

REVIEW ARTICLE 

Relevance of leech therapy in contemporary medicine: A mini-review

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Information about the article:

Received: March, 17, 2019

Accepted: June 3, 2019

Published online: July 1, 2019

Cite this article:

Ghosh S. Relevance of leech therapy in contemporary medicine: A mini-review. Quest International Journal of Medical and Health Sciences. [internet], 2019 [2019/7/1]; 2(1):8-12. Available from: <http://www.qiup.edu.my/wp-content/uploads/2019-3.pdf>

Publisher

Quest International University Perak (QIUP), No.227, Plaza Teh Teng Seng (Level 2), Jalan Raja Permaisuri Bainun, 30250 Ipoh, Perak Darul Ridzuan,

e-ISSN: 2636-9478

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ABSTRACT

Medicinal leech therapy has been used for centuries. Its popularity reached its peak in the early part of the 19th century and then plummeted for about a century only to resurge after the mid-20th century. Leeches feed on blood by anchoring themselves on the skin of vertebrates and in the process inject saliva into the host. Leech saliva contains more than 100 bioactive molecules of which more than 20 have been identified with useful healing properties. It has antithrombin, antiplatelet, analgesic, anti-inflammatory, antimicrobial, vasodilatory and other properties that are beneficial in the treatment of cardiovascular diseases, arthritis, carcinomas, diabetes mellitus. Leech therapy is used by plastic and reconstructive surgeons for replantation of digits, salvage of failing flaps etc. Leech therapy has a huge potential for future therapeutics.

Keywords

Antithrombin, deep vein thrombosis, hirudin, leech, leech therapy, saliva

Introduction

Medicinal leech therapy can be traced back to the early civilization of mankind. Hirudotherapy is a Latin term used for the medicinal application of leeches to treat diseases. The importance of leeches in ancient treatment is evident from the fact that this word was derived from the Anglo-Saxon word of physician –'laece'. [1, 2] The uses of leeches were traced to 1500 BC in the paintings of the Pharaohs of Egypt and writings in Sanskrit in India from 1300 BC. [1, 3] Its medicinal use was recommended by Hippocrates (460-370 BC) [1], Galen (130-201 AD) [4, 5], Avicenna (980-1037 AD), Ibn Maseehi (1233-1286 AD) and so on. [1, 4] Many scholars including Hippocrates and Galen hypothesized that illnesses are due to the collection of inappropriate blood and the removing of such disease-related blood, causes alleviation of a wide variety of illnesses. [1, 4] Perhaps the first written reference of leeching was made in a poem by Nicander of Colophon (185 – 135 BC), a Greek physician and poet. [6]

In the early nineteenth century, leeching gained high popularity and leech trading became so lucrative that they eventually became an endangered species. But as modern medicine developed to find ready solutions of many common ailments, the leeching practice fell drastically by the end of the 19th century. [1] Again, hirudotherapy resurged in the mid-20th century in various specific medical fields as a healing property which modern drugs and techniques cannot parallel.

Biology of Leeches

Leeches belong to the Phylum Annelida and class Hirudinea which lists more than 300 species of leeches. [7, 8] The hematophagous (bloodsucking) leeches though found in most parts of the world are of greatest abundance in North America, Europe and South East Asia. [7] They live in aquatic environments (freshwater, ponds, streams, lake and the sea) as well as in moist terrestrial regions. [7, 8] The most popular species for therapeutic purpose is *Hirudo Medicinalis* [8] from a freshwater habitat and it can grow about three times its resting size on feeding. They can feed up to 20 ml of blood within 10 – 30 minutes before dropping. [9, 10] The bloodsucking species of leeches feed on the skin of many types of vertebrates using their suckers containing blade-like jaws with teeth to slit the skin of the host. The incision in the skin is followed by secretion of hirudin, a potent anticoagulant. [6] Leeches also secrete an anaesthetic which dampens the pain and keeps the host oblivious to the attack. [7]

Active Principles in Leech Saliva

Modern medicine has now focussed its attention because of the potential utilities of leech saliva. The earliest established facts about leeches were their ability to suck out blood and the introduction of saliva having anticoagulant, analgesic and anaesthetic properties. In the course of time, the scope of

leech therapy expanded to the treatment of hematoma, congested limbs and some eye diseases. [11]

Secretions of leeches contain more than 100 bioactive molecules of which the mechanism of action of more than 20 have been well established and many more awaiting evaluations. These molecules include hirudin, hirustatin, hyaluronidase, calin, destabilase, hirustasin, histamine-like molecule, complement inhibitors, saratin, caline, thrombacin, acetylcholine, bdellins, chloromycetin, trypsin inhibitor, eglins, carboxypeptidase-A inhibitor, Factor X inhibitor, collagenase etc, which have anticoagulant, anti-inflammatory, analgesic, antimicrobial, vasodilator, matrix degradation and many more activities. [6,12]

Application of Leeches in Modern Medicine:

Extract of leeches has been identified with antimicrobial effect for the presence of destabilise a protein with lysozyme-like activity [13]. Others reported isolation of antimicrobial peptides (AMPs) from leech saliva that attack gram negative/positive bacterial strains and activate immune response of attacked cells. [14, 15]

Leech treatment has been successfully used in arthritis. It has been reported to provide more relief than diclofenac in a randomized controlled trial. [16] Leech salivary secretion was reported to inhibit DING protein, an autoantigen in synovial fluid of arthritis patients. [17] Reports showed that pain and disability in osteoarthritis patients improved after leeching and such effects lasted for at least 2 months. [18]

A protein called ghilanten was isolated from leech saliva has been reported to have an antimetastatic function. Ghilanten and a synthetic hirudin preparation inhibit metastasis of tumour cells in a wide range of malignancies including pulmonary, breast and colorectal carcinoma, leukaemia and lymphoma [19, 20]. Owing to the presence of bioactive molecules with anti-Factor Xa, antithrombin, antiplatelet, anti-inflammatory and vasodilator activity along with the presence of enzymes like hyaluronidase, collagenase, acetylcholine and histamine-like substance, medicinal leech therapy has proved to be promising for reconstructive surgeries, skin flap transplantation, microsurgery for replantation of amputated digits or extremities and the management of cardiovascular diseases (CVDs), diabetes mellitus, hypertension, hypercoagulability, varicose veins, deep vein thrombosis (DVT), haemorrhoids, thrombophlebitis, reconstructive surgeries, replantation of organs, skin flaps etc. [21- 23]

Cardiovascular diseases (CVDs) are the number one cause of death globally [24]. Hirudotherapy is emerging as an alternative remedy owing to its multipronged action to reverse the pathophysiology of CVD. Leeches secrete hirudin, a potent anticoagulant, having an inhibitory effect on both free and clot-bound thrombin. [25, 26] Hirudin is recognized to be a thrombin inhibitor par excellence and reported to be better than heparin in the management of patients with unstable angina and deep vein thrombosis. [27] Unlike heparins, hirudin does not require the endogenous

antithrombin-III for its action, so it is a preferred drug in antithrombin III deficiency states like disseminated intravascular coagulation (DIC) syndrome. Another advantage of hirudin is it inhibits the growth of thrombus by blocking thrombin-fibrin binding while thrombin bound fibrin is resistant to heparin inactivation. [27, 28] It is quite logical that lepirudin and desirudin which are two analogues of hirudin that have been approved by the FDA and has been used after hip and knee replacement surgery [29]. In addition to its antithrombin activity, leech saliva also inhibits the process of coagulation in multiple other sites. After an injury, clotting Factor X is activated by both intrinsic and extrinsic pathways of coagulation [30]. Leech saliva contains potent Factor Xa inhibitors like ghilanten [31] and therostatin. [32] It also contains calin which inhibits platelet activation and aggregation by inhibiting collagen and von Willebrand factor. [33]

Leech treatment in phlebitis demonstrated amelioration of oedema, reduction of pain, better mobility and restoration of skin colour. [6] In skin flap transplantation, the common complications are slow blood flow, venous congestion and cyanosis. Leech saliva contains vasodilators such as histamine-like substance, acetylcholine and carboxypeptidase-A which improves blood flow. It also contains hirudin that inhibits platelet aggregation and Factor Xa inhibitor. [34]

Leeching has been used in Indonesia as a successful remedy for diabetes mellitus (DM). [35] Leech saliva contains the ingredients to relieve the cardiovascular complications of DM including inflammation, oxidative stress, atherosclerosis, hypertension, disorders of platelet aggregation and coagulation and vascular complications leading to ischemia in extremities. [13]

Drawbacks of Medicinal Leech Therapy

Some of the drawbacks of leech treatment are, a) negative patient perception: acceptability of leech treatment is low among patients and their families due to unfamiliarity, fear and other concerns [36], b) uncertainty of leech attachment: it might move from impaired tissue to adjacent healthy tissue if the flap is not protected, c) excessive blood loss: oozing of blood is a common complication, d) relatively high cost of treatment: cost of leech farming, transport, preservation, number of leeches employed and cost of facilities and supervision of staff for long hours [37], e) possibility of infection [38] and, f) low rate of blood removal to relieve congestion.

Conclusion

Recently mechanical devices have been developed to replace the use of leeches for treating venous congestion [36]. Further research and advancement in medical sciences will be required to gradually replace the current medical uses of leeches. On the other hand, research on unexplored bioactive molecules of many common and wild species of leeches has

huge potentials which might determine the future therapeutics.

Abbreviations

antimicrobial peptides (AMPs), cardiovascular diseases (CVDs), deep vein thrombosis (DVT), disseminated intravascular coagulation (DIC)
diabetes mellitus (DM)

Competing interests

None declared.

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