



## Medicinal leech therapy (Hirudotherapy) : A brief overview

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### A B S T R A C T

**Keywords:**  
Hirudotherapy  
Medicinal leech  
Hirudin

Hirudotherapy is a treatment using medicinal leeches. *Hirudo medicinalis*, have been used to treat patients for centuries. In the past, leeches have proved to be an effective treatment for a number of conditions including battle wound treatment. Currently leeches may be used to assist in the treatment of abscesses, arthritis, glaucoma, myasthenia gravis, thrombosis and some venous disorders. Medical leeches may also be used in plastic surgery and in some blood circulatory problems. During feeding, leeches secrete a complex mixture of different biologically and pharmacologically active substances into the wound. Hirudin is the prominent constituent of leech saliva. It is sometimes used to describe all the active constituents in the leech saliva. This paper outlines the potential use of leech therapy in current medical care in India.

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### 1. History of hirudotherapy

In medieval and early modern medicine, *Hirudo medicinalis* were used to remove blood from patients in an attempt to balance the 'biological humours'. In Ayurvedic or traditional Indian Medicine, these three humours are referred to as *vata*, *pitta* and *kapha*, and in Unani or Traditional Arabian Medicine they have been depicted as four humours: black bile, yellow bile, blood and phlegm. The 'biological humours' are perceived as an integral aspect Ayurvedic and Arabian Medicine philosophy. Equilibrium between the 'biological humours' is seen to be essential for the proper functioning of the human body.<sup>1</sup>

Hirudotherapy was introduced by Avicenna in 'Canon of Medicine' in 1020. More recently the medicinal use of leeches was introduced by Abd-el-latifal-Baghdadi in 12th century, who claimed that leeches could help to promote cleaning tissues after surgical operations.<sup>2</sup>

Medicinal leeches appear to provide one method of reducing blood coagulation, relieving venous pressure from pooling blood, especially after plastic surgery and to stimulate blood circulation.<sup>3</sup> As hirudin is present in minuscule amounts, it is synthesised using recombinant technique.

The Composition of leech saliva is tabulated below:

Sno	Constituent	Function
1	Hirudin	Inhibits blood coagulation by binding to thrombin
2	Calin	Inhibits blood coagulation by blocking the binding of Von willebrand factor to collagen. Inhibits collagen-mediated platelet aggregation
3	Destabilase	Monomerizing activity. Dissolves fibrin
4	Hirustatin	Inhibits kallikrein, trypsin, chymotrypsin, and neuropholic cathepsin G
5	Bdellins	Anti-inflammatory, inhibits plasmin, trypsin and acrosin
6	Hyaluronidase	Increases intestinal viscosity and antibiotic action
7	Tryptase inhibitor	Inhibits proteolytic enzymes of host mast cells
8	Eglins	Anti-inflammatory. Inhibit the activity of $\alpha$ -chymotrypsin chymase, substilisin, elastase and cathepsin G
9	Factor Xa inhibitor	Inhibits the activity of coagulation factor Xa by forming equimolar complexes
10	Carboxypeptidase-A	Increases the inflow of blood at the bite site of inhibitors
11	Acetylcholine	Vasodilator
12	Histamine like	Vasodilator

### 2. Research on leeches<sup>4,5</sup>

Leeches live in water and commonly feed on decaying plant material. They detect humans by skin oils, blood, heat, and even the carbon dioxide we breathe. Leech saliva is currently being explored to detect specific medicinal compounds which may be developed to enhance blood anticoagulant and clot-digesting properties in order to develop drugs for the treatment of cardiovascular diseases such as myocardial infarction or stroke. Leeches have also been used in

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the past to remove congested blood in order to encourage normal circulation to return to damaged or infected body tissue, thus helping to prevent the onset of gangrene.

### 3. Hirudotherapy<sup>6</sup>

Leeches absorb blood either through their proboscis which is used to puncture the skin or by bite. This is similar to a mosquito bite and is not painful due to the release of a histamine-like substance. Leech saliva also contains an anaesthetic so that patients do not feel the bite. In addition the saliva has a chemical preventing blood clotting. However there may be occasions such as cold skin, smoking or age related issues that may affect the anaesthetic qualities of a leech bite. This can be resolved by warming and cleaning the skin.

### 4. Mode of action of hirudotherapy<sup>7,8</sup>

The mechanism of action appears to be the secretion of biologically active substances from the salivary glands of the leech onto living organisms. There are 100 different of bioactive materials in leech saliva. The most common found is hirudin, a substance which oppresses the process of blood clotting. Secretions from the leeches salivary glands also contain anti-inflammatory, bacteriostatic, and analgesic actions. These eliminate micro-circulation disorders and, restore the damaged vascular permeability of tissues and organs, eliminate hypoxia, reduce blood pressure, increase immunity, increase the bioenergetic status of the organism.

The mechanism of oppressing thrombin, blocks the action of thrombin and the transition of fibrinogen into fibrin. Secretions from the salivary glands of medicinal leeches also block the attachment of thrombocytes and this completely suppresses their aggregation on the surface of collagen. Thus, medicinal leeches saliva secretions has a direct influence upon cellular and plasma factors associated with blood clotting.

Currently hirudotherapy is used extensively by reconstructive surgeons to remove stagnant blood from a skin flap when managing reattached limbs. Stagnant blood pooling in wounds can lead to increased venous pressure. This may inhibit the flow of fresh oxygenated arterial blood from entering the area and supplying the wound with oxygen and nutrients. By reducing venous blood using hirudotherapy, blood pooling pressure can be reduced in order to save limbs or flaps. Leeches are extremely well suited for this process since their saliva contains important biochemical substances including vasodilators, anti coagulants and anesthetics.

Contrary to popular belief, Leeches commonly only absorb about 5 ml of blood. However, if more leeches are applied to the affected site their impact is enhanced. After treatments lasting between 3 and 7 days, damaged veins have usually healed sufficiently so that blood pooling is considerably minimised in the limbs. As a result the affected area will resume normal colour and venous pressure, encouraging blood flow to damaged tissue cells, to enhance wound healing.

### 5. Clinical trials

#### 5.1. Venous disorders

In 1995, a study was conducted to assess the efficacy and associated complications of a leech therapy protocol for patients with head and neck tissue transfer, for whom flap viability was threatened by surgically unsalvageable venous obstruction. Of 450 free tissue transfers to the head and neck region performed 1995 and October 2000, 8 patients (1.8%) developed venous obstruction not considered salvageable by conventional surgical or thrombolytic therapy.

All 8 patients were placed on a protocol using leeches, intensive care unit monitoring, antithrombotic pharmacotherapy, regular hematologic evaluation, blood transfusions as needed and antibiotic prophylaxis for *Aeromonas hydrophila*. The main outcome measures included flap salvage rate, number of leeches used per patient, time required for inosculation, duration of intensive care unit admission, transfusion requirement per patient, and complications during leech therapy.

All 8 flaps survived with the application of this protocol. Approximately 215 leeches were used per patient, and the average time needed for inosculation was 6.6 days. The average duration in the intensive care unit was 9.6 days.

At the end of the study, it was concluded that aggressive application of the presented leech therapy protocol can salvage free tissue transfers with venous obstruction that are otherwise unsalvageable. Thus, judicious application of this protocol for flap preservation is essential.<sup>9</sup>

#### 5.2. Sialadenitis

Twenty patients with chronic inflammatory and dystrophic diseases of the salivary glands (sialadenitis, sialadenosis) were examined and treated using hirudotherapy. Positive clinical shifts were observed in 50% patients; the most pronounced therapeutic effect was observed in patients with sialadenosis. Hirudotherapy was ineffective in patients with chronic parenchymatous parotitis paralleled by Sjogren's syndrome.<sup>10</sup>

Hirudotherapy was used in the treatment of 39 patients (10 male and 29 female) aged 28–58 years with chronic sialadenitis and sialadenosis. The control group consisted of 15 normal subjects without salivary glands diseases. Lipid peroxidation and antioxidant defense parameters were studied. Hirudotherapy led to an improvement in the clinical status for the majority of patients with sialadenosis in addition to the content of superoxide dismutase normalized and ceruloplasmin level increased. The status of patients with sialadenitis also improved; catalase and glutathione peroxidase levels and superoxide dismutase normalized and ceruloplasmin levels increased. The best therapeutic effect was attained in patients with sialadenitis. No appreciable improvement was observed in patients with chronic parenchymatous parotitis in the presence of Sjogren's syndrome.<sup>11</sup>

#### 5.3. Osteoarthritis

An 87-year-old woman with severe joint pain due to osteoarthritis of the knee presented with side effects from fentanyl therapy. She was subsequently treated in an inpatient setting with leeches, phytotherapy, physiotherapy and three single doses of metamizol. Pain reduction was assessed with a numeric rating scale (0–10; 0 = minimum; 10 = maximum), mobility by walking distance, and activities of daily living by Barthel index.<sup>12</sup>

The association between complementary therapy and the changes observed in the patient under treatment were evaluated using cognition-based medicine. Under complementary therapy, the patient experienced a clear reduction in pain (from 8 to 3 points on the numeric rating scale); regained the ability to walk (increase in walking distance from 0 to 70 m); and showed improvements in activities of daily living (increase in Barthel index from 45 to 65).

A further study focused upon 113 patients with advanced osteoarthritis of the knee. The patients were randomized to a single treatment group, group I (single leech application,  $n = 38$ ), a double treatment group, group II (double application,  $n = 35$ ), and a control group ( $n = 40$ ). The second treatment in group II took place after an interval of 4 weeks. The treatment in the control group was

simulated with the help of an “artificial leech”. Results were documented with the KOOS and WOMAC scores and also a visual analog scale for pain. Changes in the use of pain medication were monitored over 26 weeks.

An improvement in KOOS and WOMAC scores, and also in VAS, was found in all 3 groups following treatment. These improvements were statistically significant for treatment groups I and II during the complete follow-up period. The reduction in individual requirements for pain medication was also statistically significant. The greatest improvement was seen in the group treated twice with the leeches, with a long-term reduction of joint stiffness and improved function in the activities of daily living.<sup>13</sup>

#### 5.4. Advantages of hirudotherapy<sup>1,3</sup>

- More concentration of drug is required to reduce nidus of inflammation in blood, so that it causes allergies and strikes several reactions on liver and kidney. At this time, hirudotherapy is useful; to restore blood circulation in nidus of inflammation, improve immune protection and regeneration of tissues.
- The content of leech saliva inhibits the growth of bacteria. Hirudin has bacteriostatic and bactericidal action.
- The secretion of saliva-penetration of enzymes galuronidase, is capable of inactivating the action of galuron acid, which is the cementing substance for conjunctive tissues.
- Improves the lung ventilation and unloading of the heart.
- The lipotropic enzyme in leech saliva may be used for atherosclerotic defect of vessels irrespective of primary localization of atherosclerosis.
- Reduction of swelling, the dissolution of organised blood clot and increased local immunity.

#### 5.5. Potential problems of hirudotherapy<sup>1,2,4</sup>

Medicinal leeches (*hirudo medicinalis*) are increasingly used as a useful therapeutic option in various medical and surgical settings. The potential complications associated with this therapy include infections with *Aeromonas* species, bleeding, anemia, and allergic reactions. We describe a patient who developed thrombotic

microangiopathy and acute renal failure following leech therapy. It is proposed that the series of non-human proteins within leech saliva may be capable of injuring the endothelium.

## 6. Conclusion

Leeches currently perform an effective job of removing pooled blood from wounds than any other medicinal therapy. Hirudotherapy increases nutrients of the tissues, so that wound healing is enhanced, so promoting healing. They are also easy to use. Despite having been in recorded medical use for centuries, research continues to be conducted into this therapy. It is suggested that Hirudotherapy is an effective remedy that can assist in the management of a range of wounds and wound healing and possibly in the care of different diseases. Hirudotherapy is also a treatment with rare side-effects.

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