protocols vary, but sessions typically last 30-60 minutes and are conducted several times a week.

Combination with Standard Care:

TMR is often used in conjunction with standard wound care practices, including debridement, infection control, and appropriate wound dressings, to maximize healing outcomes.

EFFICACY AND EVIDENCE :

Healing Rates:

Clinical studies have indicated that TMR can significantly enhance the healing rates of DFUs. Patients receiving TMR treatment show faster reduction in wound size and increased rates of complete wound closure compared to those receiving standard care alone.

IV. CONCLUSION:

The advanced method of treatment of DFU offering, enhanced healing through its rich concentration of growth factor and regenerative tissue. Chronic diabetes foot ulcer can lead to amputation, Hence this all methods are used in enhancement of cellular function, improve blood flow, reduce inflammation, alleviates Pain, thus promote effective wound healing. Absorb exudates, Control infection / odor and be effective in treating diabetic foot wounds.

REFERENCE :

- [1]. Peter G Wirsing et al. Int Wound J. 2015Dec. Wireless micro current stimulation—an innovative electrical stimulation method for the treatment of patients with leg and diabetic foot ulcers. PMID:24373098 PMID: PMC7950994.DOI: 10.1111/iwj.12204.

- [2]. Frederik S Bang et al. Wound Repair Regen. 2024. The effect of VEGF stimulation in diabetic foot ulcers: A systematic review. PMID: 38494793 DOI: [10.1111/wrr.13171](https://doi.org/10.1111/wrr.13171).
- [3]. Jiali Xiang Shumin Wang Yang He Lei Xu Shanshan Zhang. iZhengyi Tang. Reasonable Glycemic Control Would Help Wound Healing During the Treatment of Diabetic Foot Ulcers. <https://doi.org/10.1007/s13300-018-0536-8>.
- [4]. Jayalal. J. A.¹, Edwin Kins Raj.S², Baghavath.P.R.², Mahesh.L Jonathan³, Kiruba³, Ajish³. THE EFFECT OF PLATELET DERIVED GROWTH FACTOR ON DIABETIC FOOT ULCERS: A PROSPECTIVE RANDOMISED CONTROL STUDY. International Journal of Academic Medicine and Pharmacy (www.academicmed.org)ISSN (O):2687-5365; ISSN (P): 2753-6556.
- [5]. Fahmida Alam, ¹ Md. Asiful Islam, ¹ Siew Hua Gan, ¹ and Md. Ibrahim Khalil ², Honey: A Potential Therapeutic Agent for Managing Diabetic Wounds. Evid Based Complement Alternat Med. 2014;2014: 169130. Published online 2014 Oct 15. DOI: [10.1155/2014/169130](https://doi.org/10.1155/2014/169130). PMID: 25386217 | PMC4216698
- [6]. Atieh Abedin-Do, ^{1,2} Ze Zhang, ² Yvan Douville, ² Mireille Méthot, ² and Mahmoud Rouabhia¹. Effect of Electrical Stimulation on Diabetic Human Skin Fibroblast Growth and the Secretion of Cytokines and Growth Factors Involved in Wound Healing. Biology (Basel), 2021 Jul; 10(7):641 .Published online 2021 Jul 9. DOI: [10.3390/biology10070641](https://doi.org/10.3390/biology10070641) PMID: 34356496 | PMC8301053
- [7]. Gill Norman, Chunhu Shi, En Lin Goh, Elizabeth MA Murphy, Adam Reid, Laura Chiverton, Monica Stankiewicz, and Jo C Dumville. Negative pressure wound therapy for surgical wounds healing by primary closure. Cochrane Database Syst Rev. 2022; 2022(4):CD009261. Published online 2022 Apr 26. DOI: [10.1002/14651858.CD009261.pub7](https://doi.org/10.1002/14651858.CD009261.pub7) PMID: 35471497 | PMC9040710
- [8]. Miguel A. Ortega, ^{1,2,3,*} Oscar Fraile-Martinez, ^{1,2,*} Cielo García-Montero, ^{1,2} Enrique Callejón Peláez, Miguel A. Sáez- ^{1,2,5} Miguel A. Álvarez-Mon, ^{1,2} Natalio García-Honduvilla, ^{1,2} Jorge Monserrat et al. A General Overview on the Hyperbaric Oxygen Therapy: Applications, Mechanisms and Translational Opportunities. Medicina (Kaunas). 2021 Sep; 57(9): 864. Published online 2021 Aug 24. DOI: [10.3390/medicina57090864](https://doi.org/10.3390/medicina57090864) PMID: 34577787 | PMC8465921
- [9]. Peter Everts, ^{1*} Kentaro Onishi, ² Prathap Jayaram, ³ José Fábio Lana, ⁴ and Kenneth Mautner⁵. Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020. Int J Mol Sci. 2020 Oct; 21(20): 7794. Published Online 2020 Oct 21. DOI: [10.3390/ijms21207794](https://doi.org/10.3390/ijms21207794) PMID: 33096812 | PMC7589810
- [10]. Letizia Ferroni et al. Eur J Histochem. 2017. Treatment of diabetic foot ulcers with Therapeutic Magnetic Resonance (TMR®) improves the quality of granulation tissue. ¹ University of Padua. letiziaferroni@unipd.it. PMID: 29046049 | PMC5572111 DOI: [10.4081/ejh.2017.2800](https://doi.org/10.4081/ejh.2017.2800).