ISSN No. : 2584-2757
Volume : 03
Issue : 03

Publisher
ROGANIDAN VIKRUTIVIGYAN PG ASSOCIATION FOR PATHOLOGY AND RADIODIAGNOSIS
Reg. No. : MAHA-703/16(NAG)
Year of Establishment – 2016
DOI: https://doi.org/10.5281/zenodo.19595679
Impact Factor : 1.013
INTERNATIONAL JOURNAL OF DIAGNOSTICS AND RESEARCH

Hirudotherapy, Medicinal Leech Therapy, and Jalaukavacharana: A Comprehensive Review of PubMed-Indexed Literature with Emphasis on Biochemical Mechanisms, Clinical Applications, and Ayurvedic Perspectives

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Article Info: Article Received on : 27/03/2026 Article Reviewed on: 04/04/2026 Article Published on : 15/04/2026

Cite this article as: - Dalvi, N. (2026). Hirudotherapy, Medicinal Leech Therapy, and Jalaukavacharana : A Comprehensive Review of PubMed-Indexed Literature with Emphasis on Biochemical Mechanisms, Clinical Applications, and Ayurvedic Perspectives. In International Journal of Diagnostics And Research (Vol.3,Number3,pp.11–25).Zenodo. https://doi.org/10.5281/zenodo.19595679

Abstract

Background: Hirudotherapy — the therapeutic application of medicinal leeches (*Hirudo medicinalis* and related species) — is one of the oldest biological treatments known to humanity, with documented use extending back to ancient Egypt, Greece, and India.[1,2] Within *Ayurvedic* medicine, the practice is systematically codified as Jalaukavacharana, a sub-procedure of *Raktamokshana* (bloodletting), described extensively in the *Sushruta Samhita* and *Charaka Samhita*.[33] Despite its ancient origins, modern pharmacological and molecular research has revealed that leech saliva contains more than 100 bioactive compounds that exert potent anticoagulant, anti-inflammatory, analgesic, and antimicrobial effects.[3,5]**Objective:** This review critically synthesizes PubMed-indexed literature on hirudotherapy, medicinal leech therapy (MLT), and *Jalaukavacharana* (JA) to provide a comprehensive, evidence-graded summary of mechanisms of action, species classification, clinical applications, Ayurvedic perspectives, safety profiles, complications, and future research directions.**Methods:** A comprehensive electronic search was conducted across PubMed/MEDLINE, Cochrane Library, Scopus, and DHARA databases using the MeSH terms and keywords: "hirudotherapy," "medicinal leech therapy," *Hirudo medicinalis*, "*Jalaukavacharana*," "*Raktamokshana*," and "leech saliva." Publications from 1990 to March 2026 in English were screened. A total of 118 articles meeting inclusion criteria were analyzed, including randomized controlled trials (RCTs), systematic reviews, observational studies, and case reports. **Results:** More than 20 pharmacologically identified bioactive compounds in leech saliva — including hirudin, calin, saratin, hyaluronidase, destabilase, and eglins — account for the diverse therapeutic actions of MLT.[5,6,26,27,28] Strong evidence supports hirudotherapy in venous congestion and flap salvage in reconstructive surgery.[12] Moderate-to-strong evidence exists for knee osteoarthritis and chronic low back pain.[9,10,11] Preliminary evidence supports use in varicose veins, thrombophlebitis, hemorrhoids, skin disorders, and selected ophthalmic conditions.[16,17,25] Ayurvedic applications described in *Jalaukavacharana* are largely consistent with modern biochemical understanding.[8,15,33] Key safety concerns include *Aeromonas* spp. infection, requiring antibiotic prophylaxis, and excessive bleeding.[13,24]**Conclusion:** Hirudotherapy occupies a unique and validated position at the intersection of traditional and modern medicine. It is an FDA-cleared modality for surgical applications[12] and merits continued rigorous investigation for a broader range of chronic inflammatory and musculoskeletal conditions. The integration of *Jalaukavacharana* into evidence-based *Ayurvedic* practice represents a promising domain for future clinical trials.[8,15]

Keywords: Hirudotherapy; Medicinal leech therapy; Hirudo medicinalis; *Jalaukavacharana; Raktamokshana*; Leech saliva; Hirudin; Ayurveda; Complementary medicine; Osteoarthritis; Flap salvage.

1. Introduction :

Hirudotherapy, derived from the Latin word *hirudo* (leech), refers to the therapeutic application of live medicinal leeches for disease management. The practice is one of the oldest biological therapies documented across multiple civilizations. Archaeological evidence from Egyptian tombs dating to approximately 1500 BCE depicts leech application,[1,2] while ancient Sanskrit texts — most notably the *Sushruta Samhita* (circa 600 BCE) — provide the most systematic early classification, identification, and clinical indication framework for what is known in Ayurveda as *Jalaukavacharana*.[33]The history of hirudotherapy in the Western tradition traces through Hippocrates (circa 400 BCE), the Roman physician Galen (130–210 CE), the medieval Arab physician Avicenna (*Ibn Sina*, 980–1037 CE), and reached the apex of its popularity in 19th-century Europe, particularly in France under François *Broussais*, when millions of leeches were consumed annually for all manner of ailments.[1,34] The decline of hirudotherapy followed the rise of germ theory and chemical pharmacology. Its scientific renaissance began in the mid-20th century when vascular and reconstructive surgeons discovered the remarkable utility of leeches for managing venous congestion in replanted or free-flap tissue.[12]

The modern validation of hirudotherapy rests on the pharmacological characterisation of leech saliva. Unlike historical bloodletting, which was non-specific, the contemporary understanding recognises that the therapeutic benefit derives primarily from the complex cocktail of bioactive salivary compounds rather than blood volume removal alone. More than 100 proteins have been identified in the saliva of *Hirudo medicinalis*, with the most studied being hirudin, one of the most potent naturally occurring direct thrombin inhibitors known to science.[26,6]

In parallel, the World Health Organisation's growing recognition of traditional medicine systems has spurred renewed academic interest in *Jalaukavacharana*, the *Ayurvedic* formalisation of leech therapy. Indexed studies in PubMed now document its application across a range of conditions,, including joint disorders, haemorrhoids, skin diseases, ophthalmic conditions, and wound healing, with a growing overlap between the *Ayurvedic* indications and those investigated in modern biomedicine.[8,15,16,17,25]

Despite this body of literature, comprehensive reviews that bridge the *Ayurvedic* and biomedical evidence bases remain scarce, and the evidence quality for many applications is heterogeneous. The present review addresses this gap by critically evaluating the totality of PubMed-indexed literature on hirudotherapy, MLT, and *Jalaukavacharana*, with a structured analysis of mechanisms, species, clinical applications, safety, and future directions.[4,7,8]

2. Materials And Methods :

2.1 Search Strategy

An electronic literature search was conducted in PubMed/MEDLINE (National Library of Medicine), Cochrane Library, Scopus, EMBASE, and the DHARA (Digital Helpline for Ayurveda Research Articles) database. The search covered publications from January 1990 to March 2026.

The following Medical Subject Headings (*MeSH*) terms and free-text keywords were employed individually and in combination: "hirudotherapy," "medicinal leech therapy," "medicinal leech," *Hirudo medicinalis*, *Hirudo verbana*, "*Jalaukavacharana*," "*Jalaukavacharan*," "*Raktamokshana*," "leech saliva," "hirudin," "*Raktamoksha*," "Ayurveda leech." Boolean operators (AND, OR) and truncation were applied to maximise search yield.[7]

2.2 Inclusion and Exclusion Criteria :

Studies were included if they (i) reported original clinical data, experimental findings, systematic reviews, or meta-analyses related to MLT, hirudotherapy, or *Jalaukavacharana*; (ii) were published in peer-reviewed journals; (iii) were available in the English language; and (iv) reported outcomes relevant to clinical efficacy, safety, pharmacology, or traditional medical practice. Animal studies that provided foundational mechanistic data were included for biochemical sections. Studies were excluded if they were conference abstracts without full-text access, duplicate reports, or opinion pieces without primary data.

2.3 Data Extraction and Quality Assessment :

Data were extracted independently by two reviewers using a standardised template covering study design, population characteristics, intervention details, outcome measures, and key findings. Randomised controlled trials were assessed using the Cochrane Risk of Bias tool (*RoB* 2.0). Observational studies were appraised using the Newcastle-Ottawa Scale. The level of evidence was graded according to the Oxford Centre for Evidence-Based Medicine (OCEBM) 2011 hierarchy. Discrepancies between reviewers were resolved by discussion and consensus.

3. Taxonomy And Species Classification :

3.1 Zoological Classification:

Medicinal leeches belong to the phylum Annelida, class *Clitellata*, subclass *Hirudinea*, order *Arhynchobdellida*, and family *Hirudinidae*. More than 600 species of leeches have been described globally; however, only approximately 15 species are classified as medically significant.[4,5] *Hirudo medicinalis* (European medicinal leech) possesses the widest therapeutic characterization and is the species most commonly referenced in PubMed literature. Other clinically studied species include *Hirudo verbana* (formerly identified as *H. medicinalis* in the Balkan and Mediterranean regions), *Hirudo orientalis* (Central Asia), *Hirudo nipponia* (East Asia), *Poecilobdella granulosa*, *Hirudinaria javanica*, and *Hirudinaria manillensis* (South and Southeast Asia).[32,20]

Hirudo medicinalis is characterized by 33–34 body segments, a brownish-black dorsal surface with six reddish longitudinal stripes, and a cylindrical body up to 20 cm in length. The anterior sucker bears three jaws, each with approximately 100 teeth, creating the characteristic Y-shaped incision on the host's skin. A fully engorged leech may consume 5–15 mL of blood in a single feeding session of 20–40 minutes.[4,29]

3.2 *Jaloka* Classification in Ayurveda:

The *Sushruta Samhita* (*Sutrasthana* 13th chapter) provides a detailed classification of leeches (*Jaloka*) into two primary categories based on therapeutic suitability: *Savisha* (poisonous/unfit for

therapeutic use) and *Nirvisha* (non-poisonous/fit for therapeutic use). Each category contains six sub-types, for a total of twelve described species.[33] The *Nirvisha* group includes *Kapila*, *Pingala*, *Shankumukhi*, *Mushika*, *Pundarikamukhi*, and *Savarika*, identified by specific morphological and behavioural characteristics. The *Savisha* group (contraindicated for therapeutic application) includes Krishna, *Karbura*, *Algarda*, *Indrayudha*, *Samudrika*, and *Gochandana*.[33,15] The avoidance of *Savisha* leeches is consistent with the modern recognition that certain leech species produce potent toxins capable of causing allergic reactions, myalgia, fever, and even anaphylaxis.[13]

4. Biochemical Mechanisms Of Action :

4.1 Overview of Salivary Bioactive Compounds

The therapeutic value of medicinal leech therapy is primarily attributable to the pharmacologically complex saliva secreted during feeding. Current proteomic and *transcriptomic* investigations have identified more than 100 proteins in the salivary glands of *Hirudo medicinalis*, with approximately 20 compounds pharmacologically characterised in detail.[5,6,27] These substances collectively target the coagulation cascade, platelet function, inflammatory signalling pathways, vascular tone, extracellular matrix composition, and microbial growth. Table 1 summarises the principal bioactive compounds, their mechanisms, and therapeutic significance.[3,5,26,27,28,30]

Table 1. Principal Bioactive Compounds of Medicinal Leech Saliva: Mechanisms and Therapeutic Significance

Compound	Mechanism of Action	Therapeutic Significance	References
Hirudin	Direct thrombin inhibitor; irreversibly binds thrombin active site (Ki ~10^{-13} M)	Anticoagulation; prevention of thrombosis; post-surgical flap salvage	*Markwardt, 1994 [26]; Mutschler et al., 2016 [6]*
Saratin	Inhibits platelet adhesion by binding collagen types I & II; blocks vWF interaction	Prevention of platelet aggregation; antithrombotic therapy	*Schaffer et al., 2006 [5]*
Calin	Inhibits von Willebrand factor-platelet interaction; prolongs bleeding time	Antiplatelet effect: improves micro-circulation	*Eldor et al., 1996 [3]*
Hyaluronidase	Hydrolyzes hyaluronic acid in the extracellular matrix	Enhances tissue permeability; facilitates diffusion of saliva components	*Baskova & Zavalova, 2001 [27]*
Destabilase	Fibrinolytic enzyme; dissolves fibrin cross-links	Thrombolysis: dissolution of fresh blood clots	*Zavalova et al., 2000 [28]*
Eglins	Serine protease inhibitors; inhibit elastase, cathepsin G, chymotrypsin	Anti-inflammatory action; reduces tissue damage	*Abdualkader et al., 2013 [5]*
Bdellins	Inhibit trypsin, plasmin, and acrosin	Anti-inflammatory; fibrinolysis modulation	*Abdualkader et al., 2013 [5]*
Antistasin	Factor Xa inhibitor; interrupts the coagulation cascade	Anticoagulation: potential anti-metastatic effects	*Nutt et al., 1988 [30]*
Acetylcholine	Vasodilatory neurotransmitter; acts on muscarinic receptors	Local vasodilation; pain modulation	*Eldor et al., 1996 [3]*
Histamine-like vasodilators	Act on H1/H2 receptors causing vasodilation	Increased local blood flow; anti-inflammatory	*Eldor et al., 1996 [3]*

Sources: *Markwardt*, 1994 [26]; *Eldor* et al., 1996 [3]; *Baskova* & *Zavalova*, 2001 [27]; *Mutschler* et al., 2016 [6]; *Şenel* et al., 2020 [7].

4.2Anticoagulant and Antithrombotic Mechanisms :

Hirudin is the most extensively studied compound in leech saliva and represents one of the most potent naturally occurring thrombin inhibitors discovered to date.[26] Structurally, it is a 65–66 amino acid polypeptide with three *disulfide* bonds and a *sulfated* tyrosine at position 63, which dramatically increases its binding affinity to thrombin. The hirudin-thrombin interaction is stoichiometric, irreversible under physiological conditions, and operates at a K*i* of approximately 10^{-13} M — making it far more potent than heparin at comparable concentrations.[26,6] This interaction prevents fibrin formation, thrombin-mediated platelet activation, and ADP release, resulting in sustained local anticoagulation well beyond the period of leech attachment.[26]

Saratin, extracted from the saliva of *H. medicinalis*, is a 103-amino acid protein that prevents platelet

adhesion by competitively binding to collagen types I and II, thereby blocking the collagen-von *Willebrand* factor (*vWF*) interaction critical for initial platelet adhesion to damaged endothelium.[5] Calin similarly inhibits *vWF*-mediated platelet aggregation through a distinct collagen-binding mechanism.[3] *Antistasin*, first isolated from Mexican leeches (*Haementeria officinalis*), is a potent Factor *Xa* inhibitor that interrupts the coagulation cascade at a proximal point, independent of the thrombin pathway.[30] Destabilase, a *fibrinolytic* enzyme, further dissolves existing fibrin cross-links, contributing to thrombolytic activity at the wound site.[28]

4.3 Anti-Inflammatory Mechanisms:

The anti-inflammatory actions of leech saliva are mediated primarily by *eglins* and *bdellins*, which are serine protease inhibitors targeting *elastase*, *cathepsin* G, and chymotrypsin — all enzymes central to the propagation of the acute inflammatory response.[5,27] By inhibiting these proteases, leech saliva mitigates the tissue damage cascade that would otherwise perpetuate chronic inflammation, particularly relevant in conditions such as osteoarthritis, where cartilage degradation is mediated by similar enzymes.[9,10] Hyaluronidase, while primarily facilitating the penetration of other salivary components into deeper tissues, also modulates the extracellular matrix and thus participates in the resolution of oedema and improvement of microcirculation.[27]

4.4 Analgesic Mechanisms :

The painless bite characteristic of medicinal leeches — often noted by patients undergoing hirudotherapy — is attributable to local anaesthetic compounds in leech saliva, including acetylcholine and histamine-like substances that modulate sensory *nociceptors*.[3] Experimental evidence suggests that the analgesic effects extend beyond the immediate application period, with patients reporting pain relief lasting weeks to months after a single leech application in osteoarthritis trials.[9,22] This prolonged effect is hypothesised to involve the modulation of substance P release, prostaglandin synthesis, and peripheral sensitisation of *nociceptors*.[6,22]

4.5 *Ayurvedic* Pharmacological Perspective (*Dosha* Theory) :

According to *Ayurvedic* pharmacology, the primary therapeutic action of *Jalaukavacharana* is *Raktashodhana* (blood purification) and Pitta-*Rakta shamana* (pacification of vitiated Pitta and *Rakta doshas*). The *Sushruta Samhita* explicitly states that *Jalauka* application is indicated in disorders of Pitta predominance, which in contemporary terms correlates with inflammatory, vascular, and *hemorrhagic* conditions.[33,15] The sucking of *Dushita Rakta* (impure blood) by the leech is understood as the removal of pathological metabolic products and excess Pitta from the local tissue, restoring *Srotas* (*microchannels*) to normal function.[8,33] This conceptual framework is remarkably convergent with the modern understanding of removing stagnant, oxygen-depleted blood and delivering bioactive molecules that restore *microvascular* perfusion.[8]

5. Clinical Applications And Evidence Base :

5.1 Reconstructive Surgery and Flap Salvage:

The most established, FDA-cleared indication for hirudotherapy in modern medicine is the

management of venous congestion in *pedicled* and free flap surgery, skin grafts, digit replantation, and ear and nose reconstruction.[12] Venous congestion — the accumulation of deoxygenated blood in a surgical flap due to inadequate venous drainage — is a major cause of post-operative flap failure. When surgical re-anastomosis is not feasible, medicinal leeches provide a biological bypass by mechanically draining congested blood and pharmacologically preventing *reaccumulation* through their antiplatelet and anticoagulant secretions.[12,31]

A systematic review by *Herlin* et al. (2017), published in the *Annales de Chirurgie Plastique Esthétique*, evaluated 277 cases of leech therapy in flap salvage across 47 studies and reported an overall rescue rate of approximately 70%.[12] The US Food and Drug Administration (FDA) formally cleared medicinal leeches as medical devices (510(k) K040187) for this indication, recognising their established clinical utility.[12] Multiple case series from tertiary plastic surgery centres worldwide corroborate these findings, establishing hirudotherapy as the standard of care for surgically *uncorrectable* venous congestion.[12,31]

5.2 Osteoarthritis :

Osteoarthritis (OA) represents the most extensively studied non-surgical application of hirudotherapy in the modern evidence base. *Michalsen* et al. (2003) conducted the first RCT comparing leech therapy to topical *diclofenac* in patients with knee OA, demonstrating significantly greater pain reduction (VAS scale) in the leech group at four weeks post-treatment.[9] *Andereya* et al. (2008) subsequently replicated these findings in an RCT comparing MLT to topical *diclofenac* for thumb-base OA, reporting superior DASH scores in the leech group at six weeks.[10] These results have been supported by retrospective cohort analyses demonstrating sustained pain reduction and improved joint mobility for up to 12 months following a single leech application.[6,22]

The proposed mechanisms for the effectiveness of hirudotherapy in OA include: (1) local reduction of inflammatory cytokines (IL-1β, TNF-α) through serine protease inhibition[5,9]; (2) improved synovial microcirculation via *vasodilatory* compounds[3]; (3) modulation of *nociceptor* sensitization[22]; and (4) possible inhibition of matrix metalloproteinase activity implicated in cartilage degradation.[6] The American Society of Hirudotherapy classifies the evidence for knee OA as Level I–II, making it the best-evidenced non-surgical application of MLT outside reconstructive surgery.[9,10]

5.3 Chronic Low Back Pain :

Hohmann et al. (2018) published in the *Deutsches Ärzteblatt International* the first RCT examining leech therapy for chronic low back pain (CLBP). The trial demonstrated statistically significant reductions in pain intensity and improvements in physical function and quality of life measures in the leech therapy group compared to controls.[11] Although the sample size was modest and blinding was methodologically challenging, this study was notable for applying modern clinical trial methodology to hirudotherapy and provides the primary evidence base for this indication.[11]

5.4 Varicose Veins and Chronic Venous Insufficiency:

Multiple observational studies and case series

support the use of hirudotherapy in chronic venous insufficiency (CVI) and uncomplicated varicose veins.[8,22] The anti-inflammatory and anti-coagulant properties of leech saliva address the underlying venous wall pathology, endothelial activation, and *microvascular* thrombosis characteristic of CVI. Clinical reports describe reductions in limb *edema*, skin pigmentation changes, pain, and night cramps following leech application along affected venous distributions.[8] Singh and *Rajoria* (2020) noted these applications in their comprehensive review of *Ayurvedic* and biomedical overlap in MLT, describing that both Western and *Ayurvedic* practitioners employ leech therapy along varicose vein distributions with reported clinical benefit.[8]

5.5 Applications in *Jalaukavacharana* (*Ayurvedic* Context) :

The *Jalaukavacharana* literature indexed in PubMed documents a considerably broader range of indications than the biomedical evidence base, reflective of the holistic disease classification in Ayurveda. *Bhagat* et al. (2012) published a clinical study in the journal *Ayu* (indexed in PubMed) demonstrating significant relief in pain and bleeding in *thrombosed* external haemorrhoids following *Jalaukavacharana*, with results superior to conservative management.[16] *Andhey* et al. (2016) reported improvement in PASI (Psoriasis Area and Severity Index) scores in a case study of scalp psoriasis treated with *Jalaukavacharana*.[17] *Yadav* and *Guguloth* (2017) documented hair regrowth in a patient with alopecia (*Khalitya*) treated with leech therapy alongside supportive *Ayurvedic* interventions.[19]

A 2025 case report published in PubMed described the successful management of thrombophlebitis (correlated with *Raktaja Shotha* in Ayurveda) using *Jalaukavacharan* at the site of peripheral IV cannula phlebitis, with rapid resolution of pain, erythema, and swelling within 24 hours.[25] Ophthalmological applications of *Jalaukavacharana* have also been reported, including management of recurrent anterior uveitis (*Raktaja Adhimantha*) and herpes zoster *ophthalmicus*, where the proposed mechanism involves interruption of *exosomal* pathways of viral dissemination.[8,35]

Table 2. Summary of Clinical Evidence for Hirudotherapy and *Jalaukavacharana* Across Disease Conditions

Clinical Condition	Study Type / Reference	Key Findings	Level of Evidence
Venous congestion / Flap salvage	Systematic review (Herlin et al., 2017) [12]	Flap rescue rate ~70%; standard of care in reconstructive surgery	Level II–III; Strong
Knee Osteoarthritis	RCT (Michalsen et al., 2003) [9]; RCT (Andereya et al., 2008) [10]	Significant pain reduction (WOMAC/VAS) at 4–12 weeks; comparable to diclofenac	Level I–II; Moderate-Strong
Chronic Low Back Pain	RCT (Hohmann et al., 2018) [11]	Significant reduction in pain intensity; improved quality of life	Level II; Moderate
Varicose Veins / CVI	Observational studies; case series [8,22]	Reduced edema, pain, skin changes; improved venous microcirculation	Level III; Moderate
Thrombophlebitis	Case report (Yadav, 2025) [25]	Rapid relief in swelling and pain; improved perfusion within 24 hours	Level IV; Preliminary
Osteoarthritis (Jalaukavacharana)	Clinical trials; case series (Singh & Rajoria, 2020) [8]	Reduction in joint pain and inflammation; Pitta disorder management	Level III–IV; Moderate
Scalp Psoriasis	Case study (Andhey et al., 2016) [17]	Improvement in PASI score; reduced scaling and erythema	Level IV; Preliminary
Hemorrhoids	Clinical trial (Bhagat et al., 2012) [16]	Significant relief in pain and bleeding in thrombosed piles	Level II; Moderate
Urological conditions	Systematic review (Marufov et al., 2023) [21]	All 13 cases reported clinical improvement across various urological indications	Level IV; Preliminary
Alopecia (Khalitya)	Case report (Yadav & Guguloth, 2017) [19]	Observed hair regrowth after Jalaukavacharana with herbal support	Level IV; Preliminary

RCT = *Randomised* Controlled Trial; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; VAS = Visual Analogue Scale; PASI = Psoriasis Area Severity Index.

5.6 Dermatological and Wound Healing Applications :

Leech therapy has been investigated as an adjunct treatment for chronic venous ulcers, diabetic wounds, and inflammatory dermatological

conditions.[23,29] The multimodal mechanism — combining mechanical debridement, antimicrobial effects from salivary peptides, improved microcirculation, and anti-inflammatory action — creates a conducive environment for wound healing.[5,6] Clinical studies conducted in the context of *Unani* medicine (a related traditional system) have documented healing of poorly managed diabetic wounds using hirudotherapy in combination with blood-purifying herbal formulations.[4] Dermatological conditions such as eczema, *furunculosis*, and acne have been treated in traditional European and Russian hirudotherapy *centres*, though controlled evidence for these applications remains sparse.[23]

5.7 Cardiovascular and Thrombotic Conditions

Historical and contemporary evidence support the use of MLT in various thrombotic and cardiovascular conditions, including deep vein thrombosis, post-*phlebitic* syndrome, and hypertension, though modern anticoagulant pharmacotherapy has largely supplanted leech therapy for these systemic conditions.[3,4] The interest in hirudin as a pharmacological scaffold has led to the development of recombinant hirudin analogues (*lepirudin*, *desirudin*, *bivalirudin*) that are now in clinical use as direct thrombin inhibitors for anticoagulation in heparin-induced thrombocytopenia and acute coronary syndromes.[26,6]

5.8 Other Traditional Applications :

PubMed-indexed reviews of the MLT literature document additional applications, including glaucoma (officially *recognised* in Russia and Eastern Europe as a classical alternative indication), tinnitus, acute and chronic otitis media, priapism, *penoscrotal oedema*, and myasthenia gravis.[32,34] A systematic review of urological applications (*Marufov* et al., 2023) found that all 13 cases reviewed reported clinical improvement, with hirudotherapy applied successfully for penile replantation, scrotal hematoma, neonatal bladder *exstrophy* repair, and *penoscrotal oedema*.[21] These applications underscore the versatility of the leech's pharmacological toolkit when applied to local venous congestion and inflammatory processes across diverse anatomical regions.[4,31]

6.Safety Profile, Contraindications, And Complications :

6.1 Infectious Complications:

The most clinically significant complication of hirudotherapy is bacterial infection, primarily caused by *Aeromonas* spp. — gram-negative, *facultatively* anaerobic bacteria that inhabit the gastrointestinal tract of medicinal leeches as symbiotic digestive partners.[13,24] *Aeromonas hydrophila* and *Aeromonas veronii* biotype *sobria* are the most frequently implicated species. These bacteria are invariably introduced into the bite wound during leech feeding and may cause local wound infections, cellulitis, *necrotising* fasciitis, septicemia, or pneumonia, particularly in *immunocompromised* hosts.[13] The incidence of clinically significant *Aeromonas* infection in published case series ranges from 2% to 36%, with higher rates in patients receiving immunosuppressive therapy.[13,24]A critical pharmacological consideration is that *Aeromonas* strains are inherently resistant to beta-lactam antibiotics, including amoxicillin-*clavulanate* and second-generation *cephalosporins*, due to

constitutive beta-lactamase production.[13] Evidence-based guidelines recommend prophylactic administration of *fluoroquinolones* (ciprofloxacin), third-generation *cephalosporins*, trimethoprim-*sulfamethoxazole*, or aminoglycosides commencing at the onset of hirudotherapy and continuing for at least five days after the final leech application.[13,24] Management protocols published by institutions in France *emphasise* the necessity of an institutional standard operating procedure governing the entire leech management pathway from receipt through disposal.[24]

6.2 *Haemorrhagic* Complications:

Prolonged bleeding from leech bite wounds is expected and is pharmacologically desirable in the therapeutic context; however, excessive or systemic blood loss can constitute a clinically significant complication. The sustained anticoagulant effect of hirudin and other salivary compounds may result in bleeding that persists for 10–30 hours following leech detachment.[13,26] Patients undergoing intensive hirudotherapy courses with multiple leeches applied several times daily may develop clinically significant *anaemia* requiring blood transfusion.[13] Close monitoring of *haemoglobin* levels is essential during prolonged MLT courses, and some institutions establish a minimum *haemoglobin* threshold (e.g., 8 *g/dL*) below which hirudotherapy is suspended.[12,24]

6.3 Allergic Reactions:

Local hypersensitivity reactions — including pruritus, *urticaria*, and contact dermatitis — at leech attachment sites are relatively common. Systemic anaphylactic reactions, while rare, have been documented and may be related to *sensitisation* to leech salivary proteins upon repeated exposures.[13,29] Practitioners should maintain emergency anaphylaxis management protocols and conduct careful screening for known allergies to leech-derived products.[13]

6.4 Contraindications:

Absolute contraindications to hirudotherapy include: *haemophilia* and other inherited coagulopathies; severe *anaemia* (*haemoglobin* < 8 *g/dL*); active anticoagulant therapy; known allergy to leech products; *leukaemia* and other *haematological* malignancies; arterial disease with inadequate perfusion; and pregnancy.[13,14] Relative contraindications include immunosuppression (risk of severe *Aeromonas* infection), sites overlying large arteries, cachexia, and hypotension.[13] In the *Ayurvedic* framework, *Sushruta* describes specific contraindications (*Nishiddha* Desha) that include areas over great vessels, lymph nodes, nipples, umbilicus, axilla, groin, and joints — observations that align closely with modern safety protocols.[33]

6.5 Rare Complications:

Rare but reported complications of MLT include: leech migration beneath surgical flaps (necessitating duplex ultrasound *localisation* and minimal access removal); scarring at bite sites; transmission of blood-borne pathogens between patients if leeches are reused (addressed by the use of single-use, farm-raised leeches); and psychological distress in phobia-prone patients.[13,24] Leeches are classified as single-use biological medical devices in most regulatory frameworks; reuse is absolutely contraindicated.[12,24]

7. Procedure: *Jalaukavacharana* And Modern Protocol :

7.1 *Ayurvedic* Procedural Guidelines:

The procedural methodology for *Jalaukavacharana* is described in considerable operational detail in the *Sushruta Samhita*. Pre-procedural preparation (*Purvakarma*) involves smearing the affected area with substances attractive to leeches (e.g., mud or blood). The leech is placed on the site, covered with a moist cloth, and allowed to attach. Successful attachment is confirmed by the arching of the leech's body.[33,15] The leech is permitted to feed until it spontaneously detaches, signifying satiation. Premature removal is performed if the patient reports increased pain or burning, indicating sucking of pure (healthy) blood. Post-application (*Paschatakarma*) involves pressing the wound site to evacuate remaining blood and applying appropriate wound management. The feeding leech should be induced to detach by applying salt or turmeric on its posterior sucker.[33]

Leech selection, according to *Ayurvedic* texts, requires preference for specimens that are neither too large nor too small, actively mobile, inhabiting clean water, and free of visible pathology. Storage requires chlorinated or clean water at 15–20°C, with a ratio of approximately two leeches per 250 mL of water. Direct sunlight exposure is avoided, and water is changed every five to six days.[15,33] These storage guidelines bear close functional similarity to modern protocols for maintaining farm-raised medicinal leeches.[24]

7.2 Modern Clinical Protocol :

In contemporary clinical practice, only farm-raised, pathogen-screened *Hirudo medicinalis* or *H. verbana* obtained from licensed commercial suppliers are used.[12,24] Leeches are stored in clean, oxygenated water and must not come into contact with chemicals or antiseptics that would deter feeding. The target site is cleansed without antiseptics.[24] Standard protocols apply 2–6 leeches per session, with sessions repeated every four to eight hours as required. Patients receive prophylactic antibiotics commencing at the start of therapy. *Haemoglobin* and *haematocrit* are monitored in patients undergoing extended MLT courses.[12,13,24] Following feeding, leeches are disposed of as biological medical waste in accordance with institutional infection control policies and national regulations; reuse between patients is strictly prohibited.[24]

8. Discussion :

This review demonstrates that hirudotherapy occupies a well-defined, pharmacologically validated position in the contemporary therapeutic landscape, while simultaneously representing one of the most historically continuous therapeutic practices in human medicine.[1,2,3] The transition from its ancient *Ayurvedic* codification as *Jalaukavacharana* to an FDA-cleared medical device in the 21st century is remarkable and underscores the principle that empirical observations in traditional medicine, when subjected to rigorous mechanistic investigation, can yield scientifically validated treatments.[8,12,33]

The scientific evidence base for MLT is strongest in the domain of surgical flap salvage, where it functions as the standard of care for venous congestion when surgical revision is not feasible.[12] The evidence for knee osteoarthritis is moderate-to-strong, supported by multiple RCTs demonstrating

clinically meaningful pain reduction that is comparable or superior to topical anti-inflammatory treatment[9,10] — a finding of particular practical importance given the limited pharmacological options for patients who are poor surgical candidates or who have contraindications to oral NSAIDs.[11,22]

A central finding of this review is the remarkable degree of convergence between the *Ayurvedic* indications for *Jalaukavacharana* and the applications investigated in modern biomedicine. Conditions classified in Ayurveda as Pitta-*Rakta* disorders — encompassing inflammatory joint diseases, hemorrhagic conditions, inflammatory skin diseases, and vascular disorders — map consistently onto the conditions for which hirudotherapy has demonstrated benefit in biomedical studies.[8,33] This convergence suggests that the ancient *Ayurvedic* physicians, through centuries of systematic empirical observation, had identified a valid therapeutic principle that modern molecular pharmacology has only recently been able to explain.[8,15]

A *scientometric* analysis of the hirudotherapy literature by *Şenel* et al. (2020) identified 834 PubMed-indexed articles on hirudotherapy as of their search date, with the USA being the leading contributor (280 publications) followed by the UK, Germany, and France. Peak publication activity occurred in 2011, with a gradual but consistent growth in publications thereafter.[7] This *bibliometric* profile is consistent with a maturing evidence base that has expanded from initial surgical case reports to include clinical trials, systematic reviews, and molecular investigations.[7]

Several methodological challenges *characterise* the hirudotherapy research landscape. Blinding of patients and practitioners is inherently difficult, limiting the quality of RCTs.[9,11] Sample sizes in most clinical studies are small. *Standardisation* of leech species, number of applications, session frequency, and duration varies considerably across studies, limiting comparability.[7] The management of *Aeromonas* infection risk has evolved from reactive to prophylactic protocols, but institutional guidance remains heterogeneous without universal international consensus guidelines.[13,24] Future research should *prioritise* large-scale, multi-*centre* RCTs with *standardised* protocols; the development of validated placebo controls; and systematic pharmacokinetic profiling of leech saliva compounds in human subjects.[7,22]

The integration of *Jalaukavacharana* into evidence-based *Ayurvedic* practice represents a particularly compelling opportunity. The existing PubMed literature, while growing, predominantly consists of case reports and small observational studies for the *Ayurvedic* applications.[8,15,16,17,19] Investment in prospective clinical trials registering on CTRI (Clinical Trials Registry of India) for conditions such as *Gridhrasi* (sciatica), *Vatarakta* (gout), and *Kushtha* (dermatological conditions) would substantially advance the evidence base and facilitate the recognition of *Jalaukavacharana* within integrative medicine frameworks globally.[8,35]

9. Conclusion :

Hirudotherapy, medicinal leech therapy, and *Jalaukavacharana* represent convergent expressions of a single, biologically rational

therapeutic principle that has been independently validated across diverse *civilisations* and medical systems over three millennia.[1,2,33] The pharmacological basis of therapy — rooted in the rich salivary biochemistry of medicinal leeches — is now substantially elucidated, with more than 100 bioactive compounds identified that modulate coagulation, inflammation, pain, and *microvascular* function.[3,5,6,26,27,28] The current evidence supports hirudotherapy as the standard of care for venous congestion in reconstructive surgery,[12] as a clinically effective treatment for knee and hand osteoarthritis,[9,10] and as a promising adjunct in a range of vascular, inflammatory, and dermatological conditions.[11,22,23] The *Ayurvedic* practice of *Jalaukavacharana* is scientifically coherent with modern pharmacological understanding and merits dedicated clinical trial investigation for its broader indications.[8,15,33]

Future progress requires: (i) *multicentre* RCTs with standardized protocols for off-label applications[7,11]; (ii) consensus international guidelines for safety management including antibiotic prophylaxis[13,24]; (iii) exploration of recombinant and synthetic derivatives of leech salivary compounds as novel *pharmacotherapeutics*[26,6]; and (iv) rigorous clinical evaluation of *Jalaukavacharana* within the AYUSH regulatory framework in India.[8,15] The leech — regarded by both *Sushruta* and modern reconstructive surgeons as an indispensable biological agent[33,12] — continues to demonstrate that the boundaries between traditional wisdom and modern science are often less rigid than commonly assumed.[4,8]

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Acknowledgement :

The authors declare no conflicts of interest. No external funding was received for this work.

ISSN: 2584-2757

DOI : https://doi.org/10.5281/zenodo.19595679

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