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An evidence based approach of Unani regimen: Irsal e Alaq (Medicinal leech therapy)

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Abstract

Complementary medicine methods have a long history, but modern medicine has just recently focused on their possible modes of action. Medicinal leech therapy (MLT) or hirudotherapy, an old technique, has been studied by many researchers for possible effects on various diseases such as inflammatory diseases, osteoarthritis, and after different surgeries. *Hirudo medicinalis* has widest therapeutic usage among the leeches, but worldwide, many different species were tested and studied. Leeches secrete more than 20 identified bioactive substances such as antistasin, eglins, guamerin, hirudin, saratin, bdellins, complement, and carboxypeptidase inhibitors. They have analgesic, anti-inflammatory, platelet inhibitory, anticoagulant, and thrombin regulatory functions, as well as extracellular matrix degradative and antimicrobial effects, but with further studies, the spectrum of effects may widen. The technique is cheap, effective, easy to apply, and its modes of action have been elucidated for certain diseases. In conclusion, for treatment of some diseases, MLT is not an alternative, but is a complementary and/or integrative choice. MLT is a part of multidisciplinary treatments, and secretes various bioactive substances. These substances vary among species and different species should be evaluated for both treatment capability and their particular secreted molecules. There is huge potential for novel substances and these could be future therapeutics.

Keywords: *Hirudo medicinalis*, hydrotherapy, medicinal leech therapy

Introduction

Medicinal leech therapy (MLT) or hirudotherapy is a kind of complementary and integrative treatment method applied with blood-sucking leeches. One or more leeches are attached to the skin of problematic area and the purpose is to gain potential utilities of leech saliva that is secreted while the leeches are feeding. MLT has been used for centuries and the term leech was provided from the word “laee” (physician).

Aim and Objective

To propagate the miraculous effects and feasibility of Leech therapy in the Medical arena.

Review of literature

Irsal e Alaq (Medicinal Leech Therapy) comes under the regimen of *istefragh*. *Istefragh* is one of the *asbab e sitta e zarooriyah*. In *Istefragh*, evacuation of morbid matter (*mawad e fasida*) is done which tends to produce the disease. *Tabiyat* naturally tends to evacuate the morbid matter from the body. It is called *Istefragh e tabayi*. But otherwise when *tabiyat* fails to evacuate, then it becomes the duty of physician to evacuate it. This is called *Istefragh e sanavi*. *Istefragh e sanavi* is further divided into *Istefragh e qawi* and *Istefragh e zaef*. Medicinal Leech therapy comes under *istefragh e zaef*.

Historical background

Medicinal leeches are as old as pyramids. Records indicate the Egyptians used leech therapy 3,500 years back i.e., in 1500 BC. And leeches (often mistakenly credited as cobras) are included in the hieroglyphics painted on the walls. The 1st written document on leech therapy was by a Greek poet and physician Nicander of Colophon in 200 BC. *Al-Jalinoos* in the 1st cent AD prescribed bloodletting by leech for almost all illnesses such as simple inflammatory conditions, mental disorders and hemorrhoids. *Zakariya Razi* (10th century AD) advocated use of leech in different diseases like *Qooba* (ring worm infection), *Sa'fa* (alopecia), *Quroohe balkhiya* and *Amraze- Mafasil* (joint diseases) etc. [29] *Ibn e Sina* (980-1037AD) mentioned in his book “*Al Qanoon*” that leech can suck blood from deep veins which cannot be leeching for various skin diseases [33].

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Ismail Jurjani (12th Century) has described that if complete evacuation of the morbid material is to be intended, *Taleeq* (Leech therapy) should be performed for two consecutive days. He also advocated its benefit in skin diseases. He quotes Baghdadadi’s recommendation the application of leeches after cleaning the body through *Fasad* (venesection) and *Is’hal* (purgation) [18]. In 12th century, Abdul lateef al Bughdadi mentioned in his texts leeches could help in cleaning tissues and promote healing after surgical operations, by encouraging regrowth of microculation [8, 33] Ibn-ul-Quf al Maseehi (1233-1286 AD) says that Taleeq (Leech therapy) eliminates the morbid materials more vigorously in comparison to *Hijamat* (cupping) but lesser to *Fasad* (venesection). He emphasized the pre and post leeching procedures and stressed that cupping should also be done after performing *Taleeq* (Leech therapy). He further added that leeches should be applied before using the local drugs in *Sa’fa* (alopecia) [4]. Akbar Arzani (16th century), an Indian physician states that *Taleeq* (Leech therapy) is a substitute for Fasad (venesection) in cases of children. He mentioned its main benefit in *muzmin amraze jildiah* (chronic dermatological diseases) like *Sa’fa* (alopecia) and *Qooba* (ring worm infections) [6].

Broussais in 1700s in France treated Typhoid fever, Syphilis, Variola and TB by applying leeches. Later in the 1800’s there was such a demand of leech therapy that a wave of “*leechmania*” has spread all over Aristocracy of the European countries and America, which had later led to endangerment of the species.

Medicinal Leech

Leeches are blood sucking annelid worms. Leech has segmented bodies. Their mouth is tri radiate, they have 3 jaws and each jaw has 80-100 teeth, and gives characteristic Y shape incision at the site of bite. They have 2 suckers, anterior sucker and posterior sucker. The anterior sucker is the proboscis which is meant for feeding and attachment and the posterior sucker is meant for attachment and locomotion. The characteristic features of medicinal leeches are that they Small head, small bodies. They have Emerald green color or greenish brown color with two yellow stripes running along the body (Figure 1). Usually found in clean water lakes and ponds, covered with weeds where frogs exist [10].



Fig 1: The Medicinal Leech

Procedure of Leech Therapy

The legendary Unani scholar, *Ibne Sina* in his famous treatise “Canon of Medicine”, has described the procedure of Leech therapy in a very comprehensive manner and narrated the following steps of the whole procedure [31]: One day prior to the procedure, leech is made to vomit by putting in the water containing turmeric. Then they are transferred to clean water with wide mouth bottle. It is necessary to keep them fasting. Later on day of use active leeches are selected for the therapy. The Desired part for the procedure is localized. It is cleaned with distilled water and rubbed to make it red, before application of Leech. Application of Alcohol for cleaning purpose is avoided as the leech gets hesitant towards the smell of alcohol. If it is reluctant to bite, a tiny droplet of blood is drawn by needle prick and leech is applied. When Leech mouth gets protruded like hoof of horse, it should be determined that leech has started sucking blood. Leeches generally suck 2-20 ml of blood within 10-30 min, then drop-off spontaneously after being completely engorged with no immediate desire of more feeding [27]. Never pull Leech while removing, instead sprinkle some salt to facilitate detachment. If a leech is forcibly removed by pulling it, its teeth get embedded in the skin and can cause local irritation. Since these contain bacteria, there is also a liability for secondary wound infection. Cups are used over the site to drain out toxins after removing leech. The used leeches are then killed and disposed off.

Table 1: The saliva of Leech contains various pharmacologically active biological substances as follows: [17].

1.	<i>Hirudin</i>	Inhibits blood coagulation by binding to thrombin.
2.	<i>Calin</i>	Inhibits blood coagulation by blocking the binding of von-Willebrand factor to collagen-Mediated platelet aggregation.
3.	<i>Destabilase</i>	Monomerizing activity. Dissolves fibrin. Thrombolytic effects.
4.	<i>Hirustasin</i>	Inhibits Kallikerin, Trypsin, Chymotrypsin, Neutrophilic Cathepsin G.
5.	<i>Bdellins</i>	Anti- inflammatory, Inhibits trypsin, Plasmin, and Acrosin.
6.	<i>Tryptase inhibitor</i>	Inhibits Proteolytic enzymes of host mast cells.
7.	<i>Eglins</i>	Anti- inflammatory. Inhibits activity of alpha- Chymotrypsin
8.	<i>Ghilanten</i>	Anti metastatic.
9.	<i>17-kDa protein (Antistasin)</i>	Prevent lung cancer colonization
10.	<i>Bufrudin</i>	Thrombin inhibitor
11.	<i>Theromin</i>	Thrombin inhibitor
12.	acetylcholine and carboxipeptidase	Vasodilator
13.	Complement inhibitors	May possibly replace natural complement inhibitors, if they are deficient.

Mechanism of Action of Irsal E Alaq (Hirudotherapy)

Leech saliva contains a range of more than 100 bioactive substances that exert manifold pharmacological effects. The efficacy of leeching is based on a combination of multiple effects resulting in

Anticoagulation & Hemodilution

When a leech bites, the bite wound immediately begins to bleed and continues to bleed for several hours. This prolonged bleeding is due to the presence of hirudin and other anticoagulant substances in leech saliva. Hirudin is a potent anticoagulant in leech saliva. Leech therapy restores the micro circulation and restores the damaged vascular permeability of tissues and organs and eliminates hypoxia. The mechanism of opposing thrombin, blocks the action of thrombin and the transition of fibrinogen into fibrin. Secretions from the salivary glands of the medicinal leeches also block the attachment of thrombocytes and this completely suppresses their aggregation on the surface of the collagen. This is attributed by calin, saratin, apyrase, decorsin and collagenase [28]. These salivary secretions of leech contain components which inhibit both the coagulating and platelet-vascular wall pathways of hemostasis.⁷ Thus, medicinal leech's saliva secretion has a direct influence upon cellular and plasma factors associated with blood clotting. Inhibition of platelet aggregation and extracellular matrix degradation

Anti-inflammatory effect

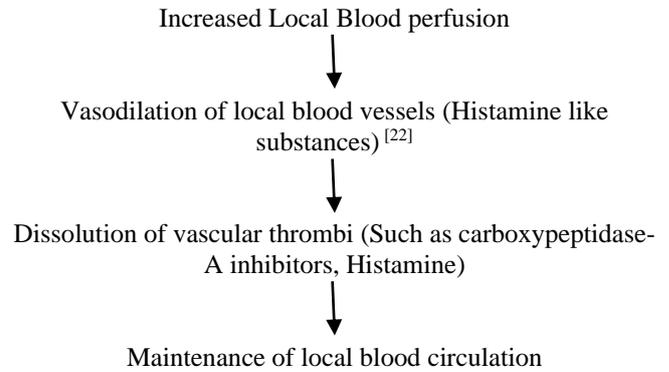
Hirudin inhibits the pro inflammatory cytokines in the inflammatory. It has been proved in osteoarthritis where the pro inflammatory cytokines were inhibited in synovial fluid by leech therapy. It also reduces inflammation and histological reduction of the synovial membrane in osteoarthritis. Apart from hirudin, Bdelins and eglins also have anti-inflammatory effect.

Immunomodulating stability

Eglin C is an inhibitor of human neutrophil elastase and cathepsin G [35]. These two enzymes are immune serine proteases in the chymotrypsin family that are stocked in azurophil granules of polymorphonuclear neutrophils and released as a part of the inflammatory response.^{20,23} Inhibition by eglin C causes decreasing levels of free oxygen radicals in neutrophils and prevents tissue inflammation and destruction. In test models, eglin C was shown to be a potential therapeutic agent for shock and emphysema [35]. Further studies are needed to show other potential effects, but the molecule itself is promising. Other isolated eglins act in similar ways, resulting in anti-inflammatory and immunomodulator effects.

Enhancing Blood Circulation

The increase in blood flow on feeding site is caused by vasodilatation, endothelial muscle relaxation and by increasing local vascular permeability. This effect is result of activities of carboxypeptidase inhibitor, acetylcholine and histamine like substance present in LS. Carboxypeptidase inhibitor of LS inhibits a metalloproteinase which is responsible for the cleavage of kinin in blood plasma. This increased kinin result in blood flow to the feeding site [19].



Enhancing Lymph Circulation

A controlled study of wound-healing in rats, using an electric wound model, showed that leeching decreased local necrotic and inflammatory reactions, accelerated epithelization and granulation, increased the amount and balance of macrophage activity and enhanced the synthesis of new blood and lymphatic vessels [26].

The impact of leech saliva on wounds' local blood and lymph microcirculation appears an essential feature of wound healing, although details of the processes involved await further exploration [2].

Antimicrobial effect

To date, only two main molecules, destabilase and chloromycetin, have been shown to have antimicrobial activity. As previously stated, destabilase has β -glycosidase activity, which directly disrupts β 1-4 bonds that are important in the peptidoglycan layer in bacterial cell walls. It is clear that this action is similar to that of lysozyme (muramidase) that is commonly found in human saliva and lachrymal fluid. Other studies have shown that antimicrobial activity does not only depend on glycosidase enzymatic activity, but it also has nonenzymatic components. Even the denaturated form destabilase shows a dose-dependent bacteriostatic effect on *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Chloromycetin is a potent antibiotic found in leech secretions, but unfortunately the data are limited about this molecule. Additionally, theromacin, theromyzin, and peptide B have been isolated as antimicrobial peptides [2].

Tissue Neogenesis

When a concerned part with tissue hypoxia is subjected to leech therapy, the leeches suck morbid blood and increase local blood and lymph circulation. This is probably due to the action of hirudin and hyaluronidase (Penetration factor), which not only improves blood circulation, but also the capacity of capillary-tissues exchanging. There is a complex beneficial interplay of all the leech's salivary secretions which helps in the wound healing and tissue neogenesis.

Segmental (reflex) counterirritation and anti-nociception

Leech therapy is said to induce pain relief through antinociceptive effects and counter irritation. The leech saliva contains a number of pharmacologically active biological substances such as hirudin and hyaluronidase which are proved to have analgesic, anti-inflammatory, and anesthetic activities [24].

Other possible actions

Many *in vitro* studies have indicated the anticancer effects of leech saliva extracts. Since coagulation is related to metastasis and tumor progression, blocking the cascade can have an antitumor effect. Hirudin has been studied in this regard, with promising results for metastasis, especially from mesothelioma. In addition, other anticoagulant derivatives are claimed to have similar effects, as well as reducing cell growth and tumor angiogenesis. The extracts have been found to induce apoptosis and cell differentiation and cause cell cycle arrest. The main mechanisms of action seem to depend on suppressing oncogenic gene expression and up regulating apoptotic chains. Effects against cell degeneration have also been reported. Eglin C, bdellastasin, destabilase, bdellins, and hirudin are cytoprotective and exert positive stimulatory actions, especially on neurons, but these studies are only at the preliminary stage [2].

Indications of Leech Therapy

Cardiovascular Diseases

Leech therapy has been advocated in many cardiovascular diseases such as Arterial HTN, IHD such as MI. Since the early days of the 20th century, people have been using leeches to treat cardiovascular diseases because of the Hirudin enzyme in the leeches saliva, a substance which has systemic anticoagulative effects. It was first isolated from *H. medicinalis* and was shown to possess a potent inhibitory effect on both free and clot-bound thrombin. It dissolves fibrin, Stops thrombus formation, Relieves hypoxia and helps in better blood circulation. Also, Hirudin stimulates segmental reflex mechanisms and this contributes to the treatment of cardiovascular diseases. Apart from this it also helps in atherosclerosis of limbs. Furthermore, other thrombin inhibitors were identified from different leech species. For instance, bufrudin was isolated from *H.*

manillensis with a chemical structure closely similar to hirudin. A tight-binding thrombin inhibitor named haemadin was identified from the whole body extract of the leech species *Haemadipsa sylvestris*. Another antithrombin named granulin-like was isolated from the leech species *H. nipponia*. Finally, a human granulocyte and monocyte protein inhibitor known as theromin was characterized from the head extract of *Theromyzon tessulatum* leech species with an antithrombin activity [3].

Vascular congestion

Leech therapy is of great help in varicose veins, varicose ulcers and engorged hemorrhoids. It helps in venous decongestion, reversal of edema, Decreasing hyper pigmentation and Healing of varicose ulcer. The antimicrobial and antibacterial properties of leech saliva help in the healing of open sores in complicated venous congestion.

Varicose Vein

Zakaria Razi, Ibn Sina, Ismail Jurjani etc have mentioned *fasad in dawali* but M. Azam Khan and A. Arzani mentioned *taleeq* in varicose vein. The effect of leech therapy in varicose vein is due to the biochemical present in the saliva of the leech which contains anticoagulant, thrombolytic, anti-inflammatory, antibiotic, anesthetic and analgesic properties. Hirudin and calin are anticoagulants. Enzyme Destabilase has thrombolytic effect. Histamine like substances, acetylcholine and carboxipeptidase has vasodilator effect. Anticoagulant, thrombolytic and vasodilators present in saliva of leech produce prolonged bleeding and hypovolumic haemodilution of the blood which reduces pressure at the vessels and excretion of metabolites at the site of microcirculatory units [24].



Fig 2: Shows the difference of results in the therapies in the course of varicose veins [13]

Deep vein thrombosis

This condition commonly occurs after the operation under general anesthesia, when the calf muscles remain idle and fail to maintain the normal flow of blood within the deep veins, thus causing thrombosis. It also occurs following child birth, immobility or any debilitating diseases. The condition is asymptomatic, only 1/4th of the patients produce symptoms and signs [31]. Avicenna (980-1037 AD) delineated in his book "Canon of Medicine" that leech can suck blood from deep veins which cannot be reached by the conventional wet cupping and he recommended leeching for skin diseases [24]. Many studies revealed that hirudin is more effective than heparin in preventing deep venous

thrombosis. Furthermore, and unlike heparins, hirudin has a promising prophylactic activity in patients who are at a high-risk of developing cardiovascular events because it can hinder thrombus growth due to its ability to block thrombin-fibrin binding [30].

Skin Diseases

Ibn e Sina considered leech therapy as the best for skin diseases. Medicinal Leech therapy helps in curing Dermatitis, Psoriasis, Eczema and many other bacterial and fungal infections. Hakeem Syed Abdul Hameed Bhopali in his book *Takmeelut Tib* mentions with reference to some experts that leeches absorb only *Fasid khoon* (contaminated

blood) and they are very beneficial in chronic skin diseases like *Sa'fa* (alopecia) and *Qooba* (ring worm) etc. [11] It also helps in the management of Diabetic Ulcer, Quruhe Asratul Indamal (Non-healing Ulcer), Leprotic wound by tissue neogenesis mechanism. Leech application has peripheral vasodilator effect due to presence of vasodilator constituents in the saliva of leech which improves blood circulation and corrects the ischemia around the wound thus promotes wound healing. Leech application has anti-inflammatory action on nerves due to presence of substances like Bdelins and Eglins which prevents leucocytic accumulation in the surrounding vessels, thus inhibits release of inflammatory factors which causes chronic wound formation [30]. Apart from this Leech therapy also helps in many inflammatory conditions such as Thrombophlebitis, Filariasis, Cellulitis, Lymphadenopathy.

Reconstructive & Skin graft surgeries

Leech therapy has been used to treat acute postoperative venous congestion since the 1960s. In this indication, leeching has now got a big boost as an internationally established modality that can be classified as a standard treatment method. Venous congestion and subsequent thrombosis are serious and feared complications of skin flap transplantation and limb reconstruction surgery. The successful use of leeches to treat postoperative venous congestion after plastic and reconstructive surgery was mentioned by Dieffenbach as early as 1827. Leech therapy helped to restore microcirculation in the post operative part & helped in the healing process in reconstructive surgeries, thereby decreasing the risk of necrosis which develops as a complication. Objective proof of the improvement of blood flow was later provided by Doppler laser studies performed by Hayden [1].

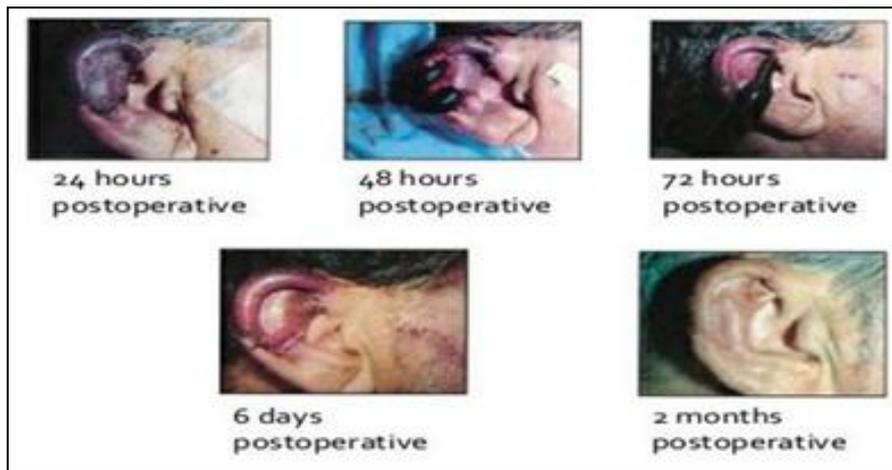


Fig 3: Showing the usage of Leech therapy in Postoperative Reconstructive surgery.¹⁵

Audiology and ear abnormalities

Greek physicians like Galen used leeches for bloodletting and for treating rheumatic pains, gout, all types of fever and hearing loss. It was reported that leeches and their salivary secretion were successfully used for the treatment of tinnitus, acute and chronic otitis. Leeching has been applied in sudden hearing loss. In such cases, the therapist used just two leeches; one behind the ear and the other one over the jaw in front of the ear, and the treatment was repeated 2-3 times at intervals of 3-4 days. Despite the unexplained reasons of tinnitus, leeches were proven to be of great benefits in the treatment of this disorder.

Gynecological Disorders

Medicinal Leech therapy has best results in gynecological disorders. It has been found that leech therapy is very beneficial to women who are suffering from Endometriosis. The saliva in leeches is rich with enzymes that can prevent coagulation of blood which leads to blood clots. Once these enzymes have dissolved the blood clots and restored a normal flow of blood into the uterus, toxins are flushed away. Another important compound in leech's saliva is the anti-inflammatory enzymes, which aid in the reduction of inflammation. Once inflammation subsides, blood can flow freely into vessels, which are further dilated by the vasodilator agents in leech's saliva. Apart from that Medicinal Leech therapy has also shown beneficial results in PID, Ovarian Cyst & Uterine Fibroid.

Infertility

The first person to use leech therapy in infertility field was Egyptian Queen Cleopatra [14]. The power of biochemical substances released by leech saliva has positive effects on the nervous system & on the local tissue. It gets relieved of hypoxia and organ performs to its best capability. Most recently in London, a woman at age 45 credits Leech therapy with helping conceive. She had history of Precancerous Uterine fibroid & she used about 500 Leeches for the treatment [16]. Apart from this Leech saliva has nutrients, which improves Immunity for a better pregnancy. Leech therapy speeds up metabolism and fights Obesity and Diabetes, which may also be a secondary factor to infertility.

Cosmetology

Leech therapy ensures good blood flow to skin making it radiant and free from premature wrinkles. The Medicinal leech has the highest Collagen enzyme in the world & Collagen is the main component of connective tissue. This particularly slows the aging process, the most wanted in the cosmetic world. The methods of slowing the skin aging with leeches' application have been known since ancient times, Japanese Geishas, famous for their beauty, with a smooth alabaster skin tone, were treated with face and body masks-sophisticated most organic hirudo-mask were applied for extraordinary results. In XIX Century France using Leeches for a healthy-looking skin and blushing cheeks was "a must"

routine for women. For an immediate blood flow into cheeks leeches were placed behind the ears, the area that the post-leeching marks were unnoticeable and hidden under the hair ^[12]. Apart from this it is also used to reduce Pigmentation, Cellulite and Acne.

Side effects

Although the bite of a leech is felt as a slight pain on the intact skin, this is not relevant in the case of recently reattached digits and flaps, where the skin is anesthetic. Slight localized itching of the Y-shaped bite site persisting for several hours and up to 3 days is the most common (37.3–75%) adverse effect of leech therapy. Use of 5% potassium permanganate, cold compresses, 10% baking soda paste, Golden Star balm, or Fenistil gel on the affected skin areas can be for more pronounced cases. In severe cases of generalized itching, topical corticosteroids and oral antihistamines should be prescribed. Signs of regional lymphadenitis, slight swelling, and pain of regional lymph nodes on the side of leech application and subfebrile temperature can occur in 6.4–13.4% of the treated patients and usually appears after 3-4 leech applications. Apparently, such adverse reactions never appear when leeches are applied on oral, nasal, or vaginal mucosa.⁹ Symbiotic bacteria such as *Aeromonas hydrophila* and *Aeromonas veronii*, living in the intestinal tract of the leech, may cause infections in 4–20% of the patients, mostly in reconstructive surgeries ^[21]. Postprandial *Aeromonas hydrophila* cultures and antibiotic levels of enteric aspirates from medicinal leeches applied to patients receiving antibiotics.⁵ *Aeromonas* infections more frequently develop in very sick and immunosuppressed patients. When applied on intact skin, for example, in patients treated for osteoarthritis, local pain, arterial hypertension, and different forms of spondylosis and dorsopathies, *Aeromonas* infections are extremely rare ^[9].

Contraindications

Contraindications related to hirudotherapy include arterial insufficiency, hemophilia, hemorrhagic diathesis, hematological malignancies, expressed and firm anemia, expressed and firm hypotension, sepsis, HIV-infection, decompensated forms of hepatobiliary diseases, any form of cachexia, and individual intolerance to leeches. Leech therapy is also not recommended in pregnancy and lactation, in patients with an unstable medical status, history of allergy to leeches or severe allergic diathesis, disposition to keloid scar formation, arterial insufficiency, and in those using anticoagulants, immunosuppressants, and some vasoactive drugs such as *Ginkgo biloba* products ^[9].

Conclusion

Hirudo Therapy is a miraculous therapy under Unani tibb which detoxifies body, Fights specific illnesses & boosts Immunity, provided used safely and precautiously.

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