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THE AYURVEDIC THERAPEUTIC POTENTIAL OF *VITIS QUADRANGULARIS* LINN. (*ASTHISAMHARAKA*): A COMPREHENSIVE ETHNOPHARMACOLOGICAL REVIEW

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ABSTRACT

Vitis quadrangularis, known in Ayurveda as *Asthisamharaka*, is a perennial plant with a rich history of use in traditional medicine for skeletal and metabolic disorders. This review aims to provide a comprehensive synthesis of its traditional Ayurvedic applications and to critically evaluate the modern scientific evidence supporting its therapeutic potential. A systematic literature search was conducted across classical Ayurvedic texts and modern scientific databases, including PubMed, Scopus, and Google Scholar, to collate information on the plant's botany, phytochemistry, and pharmacology. In Ayurveda, *Asthisamharaka* is primarily indicated for *Asthibhagna* (bone fracture) and *Sandhigatavata* (osteoarthritis), an application directly reflected in its name, which translates to "bone setter." Phytochemical analysis reveals a rich profile of bioactive compounds, including ketosteroids, triterpenoids, flavonoids, and stilbenes, which are believed to underpin its medicinal properties. Preclinical studies robustly demonstrate its osteogenic and anti-osteoporotic effects, showing that its extracts enhance osteoblast proliferation and mineralization, inhibit osteoclastogenesis, and modulate key signaling pathways and cytokine profiles. Clinical trials in humans have validated its efficacy in accelerating fracture healing, reducing joint pain, and managing weight and metabolic syndrome parameters. While its effect on established osteoporosis is more focused on slowing bone loss than rebuilding bone mineral concludes that there is a strong correlation between the traditional Ayurvedic uses of *Asthisamharaka* and its scientifically validated pharmacological activities, particularly in bone health. Further high-quality, long-term clinical trials are warranted to fully integrate this potent Ayurvedic remedy into evidence-based clinical practice.

Keywords: *Vitis Quadrangularis, Asthisamharaka, Hadjor, Ayurveda, Fracture Healing,Osteoporosis, Phytochemistry.*

1. INTRODUCTION

Vitis quadrangularis: An Ethnomedicinal Overview

Cissus quadrangularis L., a synonym of *Vitis quadrangularis*, is a perennial succulent plant belonging to the Vitaceae (grape) family.[1] Native to the hotter, drier tropical and subtropical regions of India, Sri Lanka, Africa, and Southeast Asia, this climbing herb has been a cornerstone of traditional medicine for millennia.[3] It is characterized by its remarkable resilience and distinctive morphology, which have earned it a variety of descriptive common names, including Veldt Grape, Devil's Backbone, Adamant Creeper, and Square-stalked Vine.[1] Its long-standing application is not confined to a single medical system; it holds a prominent place in Ayurveda, Siddha, and traditional African medicine, where it is employed to treat a wide spectrum of ailments ranging from musculoskeletal injuries and gastrointestinal issues to metabolic and menstrual disorders.[1] The plant's versatility and widespread use across diverse cultures underscore its significant ethnopharmacological importance and have made it a subject of intense modern scientific investigation.

The Doctrine of Signatures in Ayurveda: *Asthisamharaka* as the "Bone Setter"

In Ayurvedic philosophy, the principle of "*Yatra aakrutihi tatra gunaaha vasanti*"—which translates to "where there is a specific form, specific properties reside"—often guides the understanding of a plant's therapeutic action.[11] This concept, similar to the Western "Doctrine of Signatures," posits that a plant's physical characteristics can reveal its medicinal use.

Vitis quadrangularis is a quintessential example of this doctrine. Its thick, fleshy stem is distinctly quadrangular and segmented by nodes, bearing a striking resemblance to the structure of bones and joints in the human body.[11]

This morphological similarity is powerfully reflected in its primary Sanskrit name, *Asthisamharaka*, which literally means "that which prevents the destruction of bones" or, more simply, the "bone setter".[1] This nomenclature is not merely symbolic; it is a direct ethnopharmacological signpost that has pointed toward its principal therapeutic application for centuries. Other Sanskrit synonyms further reinforce this identity:

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Asthishrinkhala translates to "chain of bones," alluding to its stem's appearance and its role in skeletal integrity, while *Vajravalli*, meaning "diamond-like creeper," speaks to its ability to impart strength and resilience to the body.[11] The remarkable consistency of this naming convention and its associated use provides one of the most compelling cases of ethnopharmacological validation. The empirical observations of ancient physicians, who identified the plant's profound effect on bone healing, were codified in a name that has directly guided and been subsequently validated by modern scientific inquiry. This represents a successful application of reverse pharmacology, where traditional knowledge provides a highly accurate starting point for contemporary drug discovery and validation.

Rationale and Objectives of the Current Review

The use of *Vitis quadrangularis* has surged in recent years, with extracts being incorporated into numerous nutraceutical products for bone health, joint support, and weight management. This growing commercial interest is paralleled by an expanding body of scientific literature. However, despite this wealth of traditional knowledge and modern research, there remains a need for a comprehensive review that critically synthesizes these two domains.[17] Many existing studies focus on specific aspects of the plant's pharmacology, but a holistic evaluation that bridges the classical Ayurvedic framework, including its properties, actions, and formulations, with contemporary evidence from phytochemical, preclinical, and clinical studies is lacking.

Therefore, this review has been undertaken with the following objectives:

1. To document the complete botanical, taxonomic, and classical Ayurvedic profile of *Asthisamharaka*, including its nomenclature and pharmacological properties (*Ras Panchak*).
2. To systematically review the known phytochemical constituents of *Vitis quadrangularis* and their potential contributions to its bioactivity.
3. To critically evaluate the preclinical (*in-vitro* and animal) and clinical evidence supporting its diverse therapeutic uses, with a primary focus on its renowned effects on bone health and emerging applications in metabolic and inflammatory conditions.
4. To synthesize these findings to elucidate the plausible mechanisms of action that underpin its traditional uses.
5. To identify the limitations and gaps in the current body of research and to propose future directions for study that could further validate its clinical utility.

2. MATERIAL AND METHODS

A systematic literature search was performed across classical Ayurvedic texts and modern scientific databases (PubMed, Scopus, Google Scholar) using relevant keywords. Preclinical, clinical, and traditional studies were selected based on inclusion criteria, and the extracted data were narratively synthesized to correlate traditional knowledge with contemporary scientific evidence.

Study Selection: Inclusion and Exclusion Criteria

Studies were selected for inclusion based on their relevance to the review's objectives. The inclusion criteria were as follows: (1) studies published in the English language; (2) original research articles, including *in-vitro* experiments, animal studies, and human clinical trials investigating the pharmacological or therapeutic effects of *Vitis quadrangularis*; (3) review articles summarizing its phytochemistry, traditional uses, or pharmacological activities; and (4) classical Ayurvedic texts and commentaries describing *Asthisamharaka*.[21]

The exclusion criteria were: (1) studies not directly relevant to the therapeutic applications or scientific evaluation of *Vitis quadrangularis*; (2) publications in languages other than English; (3) anecdotal reports, conference abstracts, or unpublished data lacking peer-review and sufficient detail for critical assessment; and (4) studies where *Vitis quadrangularis* was part of a polyherbal formulation without a clear delineation of its specific contribution.[23]

Data Extraction and Synthesis Approach

Data from the selected studies were systematically extracted and organized. Key information recorded included study design (e.g., RCT, animal model), subject or model characteristics, intervention details (extract type, dosage, duration), outcome measures, and principal findings.[21] The extracted information was then synthesized narratively and structured thematically according to the IMRAD format of this review. A critical analysis was performed to identify patterns, correlations, and discrepancies in the literature, with a particular focus on connecting the traditional Ayurvedic concepts of action (

Karma) and properties (*Guna*) with modern, evidence-based mechanisms of action.

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3. RESULTS

Botanical and Taxonomic Profile

Taxonomy: *Vitis quadrangularis* is scientifically classified within the plant kingdom as follows:

- **Kingdom:** Plantae
- **Phylum:** Tracheophyta
- **Class:** Magnoliopsida
- **Order:** Vitales
- **Family:** Vitaceae
- **Genus:** *Cissus*
- **Species:** *Cissus quadrangularis* L. [1]

Morphology: It is a deciduous, succulent, climbing plant that can reach lengths of up to 15 meters.[4] Its most distinguishing feature is its stem, which is thick, fleshy, glabrous (smooth), and distinctly quadrangular (four-angled), with constrictions at the nodes.[1] These stems often appear leafless, especially in older plants, as they are capable of photosynthesis.[4] Simple, long tendrils emerge from the nodes, opposite the leaves, allowing the plant to climb.[28] The leaves, when present, are simple or 3-lobed, broadly ovate, with a serrated margin.[5] The plant produces small, inconspicuous, greenish-white or yellowish flowers arranged in umbellate cymes.[5] The fruit is a globose, fleshy berry that turns red or dark purple to black when ripe and typically contains a single seed.

Fig 1: *Vitis quadrangularis* [51,52]

Distribution and Habitat: *Vitis quadrangularis* is widely distributed throughout the hotter, drier parts of the world. Its native range includes tropical Africa, the Arabian Peninsula, India, Sri Lanka, and extends through Southeast Asia to the Philippines.[4] It thrives in a variety of habitats such as scrublands, thickets, Acacia woodlands, and on termite mounds, from sea level up to elevations of 2,250 meters.[4] It is also commonly cultivated in gardens for both medicinal and ornamental purposes.[4]

Propagation: The plant is typically propagated vegetatively using mature stem cuttings. This method is most successful when carried out during the warmer, wetter months of June and July, allowing for rapid development of new shoots and roots.[3]

Classical Ayurvedic Description and Properties

Nomenclature in Ayurvedic Texts

The rich therapeutic history of *Vitis quadrangularis* is encapsulated in its diverse nomenclature across Sanskrit and various vernacular languages. The names often describe its morphology or its primary medicinal function, providing valuable insight into its traditional perception.

Table 1: Vernacular and Ayurvedic Nomenclature of *Vitis quadrangularis*

Language/System	Name(s)	Etymological Significance/Note	Source(s)
Sanskrit	*Asthisamharaka*, *Asthisamhari*, *Asthisamdhani*	"Bone setter," "that which unites bones"	1

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	Asthishrinkhala, *Asthiyuk*	"Chain of bones," "joins bones" (refers to stem morphology)	11
	Vajravalli, *Vajrangi*	"Diamond-like creeper," "strong body" (denotes strengthening property)	11
	Granthimana	"Knotted stem"	11
	Chaturdhara	"Having four edges" (refers to quadrangular stem)	11
Hindi	*Hadjod*, *Hadjora*, *Harsankari*	"Bone joiner"	1
English	Veldt Grape, Devil's Backbone, Adamant Creeper, Bone Setter	Descriptive names referring to its habitat, appearance, and use	1
Tamil	*Pirandai*, *Perandai*	Common regional name	1
Telugu	*Nalleru*	Common regional name	7
Malayalam	*Changalam Paranda*	"Chain-like plant"	11
Bengali	*Harjora*	"Bone joiner"	6

This table centralizes the diverse nomenclature, providing a cross-reference for researchers working with different texts or regional traditions. The etymology of the Sanskrit names provides direct insight into the perceived qualities and actions of the herb, a foundational concept in Ayurvedic pharmacology.

Ayurvedic Pharmacology (*Ras Panchak*) and *Dosha* Karma

In Ayurveda, the pharmacological profile of a substance is defined by its *Ras Panchak*, or the five attributes of action. For *Asthisamharaka*, these are generally described as follows:

- **Rasa (Taste):** Predominantly *Madhura* (Sweet) with an associated *Katu* (Pungent) taste.[7]
- **Guna (Qualities):** *Laghu* (Light), *Ruksha* (Dry), and *Sara* (Mobile/Unstable).[7] The lightness and dryness contribute to its ability to penetrate tissues and reduce excess fluid (*Kapha*).
- **Virya (Potency):** *Ushna* (Hot/Heating).[7] The hot potency is crucial for pacifying the cold nature of *Vata* and *Kapha doshas* and for stimulating digestive and metabolic fire (*Agni*).
- **Vipaka (Post-digestive Effect):** There is some variation among classical texts. Some sources state the *Vipaka* is *Katu* (Pungent), while others report it as *Madhura* (Sweet).[7] This variation can influence its long-term systemic effects.
- **Dosha Karma (Action on Doshas):** Due to its combination of tastes and qualities, it is primarily considered *Kapha-Vatahara* (pacifies both *Kapha* and *Vata doshas*).[7] Its hot potency can aggravate *Pitta dosha* if used in excess.

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Table 2: Summary of Ayurvedic Properties (*Ras Panchak*) of *Asthisamharaka* Across Classical Texts

Nighantu (Text)	*Rasa (Taste)*	*Guna (Qualities)*	*Virya (Potency)*	*Vipaka (Post-digestive Effect)*
Bhavprakash Nighantu	*Madhura, Katu*	*Laghu, Ruksha*	*Ushna*	*Madhura*
Adarsha Nighantu	*Kashaya, Madhura*	*Laghu, Ruksha*	*Ushna*	*Katu*
Kaiyadev Nighantu	*Madhura*	*Guru, Ruksha*	*Ushna*	*Katu*
Shaligram Nighantu	*Madhura*	*Laghu, Ruksha*	*Ushna*	*Katu*

This table provides a nuanced view for scholars and researchers by showing both the consensus and the subtle disagreements among classical authorities, which can have implications for its formulation and long-term use.

Traditional Formulations and Therapeutic Indications (*Rogaghnata*)

Asthisamharaka is mentioned in some of the most revered Ayurvedic treatises. The *Sushruta Samhita*, a foundational text on surgery, describes its use in the polyherbal formulation *Lakshadi Guggul* for *Asthibhagna chikitsa* (treatment of bone fractures), where it acts as a bone tonic or setter.[12] The 11th-century text *Chakradatta* mentions *Asthisamharakadi choorna* (a powdered formulation) and *Asthisamharaka siddha ghrita* (a medicated ghee) for the treatment of bone diseases (*Asthiroga*).[15]

Its traditional therapeutic indications (*Rogaghnata*) are extensive, with a clear emphasis on musculoskeletal health. Key uses include:

- **Asthibhagna (Bone Fracture):** Its primary and most famous application, promoting rapid union of fractured bones.[1]
- **Sandhigatavata (Osteoarthritis):** Used to strengthen joints, reduce pain and swelling, and manage degenerative joint diseases.[1]
- **Arsha (Hemorrhoids):** The stem is used to treat piles, likely due to its anti-inflammatory and hemostatic properties.[7]
- **Digestive and Metabolic Disorders:** It is considered a *Pachana* (digestive aid) and *Deepana* (appetizer) and is used for indigestion, worm infestation (*Krumi*), and to relieve constipation (*Sara* property).[7]
- **Other Uses:** It is also traditionally indicated for asthma, irregular menstruation, epistaxis (nosebleeds), scurvy, and as a general tonic (*Balya*), aphrodisiac (*Vrushya*), and rejuvenative (*Rasayana*) agent.[7]

Phytochemical Constituents

The diverse therapeutic actions of *Vitis quadrangularis* are attributed to its complex and rich phytochemical profile. Modern analytical techniques have identified numerous bioactive compounds, many of which provide a scientific basis for its traditional uses.

Major Bioactive Compounds

The plant contains several classes of pharmacologically active compounds, with the stem being the most studied part.

Table 3: Key Phytochemical Constituents of *Vitis quadrangularis* and Their Associated Bioactivities

Class of Compound	Specific Examples	Associated Bioactivities	Source(s)
Steroids	Anabolic ketosteroids, Friedelin, β-sitosterol, Stigmasterol	Osteogenic, Anti-inflammatory, Anti-osteoporotic,	[17]

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		Cholesterol-lowering	
Triterpenoids	α- and β-amyrins, δ-amyrone, Lupeol	Anti-inflammatory, Analgesic, Gastroprotective	23
Flavonoids	Quercetin, Kaempferol, Isorhamnetin, Daidzein, Genistein	Antioxidant, Anti-inflammatory, Chondroprotective, Anti-diabetic	36
Stilbenes	Resveratrol, Piceatannol, Pallidol, Quadrangularins A, B, C	Antioxidant, Anti-inflammatory, Cardioprotective, Neuroprotective	37
Phenolic Compounds & Glycosides	Gallic acid derivatives, Tannins, Iridoids (e.g., catalpol derivatives)	Antioxidant, Astringent, Antimicrobial, Anti-inflammatory	34
Vitamins & Carotenoids	Vitamin C (Ascorbic acid), β-carotene (pro-vitamin A)	Antioxidant, Collagen synthesis, Immune support, Bone health	9
Fatty Acids	n-Hexadecanoic acid, Octadecatrienoic acid	Nutritional, Anti-inflammatory precursors	34

This table is crucial as it directly connects the plant's chemistry to its biological function, providing a clear, evidence-based rationale for its therapeutic actions and moving beyond traditional descriptions to molecular mechanisms.

Nutritional Composition

Beyond its specific bioactive compounds, *Vitis quadrangularis* is also a rich source of essential nutrients that are vital for musculoskeletal health. It contains high concentrations of Vitamin C (ascorbic acid), which is a critical cofactor for collagen synthesis—the primary protein in the bone matrix.[9] It is also a good source of β-carotene (a precursor to Vitamin A) and key minerals, most notably calcium and phosphorus, which are the fundamental building blocks of bone tissue.[1] This nutritional profile complements its pharmacological actions, providing the raw materials necessary for the bone repair and strengthening processes it stimulates.

Preclinical Pharmacological Evidence

An extensive body of preclinical research, spanning *in-vitro* cell culture systems and various animal models, has been conducted to investigate the mechanisms behind the traditional claims for *Vitis quadrangularis*. This research provides strong scientific validation for its primary therapeutic roles.

Osteogenic and Anti-osteoporotic Mechanisms

The most heavily researched area is the plant's effect on bone health, confirming its traditional role as *Asthisamharaka*.

- ***In-vitro* studies:** Multiple studies using osteoblast-like cell lines (e.g., SaOS-2, MC3T3-E1) have demonstrated that extracts of *V. quadrangularis* directly promote bone formation. The extracts have been shown to enhance osteoblast proliferation, differentiation, and the subsequent mineralization of the extracellular matrix.[50] Mechanistically, this is achieved through several pathways. The extract upregulates the activity of alkaline phosphatase (ALP), a key early marker of osteoblast differentiation, an effect mediated at least in part through the p38 mitogen-activated protein kinase (MAPK) signaling pathway.[50] Furthermore, it increases the expression of critical growth factors like insulin-like growth factor I (IGF-I) and IGF-II, which are potent stimulators of bone formation.[17] Concurrently,

V. quadrangularis exerts a powerful anti-resorptive effect by directly inhibiting the formation of osteoclasts, the cells responsible for breaking down bone. It has been shown to suppress RANKL-induced osteoclastogenesis in mouse bone marrow cells in a dose-dependent manner, without causing cytotoxicity.[52]

- **Animal studies:** These *in-vitro* findings are strongly corroborated by animal studies. In models of bone fracture in rats, dogs, and rabbits, administration of *V. quadrangularis* extract has consistently been shown to accelerate the healing process, leading to faster callus formation, increased tensile strength of the healed bone, and quicker mineralization.[17] Its anti-osteoporotic potential has been extensively studied in ovariectomized (OVX) rat models, which mimic postmenopausal osteoporosis. In these models, oral administration of the extract effectively prevents the bone loss induced by estrogen deficiency, preserves bone mineral density (BMD), and maintains the integrity of the bone micro-architecture.[17] A key mechanism underlying this effect is its ability to modulate the host immune system. Postmenopausal bone loss is driven by pro-inflammatory cytokines that stimulate osteoclast activity. *V. quadrangularis* has been shown to shift the systemic cytokine balance away from this pro-resorptive state by decreasing levels of osteoclastogenic cytokines like TNF-α, IL-6, and IL-17, while simultaneously increasing levels of anti-osteoclastogenic cytokines such as IFN-γ, IL-4, and IL-10.[52]

Anti-inflammatory and Analgesic Activity

The traditional use of *Asthisamharaka* for painful joint conditions like *Sandhigatavata* is supported by strong evidence of its anti-inflammatory and analgesic properties.

- ***In-vitro* studies:** Extracts have been shown to inhibit key enzymes in the inflammatory cascade, including cyclooxygenase-1 (COX-1), COX-2, and 5-lipoxygenase (5-LOX), which are responsible for the synthesis of prostaglandins and leukotrienes.[22] This provides a direct mechanism for its pain and inflammation-relieving effects. Furthermore, in models of osteoarthritis, the extract has demonstrated a chondroprotective effect by inhibiting the inflammatory responses induced by IL-1β in human chondrocytes, thereby preventing the degradation of cartilage.[57]

- **Animal studies:** In standard animal models of inflammation, such as carrageenan-induced paw edema in rats, *V. quadrangularis* extract significantly reduces swelling.[58] Its analgesic effects have been confirmed in models like the acetic acid-induced writhing test and the hot plate test, demonstrating efficacy against both visceral and thermal pain.[59] Mechanistic studies suggest that its pain-relieving action is mediated through both central and peripheral pathways, involving the opioidergic and serotonergic systems.[59]

Effects on Metabolic Syndrome, Obesity, and Diabetes

Emerging research has highlighted the potential of *Vitis quadrangularis* in managing components of metabolic syndrome, aligning with its traditional use as a digestive and metabolic aid. Preclinical studies have shown that its extracts can improve insulin sensitivity and lower blood glucose levels in alloxan-induced diabetic rat models.[62] It also improves lipid profiles and inhibits the accumulation of fat.[63] One of the proposed mechanisms for its weight management effects is its ability to inhibit key digestive enzymes. In-vitro studies have demonstrated that it can inhibit pancreatic lipase, α-amylase, and α-glucosidase, which would reduce the digestion and absorption of dietary fats and carbohydrates, respectively.[64]

Gastroprotective and Other Ancillary Activities

Consistent with its use in Unani medicine for gastritis, *V. quadrangularis* has demonstrated significant gastroprotective activity. It has shown bactericidal effects against *Helicobacter pylori*, a primary cause of gastric ulcers, and has been found to protect the gastric mucosa from damage induced by NSAIDs like aspirin.[10] This activity is complemented by its potent antioxidant properties, which help to mitigate oxidative stress, a key factor in many chronic diseases.[3] The plant also exhibits broad-spectrum antimicrobial activity against various bacteria and fungi.[18]

Clinical Evidence from Human Trials

The promising results from preclinical studies have led to a number of human clinical trials investigating the efficacy of *Vitis quadrangularis* for various conditions.

Efficacy in Fracture Healing

Several clinical studies and case reports have provided direct evidence for the traditional use of *V. quadrangularis* in accelerating fracture healing. In a pilot study involving patients with maxillofacial fractures treated with open reduction and internal fixation, those who received supplementary *V. quadrangularis* capsules (500 mg, thrice daily for 6 weeks) experienced a significant reduction in pain, swelling, and fragment mobility compared to a control group.[68] Radiographic evaluation showed clearer and faster signs of bone healing in the treatment group by day 21.[68] Another study on young adults with mandible fractures found that supplementation with 300 mg of dried stem extract significantly increased serum levels of osteopontin, a protein crucial for bone remodeling and healing, suggesting an

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enhanced rate of recovery.[69] These clinical findings directly validate its Ayurvedic name and primary indication.

Role in Osteoporosis and Osteopenia

The application of *V. quadrangularis* for chronic bone loss conditions like osteoporosis has yielded more nuanced results. A randomized, placebo-controlled trial in over 100 postmenopausal women with osteopenia investigated the effects of daily supplementation with 1.2 g or 1.6 g of the extract for 24 weeks.[70] The study found that while the supplement did not lead to a statistically significant increase in bone mineral density (BMD) at the lumbar spine or hip compared to placebo, it did have a significant effect on bone turnover markers. Specifically, it significantly reduced the levels of procollagen type 1 amino-terminal propeptide (P1NP), a marker of bone formation, while levels of C-terminal telopeptide (CTX), a marker of bone resorption, remained stable. In the placebo group, both markers tended to increase.[71] This suggests that in a state of chronic bone loss, the primary effect of

V. quadrangularis is to slow down the overall rate of bone remodeling, thereby delaying or preventing further bone loss, rather than actively rebuilding lost bone mass. This is a critical distinction from its role in acute fracture healing, where its anabolic properties are more pronounced. A separate systematic review and meta-analysis of seven studies found that the intervention was significantly associated with increased serum parathyroid hormone levels, but had no significant effect on other markers like calcium, phosphorus, or alkaline phosphatase.[20]

Application in Weight Management and Metabolic Syndrome

Several well-designed, randomized, double-blind, placebo-controlled trials have demonstrated the efficacy of *V. quadrangularis* in weight management. In a study on overweight and obese individuals, daily supplementation with a standardized extract (CQR-300, 300 mg/day) for 8-10 weeks resulted in statistically significant reductions in body weight, body fat percentage, waist circumference, fasting blood glucose, total cholesterol, LDL-cholesterol, and triglycerides when compared to placebo.[63] These beneficial effects were observed even without accompanying dietary restrictions.[73] Some studies hypothesize that its mechanism of action may involve appetite control, as supplementation was associated with an increase in plasma serotonin levels, a neurotransmitter known to influence satiety.[63]

Alleviation of Joint Pain

The analgesic and anti-inflammatory properties observed in preclinical models have been tested in a clinical setting for exercise-induced joint pain. A pilot study was conducted on 29 healthy, exercise-trained men who reported chronic joint pain.[74] After an 8-week course of supplementation with 3200 mg of

V. quadrangularis daily, the participants showed a statistically significant improvement in their joint pain scores. The mean total score on the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index decreased by approximately 31%, indicating a substantial reduction in pain and improvement in joint function.[74]

Table 4: Overview of Human Clinical Trials on *Vitis quadrangularis*

Condition Studied	Study Design	Participants	Intervention (Dosage, Duration)	Key Outcomes	Conclusion	Source(s)
Maxillofacial Fracture	Pilot Study	9 patients	500 mg capsule, 3x/day for 6 weeks	Reduced pain, swelling, mobility; faster radiographic healing	Accelerates healing of jaw fractures	68
Mandible Fracture	RCT	60 adults	300 mg dried stem capsule/day for 8 weeks	Significantly increased serum osteopontin levels	Promotes fracture healing	69
Osteopenia (Postmenopausal)	RCT	134 women	1.2 g or 1.6 g extract/day	No significant change in BMD;	Delays bone loss by slowing	70

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			for 24 weeks	significant reduction in bone turnover marker (P1NP)	bone remodeling	
Weight Management	RCT	168 overweight/obese adults	300 mg (CQR-300)/day for 6-8 weeks	Significant reduction in weight, body fat, waist size, blood glucose, cholesterol, triglycerides	Effective for weight loss and improving metabolic parameters	63
Exercise-Induced Joint Pain	Pilot Study	29 exercise-trained men	3200 mg/day for 8 weeks	~31% reduction in total WOMAC pain score	Reduces joint pain in healthy, active men	74

This table provides a clear overview of the current state of human evidence, translating preclinical promise into tangible clinical outcomes.

Safety, Toxicology, and Drug Interactions

Across human clinical trials, *Vitis quadrangularis* has demonstrated a favorable safety profile. It is generally well-tolerated and considered possibly safe for oral use in adults for periods of up to 10 weeks.[13] The reported side effects are typically mild and infrequent. In some studies, a small number of participants experienced adverse effects such as headache, intestinal gas, dry mouth, diarrhea, and insomnia.[13]

Certain precautions are warranted. Due to a lack of sufficient reliable information, its use should be avoided during pregnancy and breastfeeding.[13] Because of its potential to lower blood sugar levels, individuals taking medications for diabetes should use it with caution and monitor their blood sugar closely to prevent hypoglycemia.[13] For the same reason, it is recommended to discontinue use at least two weeks prior to any scheduled surgical procedure to avoid interference with blood sugar control during and after surgery.[13] Animal toxicology studies have further supported its safety, showing no significant toxic effects even at doses much higher than those used therapeutically in humans.[17]

4. DISCUSSION

Synthesis of Evidence: Correlating Ayurvedic Use with Modern Science

The body of evidence reviewed here presents a compelling case for the validation of the traditional Ayurvedic wisdom surrounding *Vitis quadrangularis*. There is a remarkable and direct correlation between its classical indications and its scientifically demonstrated pharmacological activities. The Ayurvedic concept of *dosha* provides a framework for understanding its application. Degenerative bone and joint diseases, such as *Sandhigatavata* (osteoarthritis), are primarily considered disorders of *Vata dosha*, which is characterized by qualities of cold, dryness, and catabolism. The *Ushna Virya* (hot potency) of *Asthisamharaka* directly counteracts the cold nature of *Vata*, while its anabolic and strengthening properties combat the degenerative aspect of the *dosha*. This aligns perfectly with modern findings of its potent anti-inflammatory, analgesic, and chondroprotective effects.

Most significantly, the Ayurvedic actions of *Asthi sthapana* (bone strengthening) and *Sandhaniya* (union promoting) are unequivocally supported by modern research. The observed enhancement of osteoblast activity, upregulation of bone-specific growth factors, and inhibition of bone-resorbing osteoclasts provide a clear molecular basis for the accelerated fracture healing seen in both preclinical and clinical studies. This convergence of ancient observation and modern mechanistic insight exemplifies how traditional medical systems can provide a valuable and accurate roadmap for contemporary pharmacological research.

Mechanistic Insights into Osteoprotective Effects

The osteoprotective effects of *Vitis quadrangularis* are not attributable to a single mechanism but rather to a multi-target, synergistic action of its diverse phytochemical constituents. Based on the available evidence, a comprehensive

mechanism can be proposed that operates on four distinct levels:

- **Anabolic/Osteogenic Action:** The plant's extracts, likely through their content of anabolic ketosteroids and other compounds, directly stimulate the cells responsible for bone formation. They promote the proliferation and differentiation of osteoblasts and enhance the mineralization process, which is the final step in creating new bone tissue. This action is mediated through key cellular signaling pathways, including the MAPK and IGF pathways.
- **Anti-catabolic/Anti-resorptive Action:** Simultaneously, it curbs the process of bone breakdown. It achieves this by inhibiting the formation and functional activity of osteoclasts, the cells that resorb bone. This suppression of the RANKL pathway is crucial for shifting the balance of bone remodeling from net loss towards net gain or maintenance.
- **Immunomodulatory Action:** Chronic inflammation is a key driver of bone loss, particularly in conditions like postmenopausal osteoporosis and rheumatoid arthritis. *V. quadrangularis* modulates the immune system to create a more favorable environment for bone health. It reduces the production of pro-inflammatory, pro-resorptive cytokines (TNF-α, IL-6, IL-17) and increases anti-inflammatory, anti-resorptive cytokines (IFN-γ, IL-4, IL-10), effectively dampening the inflammatory fire that fuels bone destruction.
- **Nutritional Support:** The herb provides a rich source of the fundamental building blocks for bone: calcium, phosphorus, and Vitamin C. This nutritional contribution ensures that the stimulated bone-building cells have the necessary raw materials to synthesize a healthy and robust bone matrix.

Emerging Therapeutic Applications Beyond Bone Health

While bone health remains its primary application, the evidence strongly suggests that the therapeutic potential of *Vitis quadrangularis* extends to other interconnected areas of health. Its demonstrated efficacy in reducing body weight, improving lipid profiles, and lowering blood glucose levels positions it as a promising multi-component therapy for metabolic syndrome. This is particularly relevant as obesity and metabolic dysfunction are increasingly recognized as risk factors for poor skeletal health, creating a vicious cycle of comorbidity. The plant's ability to systemically reduce inflammation and oxidative stress appears to be a unifying mechanism that benefits both the metabolic and skeletal systems. This holistic action aligns with the Ayurvedic approach of treating the entire system rather than isolated symptoms.

Furthermore, its proven ability to reduce exercise-induced joint pain opens up significant applications in the field of sports medicine. It can be utilized not only for the recovery from acute injuries like fractures but also for the chronic management of joint stress and pain experienced by athletes and physically active individuals, potentially improving performance and career longevity.

Limitations of Current Research and Gaps in Knowledge

Despite the promising body of evidence, the current research on *Vitis quadrangularis* is not without limitations. A significant portion of the human clinical trials consists of small pilot studies, which, while indicative, lack the statistical power of large-scale research.[19] There is also considerable heterogeneity across studies in terms of the type of extract used (e.g., aqueous, ethanol, petroleum ether), dosage, and duration of treatment. This lack of standardization makes it difficult to compare results across studies and to establish a definitive, evidence-based dosing regimen for specific conditions.

Moreover, while its primary use for bone health is well-studied, many of its other traditional indications remain largely unexplored by modern science. For instance, its Ayurvedic use for gynecological disorders (*Pradara*) and as an aphrodisiac (*Vrushya*) has not been investigated scientifically. Similarly, the claim that it is used in bodybuilding supplements as an alternative to anabolic steroids lacks direct clinical evidence demonstrating an effect on lean muscle mass, although some studies have noted an increase in creatinine, which could indirectly suggest this.[17]

Future Research Directions and Clinical Implications

To bridge these gaps and fully realize the clinical potential of *Vitis quadrangularis*, future research should focus on several key areas. There is a pressing need for larger, multicenter, randomized controlled trials with long-term follow-up to confirm its efficacy and safety, particularly for chronic conditions like osteoporosis and metabolic syndrome. These studies should prioritize the use of standardized extracts to ensure reproducibility and to establish clear dose-response relationships.

Further research should also aim to isolate and characterize the specific bioactive compounds responsible for its therapeutic effects. Investigating the structure-activity relationships of its unique ketosteroids, flavonoids, and stilbenes could lead to the development of new, more potent pharmaceutical agents. Head-to-head clinical trials comparing standardized *V. quadrangularis* extracts to conventional standard-of-care treatments (e.g., bisphosphonates for osteoporosis) would be invaluable for defining its place in the therapeutic armamentarium. Finally, exploring its

synergistic effects within traditional polyherbal formulations, such as *Lakshadi Guggul*, could provide insights into the complex interactions that may enhance its efficacy, reflecting the holistic principles of Ayurvedic medicine.

5. CONCLUSION

Vitis quadrangularis, revered in Ayurveda as *Asthisamharaka*, stands as a powerful example of a traditional remedy whose historical use is being progressively validated by modern science. The convergence of evidence from classical texts, extensive preclinical research, and a growing number of human clinical trials is remarkable. Its primary Ayurvedic indication for promoting bone healing is strongly supported by robust data demonstrating its multi-target mechanism, which includes direct osteogenic and anti-resorptive actions, immunomodulation, and nutritional support. Beyond its role as a "bone setter," it has emerged as a potent therapeutic agent for managing joint pain and key components of metabolic syndrome, including obesity and dyslipidemia, largely through its systemic anti-inflammatory and antioxidant effects. While the existing evidence is highly promising, the field must now move towards more rigorous, large-scale, and standardized clinical research. Such efforts are essential to establish definitive clinical guidelines and to fully integrate this ancient and valuable botanical medicine into the framework of contemporary, evidence-based healthcare.

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