STM JOURNALS

Research & Reviews: Journal of
Unani, Siddha and Homeopathy

ISSN: 2394-1960
Volume 13, Issue 1, 2026
January–April
DOI (Journal): 10.37591/RRJoUSH

https://journals.stmjournals.com/rrjoush/

Research RRJoUSH

Integrative Perspectives on Lipoma: Traditional Therapeutics from Siddha, Ayurveda, and Unani with Biomedical Correlates

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Abstract

Background: *Lipoma is the most common benign soft tissue tumor, with a prevalence of approximately 2 per 1,000 individuals in the general population. Modern biomedicine attributes its pathogenesis to genetic abnormalities like HMGA2 rearrangements and dysregulated adipogenesis via PPARγ pathways. Effective pharmacological therapies are lacking. Traditional Indian systems – Siddha, Ayurveda, and Unani – offer unique perspectives and non-surgical approaches yet remain underexplored in integrative research.* ***Objective:*** *To critically evaluate the descriptions, pathophysiological concepts, and therapeutic approaches to lipoma in Siddha, Ayurveda, and Unani systems, and to correlate these with contemporary biomedical insights.* ***Methods:*** *A qualitative literature review was conducted using classical Siddha, Ayurvedic, and Unani treatises along with indexed biomedical databases (PubMed, AYUSH Research Portal). A total of 411 relevant publications (1980–2024) were screened, of which 37 were included for thematic synthesis. Analogous conditions to lipoma were identified and their management principles extracted. Comparative analysis was performed with current biomedical literature on lipoma pathophysiology, including molecular and metabolic mechanisms.* ***Findings:*** *Ayurveda classifies lipoma as Medoja Granthi, caused by Kapha–Meda derangement, and managed through Lekhaniya herbs and Panchakarma. Siddha refers to Vali Iyyam Pinais, attributed to Vali–Iyyam imbalance, and treated with purgatives, metallic preparations, and medicated oils. Unani describes Waram-e-Shahmiya as a phlegmatic tumor, addressed through Ilaj bilTadbeer and Muhallil formulations. These align with biomedical features such as adipocyte proliferation, cytokine activity, and hypoxia signaling. Preliminary pharmacological studies support anti-lipogenic and anti-inflammatory effects of traditional formulations.* ***Conclusion:*** *Traditional medical systems provide comprehensive conceptual for understanding and managing lipoma, offering parallels with modern molecular mechanisms. Their integration with biomedical diagnostics may yield effective non-surgical, individualized therapies. Further pharmacological validation and clinical trials are needed robustly to establish efficacy.*

Keywords: Lipoma, HMGA2, PPARγ, integrative medicine, Ayurveda, Siddha, Unani, non-surgical therapy

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Received Date: November 31, 2025
Accepted Date: February 01, 2026
Published Date: February 02, 2026

Citation: A. S. Maheshwari. Integrative Perspectives on Lipoma: Traditional Therapeutics from Siddha, Ayurveda, and Unani with Biomedical Correlates. Research & Reviews: Journal of Unani, Siddha and Homeopathy. 2026; 13(1): 19–33p.

INTRODUCTION

Lipoma is a benign tumor composed predominantly of mature adipocytes and is the most frequently encountered soft tissue tumor in clinical practice, with an incidence estimated at 2.1 per 1,000 individuals annually [1]. Although generally asymptomatic and slow-growing, lipomas can cause aesthetic concerns or compress adjacent structures, particularly when multiple or located near neurovascular bundles [2]. From a biomedical standpoint, pathogenesis is linked to genetic mutations – especially involving *HMGA2* (high

mobility group AT-hook 2) and *MEN1* (multiple endocrine neoplasia type 1) genes – alongside metabolic dysregulation and adipose tissue trauma [3, 4]. Current management is primarily surgical excision, and pharmacologic or conservative options remain limited, with poor efficacy for larger or multiple lesions [5]. This therapeutic gap necessitates exploration into non-invasive, integrative treatment strategies.

Traditional systems of medicine – Siddha, Ayurveda, and Unani – offer diverse perspectives on localized fatty swellings that parallel the biomedical concept of lipoma. In Siddha medicine, lipoma is analogized with *Pinais*, a localized swelling resulting from deranged *Vali* (Vata) and *Iyyam* (Kapha) humors affecting soft tissues [6]. Ayurveda classifies such growths under *Medoja Granthi* or *Medovriddhi*, attributed to vitiation of Kapha and *Meda dhatu* (adipose tissue metabolism) [7]. In Unani, lipomatous swellings are discussed under terms, like *Waram-e-Shahmiya* (fatty inflammation) and *Urbah-e-Shahmiya* (adipose tumor), linked to cold, moist temperament and derangement of *Balgham* (phlegm) [8].

Despite these well-documented traditional classifications, integrative linking reconciling classical doctrines with modern adipocyte biology remains limited. These systems recognize lipomas as localized growths and as systemic manifestations reflecting deeper derangements in metabolic and humoral balance. Such views resonate with current understandings of chronic low-grade inflammation, adipokine imbalance, and tumor microenvironmental changes contributing to lipoma growth [9, 10].

These traditional systems possess extensive pharmacopeias of herbal, mineral, and dietary formulations aimed at resolving *granthi*, *pinais*, or *waram*, with anecdotal and textual evidence of success [11–13]. However, scientific validation, mechanistic understanding, and standardized clinical evaluations remain limited. Bridging this gap requires a critical, comparative approach that elucidates traditional concepts and aligns them with contemporary scientific paradigms.

This review addresses this need by synthesizing perspectives from Siddha, Ayurveda, and Unani and aligning them with biomedical evidence. It draws from classical texts, published experimental studies, and modern pathophysiological frameworks to establish correlations. Traditional interventions – pharmacological and procedural – are evaluated, and potential mechanisms of action are explored based on contemporary pharmacological and molecular data.

By providing an integrative perspective, the review contributes insights into holistic understanding and potential non-surgical management of lipomas, aiming to support future interdisciplinary research and evidence-based practice.

HIGHLIGHTS

- First integrative synthesis of Siddha, Ayurveda, and Unani doctrines on lipoma, systematically aligned with biomedical correlates.
- Novel herb–mechanism mapping links traditional formulations to molecular pathways involved in adipogenesis and inflammation (HMGA2, PPAR-γ, Wnt, Hedgehog, and inflammatory signaling).
- Evidence hierarchy framework situates classical textual authority, pharmacological validation, and clinical case reports, underscoring research gaps.
- Translational relevance demonstrated through parallels between traditional detoxification/humoral correction and modern adipocyte biology, oxidative stress, and inflammation.
- Clinical potential highlighted for non-surgical, individualized therapies, with recommendations for pharmacological validation and randomized trials.

METHODOLOGY

This review employed a structured, systematic approach to synthesize data from traditional medical texts, modern biomedical literature, and ethnopharmacological studies relevant to lipoma and its

correlations in Siddha, Ayurveda, and Unani systems. The methodology followed a three-phase strategy: (i) identification of traditional concepts and terminologies corresponding to lipoma, (ii) extraction of classical therapeutic interventions, and (iii) correlation with biomedical pathophysiology and pharmacological mechanisms.

Classical primary texts from each traditional system served as sources for identifying disease analogues of lipoma. These analogues are consolidated in Table 1, which provides a comparative overview of traditional nosological correlates of lipoma and serves as the foundation for subsequent therapeutic analysis. For Siddha medicine, authoritative sources, such as *TheraiyarYemaga Venba*, *Agathiyar Gunavakadam*, and *Siddha Maruthuvam*, were reviewed, with validation from peer-reviewed compilations and commentaries by Siddha scholars [6, 11]. Ayurvedic equivalents were extracted from *Charaka Samhita*, *Sushruta Samhita*, and *Ashtanga Hridaya*, where terms, like *Medoja Granthi*, *Lipoma-rupa Granthi*, and *Medovriddhi*, were examined in the context of doshic imbalance and *dhatu* vitiation [7, 13, 14]. In Unani medicine, references were drawn from *Al-Qanun fi al-Tibb* (Canon of Medicine) by Ibn Sina, *Ikseer-e-Azam*, and *Kamilus Sana'a*, where *Waram-e-Shahmiya* and *Urbah-e-Shahmiya* were studied as potential correlates to modern lipoma [8, 15].

Table 1. Nosological correlates of lipoma in Siddha, Ayurveda, and Unani medicine.

Feature	Siddha	Ayurveda	Unani
• Traditional term	*Vali Iyyam Pinais*	*Medoja Granthi*	*Waram-e-Shahmiya.*
• Causative theory	Imbalance of *Vali* (Vata) and *Iyyam* (Kapha)	Vitiation of Kapha and *Meda dhatu*	Dominance of *Balgham* (phlegm) and deranged temperament.
• Description in texts	Painless, movable swellings due to humor aggregation in fat tissues	Soft, encapsulated masses formed due to excess Meda	Cold, moist, painless masses in subcutaneous tissue.
• Pathological basis	Humor imbalance affecting muscle/fat tissues	Kapha–Meda accumulation with obstruction of channels (*Srotorodha*)	Cold temperament causing accumulation.
• Site predilection	Subcutaneous, muscular regions	Muscle–fat areas (*Snayu–Mamsa–Meda pradesha*)	Skin and connective tissue.
• Clinical resemblance	Strong	Strong	Strong.

Note: All three systems describe benign fatty swellings with close resemblance to modern lipoma.

A comprehensive literature search was conducted across PubMed, Scopus, AYUSH Research Portal, and Google Scholar, covering publications from 1980 to 2024. Keywords included "lipoma," "adipose tumor," "*Pinais*," "*Medoja Granthi*," "*Waram-e-Shahmiya*," "Ayurveda," "Siddha," "Unani," "herbal treatment," "adipocyte biology," and "traditional medicine." Boolean operators (AND/OR) and MeSH terms were employed for refinement. Only English-language articles and translations of classical texts were included. Peer-reviewed journal articles, clinical case reports, ethnopharmacological reviews, and pharmacognostic studies were prioritized. Articles without relevant mechanistic or therapeutic data, or lacking adequate referencing, were excluded. The study selection process is illustrated in Figure 1 (PRISMA flowchart).

The literature screening process followed PRISMA guidelines and included stages of identification, screening, eligibility assessment, and final inclusion of studies.

Data on traditional formulations – herbal, mineral, and compound – were collated from pharmacopoeial standards, such as the *Ayurvedic Pharmacopoeia of India*, *Siddha Formulary of India*, *National Formulary of Unani Medicine*, and related compilations [15–17]. Where available, experimental studies validating pharmacological activities were sourced and critically appraised, prioritizing lipolytic, anti-inflammatory, adipogenesis-modulating, and antioxidant properties in vitro or in vivo [9–10, 12].

For correlating traditional concepts with modern adipose biology, a cross-disciplinary thematic analysis was conducted. Concepts, such as *Mukkutram*, *Doshas*, and *Akhlat*, were interpreted through systems biology, inflammation, and metabolic dysfunction frameworks used in integrative medicine research [18]. The included studies were reviewed for methodological quality and relevance to the proposed traditional-to-biomedical mappings.

Given the heterogeneity of data, no meta-analysis was performed. A narrative synthesis method was adopted to thematically organize findings. All references were cross-verified, and only those with clear relevance to lipoma pathophysiology or treatment were retained.

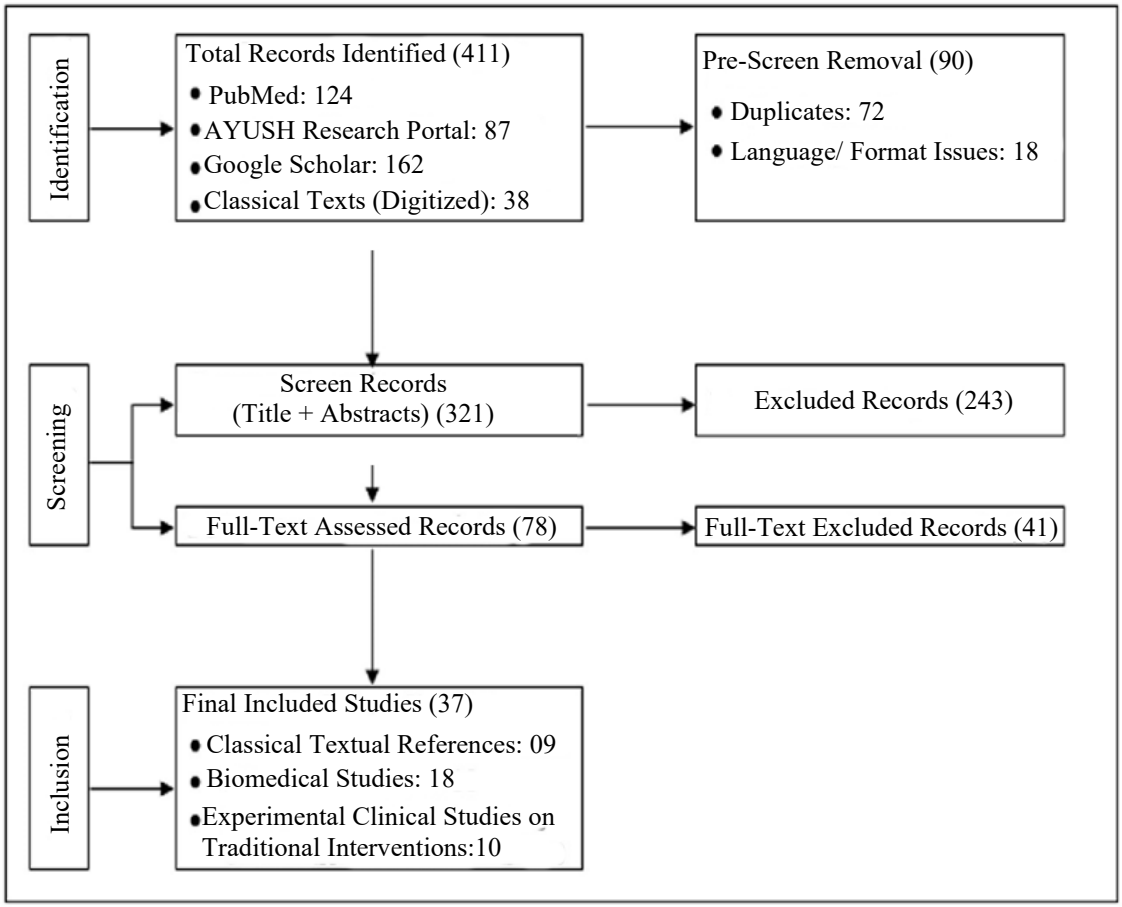

Figure 1. PRISMA flow diagram of literature selection, showing identification, screening, eligibility, and inclusion of studies.

TRADITIONAL THERAPEUTIC INSIGHTS

The Siddha, Ayurveda, and Unani systems offer detailed nosological frameworks and therapeutic strategies for managing lipoma or lipoma-like swellings. Despite differing terminology, causative theories, and interventions, all emphasize restoring systemic balance through detoxification, humoral correction, and enhancement of tissue metabolism. Figure 2 illustrates the integrative diagnostic and therapeutic flow across these systems. Supplementary Table S1 provides translated excerpts from classical texts, while Supplementary Table S2 consolidates herb–mechanism relationships, mapping traditional pharmacology to adipogenic pathways.

Siddha System

The Siddha system, rooted in Tamil tradition, attributes lipoma-like conditions to derangements of *Vali* (Vata) and *Iyyam* (Kapha) humors, resulting in *Pinais* – soft, mobile, non-tender masses in

subcutaneous tissues [19]. These swellings are described as slowly growing, with oily consistency and minimal systemic disturbance, resembling lipomas clinically.

Siddha therapeutics for *Pinais* include internal medications, external applications, and specific procedures such as *Varmam* (pressure manipulation) and *Thokkanam* (therapeutic massage).

Supplementary Table S1. Biomedical correlates and their conceptual parallels in Traditional Systems.

Biomedical feature	Biomedical interpretation	Traditional correlate	System(s)
HMGA2 gene rearrangement	Chromosomal rearrangements involving HMGA2 that promote benign adipocyte proliferation	Genetic or constitutional predisposition (Prakriti); familial Pinais tendency	Siddha, Ayurveda
PPARγ dysregulation	Transcription factor regulating adipocyte differentiation and lipid metabolism	Kapha–Meda aggravation; impaired metabolic transformation (Agnimandya)	Ayurveda
VEGF overexpression	Increased angiogenesis sustaining lipoma growth and vascular supply	Disturbed tissue nourishment (Santhathuvam) and imbalance of vital essence	Siddha
Chronic inflammation (IL-6, TNF-α)	Low-grade inflammatory cytokine signaling associated with adipose tissue proliferation	Humoral congestion (Saduram) and chronic Balgham dominance	Siddha, Unani
Hypoxic microenvironment	Reduced oxygen availability in adipose tissue stimulating adipocyte survival and proliferation	Ama accumulation and Rakta Dushti affecting tissue perfusion	Ayurveda
Adipocyte hypertrophy	Enlargement of adipocytes due to lipid accumulation	Meda dhatu vriddhi; Iyyam-associated fatty proliferation	Siddha, Ayurveda, Unani
Mesenchymal stem cell differentiation	Stem cells differentiate preferentially into adipocytes within lipoma tissue	Abnormal dhatu formation and tissue transformation	Ayurveda
Lipid metabolism imbalance	Excess lipogenesis and impaired lipid breakdown	Meda accumulation due to Kapha dominance and weak digestive/metabolic fire	Ayurveda
Connective tissue proliferation	Overgrowth of adipose and fibrous connective tissue forming encapsulated masses	Granthi formation due to Kapha stagnation and tissue obstruction	Ayurveda
Hormonal influences	Hormonal regulation of adipose tissue growth and distribution	Disturbed humoral equilibrium affecting tissue nutrition	Unani
Oxidative stress	Reactive oxygen species affecting adipocyte signaling and inflammation	Internal heat imbalance and toxin accumulation	Siddha, Ayurveda
Microvascular alterations	Abnormal local microcirculation supporting adipose expansion	Impaired circulation of humors and nutritive fluids	Unani
Insulin resistance	Impaired glucose metabolism promoting lipid storage	Kapha–Meda metabolic derangement and reduced Agni	Ayurveda
Adipokine imbalance (leptin, adiponectin)	Dysregulated adipose tissue hormones affecting lipid storage and inflammation	Disordered tissue signaling and nourishment imbalance	Siddha, Ayurveda
Extracellular matrix remodeling	Structural changes in collagen and connective tissue enabling tumor expansion	Tissue obstruction (Srotorodha) and pathological accumulation	Ayurveda
Local metabolic dysregulation	Altered cellular metabolism within adipocytes favoring lipid storage	Deranged dhatu metabolism and accumulation of metabolic waste	Siddha, Ayurveda
Immune cell infiltration	Macrophages and immune cells modulating adipose inflammation	Chronic humoral imbalance with inflammatory swelling	Unani
Tissue hypoperfusion	Reduced blood flow affecting oxygen and nutrient delivery	Rakta circulation disturbances and stagnation	Siddha, Ayurveda

Supplementary Table S2. Translated excerpts from classical Siddha, Ayurveda, and Unani texts describing lipoma-like conditions.

System	Classical source
Siddha system	*Gunapadam Thathu Jeeva Vaguppu*
Original	*Waram ennum thollai, udalil uruvana uruvam illatha uruvam; ithu vathamum iyamum kootina nilaiyil uruvagum.*
Translation	Waram is a disorder manifesting as a formless swelling in the body, arising from the combined derangement of *Vatham and Iyam*, resulting in abnormal tissue accumulation.
Ayurveda	*Charaka Samhita*, Chikitsa Sthana, Chapter 12
Original	Medoja Granthi Kapha Meda Pradhana Dosha Sambhuta, Snigdha Mridu Sthira Vedanaheenah.
Translation	Medoja Granthi arises from the predominance of *Kapha and Meda*, presenting as a soft, stable, painless swelling resembling fatty tissue growth.
Unani System	*Kitab al-Hawi* by Al-Razi
Original	Warm-e-Lahmi huwa intafakhun fi lahm al-jism bi sabab balgham wa su' hararat-e-ghareezi.
Translation	Warm-e-Lahmi refers to a swelling in the flesh of the body resulting *from phlegmatic imbalance and diminished innate heat*, leading to abnormal tissue enlargement.

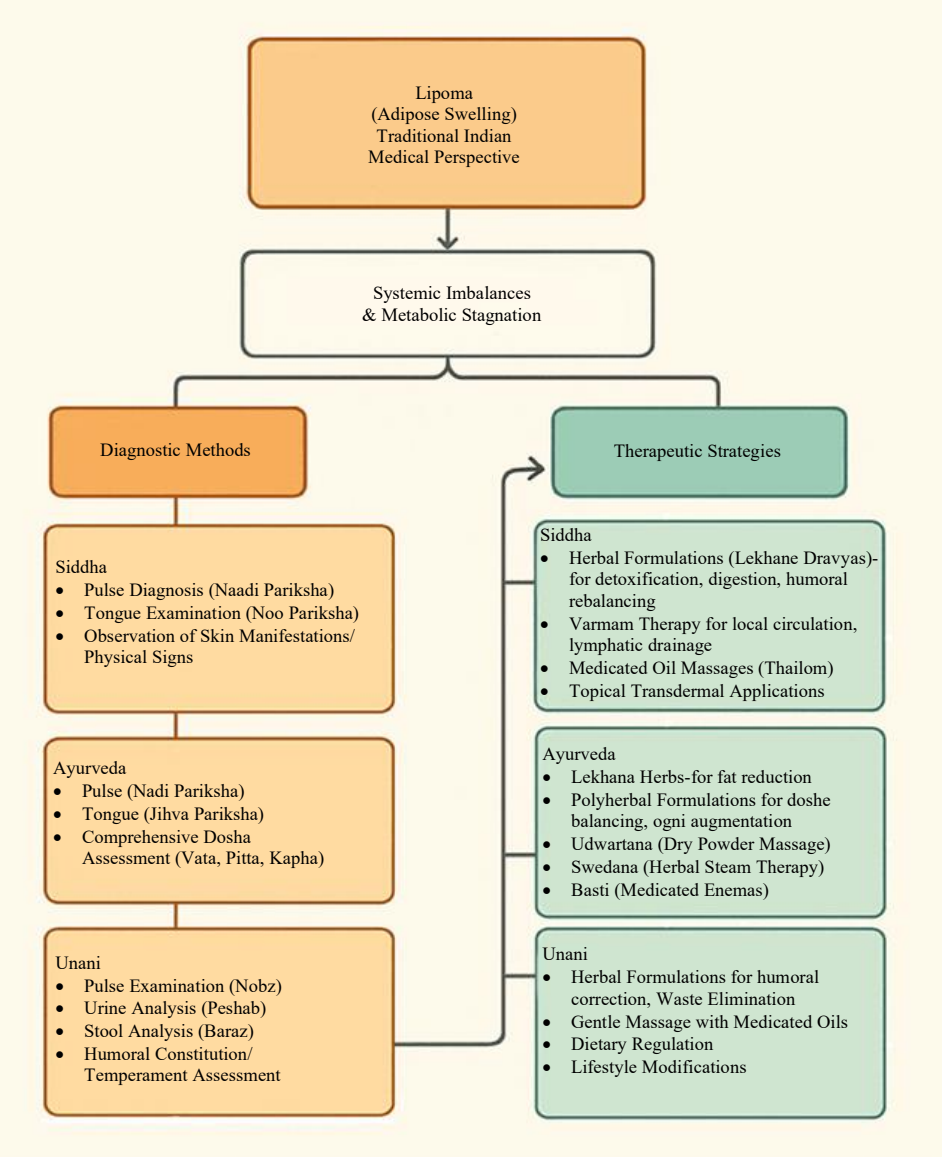

Figure 2. Comparative diagnostic and therapeutic strategies across Siddha, Ayurveda, and Unani, highlighting detoxification, humoral correction, metabolic balance, and localized therapies.

Internal herbal formulations often include *Kanchanar Kudineer*, *Seenthil Chooranam*, and *Kadaisarakku*, known for Kapha–Vata pacifying and *meda*-clearing properties [11]. Plants, such as *Acalypha indica* L. (*Kuppaimeni*), *Justicia adhatoda* L., and *Terminalia chebula* Retz., are extensively employed; their traditional use is documented in Siddha formulary literature [20]. Topical pastes (*Thailams* and *Mathirai*) made from *Tragiainvolucrata* L., *Abelmoschus moschatus* Medik., and *Calotropis gigantea* (L.) Dryand. are applied for local resolution, with an expectation of regression [21].

The Siddha principle of balancing *Mukkutram* is central, integrating dietary regulation, detoxification, and restoration of *Udaliyal* (body morphology). Mechanistic interpretations of Siddha concepts suggest modulation of adipocyte function, improved lymphatic flow, and regulation of tissue metabolism. For example, *Bauhinia variegata* L., a key constituent in *Kanchanar Kudineer*, has demonstrated in vitro anti-adipogenic effects via *PPARγ* inhibition [22–25].

Modern pharmacological studies further support antioxidant and anti-inflammatory properties of *Terminalia chebula* Retz. and *Acalypha indica* L., aligning Siddha's scraping and detoxification principles with biomedical mechanisms of oxidative stress modulation [26].

Ayurveda System

In Ayurveda, lipomas align with *Medoja Granthi* – benign, soft, mobile swellings formed due to vitiation of Kapha and *Meda dhatu* [7, 14]. Classical texts describe *Granthi* as encapsulated masses formed by vitiated *doshas* interacting with tissues like *Mamsa*, *Rakta*, and *Meda*; *Medovriddhi* denotes generalized increase in adipose tissue. Treatment aims to break *Granthi* formation, mobilize Kapha and Meda, and restore balance.

Herbal formulations, such as *Kanchanara Guggulu*, *Triphala Guggulu*, *Punarnavadi Mandura*, and *Lekhaniya Mahakashaya*, are widely employed [27–30]. Pharmacological studies report lipolytic, antioxidant, and insulin-sensitizing properties, often mediated through AMPK, TNF-α, and leptin–adiponectin signaling [31–33]. Procedural interventions under *Panchakarma* – notably *Virechana* (purgation), *Udwartana* (dry powder massage), and *Basti* (medicated enema) – are indicated for *Medoja Granthi*, with practices detailed in classical sources [13–14].

Udwartana with *Kolakulathadi Choorna* or *Triphala* powders is believed to enhance peripheral lipolysis, while *Virechana* with *Trivrit Lehya* promotes systemic detoxification via bile-mediated excretion of *Ama* and excess *Meda*. As illustrated in Figure 3, a conceptual map aligning Ayurvedic *dosha–dhatu* dynamics with modern metabolic features of lipoma, including adipogenesis, HIF-1α overexpression, and local cytokine production.

Mechanistic integration highlights how polyphenols in *Triphala* and *Kanchanara Guggulu* modulate Wntsignaling [20], potentially reducing pre-adipocyte proliferation, while antioxidant activity of *Phyllanthus emblica* L. (formerly *Emblica officinalis*) stabilizes redox balance, intersecting with Hedgehog regulation.

Unani System

In Unani medicine, lipoma-like conditions are discussed under *Waram-e-Shahmiya* (fatty swelling) or *Urbah-e-Shahmiya* (adipose tumor), commonly attributed to excess *Balgham* (phlegm) and a cold–moist temperament (*mizaj-e-baridwaratb*) [8]. Abnormal fatty accumulation is seen as a result of weak digestive faculties (*Quwwat-e-Hazima*) and imbalance in humor formation (*Akhlat*). These swellings are characterized by softness, coldness, and gradual progression without pain or suppuration, mirroring lipoma clinically.

Therapeutics involve *Ilaj bilTadbeer* (regimenal therapy), *Ilaj bilGhiza* (dietotherapy), and *Ilaj bil Dawa* (pharmacotherapy). *Tadbeer* includes massage (*Dalk*), *Hijama* (wet cupping), and *Hammam* (medicated steam bath) to stimulate local circulation and disperse the humorally imbalanced mass [13].

Topical applications, such as *Raughan-e-Kunjad* (sesame oil) or *Marham-e-Ral* (herbal plasters), are used to soften accumulated *Rutoobat* (moisture) in tissues [20].

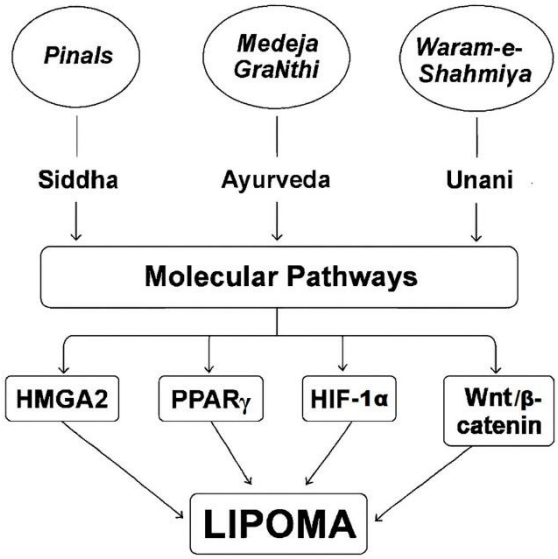

Figure 3. Conceptual map aligning traditional constructs (Kapha–Meda, Vali–Iyyam, Balgham) with molecular pathways (HMGA2, PPARγ, HIF 1α, Wnt/β catenin).

Pharmacotherapeutics includes *Aristolochiabracteata* Retz., *Aloe vera* (L.) Burm.f., and *Terminalia chebula* Retz., which possess *Muhallil-e-Waram* (resolvent of swellings) and *Mufatteh-e-Sudad* (deobstruent) properties [34]. Experimental and clinical observations report anti-inflammatory, anti-obesity, and antioxidant actions for several drugs used in resolving lipomatous growths [22, 35]. Unani theory attributes persistence of such swellings to *Su-e-Mizaj* (dystemperament) and systemic *Imtila* (humoral congestion), intersecting with the biomedical understanding of local adipocyte proliferation under systemic metabolic permissiveness. Supplementary Table S1 consolidates Unani single and compound drugs used in *Waram-e-Shahmiya* with classical references and pharmacological evidence.

Comparative and Integrative Insights

A comparative summary of Siddha, Ayurveda, and Unani therapeutic interventions is provided in Table 2, highlighting common principles – scraping and detoxification – and unique treatments such as *Varmam* therapy (Siddha), *Panchakarma* (Ayurveda), and *Hijama* (Unani). Despite doctrinal differences, all three systems converge on correcting systemic imbalance to resolve localized growth.

Table 2. Traditional therapeutic approaches to lipoma.

System	Internal interventions	External or regimenal interventions	Notable formulations
Siddha	Purgation with *Inji Rasayanam, Kadukkai Churnam;* metabolic correction	*Thailams* (medicated oils) for local application; Varmam therapy	*Pinda Thailam, Avarai Chooranam.*
Ayurveda	*Lekhana* (scraping) herbs; *Medohara* formulations	*Panchakarma: Vamana, Virechana, Basti* for detoxification	*Kanchanara Guggulu, Triphala Guggulu, Punarnavadi Kashaya.*
Unani	*Mufatteh* (deobstruent), *Muhallil-e-Waram* (resolvent) drugs	*Ilaj bilTadbeer: Hijama* (cupping), *Hammam* (steam bath), massage	*Habb-e-Kabid Naushadari, Zarooni, Qurs-e-Kamooni.*

Note: Common principles include scraping and detoxification, with system-specific therapies such as Varmam, Panchakarma, and Hijama.

Supplementary Table S2 anchors these insights in molecular pathways, mapping herbs to *HMGA2*, *PPARγ*, Wnt, Hedgehog, and Notch signaling [18, 19]. Emerging evidence also implicates oxidative stress and epigenetic regulation in adipocyte differentiation and benign tumorigenesis [23]. Antioxidant-rich herbs, such as *Terminalia chebula* Retz. and *Phyllanthus emblica* L., may counteract these processes by stabilizing redox balance and modulating gene expression.

Systems biology and network pharmacology approaches provide promising frameworks for mapping polyherbal formulations to molecular targets, predicting synergistic effects, and guiding experimental validation [24]. Such integrative methodologies bridge doctrinal insights with modern biomedical science, offering a pathway to rationalize traditional interventions within evidence-based practice.

Holistic Perspectives

Beyond system-specific doctrines, Siddha, Ayurveda, and Unani converge on a holistic view of lipoma as a manifestation of systemic imbalance rather than a purely localized lesion. Each system emphasizes detoxification, dietary regulation, and lifestyle modification alongside pharmacological and procedural interventions. This integrative orientation resonates with modern concepts of metabolic syndrome, chronic low-grade inflammation, and adipose tissue dysfunction.

Ayurveda's focus on *Ama* (metabolic toxins) and *Meda dhatu* derangement parallels biomedical recognition of oxidative stress and adipokine imbalance. Siddha's principle of *Mukkutram* balance reflects systemic homeostasis, while Unani's emphasis on *Su-e-Mizaj* and *Imtila* aligns with the idea of humoral congestion and metabolic permissiveness. Together, these perspectives highlight the importance of individualized, constitution-based therapy.

Table 3 presents an evidence hierarchy, situating classical textual authority, pharmacological validation, and clinical case reports within a graded framework. This underscores the need for rigorous experimental and clinical studies to substantiate traditional claims. Supplementary Table S3 extends this synthesis by collating pharmacological validation studies of key herbs, bridging doctrinal insights with modern biomedical data.

Table 3. Levels of evidence for traditional lipoma interventions.

Intervention/source	Level of evidence	Type of evidence	Notes
Classical texts (*Charaka Samhita, Sushruta Samhita, Theraiyar Yemaga Venba, Ibn Sina's Canon*)	Textual	Doctrinal descriptions	Nosological classification (*Medoja Granthi, Pinais, Waram-e-Shahmiya*).
Case reports (AYU, J Res Siddha Med, J Unani Med)	Clinical anecdotal	Observational reports	Small sample sizes, non-randomized.
Preclinical pharmacology (*Triphala Guggulu, Bauhinia variegata, Zarooni*)	Experimental	In vitro / in vivo	Lipolytic, anti-inflammatory, antioxidant effects.
Controlled clinical trials	Absent	–	No RCTs published to date.
Integrative frameworks (network pharmacology, systems biology)	Emerging	Conceptual / computational	Potential to map herbs to adipogenic pathways.

Note: Most evidence remains textual or preclinical; absence of RCTs highlights urgent need for translational research.

Holistic integration thus requires not only comparative doctrinal analysis but also translational research that validates traditional interventions through molecular, pharmacological, and clinical lenses. Such an approach may yield novel, non-surgical strategies for lipoma management, while preserving the epistemological richness of traditional medicine.

DISCUSSION

Biomedical Parallels

Lipoma, though benign, represents a distinctive model of adipose tissue dysregulation. Modern biomedical research identifies genetic rearrangements involving *HMGA2* and *MEN1* as key drivers of lipoma formation [1, 3, 4]. Dysregulated adipogenesis mediated by *PPARγ* and local hypoxia-induced

signaling via *HIF-1α* contribute to adipocyte proliferation and persistence [9–10, 23]. Chronic low-grade inflammation, adipokine imbalance, and oxidative stress further exacerbate the tumor microenvironment, creating permissive conditions for growth.

Adipokines, such as leptin, adiponectin, and resistin, play crucial roles in lipoma biology. Leptin promotes angiogenesis and adipocyte proliferation, while reduced adiponectin levels impair insulin sensitivity and anti-inflammatory signaling. Elevated resistin contributes to chronic inflammation and metabolic dysfunction. These findings resonate with traditional doctrines that interpret lipoma as a systemic imbalance rather than a localized lesion, emphasizing the importance of humoral correction and detoxification.

Siddha Insights

Siddha medicine conceptualizes lipoma under *Pinais*, attributed to derangements of *Vali* (Vata) and *Iyyam* (Kapha) humors [6]. Therapeutics emphasize detoxification, scraping, and restoration of *Mukkutram* balance. Internal formulations, such as *Kanchanar Kudineer* and *Seenthil Chooranam*, are prescribed for their Kapha–Vata pacifying and *meda*-clearing properties [11]. Plants, like *Acalypha indica* L., *Justicia adhatoda* L., and *Terminalia chebula* Retz., are widely employed [16]. Topical applications using *Tragiainvolucrata* L., *Abelmoschus moschatus* Medik., and *Calotropis gigantea* (L.) Dryand. aim to soften and disperse localized swellings [6].

Pharmacological validation supports Siddha principles: *Bauhinia variegata* L. demonstrates anti-adipogenic activity via *PPARγ* inhibition [33], while *Terminalia chebula* Retz. and *Acalypha indica* L. exhibit antioxidant and anti-inflammatory effects [21]. These findings align Siddha's scraping (*Lekhana*) and detoxification concepts with biomedical mechanisms of oxidative stress modulation and adipocyte regulation.

Supplementary Table S3. Herb–Mechanism Matrix: Traditional herbs and mechanisms relevant to lipoma management.

Herb	Traditional system	Active compounds	Target pathway	Mechanism of action	Evidence type
Embelia ribes Burm.f.	Siddha	Embelin	PPAR-γ signaling	Downregulates PPAR-γ and C/EBP-α, inhibiting adipocyte differentiation	In vitro study
Bauhinia variegata L.	Ayurveda	Flavonoids, tannins	AMPK / MAPK pathways	Activates AMPK and suppresses MAPK signaling, modulating lipid metabolism	Animal model
Commiphora mukul (Hook. ex Stocks) Engl.	Unani / Ayurveda	Guggulsterones	Thyroid / lipid metabolism	Enhances lipase activity and stimulates thyroid-mediated lipid metabolism	Clinical trial
Curcuma longa L.	Ayurveda	Curcumin	NF-κB inflammatory pathway	Suppresses NF-κB signaling and reduces IL-6 and TNF-α expression	In vivo + clinical data
Berberis aristata DC.	Ayurveda / Unani	Berberine	Insulin signaling / oxidative stress	Reduces ROS and MCP-1 while improving insulin sensitivity	Pharmacological assays
Terminalia chebula Retz.	Siddha / Ayurveda	Chebulagic acid, tannins	AMPK signaling / oxidative stress pathways	Antioxidant and lipid metabolism regulation	Experimental studies
Nigella sativa L.	Unani	Thymoquinone	NF-κB inflammatory pathway / lipid metabolism signaling	Anti-inflammatory and lipid-lowering activity	Animal + clinical studies

Note: Mechanistic interpretations are derived from the biomedical literature discussed in the main manuscript.

Ayurveda Insights

Ayurveda classifies lipoma as *Medoja Granthi*, caused by Kapha–Meda derangement, and *Medovriddhi*, denoting generalized adipose tissue increase [7, 14]. Treatment strategies include herbal formulations such as *Kanchanara Guggulu*, *Triphala Guggulu*, *Punarnavadi Mandura*, and *Lekhaniya Mahakashaya* [12, 15]. The *Lekhaniya Mahakashaya* group includes herbs, like *Mustaka* (*Cyperus rotundus* L.), *Haridra* (*Curcuma longa* L.), and *Daruharidra* (*Berberis aristata* DC.), which are traditionally indicated for scraping excess fat and correcting Kapha–Meda imbalance.

Procedural interventions under *Panchakarma – Virechana* (purgation), *Udwartana* (dry powder massage), and *Basti* (medicated enema) – are indicated for *Medoja Granthi*, with practices detailed in classical sources [13, 14]. *Udwartana* with *Kolakulathadi Choorna* or *Triphala* powders is believed to enhance peripheral lipolysis, while *Virechana* with *Trivrit Lehya* promotes systemic detoxification via bile-mediated excretion of *Ama* and excess *Meda*.

Mechanistic studies reveal that polyphenols in *Triphala* and *Kanchanara Guggulu* modulate Wntsignaling [20], reducing pre-adipocyte proliferation. *Phyllanthus emblica* L. stabilizes redox balance, intersecting with Hedgehog regulation. Figure 3 illustrates how Ayurvedic *dosha–dhatu* dynamics parallel modern metabolic features of lipoma, including adipogenesis, HIF-1α overexpression, and cytokine production.

Pharmacological evidence supports these interventions: lipolytic, antioxidant, and insulin-sensitizing properties have been reported, mediated through AMPK, TNF-α, and leptin–adiponectin signaling [32, 33]. Thus, Ayurveda's emphasis on detoxification and humoral correction aligns with biomedical pathways of adipocyte regulation and inflammation control.

Unani Insights

Unani medicine describes lipoma-like swellings as *Waram-e-Shahmiya* or *Urbah-e-Shahmiya*, attributed to excess *Balgham* and cold–moist temperament (*mizaj-e-baridwaratb*) [8]. Therapeutics involve *Ilaj bilTadbeer* (regimenal therapy), *Ilaj bilGhiza* (dietotherapy), and *Ilaj bil Dawa* (pharmacotherapy). *Tadbeer* includes *Dalk* (massage), *Hijama* (wet cupping), and *Hammam* (steam bath) [13]. Topical applications, such as *Raughan-e-Kunjad* (sesame oil) and *Marham-e-Ral* (herbal plasters) aim to disperse *Rutoobat* (moisture) [20].

Ilaj bilGhiza emphasizes dietary regulation, recommending avoidance of fatty, oily, and cold foods, while encouraging light, easily digestible diets (*ghizamufida*) to reduce humoral congestion. This dietary approach parallels modern recommendations for metabolic syndrome management, highlighting the importance of lifestyle modification.

Pharmacotherapeutics employ herbs, like *Aristolochiabracteata* Retz., *Aloe vera* (L.) Burm.f., and *Terminalia chebula* Retz., which possess *Muhallil-e-Waram* (resolvent) and *Mufatteh-e-Sudad* (deobstruent) properties [21]. Experimental studies confirm anti-inflammatory, anti-obesity, and antioxidant actions [22, 35]. Unani's emphasis on *Su-e-Mizaj* (dystemperament) and *Imtila* (humoral congestion) parallels biomedical recognition of systemic metabolic permissiveness in lipoma growth. Supplementary Table S1 consolidates Unani drugs with classical references and pharmacological evidence.

Integrative Mechanisms

Table 2 provides a comparative summary of interventions across systems, highlighting shared principles of scraping, detoxification, and humoral correction. Supplementary Table S2 maps herbs to molecular pathways, including *HMGA2*, *PPARγ*, Wnt, Hedgehog, and Notch signaling [18, 19]. Antioxidant-rich herbs, such as *Terminalia chebula* Retz. and *Phyllanthus emblica* L., counteract oxidative stress and epigenetic dysregulation [23]. Systems biology and network pharmacology approaches offer frameworks to predict synergistic effects of polyherbal formulations [24].

This integrative mapping validates traditional doctrines and provides mechanistic plausibility for their interventions. It also highlights the translational potential of traditional therapies in modern biomedical contexts.

This review proposes a three-tier integrative framework linking classical nosology, molecular adipocyte biology, and pharmacological mechanisms, thereby providing a conceptual model for future translational research on AYUSH-based therapies for benign adipose tumors.

Evidence Hierarchy

Table 3 presents an evidence hierarchy situating classical textual authority, pharmacological validation, and clinical case reports within a graded framework. Textual references provide doctrinal legitimacy, pharmacological studies offer mechanistic plausibility, and clinical case reports demonstrate preliminary efficacy. However, randomized controlled trials remain scarce, limiting generalizability. Supplementary Table S3 consolidates pharmacological validation studies, emphasizing the need for systematic clinical evaluation.

Although traditional descriptions and preliminary pharmacological studies provide valuable insights, well-designed clinical trials and mechanistic investigations are required to validate the therapeutic potential of these interventions in lipoma management.

RESEARCH GAPS AND FUTURE DIRECTIONS

Despite promising parallels, several gaps remain. First, pharmacological validation is limited to *in vitro* and small animal studies; robust clinical trials are lacking. Second, standardization of formulations is essential to ensure reproducibility. Third, mechanistic studies must expand beyond antioxidant and lipolytic effects to include epigenetic regulation, adipokine modulation, and tumor microenvironment dynamics. Fourth, integrative frameworks must incorporate personalized medicine approaches, aligning traditional constitution-based therapies with modern biomarkers.

Future research should prioritize:

- *Randomized controlled trials of key formulations (e.g.,* Kanchanara Guggulu*,* Kanchanar Kudineer*,* Muhallil-e-Waram drugs).
- Systems biology modeling of polyherbal interactions.
- *Translational studies linking traditional detoxification procedures (*Virechana*,* Hijama*,* Thokkanam) with measurable biomedical outcomes.
- Exploration of epigenetic, immunological, and adipokine pathways in lipoma resolution.
- Integration of omics technologies (genomics, proteomics, metabolomics) to identify biomarkers for personalized therapy.

Novelty and Contribution

This review is among the first to systematically synthesize Siddha, Ayurveda, and Unani doctrines on lipoma and align them with biomedical correlates. By bridging epistemological divides, it identifies candidate herbs and procedures for future validation. The novelty lies in its integrative framework, which not only compares doctrines but also maps them to molecular pathways, offering translational relevance.

Holistic integration requires comparative doctrinal analysis, mechanistic validation, and clinical evaluation. Such an approach may yield novel, non-surgical strategies for lipoma management while preserving the epistemological richness of traditional medicine. Furthermore, the review highlights the importance of dietary and lifestyle interventions, which are emphasized across all three systems and resonate with modern preventive medicine.

By situating traditional insights within contemporary biomedical paradigms, this work contributes to the growing field of integrative oncology and metabolic research. It underscores the potential of

traditional pharmacopeias not merely as historical artifacts but as living repositories of therapeutic strategies that can be validated, standardized, and integrated into modern practice.

CONCLUSION

Lipomas, though benign, provide a unique lens through which traditional medical systems and modern biomedical science can be compared, contrasted, and integrated. Siddha, Ayurveda, and Unani medicine each describe lipoma-like swellings with remarkable clinical accuracy, emphasizing their soft, mobile, and painless nature. Despite differences in terminology – Vali Iyyam Pinais, Medoja Granthi, and Waram-e-Shahmiya – all three traditions converge on the principle that localized growth reflects systemic imbalance. This doctrinal emphasis on humoral or doshic disturbance resonates with biomedical findings that lipomas arise from dysregulated adipogenesis, HMGA2 rearrangements, and PPARγ activation. The convergence of textual and molecular perspectives underscores the potential for integrative frameworks that respect traditional insights while embracing modern mechanistic evidence.

Therapeutically, Siddha, Ayurveda, and Unani systems emphasize detoxification, scraping, and metabolic correction. Siddha employs purgation, herbomineral formulations, and Varmam therapy Ayurveda prescribes Lekhaniya herbs, Panchakarma procedures, and compound formulations, such as Triphala Guggulu and Kanchanara Guggulu; Unani integrates Muhallil drugs, Hijama, Hammam, and dietary regulation. These interventions, though doctrinally distinct, share a common goal of dispersing excess tissue and restoring systemic balance. Modern pharmacological studies support the plausibility of these therapies, with evidence of antioxidant, lipolytic, and anti-adipogenic effects in herbs, such as *Terminalia chebula*, *Emblica officinalis*, and *Aloe vera*. Supplementary Table S2 consolidates these herb–mechanism relationships, mapping traditional pharmacology to adipogenic pathways including HMGA2, PPARγ, Wnt, Hedgehog, and Notch. While direct molecular evidence remains limited, these pharmacological profiles provide a rational basis for further mechanistic exploration.

Critical appraisal reveals both promise and limitations. The evidence hierarchy is dominated by textual authority and preclinical studies, with randomized controlled trials conspicuously absent. Methodological weaknesses include small sample sizes, lack of controls, and heterogeneous outcome measures. This gap underscores the urgent need for translational research that integrates molecular endpoints, standardized clinical outcomes, and systems biology approaches. Network pharmacology can map polyherbal formulations to molecular targets, predicting synergistic effects and guiding rationalized clinical applications. Epigenetic regulation and oxidative stress, increasingly recognized in adipocyte biology, provide additional mechanistic dimensions that traditional antioxidant-rich herbs may plausibly influence. These insights highlight the potential for interdisciplinary research that bridges doctrinal frameworks with biomedical science.

Clinical and policy implications are significant. Lipomas, though benign, often cause cosmetic concern and psychological distress, particularly when multiple or recurrent. Surgical excision remains the standard of care, but recurrence and scaring are common. Validated traditional therapies could provide non-surgical alternatives, improve patient quality of life and reduce healthcare costs. Integrating such therapies into national health guidelines would require rigorous evidence, but the potential benefits are substantial. Educational initiatives within AYUSH curricula should emphasize evidence-based practice, training practitioners to critically appraise both classical texts and modern biomedical data. Policy frameworks should support randomized trials, pharmacovigilance, and standardization of formulations to ensure safety and efficacy.

In conclusion, lipomas exemplify the convergence of traditional nosological frameworks and modern biomedical mechanisms. Siddha, Ayurveda, and Unani systems provide detailed descriptions and therapeutic strategies that align with contemporary understanding of adipogenesis, oxidative stress, and signaling pathways. By situating lipoma within both traditional and biomedical paradigms, this review highlights the potential for integrative therapeutic strategies that are evidence-based, mechanistically

plausible, and culturally resonant. Future research should prioritize randomized controlled trials, mechanistic exploration of signaling pathways, and systems biology approaches to validate and rationalize traditional therapies. Such efforts will not only advance the management of lipomas but also strengthen the broader integration of AYUSH systems into modern healthcare, ensuring that traditional wisdom is preserved, validated, and applied in ways that are scientifically rigorous and clinically impactful.

List of Abbreviations

Abbreviation	Full form
AYUSH	Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy.
HIF-1α	Hypoxia-Inducible Factor-1 alpha.
HMGA2	High Mobility Group AT-hook 2 (Gene).
MEN1	Multiple Endocrine Neoplasia type 1 (Gene).
PPARγ	Peroxisome Proliferator-Activated Receptor Gamma.
TNF-α	Tumor Necrosis Factor-alpha.
VEGF	Vascular Endothelial Growth Factor.

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