

# Leech Therapy and its Efficacy in Management of Non-Healing Ulcers - A Review

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**Abstract:** *Leech therapy is one of the most important and widely practised methods of regimental therapy used for local evacuation of morbid humours way back 3500 years also it has been suggested and successfully practiced by Greeko-Arab physicians, eminent Unani physician Ibn e Sina stated in his treatise Al Qanoon fit Tib that "Leeches evacuate blood from the deeper tissues compared to Hijama", He mentioned its efficacy such as ear, eyes, throat and skin disorders and also plays a vital role in healing of chronic non-healing ulcers, musculoskeletal diseases, thromboembolic diseases etc. According to Unani doctrine, the efficacy of leech therapy is attributed to the analgesic and resolvent activities of leeches. However, the saliva of leech contains about 100 pharmacologically active biological substances like Hirudin, hyaluronidase etc which are vasodilators, anesthetics, anti-inflammatory etc. These substances are injected into human body while sucking the blood these properties are responsible for the analgesic, anti-inflammatory and anesthetic effects of leech therapy. Leech therapy involves an initial bite, which is usually a painless bite, followed by the sucking of 5 to 15 ml of blood. Leech therapy is also used for evacuation from the parts where Hijama and Fasd cannot be applied. In Chronic Ulcers, wound healing is a combination of Regeneration and Repair of surrounding parenchymal tissues, which includes Angiogenesis and Granulation tissue formation, these things are accelerated by the components present in Leech Saliva, by inhibiting Thrombin, Platelet aggregation and fibrinolysis.*

**Keywords:** Leech therapy, Chronic wounds, Wound healing

## 1. Introduction

Regeneration and repair in combination plays a vital role in healing chronic non-healing ulcers such as Diabetic foot ulcer, varicose ulcer, Thromboangitis obliterata, is done by Angiogenesis & Granulation tissue formation.

Chronic ulcers are challenge to wound care professional and consumers.

Eminent Unani Physician Shaik ur Rayees has mentioned in his famous book Al- Qanoon Fit tib "Putrification in any organ gets started when there is destruction of Rooh e Haiwani" to that particular organ

There are 2 reasons for destruction of Rooh e Haiwani

- 1) Blood Toxicity
- 2) Interruption in blood supply.<sup>8</sup>

Wound healing is a dynamic and sequential process which involves exudative, proliferative and extracellular matrix remodeling phases. These phases are regulated by signaling molecules produced by a wide range of cells present in the extracellular matrix. The early stages of this process (homeostasis, inflammation and proliferation) prepare the tissues for the final, remodeling stage which can last for one year or more. Various factors affect wound healing. Most chronic wounds are ulcers associated with ischemia, venous stasis or pressure. The therapeutic measures used to promote and treat wound healing must be adjusted to the states of the various wound healing phases.<sup>4</sup>

Medicinal Leech Therapy is a multi-faceted therapeutic concept. It comprises the biting stimulus, blood drawing and the injection of pharmacologically-active substances found in leeches' saliva into patients' blood and tissues. It's therapeutic effects include anti-coagulation, vasodilator which induce blood and lymph flow and reduce both inflammation and pain. The pharmaceutical profile of MLT means that therapy must be restricted to the late, remodeling phase of wound healing.<sup>14</sup>

Ancient Unani Physician Ibn sena Stated in this Book Kulliyat qanoon that application of leech evacuate blood more deeper tissues when compare to Hijama & Fasd. He also mentioned its efficacy in various diseases such as Skin, Ear, Eye & Throat diseases. It also plays a vital role in healing Chronic no healing ulcers.<sup>12</sup>

It's efficacy is also mentioned in ancient book Sushruth Samhita that Leech therapy is useful in Skin, Musculoskel et al disorders and in healing of chronic ulcers.<sup>9</sup>

Conditions which interfere with the Healing of ulcers

- 1) Unhealthy condition of surrounding area
- 2) Deficient supply of healthy blood
- 3) Excessive flow of blood
- 4) Necrosis of the underlying bone<sup>1</sup>

### Classification of wounds

Basically wounds are classified as

- 1) Clean & Untidy wound

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- 2) Acute & Chronic wound
- 3) Open & Close wound.<sup>15</sup>

According to cleanliness and condition it is classified as

- 1) Clean wound - They are uninfected, no inflammation is present, and are primarily closed.
- 2) Clean-contaminated wound - These wounds lack unusual contamination. However these wounds enter the respiratory, alimentary, genital or urinary tracts under controlled conditions.
- 3) Contaminated wound - These are fresh, open wounds that can result from insult to sterile techniques or leakage from the gastrointestinal tract into the wound. Additionally, incisions made that result in acute or lack of purulent inflammation are considered contaminated wounds.
- 4) Dirty-infected wound - These wounds typically result from improperly cared for traumatic wounds. However these wounds demonstrate devitalized tissue, and they most commonly result from microorganisms present in perforated viscera or the operative field.<sup>7</sup>

Another classification is according to Acute & chronic wound

- 1) Acute wounds include abrasion, stab wound etc.
- 2) Chronic wounds includes Varicose ulcer, Diabetic ulcer, TAO, Pressure sore etc.

## 2. Historical Aspect

It has been reported that the first person to use leeches medicinally may have been Nicandros of Colophon (200-130 BC) and soon thereafter, Thmison of Laodicea (123-43 BC) a pupil of Aesculapius, Blood letting has been part of the history of medicine for more than 2500 years. Up to the end of the Middle Ages, the rationale for bloodletting originated from the ancient greek humoral theory.<sup>20</sup>

Accordingly Way back in 2500 years ago back to ancient Egypt and the beginning of civilization bloodletting and *Hirudo medicinalis* were use.<sup>9</sup>

During the Roman Era, Galen (129-189 AD) promoted leeching because he believed that bloodletting would rid the body of noxious substances produced by disease. By doing so it could restore the four humors to proper balance. Avicenna (978-1037 AD), the great Arab Physician, believed that leeches drew blood from deeper sources than did wet cupping. In his world famous book *The Canon of Medicine* (Al-qanoon-fit-Tibb) he has devoted several pages for instructions on leeching and description of leeches to be used medicinally.<sup>20</sup>

Leeching is also mentioned in medical encyclopedia from India written in Sanskrit completed between 500 BC and 200 AD.<sup>9</sup>

One reference from Medieval England refers to bloodletting by leeches in a Latin written by Aldhelm of Malmsburh (7th or 8th century AD) and may be translated as I bite unfortunate bodies with three-furrowed wounds and bestow a cure from my healing lips.<sup>3</sup>

Avicenna in his famous book the canon of medicine emphasize on the use of leeches even for skin diseases, Chronic wound healing. Later in the 12<sup>th</sup> century Abdul Latif Baghdadi wrote that leech could also be used for cleaning the tissues after surgical operations.

Hirudotherapy has also been mentioned in Ayurveda as Jalaukavacharan (Jalauka meaning leeches and Avacharan meaning application). As per Ayurveda Jalaukavacharan is one of the procedures of Raktamokshana. Raktamokshana is one of the biopurification methods mentioned in Ayurveda, in which humours vitiated in blood are expelled from the body.<sup>9</sup>

Leeching reached the height of its popularity in the middle 19<sup>th</sup> century, when it was exposed by the French physicians Francois Broussais (1722-1838). Broussais was the head of French physician of the Val De Grace Hospital in Paris and a surgeon in diseases such as typhoid fever, Syphilis, T.B, and even mental illness by applying leeches to abdomen. Broussais was in fact the biggest consumer in France, ordering 2-3 millions leeches in 1824 and his requisition rose to 42 millions in 1833. A record of 57 millions leeches was used in 1854. Between the years of 1829 and 1836, five to six millions leeches were used annually in the hospitals of Paris. In early 19<sup>th</sup> century. American physician from Georgia wrote bloodletting is the most important treatment, whenever there appears mark of local congestion, inflammation or that sluggish or torpid action which makes incapacity in the circulation vessels. He continue to discuss the use of leeches as treatment for myocarditis, peritonitis, pleuritis, hepatitis, gastritis, tonsillitis, nephritis, pneumonia, whopping cough, dysentery, hemorrhoids, acne and pimples.<sup>9</sup>

Napoleon's grant army. Broussais treated Napoleon's grant army Broussais treated Von Rosenstein, in the first printed text book on diseases of children advocated leeching for difficult dentition, tooth abscess, convulsion, scarlet fever, pleurisy, or inflamed eyes. Regarding diseases of the throat he wrote. "We know very well what an incomparable effect blistering has in a rheumatism, toothache, in common sore throat and in all colds or rheumatisms in what place so eve; so that there is reason to expect a good effect in this disease likewise. But bleeding and leeches ought, without dispute, to have been used before hand.<sup>19</sup>

The leeches was brought back into the middle domain in the middle of the 20<sup>th</sup> century, its use was called as hirudotherapy. With the advent of microsurgery including plastic and reconstructive surgeries the doctors found a use for the leech in modern medicine, primarily in the reattachment of fingers, toes, arms, ears and noses and even in breast reconstruction. In operation one of the biggest problems that arises is venous congestion, the excess blood from the injured or reattached tissue needs to be removed. If the blood is not cleared quickly, the blood begins to clot, the arteries that bring the fresh oxygenated blood will become clogged and the tissues that were reattached will decay and die.

Venous congestion may lead to edema, capillary and arterial slowing, arterial thrombosis, flap ischemia and eventual necrosis. The main reason why leeches are employed in microsurgeries is to reduce this venous congestion. After the operation, the use of leeches should be withheld as long as possible. This is due to the anesthetic in patient's body.

A leech in contact with anesthetic will not feed a phenomenon that is called as lazy leech syndrome. In 1983, Handerson et al. reported a case where leeches were used in the post operative treatment of a scalp avulsion case.<sup>9</sup>

In 2004 Leech therapy was classified by the US Food & Drug Administration (FDA) as a medicinal device.<sup>5</sup>

Properties	Non poisonous leeches	Poisonous leeches
Head	Tiny Head	Large Head (When compared to non poisonous leech)
Body cover's with hair	No	Yes
Line's on body	2 yellow stripes Emerald green colour	Blue stripe Chameleon colour
Found in water	Water which has weed & frogs	Dirty water
Tail	Round, thin, Mouse like tail.	-

Ayurveda by the name Poisonous leeches produces Inflammation, Hemorrhage, Fever, Syncope, Paralysis Intractable ulcers.<sup>1</sup>

**Likely Mechanism of action:**

In chronic wound blood supply to effected organ get reduced by developing clot formation, Vaso-constriction etc, which cause ischemia and necrosis of peripheral tissue and develops debris.

This debris occupies the surface of ulcers & delayed wound healing.

However, the saliva of leech contains about 100 pharmacologically active biological substances like Hirudin, hyaluronidase etc which are vasodilators, anesthetics, anti-inflammatory etc.

These substances are injected into human body by the leech while sucking blood which induce analgesic, anticoagulant, antiplatelet aggregation anti-inflammatory substances, anesthetic agents and gelatinous substances.<sup>5</sup>

Leeches suck the excess blood to reduce the swelling in the tissue, and promote healing by allowing fresh oxygenated blood to reach the area until normal circulation can be restored which helps in the process of regeneration and

**Description of Leech**

Eminent Unani Physician classified leeches in 2 categories as poisonous & Non poisonous in his famous book Al qanoon fit tib.

Also the same has been mentioned in Ayurvedic famous book Sushruta samhita and describe 12 different leeches (6 poisonous, 6 non poisonous).

Properties of poisonous & Non poisonous leeches has been described in Table 1,

repair of surrounding parenchymal tissues which includes angiogenesis and granulation tissue formation.<sup>16</sup>

In review of the function of various active substances which has varied function on ulcer.

The leech therapy is classified as follows.

- 1) Inhibit Thrombin/ Factor Xa activity Inhibitor
  - Hirudin
  - Factor Xa Inhibitor
- 2) Platelet aggregation inhibit group
  - Seratin
  - Calin
  - Apyrase
  - Leech anti platelet protein
- 3) Fibrin dehydrating group
  - Destabilase
- 4) Anti inflammatory group
  - Bdelins
  - Eglins C
- 5) Vasodilators / Increase bloodflow
  - Histamine like substances
  - Acetylcholine
  - Caroxypeptidase-A
- 6) Microbial peptide group
  - Hirudomacin
  - Hyalourinidase

Constituents of leech saliva are described in Table 2.

S. No.	Constituent	Function
1	Hirudin	Inhibits blood coagulation by binding to thrombin.
2	Factor Xa inhibitor	Inhibits the activity of coagulation factor Xa by forming equimolar complexes.
3	Seratin	Prevents the platelet adhesion & intimal hyperplasia
4	Decorsin	A glycoprotein which inhibit platelet aggregation
5	Calin	Inhibits blood coagulation by blocking the binding of von Willebrand factor to collagen, Inhibits collagen mediated platelet aggregation.
6	Destabilase	Monomerizing activity. Dissolves fibrin. Thrombolytic Effects.
7	Bdelins	Anti-inflammatory. Inhibits trypsin, plasmin, acrosin.
8	Eglin C	Anti inflammatory
9	Apyrase	Anti inflammatory

		Inhibitor of ADP-Induce platelet aggregation.
10	Histamine like substances	Vasodilators Increase blood flow at bite site
11	Acetylcholine	Vasodilators
12	Caroxypeptidase-A	Increase inflow of blood at bite site
13	Hylarourinidase	Increase intestinal viscosity ans antibiotic action.
14	Anesthetic agent	Anesthetic action

### Hirudin

- It is an acidic polypeptide which is secreted by salivary glands of *Hirudo Medicinalis*.
- It has been demonstrated to possess potent antithrombotic effect.
- It is a 7.1-KDa protein irreversible binding to thrombin by binding to thrombin, it hinders blood coagulation.<sup>18</sup>
- It contains 3 pairs of disulphide bonds have been proved in the N-end of hirudin (CyS6-CyS14, Cys16-Cys28, CyS32-CyS39) which foam compact structure & bind to active site of thrombin
- Thrombin exerts a significant role in the clotting system .It converts fibrinogen to fibrin & facilitates the stabilization of fibrin and the amplification of fibrin formation by activating facto XIII, V, as well as VII.<sup>11</sup>
- Thus this component helps to prevent the clotting and enhance the flow of blood towards the effected side.

### Factor Xa inhibitor

Factor Xa works both extrinsic & intrinsic pathway, it is also a pro-thrombin activator which converts pro-thrombin to thrombin.

Factor Xa inhibitor hinder the coagulation factor Xa activity, it plays a vital role to reduce clot formation, enhance the blood flow towards effected side and accelerate the healing of chronic ulcers.

### Bdellins

A proteinase inhibitor Bdellins is been extracts of leech saliva which acts as inhibitor for trypsin, plasmin & acrosin. It is most essential anticoagulants currently described from medicinal leeches and it also plays a significant role to inhibit clotting, acts as anti inflammatory effects.<sup>18</sup> Trypsin does not clot the fibrinogen directly, but react with prothrombin to foam thrombin. Thus Bdellins display strong anti-inflammatory inhibitory activity towards the trypsin which inhibit clot formation, enhance the blood flow towards effected side and accelerate the healing of chronic ulcers.

### Eglins C

Eglin c is a natural protein from the leech *Hirudo medicinalis* which contains 70 amino acids. It powerfully prevents the chymase, alpha chymotrypsin, subtilisin, elastase, and cathepsin G activity. It also attracted particular attention as a possible therapeutic agent against various pathogenic elastic tissue agents, blood clotting disorders and inflammatory processes.<sup>18</sup>

### Calin

Platelet surface use to bind the collagen of exposed area with the help of Von Willibrand Factor of damage endothelium. Calin binds to Von Willibrand Factor & inhibits platelet

adhesion which enhance the blood flow towards effected side and accelerate the healing of chronic ulcers.<sup>6</sup>

### Apyrase

- It is an antithrombotic & anti inflammatory salivary enzyme found in saliva of *Hirudo medicinalis*
- It inhibit ADP-Induce platelet aggregation and prevents aggregation of pletelets and clot formation.
- ADP is the oldest and one of the most important agonists of platelets activation, It induce platelet shape change, exposure of fibrinogen binding site, aggregation & its importance for maintaining normal heamostasis.<sup>17</sup>
- Thus Apyrase plays a significant role in inhibit ADP-Induce platelet aggregation and prevents aggregation of pletelets and clot formation enhance the blood flow towards effected side and accelerate the healing of chronic ulcers.

### Hyalourinidase

Hyalourinidase can be used to realize various complication associated with Hyalournic acid.<sup>18</sup>

It enables the diffusion & penetration of pharmacologically active material into the tissue & possesses antibiotic features. It is also use to treat heamatomas.

### Histamine

It helps in the vasodilation of blood vessels which incease the blood flow towards the effected side.

It can produce vasodilation of submucosal arteries by in induce by the given mechanism

Activation of vascular H1 receptors results in release of nitric oxide from endothelium & activation of H3 receptors on sympathetic nerve terminals resulting in pre-synaptic inhibition of vasoconstriction tone.<sup>2</sup>

Thus the vasodilatation activity enhance blood flow towards the effected side & accelerate the healing process. (“Jalauka” meaning leeches and “Avacharan”

### Procedure of application:-

- 1) Pre-therapeutic Procedure
- 2) Therapeutic procedure
- 3) Post Therapeutic procedure

### Pre-therapeutic Procedure

#### (a) Preparation of leech

The leeches are to be preserved in fresh spring water. The water needs to be changed every day or twice daily depending on the temperature. Traditionally the leeches are being kept in earthen pots as the pores present in the pot keeps the atmosphere for the leeches cool. The temperature

should be maintained between 5 and 15 degree centigrade, fresh spring water can be used.

Leech should be held upside down to empty the stomach & sponged clean of the dirty viscid slime.<sup>13</sup>

Then they should be fed on a small quantity of blood from a goat or some other Animals.

#### **(b) Preparation of Patient.**

The part to be treated should be washed with a solution of Borax & Rubbed until it get red.

Little Clay or blood smear apply on the part of treatment for better stick.<sup>12</sup>

#### **Investigation should be done before the procedure**

- 1) Vitals & Blood Pressure
- 2) Hemoglobin estimation (Hb%)
- 3) Bleeding Time & Clotting Time (BT, CT)
- 4) HIV to avoid cross infection
- 5) Complete heamogram
- 6) Hb1AC.<sup>10</sup>

#### **Standard Operating Procedure:**

Ideally aseptic & separate room should be there which is well equipped with

- 1) Patient bed
- 2) Separate tank / Bottle for storage of leech
- 3) Dressing trolley which has sterilized gloves, gauge pieces, Normal Saline, Turmeric powder, Soap, Sufoof Habiss uddam, Dressing material.<sup>10</sup>

#### **Therapeutic Procedure**

The desired site is cleaned with wet gauze. Leech is held at its neck with finger and applied to the skin.

Once leech start sucking the blood, they are covered with wet gauge and cold water is poured on it time to time, as to make leech comfortable during sucking.

If leech do not catch the site by its own, then rub the site of leeching to increase bleeding may be required so as to facilitate the sucking procedure.

The leech when once starts sucking the blood elevates its neck, and fix its head to the supporting point of skin. Once can observe wave like movements indicating sucking of blood.

Leave it for 30 - 60 minutes.<sup>10</sup>

When leech become fully satisfied with its food, it leaves off the skin of patient and drop itself down.

If this is not happened, then patient may feel itching sensation which indicates impure blood from that spot is no more available for the leech.

In such case, a little turmeric powder is sprinkled on the sucking point of the leech and immediately the leech takes away its mouth from that point.<sup>12</sup>

#### **Post Therapeutic Procedure**

##### **(a) For Patient:**

Leech removed from site & it is cleaned with normal saline (or) other antiseptic solution.

After that apply hemostatics like gile armani, aspand sokhta, katan sokhta, damul akwain etc.

Turmeric powder should be sprinkled on bleeding side.<sup>12</sup>

Bandaging is done to arrest bleeding.

Glucose, ORS can be offered to patient.

Patient is allowed to sit for few minutes before leaving the place.

##### **(b) For leeches:**

Leech after use are kept in an empty tray.

Turmeric powder is sprinkled on its mouth just to induce vomiting, so that it induce vomit the blood.

After that leech is again washed with clean water.

At the end leech is transferred to separate jar and kept starved for normally 7 days.<sup>10</sup>

#### **Indications:**

Leech therapy is useful in Abscess, Thrombophelibitis, Eye, Ear, Throat disorders, Hypertension, Skin diseases and chronic ulcers.

According to ancient Indian physician, Leech is applied around chronic wound like Elephantiasis. Gangrenous ulcers, erosive ulcers of ear, nose, breast, also it is applicable at places where poisonous animals have bitten.<sup>12</sup>

Unani Physicians also mentioned that application of leeches are helpful where we cannot evacuate humour by hijama & fad.<sup>12</sup>

Mechanism of action of leeches in wound healing process is

- The Local necrotic and inflammatory reaction were decreased.
- The period of inflammation was reduced.
- Epithelialization and Granulation were accelerated.

#### **Precaution:**

- One should not apply Leeches to major veins like Femoral or Jugular veins and to the delicate parts like Breast, Penis, Eyelids.
- Used leeches should be kept in separate jars.

#### **Contraindication**

- Hemophilia
- Pregnancy
- Leukemia
- Anemia
- Arterial insufficiency
- Patient refuse to accept blood transfusion
- Patient refuse to undergo leech therapy
- Leech itching / Allergens
- Transmission of infectious diseases
- Hypotension
- Cold weather.

### **3. Conclusion**

These days many patients are turning up to OPD's with age to 60 years mostly as a complication of Diabetes Mellitus, Varicose veins etc. The incidence is 0.78% of the population.

Application of Medicinal Leech Therapy (MLT) is safe and cost effective procedure instead of long term usage of high dose of antibiotics, which is not only fasten the wound healing but also reduces the adverse effect of long term of antibiotics and other medication.

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Ayurveda by the name of “Jalaukavacharan” („Jalauka“ meaning leeches and „Avacharan“ Ayurveda by the name of “Jalaukavacharan” („Jalauka“ meaning leeches and „Avacharan meaning application). As per Ayurveda Jalaukavacharan is one of the procedures of Raktamokshana. Raktamokshana is one of the biopurification methods mentioned in Ayurveda, in which humours vitiated in blood are expelled from the body