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Review article

Integrative Potential of Majoon Suranjan in the Management of Varicose Veins: A Review of Unani Humoral Theory and Contemporary Molecular Mechanisms

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Abstract

Background: Chronic Venous Disease (CVD), traditionally known as *Dawali*, involves complex vascular remodelling. While the Unani System of Medicine (USM) has long utilised *Majoon Suranjan* (MS) for its resolvent (*Muhallil*) properties, its molecular interactions with modern vascular science remain underexplored.

Objectives: This review aims to synthesise classical Unani humoral theories of venous stasis with modern molecular mechanisms, with a specific focus on the regulation of Matrix Metalloproteinases (MMPs) by the bioactive constituents of *Majoon Suranjan*.

Methods: A comprehensive analysis of classical Unani texts (e.g., *Al-Qanun Fi'l Tibb*) was integrated with contemporary pharmacological data and bibliographic trends (2014–2024) regarding *Majoon Suranjan* (MS) and chief ingredient *Colchicum luteum* and its primary alkaloid, colchicine.

Results: The study identifies a significant conceptual convergence between the Unani "atrabilius matter" (*Sauda*) and modern hemorheological stasis. Mechanistically, the *Muhallil* action of *Majoon Suranjan* aligns with the inhibition of MMP-9 and the NLRP3 inflammasome, which prevents the degradation of the extracellular matrix (ECM) and stabilises the venous wall. Furthermore, the polyherbal synergism of ingredients like *Zingiber officinale* and *Piper longum* enhances microcirculation and mitigates tropolone alkaloid toxicity.

Conclusion: *Majoon Suranjan* serves as a scientifically plausible integrative therapy for varicose veins. Future clinical research utilising Doppler-derived hemodynamic and proteomic profiling is recommended to establish its role in standard vascular care.

Keywords: *Majoon Suranjan*, Varicose Veins, *Dawali*, *Colchicum luteum*, Matrix Metalloproteinases (MMP-9), Unani Medicine, Colchicine.

Introduction

The Unani System of Medicine (USM), also known as Greco-Arabic medicine, represents one of the oldest surviving comprehensive medical traditions, tracing its intellectual lineage to the teachings of Hippocrates (*Buqrat*) and Galen (*Jalinoos*). The philosophical foundation of USM rests upon the doctrine of the four humours (*Akhlat-e-Arba*): *Damm* (blood), *Balgham* (phlegm), *Safra* (yellow bile), and *Sauda* (black bile). Each humour is associated with specific primary qualities—heat, cold, moisture, and dryness—and their equilibrium defines the health status or temperament (*Mizaj*) of an individual. Within this framework, disease is viewed as a state of *Su-i-Mizaj* (dys temperament)

resulting from the qualitative or quantitative corruption of these humours (*Fasad-e-Akhlat*).¹

Dawali, the Unani term for varicose veins, is described in classical literature as a condition where the veins of the legs and feet become thick, twisted, and prominently visible, often appearing green or dark purple due to the pooling of morbid *saudavi* or *balghami* matter. Modern vascular science identifies varicose veins as a manifestation of Chronic Venous Insufficiency (CVI), affecting approximately 10–40% of the adult population globally. The risk of progression from simple varicosity to severe Chronic Venous Insufficiency (CVI) increases significantly after age 50, often leading to debilitating complications such as lipodermatosclerosis, venous

stasis ulcers (CEAP C6), and superficial thrombophlebitis.^{2,3,4}

The historical utilisation of *Suranjan* (the corm of *Colchicum luteum*) in the management of inflammatory and musculoskeletal disorders is well-documented. References to its use for treating rheumatism and joint swelling appear in the Ebers Papyrus (circa 1500 BCE). Unani scholars such as Ibn Sina (*Avicenna*) and Al-Razi endorsed its role as a powerful resolvent (*Muhallil*) and deobstruent (*Mufattih Sudad*). While traditionally indicated for *Niqris* (gout) and *Waja' al-Mafasil* (arthralgia), its modern pharmacological profile reveals a direct relevance to the pathophysiology of *Dawali*. Colchicine, its primary alkaloid, has long been recognised for its anti-mitotic and anti-inflammatory properties, but recent breakthroughs have expanded its therapeutic scope to include vascular protective effects and the reduction of major adverse cardiovascular events.^{5,6,7,8}

The polyherbal formulation *Majoon Suranjan* (MS) represents a pinnacle of Unani pharmaceutical logic.

Attributed to the Greek physician Andromachos (*In drumakhas*), MS is composed of eighteen or more medicinal plants formulated in a sugar base (*Qiwam*). This formulation exemplifies the concept of synergistic pharmacology, where primary drugs like *Suranjan* and *Turbud* (*Ipomoea turpethum*) are combined with correctives (*Musleh*) and bioavailability enhancers (*Mu'in*) to maximise efficacy and minimise the inherent toxicity of tropolone alkaloids.^{8,9,10,11}

This review aims to comprehensively evaluate the scientific validity of *Majoon Suranjan* for varicose vein management. It explores the transition from humoral stasis theories to modern molecular understandings of venous remodelling, analysing the phytochemical basis for the formulation's venotonic and anti-fibrotic actions. By synthesising bibliographic trends, clinical trial data, and pharmacological simulations, this document provides an expert-level appraisal of *Majoon Suranjan* as a bridge between traditional herbal wisdom and contemporary vascular medicine.^{11,12}

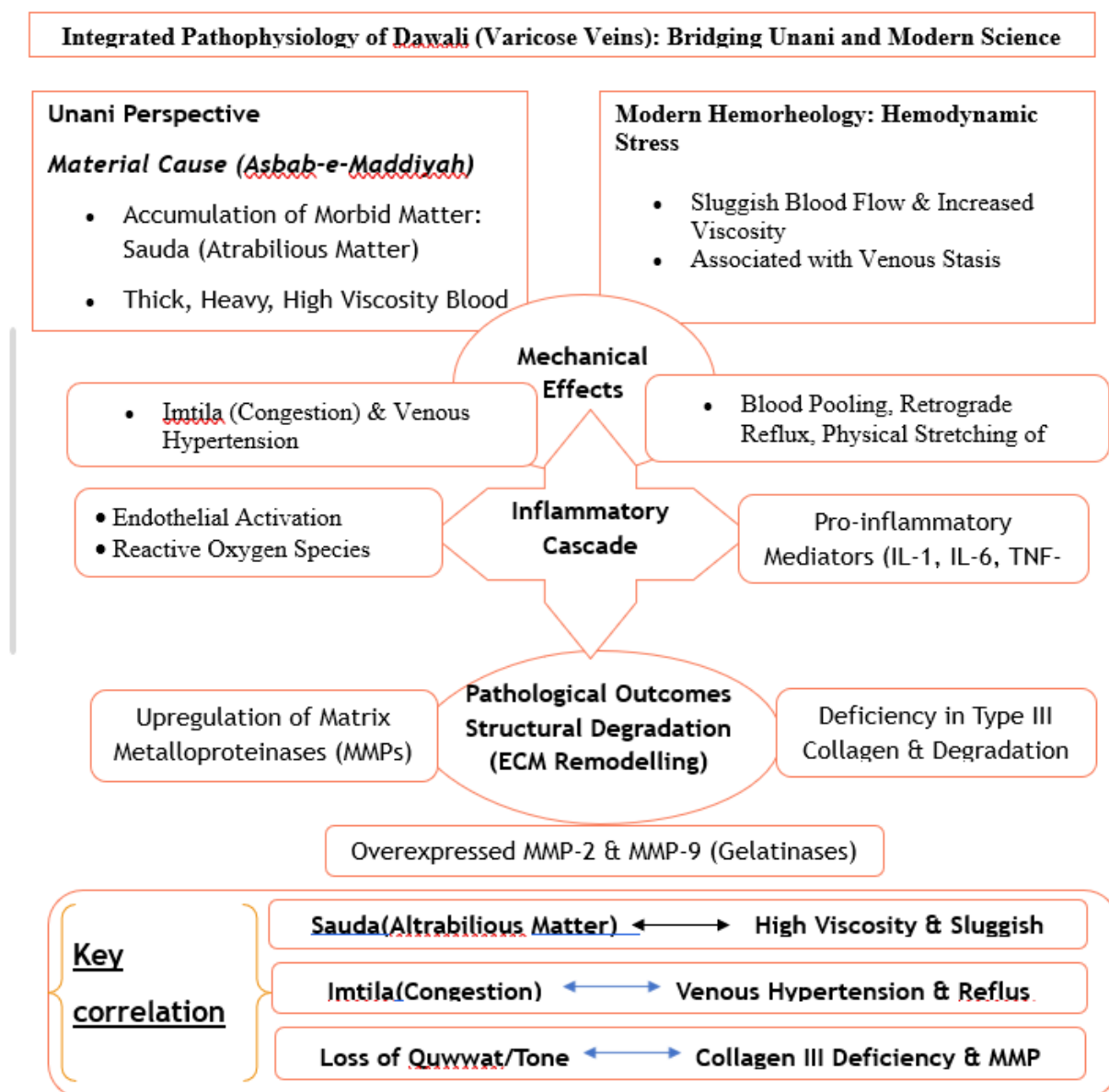


Table 1: Patho-physiology of Varicose vein (Dawali)

Parameter	Unani Paradigm (Dawali)	Modern Paradigm (Varicose Veins)
Etiology	Accumulation of sauda; maadda; sauda-producing foods; weight lifting; prolonged standing. ^{3,4,19,21}	Genetic predisposition; valve incompetence; vessel wall weakness; elevated venous pressure. ^{32,34,36}
Pathogenesis	Humour pooling causing dilatation; Su-i-Mizaj Barid Yabis (Cold/Dry) leading to loss of elasticity. ^{3,4,13,21}	Retrograde flow (reflux); endothelial activation; inflammatory cell recruitment; Matrix metalloproteinases (MMPs)-mediated ECM degradation. ^{32,33,37}
Manifestation	Thick, tortuous, green/dark veins; leg tiredness; relieved by elevation. ^{3,4,19,21,37}	Dilated, bulging cords; aching; burning; nighttime cramping; edema; pigmentation. ^{32,34}
Treatment	Mushil (Purgatives) for sauda removal; Muhallil (Resolvents); Fasd (Venesection); Taleeq (Leeching) ^{3,4,19,20,21,36,37}	Compression therapy; venoactive drugs (flavonoids); sclerotherapy; thermal ablation; vein stripping. ^{32,34}

Ethnobotany and Taxonomy of Suranjan

The plant source of colchicine is predominantly the autumn crocus or meadow saffron. *Colchicum luteum* Baker is a perennial herb characterised by starchy corms and starchy rhizomes, predominantly found in the low-temperature environments of the Kashmir Valley and the Western Himalayas. The corm is the primary medicinal part used therapeutically used in Unani medicine, although historical texts also mention the use of its flowers (*Asabe' Hurmus*).^{5,6,13}

Suranjan is traditionally classified into three distinct types based on the colour and taste of the external and internal surfaces of the corm.^{14,15}

- Type 1 (Suranjan Shirin):** Characterised by a white root and a sweet taste. This variety is commonly administered orally and forms the core of compound formulations like *Majoon Suranjan*.^{13,14,25}
- Type 2 (Reddish-Black Variety):** Considered toxic and generally avoided in oral preparations.¹⁴
- Type 3 (Suranjan Talkh):** Characterised by a slightly blackish root and a bitter taste. This variety is highly potent and historically described by Galen as potentially poisonous, requiring specific detoxification protocols (*Amal-i-Tadbir*) before medicinal use.^{24,25}

The taxonomical status of the plant is defined within the order Liliales and the family Colchicaceae, a shift from earlier classifications that placed it within the Liliaceae family.^{12,10}

Rank	Taxonomic Name
Kingdom	Plantae
Division	Tracheophyta
Class	Magnoliopsida
Order	Liliales
Family	Colchicaceae
Genus	<i>Colchicum</i>
Species	<i>Colchicum autumnale</i> L. / <i>Colchicum luteum</i> Baker

The presence of tropolone alkaloids is the defining phytochemical feature of this genus. Colchicine, the most studied of these, inhibits microtubule polymerisation by binding to tubulin heterodimers, which is essential for its anti-mitotic and anti-inflammatory effects. This binding is highly sensitive to environmental factors; for instance, exposure to light causes photoisomerisation of colchicine into lumicolchicine, which lacks affinity for tubulin and renders the drug ineffective.¹²

Pathophysiological Evolution: From Humours to Matrix Metalloproteinases (MMPs)

In the Unani perspective, *Dawali* represents a classic "material cause" (*Asbab-e-Maddiyah*) of disease, where the accumulation of morbid matter disrupts the normal function of the venous system. This "atrabilius matter" (*sauda*) is described as being thick and heavy, which conceptualises the increased viscosity and sluggish flow observed in modern hemorheological studies of venous stasis. The pooling of this viscous blood leads to an increase in *Imtila* (congestion), which physically stretches the vessel walls.^{29,30,31,32,33}

Modern research has elucidated the molecular mechanisms that underpin these ancient observations. The fundamental defect in primary varicose veins is the incompetence of venous valves, which may be inherited or acquired. This valvular failure leads to retrograde blood flow (reflux), increasing intravenous pressure. The chronic hypertension within the venous segment activates the vascular endothelium, promoting the release of Reactive Oxygen Species (ROS) and pro-inflammatory mediators such as Interleukins (IL-1, IL-6) and Tumour Necrosis Factor-alpha (TNF-alpha).^{30,33}

A central feature of this progression is the degradation of the extracellular matrix (ECM). Varicose vein walls frequently exhibit a deficiency in Type III collagen and a significant increase in the expression of Matrix Metalloproteinases (MMPs). Specifically, overexpressed MMP-9 (gelatinase B) and MMP-2 (gelatinase A) degrade the collagen and elastin fibres that provide the vein with structural integrity and elasticity. This weakening of the vein wall facilitates permanent dilation and tortuosity, aligning with the Unani

description of veins losing their elasticity and stretching

to accommodate the "heavy blood".^{34,18}

Table 2: Formulation of Majoon Suranjan ^{10,5,31,18}

Ingredient (Unani Name)	Botanical Name	Part Used	Quantity per Batch
Suranjan Shirin	<i>Colchicum luteum</i>	Corm	500g
Sana Maki	<i>Cassia angustifolia</i>	Leaf	250g
Zanjabeel	<i>Zingiber officinale</i>	Rhizome	100g
Zeera siyah	<i>Carum carvi Linn</i>	Seed	100g
Filfil Daraz	<i>Piper longum L.</i>	Fruit	100g
Asaroon	<i>Asarum europaeum L</i>	Rhizomes	100g
Qiwam Shakar Safaid	<i>Saccharum officinarum</i>	Syrup base	2.5kg

Classical Unani Action (Af'al) of Suranjan ^{6,7}

The therapeutic versatility of Suranjan is expressed through a set of specific Unani terminologies that describe its multidimensional pharmacological profile:

- Musakkin (Sedative/Analgesic):** It provides immediate relief from the acute pain associated with inflammatory crises, particularly in gout.^{4,7}
- Muhallil (Resolvent):** One of its most esteemed properties; it actively dissolves and resolves inflammatory swellings and morbid humours.^{4,7}
- Mufattih Sudad (Deobstruent):** It is used to open blockages in the vascular and lymphatic systems, as well as in the brain.^{4,7}
- Mundij (Concoctive):** It alters the consistency of morbid matter, preparing it for excretion.⁴
- Jali (Detergent):** It has a cleansing effect, which is why it is used for chronic wounds and skin lesions.⁴
- Mushil-i-Balgham (Phlegmagogue):** It specifically targets the phlegmatic humour, which is considered the root cause of many joint disorders.⁴
- Muqwwi-i-Bah (Aphrodisiac):** In specific combinations, it is used to enhance sexual vitality by improving the "spirit" and heat of the reproductive system.⁴

Modern Phytochemical and Mechanistic Insights

Contemporary pharmacological analysis has validated much of the traditional Unani perspective on Suranjan. The primary bioactive constituent, colchicine, is a neutral alkaloid that has become a cornerstone of modern gout therapy.^{24,25}

The Mechanism of Colchicine

The fundamental mechanism of colchicine involves its binding to beta-tubulin, which inhibits the assembly and polymerisation of microtubules.⁷ Microtubules are essential components of the cellular cytoskeleton, involved in mitosis, intracellular transport, and cell

motility. By disrupting these processes, colchicine exerts several effects ²⁶

Anti-inflammatory: It inhibits neutrophil chemotaxis and adhesion to the endothelium, effectively preventing the "swarming" of inflammatory cells to the site of injury or crystal deposition ²⁸

Antimitotic: It arrests cells in metaphase by preventing the formation of the mitotic spindle ²⁸

Inflammasome Inhibition: Recent research has highlighted its role in inhibiting the NLRP3 inflammasome, a key complex in the innate immune system that triggers the release of pro-inflammatory cytokines like IL-1beta and IL-18. ^{27,28,50}

Matrix Metalloproteinases (MMPs) and the Pathophysiology of Varicose Veins

To understand the deeper "Resolvent" and "Deobstruent" actions of Suranjan in vascular health, one must examine the role of matrix metalloproteinases (MMPs) in chronic venous disorders. Varicose veins are characterised by an abnormal dilation and tortuosity of the superficial veins, driven by an imbalance in the structural proteins of the vein wall. ²⁹

Synthesising Unani Actions with MMP Regulation

The traditional Unani actions of *Muhallil* (resolvent) and *Mufattih Sudad* (deobstruent) provide a clinical framework that aligns remarkably well with the modern modulation of MMPs.²⁷

The Resolvent (*Muhallil*) Action as MMP Inhibition

In Unani medicine, a *Muhallil* is a drug that helps in the resolution of inflammation and the dissolution of "morbid matter." Modern research shows that colchicine—the active principle of Suranjan—is a potent inhibitor of MMP-9 and TGF-beta 1. By binding to the active sites of MMP-9, colchicine reduces its proteolytic activity, thereby preventing the excessive degradation of the ECM that characterises the pathological remodelling of varicose veins and the heart. Furthermore, by reducing the recruitment of neutrophils (which are major sources of MMPs),

Suranjan effectively "resolves" the inflammatory milieu within the vascular wall.^{29,47,48,49}

The Deobstruent (*Mufattih Sudad*) Action and Vascular Patency

The *Mufattih Sudad* property refers to the ability to clear obstructions. In the context of chronic venous insufficiency, "obstructions" can be understood as the accumulation of degraded ECM proteins and the "pooling" of blood due to valvular failure. By regulating the balance between MMPs and their inhibitors (TIMPs), Suranjan helps restore the structural homeostasis of the vein wall.¹ Specifically, colchicine has been shown to increase the expression of TIMP-1 and TIMP-2 while reducing the expression of MMP-1 and MMP-9. This shift promotes the preservation of elastin and collagen, potentially reversing the "obstruction" caused by vascular dilation and loss of elasticity.^{30, 6,51,52}

Discussion

The management of *Dawali* through *Majoon Suranjan* provides a compelling example of how ancient humoral logic anticipates modern molecular pathophysiology. The convergence of "atrabilious matter accumulation" and "Matrix Metalloproteinase over-expression" represents two descriptive systems mapping the same biological reality: the structural failure of the venous system under chronic stress.^{6,9,10,12}

Humoral Stasis and Blood Rheology

In Unani theory, the primary pathological event in *Dawali* is the pooling of *saudavi* (black bile) blood. Sauda is inherently cold and dry (*Barid Yabis*), but when it becomes morbid, it becomes thick (*Ghaleez*) and viscous. This viscous state directly mirrors modern observations of hemoconcentration and increased shear stress in the hypoxic environment of an incompetent vein. The traditional property of *Suranjan* to "reduce the viscosity of all humours" acts as a natural rheological stabiliser, facilitating the movement of pooled blood back into the systemic circulation.^{4,5,10}

Molecular Modulation by Tropolone Alkaloids

The efficacy of *Majoon Suranjan* is deeply rooted in the pharmacology of colchicine. Unlike broad-spectrum NSAIDs that target COX enzymes non-specifically, colchicine exerts a highly targeted effect on the cellular architecture. By binding to tubulin, it disrupts the assembly of microtubules, which are essential for the migration and degranulation of neutrophils. This is critical in varicose veins, where neutrophil accumulation and activation are the primary drivers of vein wall remodelling.³⁴

Furthermore, the "anti-fibrotic" property of *Suranjan* described in modern research correlates with the Unani "Muhallil" (resolvent) action. Resolvents are drugs that dissolve morbid material and prevent its hardening into chronic lesions. Mechanistically, this is achieved through:^{30 31}

1. MMP Inhibition: Colchicine's binding affinity for MMP-9 prevents the degradation of Type III collagen,

thereby halting the structural weakening that leads to venous "snake-like" tortuosity.^{28,48}

2. NLRP3 Suppression: Inhibition of the inflammasome reduces the release of IL-beta, preventing the feed-forward inflammatory response that causes skin thickening (*Induration*) and lipodermatosclerosis (CEAP C4b).⁵⁰

3. Endothelial Protection: Colchicine prevents oxidative-stress-induced senescence in endothelial cells, preserving the vascular barrier and reducing the leakage of fluid into the interstitial space (*Oedema/Ratab*).^{30 31}

Synergism of Polyherbal Ingredients

The strength of *Majoon Suranjan* lies in the "Murakkab" (compound) nature of its formulation. Each ingredient plays a specific role in balancing the overall effect.

Vascular Deobstruent and Resolvent Action: The formulation primarily functions as a *Mufattih-e-Sudad* (deobstruent) and *Muhallil* (resolvent). *Asarum europaeum* and *Carum carvi* are specifically utilised to clear "Sudad" (vascular and lymphatic obstructions), while *Colchicum luteum* resolves the localised inflammatory swellings and "morbid humours" that characterise dilated, tortuous veins.^{29 30}

Vein Wall Stabilisation and MMP Inhibition: As established with *Colchicum luteum*, the natural colchicine in this formula acts as a potent inhibitor of matrix metalloproteinases, specifically MMP-9. This action prevents the excessive degradation of the vein wall's extracellular matrix (collagen and elastin), thereby hindering the progressive dilation and loss of tensile strength seen in varicose disease.³⁰

Enhancement of Venous Return and Circulation: *Zingiber officinale* (Ginger) and *Piper longum* (Long Pepper) provide warming and circulatory-stimulant properties. They act as natural blood thinners to prevent stagnation and the formation of micro-clots (thrombosis), while also improving microcirculation to alleviate the "heaviness" and pain associated with pooled blood in the lower extremities.²⁸

Detoxification and Humour Regulation: *Cassia angustifolia* (Senna) acts as a specialised purgative to expel excess "thick humours" (waste) from the systemic circulation. This systemic cleansing reduces the humoral burden on the vascular system, which is why it is historically prescribed for haemorrhoids, effectively varicose veins of the rectal area.^{30 28}

Pain Relief and Internal Balance: The combination provides significant analgesic (*Musakkin*) effects, reducing the discomfort, aching, and muscular stiffness caused by compromised venous drainage.¹⁸

Integrative Management and Regimental Therapies
51,3,4,5,7,13,15

Unani medicine rarely relies on drugs alone. The management of *Dawali* emphasises the integration of *Ilaj Bil-Tadbeer* (regimental therapy).

- **Fasd (Venesection):** Historically, the gold standard for immediate pressure relief in *Dawali*. By removing congested blood from the *Saphenous* vein, it dramatically lowers venous engorgement and pain.¹⁹
- **Taleeq (Leech Therapy):** Contemporary trials have validated this "Irsal-e-Alaq" practice. Leech saliva contains hirudin and other enzymes that act as anti-coagulants and thrombolytics, preventing the superficial thrombophlebitis common in CVI.³⁶
- **Exercise and Diet:** Continuous weight control and the avoidance of "heavy" foods address the *Asbab-e-Maddiyah* (material causes), preventing the regeneration of morbid humours.⁴¹

Gap Analysis and Future Outlook

While the mechanistic and traditional evidence for *Majoon Suranjan* is robust, this report identifies specific gaps that must be addressed to meet the stringent standards of PubMed or Scopus-indexed vascular journals:

1. **Quantitative Venous Hemodynamic:** Future clinical trials must include Doppler-derived reflux time and venous filling index as primary endpoints to provide objective evidence of venotonic (pnebotonics) action.
2. **Proteomic Profiling post-Majoon administration:** Measuring changes in circulating MMP levels in patients before and after a 60-day course of *Majoon Suranjan* would provide the "molecular signature" required for high-impact publication.
3. **Tadbir Standardisation:** There is a lack of data on how different *Tadbir* techniques (milk vs. ghee) affect the pharmacokinetic profile of colchicine in human subjects. Standardising the "Lumicolchicine" content as a marker of drug stability is essential.

Despite promising mechanistic evidence, the current review is limited by the scarcity of controlled clinical trials evaluating *Majoon Suranjan* specifically in patients with chronic venous insufficiency.

Conclusion

This exhaustive evaluation establishes *Majoon Suranjan* (based on *Colchicum luteum*) as a scientifically plausible and traditionally validated therapy for the management of *Dawali* and Chronic Venous Insufficiency. The formulation's multi-targeted mechanism—inhibiting the NLRP3 inflammasome, downregulating MMP-9, and stabilising blood rheology—directly addresses the pathophysiological root causes of venous remodelling. The convergence of Unani humoral theory (atrabilious stasis) and modern vascular proteomics (MMP-mediated ECM degradation) provides a robust conceptual bridge for integrative medicine. The historical safety protocols of *Amal-i-Tadbir* and the use of pharmacological correctives ensure that the drug's potent tropolone alkaloids can be harnessed safely for long-term management. Future clinical research focusing on objective CEAP and VCSS transitions will be paramount in establishing *Majoon Suranjan* as a standard-of-care botanical intervention in the global effort to manage chronic vascular diseases.

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Author Contributions:

- **Mahboob us Salam & Vijay Bhan Singh:** Conceptualization of the review, integration of modern molecular mechanisms (MMP regulation), and drafting of the manuscript.
- **Faiyaz Ahmed & Bushra Sabir:** Comprehensive analysis of classical Unani literature (e.g., *Al-Qanun Fi'l Tibb*) and synthesis of humoral stasis theories.
- **Badruddeen:** Pharmacological evaluation of polyherbal synergism and toxicological appraisal of tropolone alkaloids.
- **Minhajul Haque Ansari & Kaynat Fatima:** Data collection on bibliographic trends (2014–2024), creation of taxonomic and phytochemical tables, and refinement of the final manuscript.

Conflicts of Interest: The authors declare that there are no conflicts of interest and financial or personal relationships with other people or organizations that could inappropriately influence or bias the content of this paper.

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