



ORIGINAL RESEARCH PAPER

Homoeopathy

RENEWING THE JOINTS: A COMPARATIVE MOLECULAR REVIEW ON THE ANTI-ARTHRITIC EFFICACY OF BOERHAAVIA DIFFUSA L. VERSUS TRIBULUS TERRESTRIS L.

KEY WORDS: Boerhaavia diffusa; Tribulus terrestris; Rheumatoid Arthritis; Osteoarthritis; Synovial inflammation; Chondroprotection.

Dr N.V.Sajana

Assistant Professor, Department of Homoeopathic Materia Medica, Excel Homoeopathy Medical College, Namakkal, Tamilnadu

ABSTRACT

Chronic arthritic conditions, including Rheumatoid Arthritis (RA) and Osteoarthritis (OA), presents exceptionally large global health burden characterized by persistent synovial inflammation, articular cartilage degradation, and progressive joint deformity with pain. Traditional Indian medicine systems heavily utilize Boerhaavia diffusa L. (Punarnava) and Tribulus terrestris L. (Gokshura) to manage complex musculoskeletal pathologies and inflammatory disorders. This review presents a critical, systematic molecular evaluation of these two prominent plants concerning their therapeutic actions on articular joints. Boerhaavia diffusa, exceptionally rich in unique rotenoids (boeravinones), acts primarily through the suppression of the Nuclear Factor-kappa B (NF- κ B) and Mitogen-Activated Protein Kinase (MAPK) cascades, downstream halting pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6) and inhibiting severe periarticular osteopenia. Conversely, Tribulus terrestris, rich in steroidal saponins (protodioscin, tribulosin) and unique alkaloids, exerts anti-arthritic activities by inhibiting oxidative stress, downregulating inducible nitric oxide synthase (iNOS), and mitigating cartilage matrix erosion. While both plants demonstrate profound anti-nociceptive and anti-inflammatory properties, Boerhaavia diffusa displays superior systemic efficacy in reversing structural bone damage, suppressing systemic immunological cascade-driven edema, and moderating chronic swelling in severe rheumatoid-type models. In contrast, Tribulus terrestris provides exceptional mechanical defense, anti-apoptotic structural alignment, and highly localized targeted relief suitable for wear-and-tear osteoarthritis pathways. This exhaustive comparative breakdown establishes a comprehensive modern biochemical and clinical framework to guide targeted botanical usage in contemporary rheumatology.

1. INTRODUCTION

Musculoskeletal diseases, particularly Rheumatoid Arthritis (RA) and Osteoarthritis (OA), represent a massive global epidemic affecting millions of individuals, drastically diminishing quality of life and imposing colossal economic burdens on healthcare infrastructures globally every year. RA is classified as a highly systemic, chronic autoimmune disease characterized by aggressive, symmetrical inflammation of peripheral joints, progressive synovial hyper-proliferation (pannus formation), and subsequent irreversible erosion of marginal articular cartilage and subchondral bone¹. Conversely, OA is a multifaceted most common type of arthritis with degenerative arthropathy driven by mechanical wear, localized chondrocyte dysfunction, metabolic stress, and low-grade chronic inflammatory cascades within the cartilage matrix, resulting in the narrowing of joint spaces, osteophyte formation, and subchondral sclerosis².

Conventional therapeutic strategies for arthritic conditions rely heavily on Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), corticosteroids, and Disease-Modifying Anti-Rheumatic Drugs (DMARDs) such as methotrexate or biologic TNF- α inhibitors³. However, long-term administration of these synthetic agents is severely constrained by long term side effects such as critical gastrointestinal ulcerations, cardiovascular toxicities, severe hepatic damage, and profound systemic immunosuppression. Consequently, there is an urgent and accelerating paradigm shift toward our natural, bio-available botanical therapeutic agents derived from ancient traditional knowledge systems to achieve durable, safe, and holistic multi-target protection of joint components⁴.

Within the repository of Indian traditional medicine Boerhaavia diffusa L. (commonly known as Punarnava) and Tribulus terrestris L. (commonly known as Gokshura) are categorized as premier herbs, utilized extensively to target musculoskeletal ailments categorized broadly under Vata disease (neuromuscular and degenerative joint diseases)⁵. Punarnava, historically recognized for its profound edema-reducing, anti-inflammatory properties, is primarily deployed to manage inflammatory joint conditions accompanied by widespread soft-tissue edema and systemic fluid retention. On the other hand, Gokshura is celebrated for its strengthening and metabolic regulatory capacities, frequently utilized to alleviate localized pain, boost lower-extremity mechanical performance, and resolve urogenital-metabolic imbalances

affecting systemic joints. Although both herbs have been utilized for centuries, a modern comparative evaluation isolating their precise molecular mechanisms, cellular targets, and relative pharmacological therapeutic efficacy on joint structures remains highly scattered. This review aims to synthesize original empirical data to comprehensively determine which botanical offers superior efficacy for specific joint-related pathological pathways.

2. Phytochemical Profiling of Active Moieties

The therapeutic potential of both plants on joint is entirely dictated by their highly diverse chemical configurations. Boerhaavia diffusa possesses an exceptionally unique class of phytochemicals termed rotenoids, specifically boeravinones A, B, C, D, E, and F, which have exhibited potent, targeted systemic anti-inflammatory actions⁶. Additionally, it contains the distinct quinolizidine alkaloid punarnavine, highly active phenolic fractions, lignans (liriodendrin), and various bio-flavonoids such as quercetin and kaempferol. These molecules act synergistically to lower the cellular lipid peroxidation and suppress intracellular reactive oxygen species (ROS) that aggressively damage joint matrices.

In contrast, the secondary metabolites of Tribulus terrestris are characterized predominantly by high concentrations of steroidal saponins, categorized into furostanol and spirostanol frameworks, with protodioscin, tribulosin, dioscin, and gracillin constituting the primary bioactive components⁷. T. terrestris also features unique cinnamic acid amides collectively known as tribulusamides (A through D), along with indole alkaloids like harmine and harmaline. While the rotenoids in B. diffusa are optimized for highly rapid cellular fluid balance and intercellular cytokine dampening, the steroidal saponins of T. terrestris mimic endogenous steroid pathways, rendering them highly competent at modulating local structural cell tissue responses, modifying systemic lipid parameters, and preserving cartilage cell viability.

3. Molecular Mechanisms of Action on Articular Joints

3.1 Boerhaavia diffusa: The NF- κ B and Cytokine Suppression Axis

At the molecular baseline, Boerhaavia diffusa exerts its exceptional anti-arthritic effects by intercepting the central inflammatory command pathway: Nuclear Factor-kappa B (NF- κ B) transcription factor network. In active arthritic states, extracellular pathogen-associated or damage-associated

molecular patterns bind to chondrocyte and macrophage receptors, inducing the phosphorylation and degradation of I κ B (Inhibitor of kappa B). This releases the active NF- κ B p65 subunit to rapidly translocate into the nucleus, triggering massive transcription of aggressive pro-inflammatory cytokines, specifically Tumor Necrosis Factor- α (TNF- α), Interleukin-1 beta (IL-1 β), and Interleukin-6 (IL-6)⁸. Original scientific investigations verify that isolated boeravinone fractions strongly inhibit I κ B kinase (IKK) activation, therefore blocking NF- κ B nuclear translocation with a level of efficacy comparable to baseline corticosteroids. By neutralizing this master switch, *B. diffusa* directly shuts down downstream production of iNOS (inducible Nitric Oxide Synthase) and COX-2 (Cyclooxygenase-2), leading to an immediate drop in nitric oxide and prostaglandin E2 (PGE2) production within inflamed synovial cavities⁹. This profound cellular containment effectively neutralizes the formation of invasive hyper-proliferative synovial pannus tissue, which is directly responsible for marginal bone erosion in autoimmune polyarthritis models¹⁰.

3.2 Tribulus terrestris: The MAPK and Anti-Apoptotic Pathway

Conversely, *Tribulus terrestris* operates predominantly via the modulation of the Mitogen-Activated Protein Kinase (MAPK) signaling cascade, specifically downregulating the activation loop of p38 MAPK and c-Jun N-terminal kinase (JNK). In joints suffering from chronic mechanical friction and localized wear, the activation of p38 MAPK in chondrocytes triggers the massive synthesis of Matrix Metalloproteinases, particularly MMP-1, MMP-3, and MMP-13. These proteolytic enzymes actively catabolize the type II collagen framework and aggrecan aggregates that compose the structural integrity of the articular cartilage¹¹. Purified steroidal saponins and tribulusamides isolated from *T. terrestris* block the intracellular phosphorylation of p38 and extracellular signal-regulated kinases (ERK1/2), dramatically reducing MMP gene expression. Concurrently, *T. terrestris* exhibits extraordinary chondroprotective and anti-apoptotic properties by upwardly adjusting the cellular Bcl-2/Bax balance ratio within stressed chondrocytes¹². This specific molecular mechanism suppresses caspase-3 and caspase-9 activation cascades, directly preventing premature chondrocyte apoptosis induced by mechanical strain or localized peroxynitrite accumulation⁴.

4. Head-to-Head Comparative Efficacy Analysis: Which Herb is More Effective?

To unequivocally address which botanical displays superior joint protective efficacy, the specific pathological context of the arthritic disease state must be meticulously analyzed. When evaluated against severe, acute and chronic multi-joint, systemic auto-immune inflammatory models—such as Complete Freund's Adjuvant (CFA) induced rheumatoid polyarthritis—*Boerhavia diffusa* demonstrates clearly superior, comprehensive efficacy compared to *Tribulus terrestris*⁵. This exceptional superiority is rooted directly in *B. diffusa*'s highly potent anti-edematous action. Systemic arthritis induces rapid, severe endothelial hyper-permeability, massive periarticular soft tissue fluid accumulation, and substantial macroscopic paw swelling in animal models. The active alkaloid punarnavine and associated boeravinones modulate renal and microvascular aquaporin channels while aggressively downregulating systemic IL-6, leading to a profound reduction in localized joint volume edema and rapid clearance of highly toxic inflammatory exudates from the synovial space⁶. Radiographical and histopathological evaluations reveal that animals treated with standardized *B. diffusa* extracts experience significantly lower periarticular bone erosion, minimized osteophyte development, and preservation of cortical bone density due to direct inhibition of RANKL-induced osteoclastogenesis.

Conversely, when evaluated in models prioritizing localized mechanical cartilage erosion, chronic wear-and-tear

degradation, and metabolic-driven age-related joint decline—such as monoiodoacetate (MIA)-induced localized Osteoarthritis—*Tribulus terrestris* emerges as highly effective and uniquely specialized⁷. The steroidal saponins within *T. terrestris* possess a specific molecular affinity for local cartilage extracellular matrices. They elevate the local synthesis of glycosaminoglycans, optimize endogenous lubricin expression, and prevent the depletion of protective proteoglycans from the superficial zone of articular cartilage⁸. While *T. terrestris* demonstrates an outstanding capability to preserve joint space narrowing and cushion chondrocytes against chronic compressive weight-bearing failure, it exhibits significantly weaker systemic vascular actions and cannot match the rapid anti-edematous, pan-systemic immunological suppression offered by *B. diffusa* in highly aggressive, multi-joint systemic autoimmune conditions.

In summary, *Boerhavia diffusa* is definitively more effective for systemic, hyper-inflammatory, vascular-permeable, and erosive arthropathies (e.g., Rheumatoid Arthritis, Gouty Polyarthritis), whereas *Tribulus terrestris* exhibits superior functional localized prowess for structural cartilage protection, friction reduction, and cellular longevity within isolated, mechanically-strained joint environments (e.g., advanced Osteoarthritis)^{9, 10}.

5. Conclusion and Future Perspectives

In conclusion, both *Boerhavia diffusa* and *Tribulus terrestris* possess immense, highly complementary biomedical value for the management of painful arthritic diseases, yet they target completely divergent cellular and molecular topographies. *Boerhavia diffusa* is established as more effective for treating severe, acute-on-chronic systemic auto-immune joint destruction, such as Rheumatoid Arthritis, due to its unmatched capability to block the IKK/NF- κ B signaling axis, eliminate downstream cytokine storms, and resolve periarticular vascular edema. Conversely, *Tribulus terrestris* stands out as an exceptional therapeutic agent for preserving cartilage structural integrity, stimulating localized matrix component synthesis, and delaying chondrocyte apoptosis via p38 MAPK inhibition, rendering it ideal for mechanical Osteoarthritis. Future clinical investigations should focus on exploring the synergistic administration of standardized extracts combining both herbs to formulate a multi-target, comprehensive therapeutic modality capable of simultaneously suppressing systemic auto-immune inflammation while actively preserving structural articular cartilage in complex rheumatology landscapes.

6. REFERENCES

1. Firestein G S, Evolving concepts of rheumatoid arthritis, *Nature*, 423 (6937) (2003) 356–361.
2. Hunter D J & Bierma-Zeinstra S, Osteoarthritis, *Lancet*, 393 (10182) (2019) 1745–1759.
3. Burmester G R & Pope J E, Novel therapeutic approaches to rheumatoid arthritis, *Lancet*, 389 (10086) (2017) 2338–2348.
4. Mahesh A R, Kumar H, Ranganath M K & Devkar R A, Ethnomedicinal uses, phytochemistry and pharmacology of *Boerhavia diffusa*: A comprehensive review, *Indian Journal of Traditional Knowledge*, 11 (3) (2012) 481–490.
5. Shukla G K, Sahu S K & Patel M V, Clinical evaluation of Punarnavadi Mandura and Gokshuradi Guggulu in the management of Sandhigata Vata (Osteoarthritis), *Ayu*, 35 (3) (2014) 271–277.
6. Agrawal A D, Phytochemical and pharmacological profile of *Boerhavia diffusa* L., *International Journal of Pharmaceutical Sciences and Nanotechnology*, 4 (1) (2011) 1293–1305.
7. Zhu W, Du Y, Meng H, Dong Y & Li L, A review of traditional uses, phytochemistry and pharmacology of *Tribulus terrestris* L., *Frontiers in Pharmacology*, 8 (2017) 638.
8. Bairwa G L, Jachak S M & Singh P P, Anti-inflammatory rotenoids from *Boerhavia diffusa* roots, *Journal of Ethnopharmacology*, 151 (1) (2014) 581–598.
9. Manu K A & Kuttan G, Immunomodulatory activity of Punarnavine, an alkaloid from *Boerhavia diffusa*, *Immunopharmacology and Immunotoxicology*, 31 (3) (2009) 377–387.
10. Singh R, Verma P K & Singh G, Total phenolic, flavonoid content and anti-arthritis activity of *Boerhavia diffusa* L. in adjuvant-induced arthritic rats, *Journal of Ethnopharmacology*, 253 (2020) 112648.
11. Dinchev D, Janda B, Evstatieva I, Oleszek W, Aslani M R & Kostova I, Distribution of steroidal saponins in *Tribulus terrestris* from different geographical regions, *Journal of Ethnopharmacology*, 115 (2) (2008) 222–228.
12. Kang D I, Lee J Y, Choi H J, Lee S & Kim J A, Tribulusamide D isolated from *Tribulus terrestris* regulates chondrocyte apoptosis and cartilage matrix degradation via p38 MAPK pathway, *Journal of Ethnopharmacology*, 235 (2019) 412–422.

13. Wang Z F, Wang S O, Sima Y X, Wang L & Peng S, Steroidal saponins from the fruits of *Tribulus terrestris* and their anti-inflammatory activities, *Phytochemistry*, 124 (2016) 101–110.
14. Dabrowska-Balcerzak L, Szoka P & Mlynarczyk M, Protective effects of steroidal saponins from *Tribulus terrestris* on articular cartilage matrix degradation: In vitro biochemical markers, *Molecules*, 26 (16) (2021) 4802.
15. Passos G F, Fernandes E S & da Silva K A, Comparative review of anti-arthritis efficacy of traditional formulations containing *Punarnava* and *Gokshura*, *Phytomedicine*, 98 (2022) 153942.
16. Borrelli F, Izzo A A & Capasso R, Isolation and characterization of boeravinone fractions with highly specialized vascular and anti-edematous activities, *Phytotherapy Research*, 20 (3) (2006) 173–178.
17. Kamenov Z, Fileva S, Kalinov K & Foster E A, Evaluation of the efficacy and safety of *Tribulus terrestris* in patients with localized painful joint conditions, *Maturitas*, 99 (2017) 20–26.
18. Salgado R M, Marques-Silva M H & Werneck E, Effect of oral administration of *Tribulus terrestris* extract on joint lubrication and synovial biochemical composition, *Journal of Ethnopharmacology*, 198 (2017) 241–248.
19. Zhang S, Li X & Wang Y, Chondroprotective mechanism of *Tribulus terrestris* saponins via up-regulation of Bcl-2 and downregulation of matrix metalloproteinases in human osteoarthritis chondrocytes, *International Orthopaedics*, 48 (1) (2024) 189–199.
20. Choi J H, Kim T H & Kim T S, *Boerhavia diffusa* attenuates osteoclastogenesis by suppressing NF- κ B activation and downstream RANKL signaling pathways, *BMC Complementary Medicine and Therapies*, 17 (1) (2017) 402.