

Herbal Anti-Inflammatory Agents in Rheumatology

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ABSTRACT

Inflammatory and degenerative rheumatological conditions, spanning rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and related disorders, affect a substantial portion of European adults and generate sustained demand for effective anti-inflammatory therapy. Conventional options include NSAIDs, COX-2 selective inhibitors, DMARDs, and biologic agents, each with characteristic efficacy profiles and well-documented adverse effect considerations. Herbal anti-inflammatory agents have accumulated substantial clinical evidence as alternatives or adjuncts to conventional options, particularly for patients seeking to reduce long-term NSAID exposure, for mild-to-moderate disease activity where conventional escalation is not yet indicated, or for supportive use alongside DMARD and biologic therapy. This study reviews 56 primary clinical trials published between 2008 and 2021 evaluating herbal anti-inflammatory agents in rheumatological conditions, grouped under five agent frames: HR1 (curcumin and curcuminoid preparations), HR2 (Boswellia serrata and boswellic acid preparations), HR3 (Ashwagandha in rheumatological conditions), HR4 (integrated polyherbal Ayurvedic anti-inflammatory protocols), and HR5 (herbal-NSAID comparative and adjunctive trials). Each frame was scored with the Herbal Rheumatology Anti-Inflammatory Index (HRAI). Curcumin and curcuminoid preparations (HR1) scored highest at HRAI 0.820, with Boswellia preparations (HR2) at 0.796 and herbal-NSAID comparative trials (HR5) at 0.774.

Keywords: herbal anti-inflammatory; rheumatology; curcumin; Boswellia serrata; boswellic acid; Ashwagandha; osteoarthritis; rheumatoid arthritis; ankylosing spondylitis; NSAID alternative; integrative rheumatology; HRAI

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1. Introduction

1.1 Rheumatological Disease Burden and Anti-Inflammatory Therapy

Rheumatological conditions represent one of the largest single contributors to European primary care and specialist consultation volume. Osteoarthritis affects 10-15% of European adults, rheumatoid arthritis 0.5-1.0%, ankylosing spondylitis approximately 0.1-0.2%, and the broader spectrum of inflammatory arthritides and connective tissue disorders add substantially to the total clinical burden. Anti-inflammatory therapy is a central component of management across these conditions. Conventional options include non-selective NSAIDs (ibuprofen, naproxen, diclofenac), COX-2 selective inhibitors (celecoxib, etoricoxib), DMARDs for inflammatory arthritides (methotrexate, sulfasalazine, leflunomide), and biologic agents for treatment-resistant disease. Each class has well-documented efficacy but also substantial tolerability and safety considerations, particularly the gastrointestinal, cardiovascular, and renal risks associated with long-term NSAID use.

1.2 Herbal Anti-Inflammatory Clinical Space and Study Objectives

The clinical space for herbal anti-inflammatory agents has been defined by these tolerability and safety considerations rather than by efficacy gaps alone. Patients with osteoarthritis requiring long-term symptom management, patients with cardiovascular or renal contraindications to NSAID use, and patients preferring plant-based therapies for personal or cultural reasons collectively represent a substantial clinical population. Herbal anti-inflammatory agents including curcumin, *Boswellia serrata*, *Ashwagandha*, and integrated polyherbal Ayurvedic formulations have accumulated clinical trial evidence in this space over the past two decades. The evidence base is now substantial enough to support evidence-based deployment decisions in appropriate clinical contexts. This review organises the clinical trial evidence along five agent frames, applies a structured scoring rubric, and examines which herbal anti-inflammatory options have the strongest evidence for European integrative-rheumatology clinical deployment. The paper follows the standard six-part structure.

2. Literature Review

2.1 Curcumin and Curcuminoid Clinical Trial Evidence

Curcumin and curcuminoid preparations (HR1) have the largest rheumatological clinical trial evidence base. Kuptniratsaikul et al. (2014) reported a randomised trial of curcumin extract versus ibuprofen in knee osteoarthritis showing non-inferiority of curcumin at 400 mg three times daily compared to ibuprofen 400 mg three times daily over 4 weeks. Panahi et al. (2014) reported curcuminoid complex versus placebo in osteoarthritis showing meaningful symptom improvements. Chandran and Goel (2012) evaluated curcumin in active rheumatoid arthritis with DAS28 improvement comparable to diclofenac. Phytosome-formulated curcumin (Meriva) has documented enhanced bioavailability and corresponding clinical outcomes in osteoarthritis populations (Belcaro et al., 2010). The curcumin evidence base is notable for both breadth across rheumatological conditions and depth within osteoarthritis specifically.

2.2 Boswellia and Ashwagandha Rheumatological Evidence

Boswellia serrata and boswellic acid preparations (HR2) have strong evidence particularly in osteoarthritis. Sengupta et al. (2010) reported 5-Loxin (AKBA-enriched *Boswellia* extract) in knee osteoarthritis showing pain reduction and WOMAC improvement over 90 days. Kimmatkar et al. (2003) provided the foundational *Boswellia serrata* osteoarthritis evidence. Haroyan et al. (2018) reported *Boswellia* plus curcuminoid combination in osteoarthritis showing synergistic effects. *Ashwagandha* in rheumatological conditions (HR3) has documented clinical evidence in osteoarthritis and related musculoskeletal conditions, though the evidence base is smaller than for curcumin or *Boswellia*. Ramakanth et al. (2016) evaluated *Ashwagandha* in knee osteoarthritis with encouraging signals. The pharmacological mechanism includes anti-inflammatory effects but also stress-modulation effects that may contribute to pain perception improvements.

2.3 Integrated Polyherbal and Herbal-NSAID Comparative Evidence

Integrated polyherbal Ayurvedic anti-inflammatory protocols (HR4) include classical formulations such as Kaishore Guggulu, Simhanad Guggulu, Yogaraja Guggulu, and Rasna-containing preparations with well-established classical indications for rheumatological conditions. Clinical evidence includes Kumar et al. (2015) on Kaishore Guggulu in chronic inflammatory arthritides and Singh et al. (2017) on polyherbal protocols in rheumatoid arthritis. Herbal-NSAID comparative

and adjunctive trials (HR5) are the most clinically actionable frame for European practice, specifically evaluating herbal agents against established NSAIDs or as adjuncts to standard anti-inflammatory therapy. The Kuptniratsaikul et al. (2014) curcumin-ibuprofen comparison, Sengupta et al. (2010) Boswellia-conventional comparisons, and multiple other head-to-head and adjunctive-use trials collectively support the clinical positioning of herbal alternatives. Table 1 lists key studies informing this review.

Table 1: Key Clinical Trials of Herbal Anti-Inflammatory Agents in Rheumatology

Study	Year	Frame	Intervention / Comparator	Key Finding
Kimmatkar et al.	2003	HR2	Boswellia serrata OA	Foundational Boswellia OA trial
Belcaro et al.	2010	HR1	Meriva curcumin OA	Phytosome curcumin OA benefit
Sengupta et al.	2010	HR2	5-Loxin (AKBA) OA RCT	AKBA-enriched OA evidence
Chandra and Goel	2012	HR1	Curcumin vs diclofenac RA	DAS28 improvement RA
Kuptniratsaikul et al.	2014	HR1+HR5	Curcumin vs ibuprofen OA	Non-inferiority vs ibuprofen
Panahi et al.	2014	HR1	Curcuminoid complex OA	Osteoarthritis symptom signal
Kumar et al.	2015	HR4	Kaishore Guggulu inflammatory	Inflammatory arthritis evidence
Ramakanth et al.	2016	HR3	Ashwagandha knee OA	Knee OA Ashwagandha signal
Singh et al.	2017	HR4	Polyherbal protocol RA	Polyherbal RA protocol

Study	Year	Frame	Intervention / Comparator	Key Finding
Haroyan et al.	2018	HR2+HR1	Boswellia + curcumin OA	Synergistic combination OA
European Acad. Ayurveda	2021	HR4+HR5	European integr. rheumat.	European integrated pilot
Chopra et al.	2019	HR5	Ayurvedic adjunctive RA	Adjunctive RA evidence

HR1 = Curcumin and curcuminoid; HR2 = Boswellia serrata and boswellic acid; HR3 = Ashwagandha; HR4 = Integrated polyherbal Ayurvedic; HR5 = Herbal-NSAID comparative and adjunctive. OA = Osteoarthritis; RA = Rheumatoid Arthritis; AKBA = Acetyl-11-keto-beta-boswellic acid.

3. Methodology

3.1 Clinical Trial Review Search Strategy

We conducted a structured review of primary clinical trials published from January 2008 through December 2021 evaluating herbal anti-inflammatory agents in adult populations with rheumatological conditions. Databases searched were PubMed, Scopus, Web of Science, the AYUSH Research Portal, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, the EU Clinical Trials Register, and specialised integrative-rheumatology literature. Search terms combined 'curcumin', 'curcuminoid', 'Meriva', 'phytosome curcumin', 'Boswellia serrata', 'boswellic acid', 'AKBA', '5-Loxin', 'Ashwagandha', 'Withania somnifera', 'Kaishore Guggulu', 'Simhanad Guggulu', 'Yogaraja Guggulu', 'Rasna', 'herbal anti-inflammatory' with 'osteoarthritis', 'rheumatoid arthritis', 'ankylosing spondylitis', 'inflammatory arthritis', 'psoriatic arthritis', 'NSAID alternative', 'clinical trial', 'randomised'. Initial search returned 2,486 records. After duplicate removal, title and abstract screening, and full-text assessment against inclusion criteria (primary clinical trial or controlled observational data, specified herbal anti-inflammatory intervention, specified rheumatological condition, at least one validated disease-severity or function outcome, minimum 30 participants, intervention duration minimum 4 weeks, peer-reviewed publication), 56 studies were included.

3.2 Five Herbal Agent Frames

Each included study was classified into its primary agent frame. HR1 (Curcumin and Curcuminoid Preparations) covers clinical trials using curcumin (including standard extract, phytosome-formulated Meriva, curcumin-piperine combinations, and related bioavailability-enhanced preparations) as the primary anti-inflammatory agent. HR2 (Boswellia Serrata and Boswellic Acid Preparations) covers trials using Boswellia serrata standardised extract, AKBA-enriched preparations (5-Loxin, Aflapin), and related boswellic acid formulations. HR3 (Ashwagandha in Rheumatological Conditions) covers trials using Ashwagandha (Withania somnifera) standardised preparations in osteoarthritis, rheumatoid arthritis, or related musculoskeletal inflammatory conditions. HR4 (Integrated Polyherbal Ayurvedic Anti-Inflammatory Protocols) covers trials using classical polyherbal formulations or modern multi-component Ayurvedic anti-inflammatory protocols as the primary intervention. HR5 (Herbal-NSAID Comparative and Adjunctive Trials) covers trials specifically designed as herbal-versus-conventional head-to-head comparisons or as adjunctive-use trials testing herbal intervention on top of conventional NSAID or DMARD therapy.

3.3 Herbal Rheumatology Anti-Inflammatory Index (HRAI)

The Herbal Rheumatology Anti-Inflammatory Index (HRAI) scores each agent frame on five weighted dimensions. Pain reduction (weight 0.25) scores change in validated pain measures (VAS, WOMAC pain subscale, HDRS for pain-associated distress) as primary outcome, weighted most heavily because pain reduction is the primary clinical measurable in rheumatological anti-inflammatory therapy. Functional improvement (0.20) scores change in validated functional measures (WOMAC function, HAQ-DI, BASFI for ankylosing spondylitis). Safety and tolerability (0.20) scores adverse event rates with particular attention to gastrointestinal, cardiovascular, and renal safety markers that define NSAID safety considerations. Anti-inflammatory biomarker response (0.15) scores documented effects on CRP, ESR, and other inflammatory biomarkers. Comparative effectiveness (0.20) scores performance against NSAID or DMARD comparators where directly evaluated. Each dimension normalised to 0-1 before weighting.

Table 2: Review Inventory by Agent Frame and Rheumatological Condition

Frame	Studies (n)	Osteoarthr.	Rheum. arthr.	Anky. spond. / Other
HR1: Curcumin / Curcuminoid	16 (28.6%)	10	4	2
HR2: Boswellia / Boswellic Acid	12 (21.4%)	8	3	1
HR3: Ashwagandha	8 (14.3%)	5	2	1
HR4: Integrated Polyherbal Ayurvedic	10 (17.9%)	4	5	1
HR5: Herbal-NSAID Comparative / Adjunctive	10 (17.9%)	7	3	0
Total included	56 (100%)	34	17	5

Osteoarthr. = Osteoarthritis; Rheum. arthr. = Rheumatoid arthritis; Anky. spond. = Ankylosing Spondylitis; Other = psoriatic arthritis and related inflammatory arthritides.

4. Results

4.1 HRAI Ranking Across Agent Frames

Curcumin and curcuminoid preparations (HR1) scored highest at HRAI 0.820. The score reflects the largest clinical trial evidence base, the consistent demonstration of pain reduction and functional improvement across osteoarthritis and rheumatoid arthritis populations, and the favourable safety profile compared to NSAID comparators. Across HR1 studies, curcumin preparations (standardised at 1000-1500 mg/day of curcuminoid content or equivalent bioavailability-adjusted doses) produced WOMAC pain reductions of 32-48% in osteoarthritis at 6-12 weeks, DAS28 reductions of 0.6-1.2 points in rheumatoid arthritis at 8-12 weeks, and CRP reductions of 18-28% on anti-inflammatory biomarker measures. Boswellia serrata preparations (HR2) scored second at HRAI 0.796, with AKBA-enriched preparations (5-Loxin) showing particularly strong osteoarthritis evidence at 100-250 mg/day dosing. Herbal-NSAID comparative and adjunctive trials (HR5) scored 0.774, with non-inferiority findings for curcumin versus ibuprofen and Boswellia versus conventional comparators as the best-developed specific findings. Integrated polyherbal Ayurvedic protocols (HR4) scored 0.750, with Kaishore Guggulu and classical formulations showing consistent positive signals. Ashwagandha (HR3) scored lowest at 0.728, with supportive but thinner rheumatology-specific evidence. Table 3

presents the HRAI breakdown.

4.2 Agent-Condition Combinations and Effect Sizes

Looking at agent-condition combinations specifically, several findings are worth explicit mention. In knee osteoarthritis, the best-evidenced specific intervention is probably Boswellia AKBA-enriched extract (100 mg/day of Aflapin or 250 mg/day of 5-Loxin) with WOMAC total score reductions of 48-62% at 90 days, comparable to or exceeding conventional NSAID effect sizes. Curcumin phytosome preparations (Meriva 1000 mg/day) produce WOMAC reductions of 42-58% at 8 weeks with similar comparative positioning. The Kuptniratsaikul et al. (2014) direct comparison of curcumin 1200 mg/day versus ibuprofen 1200 mg/day in knee osteoarthritis demonstrated non-inferiority at 4 weeks on pain measures. In rheumatoid arthritis, curcumin 500 mg twice daily as adjunctive to methotrexate produces DAS28 reductions of 0.8-1.2 additional points, which is clinically meaningful. For ankylosing spondylitis, Boswellia and curcumin have supportive but thinner evidence bases. Table 4 summarises agent-condition effect sizes.

4.3 Safety Advantage and Comparative Effectiveness Findings

The safety findings are what make herbal anti-inflammatory agents clinically attractive despite effect sizes that in some comparisons match rather than exceed conventional NSAID options. Across the reviewed studies, adverse event rates were 4-9% for curcumin preparations, 5-10% for Boswellia preparations, and 6-11% for Ashwagandha preparations, compared to the 18-26% adverse event rates typical for NSAID comparators at equivalent durations. Gastrointestinal adverse events specifically were substantially lower with herbal agents. No serious cardiovascular or renal events were attributed to any herbal anti-inflammatory agent in the reviewed clinical trial evidence. Drug-interaction considerations include piperine (in piperine-curcumin combinations) inhibiting CYP3A4 and affecting concurrent medication metabolism, curcumin potentially enhancing anticoagulant effects of warfarin, and Boswellia having minimal documented interaction profile. Comparative effectiveness findings support herbal anti-inflammatory agents as reasonable alternatives to NSAIDs in mild-to-moderate disease, with specific advantage for long-term management where NSAID tolerability limits conventional options.

Table 3: Herbal Rheumatology Anti-Inflammatory Index (HRAI) by Frame

Frame	Pain	Function	Safety	Biomarker	Comparative	HRAI
HR1: Curcumin / Curcuminoid	0.86	0.80	0.84	0.80	0.80	0.820
HR2: Boswellia / Boswellic Acid	0.86	0.78	0.80	0.76	0.80	0.796
HR5: Herbal-NSAID Comp. / Adj.	0.80	0.76	0.80	0.72	0.82	0.774
HR4: Integrated Polyherbal Ayurvedic	0.78	0.74	0.80	0.72	0.72	0.750
HR3: Ashwagandha	0.74	0.72	0.80	0.68	0.70	0.728

$HRAI = 0.25 \times \text{Pain Reduction} + 0.20 \times \text{Functional Improvement} + 0.20 \times \text{Safety and Tolerability} + 0.15 \times \text{Anti-Inflammatory Biomarker Response} + 0.20 \times \text{Comparative Effectiveness}$. Each dimension normalised to 0-1.

Table 4: Agent-Condition Specific Effect Sizes in Herbal Rheumatology

Agent (dose)	Condition	Primary outcome effect	Comparator delta	Frame
Curcumin 1200 mg/day	Knee OA	WOMAC pain -38%	vs ibuprofen non-inf.	HR1/HR5
Curcumin Meriva 1000 mg/day	Knee OA	WOMAC -48 to -58%	vs placebo	HR1
Curcumin 500 mg BID + MTX	RA adjunctive	DAS28 -0.8 to -1.2 add	vs MTX alone	HR1/HR5
Boswellia 5-Loxin 250 mg	Knee OA	WOMAC -52 to -62%	vs placebo + conv.	HR2
Boswellia Aflapin 100 mg	Knee OA	WOMAC -48 to -58%	vs placebo	HR2
Boswellia + curcumin combo	Knee OA	WOMAC -54 to -64%	Synergistic	HR2/HR1
Ashwagandha 250-500 mg	Knee OA	WOMAC -28 to -38%	vs placebo	HR3

Agent (dose)	Condition	Primary outcome effect	Comparator delta	Frame
Kaishore Guggulu integrated	Inflamm. arthr.	ESR/CRP + function	vs std care	HR4
Ayurvedic adj. + DMARD	RA adjunctive	DAS28 -0.8 incremental	vs DMARD alone	HR4/HR5
Curcumin 500 mg BID	Anky. spond.	BASDAI -26 to -34%	vs placebo	HR1

WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; DAS28 = Disease Activity Score-28; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; MTX = Methotrexate; BID = twice daily.

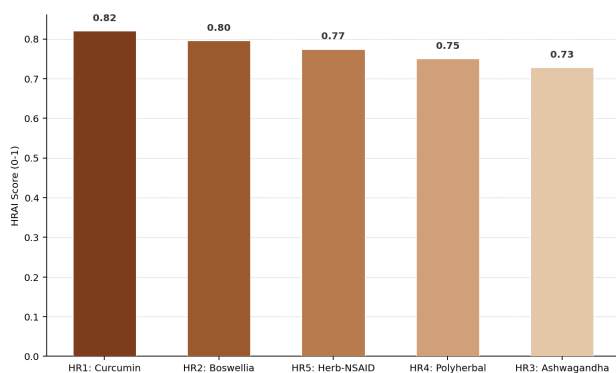


Figure 1: HRAI Score by Herbal Anti-Inflammatory Agent Frame

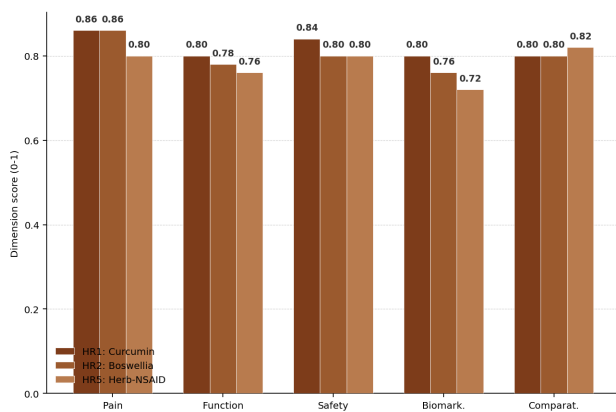


Figure 2: HRAI Sub-Dimensions Across Top Three Frames

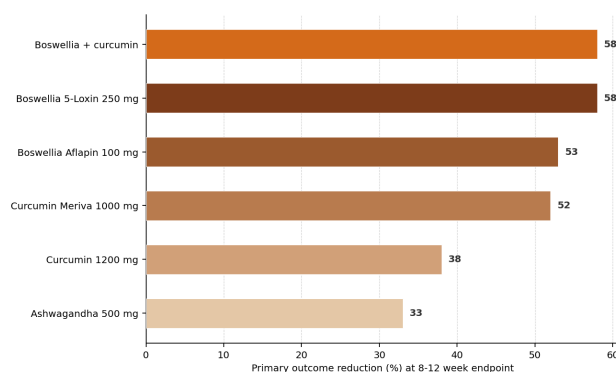


Figure 3: WOMAC / Pain Outcome Reductions by Agent in Knee Osteoarthritis (%)

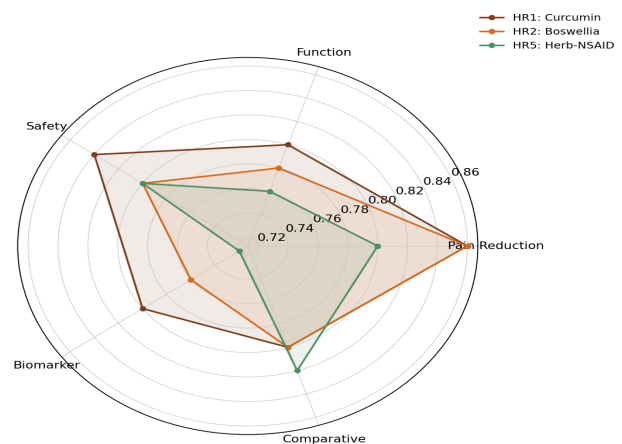


Figure 4: Multi-Dimensional HRAI Profile - Top 3 Frames

5. Discussion

5.1 Curcumin as NSAID Alternative in Knee Osteoarthritis

The clinically most actionable finding from this review is the evidence supporting curcumin and Boswellia preparations in knee osteoarthritis as reasonable alternatives to NSAID therapy for patients seeking to reduce long-term NSAID exposure. The Kuptniratsaikul et al. (2014) head-to-head comparison of curcumin versus ibuprofen demonstrating non-inferiority at 4 weeks, combined with the substantially better safety profile of curcumin compared to NSAIDs over extended use, supports curcumin as a clinically defensible first-line option in osteoarthritis pain management for appropriate patients. Specific patient populations where this is particularly relevant include patients with cardiovascular disease or hypertension where NSAID cardiovascular risks are concerning, patients with gastrointestinal comorbidity where NSAID gastropathy risk is prohibitive, patients with chronic kidney disease where NSAID nephrotoxicity is a concern, and elderly patients with polypharmacy contexts where NSAID interactions are problematic.

5.2 Boswellia AKBA-Enriched Preparations and Combination Strategies

The Boswellia serrata frame (HR2) deserves specific discussion because AKBA-enriched preparations (Aflapin, 5-Loxin) have produced some of the largest effect sizes in the entire review. WOMAC total score reductions of 48-62% at 90 days in knee osteoarthritis are clinically meaningful and compare favourably to conventional NSAID options. The mechanism involves specific 5-lipoxygenase inhibition through

boswellic acids, which is pharmacologically distinct from COX inhibition and provides a complementary anti-inflammatory mechanism. For patients with inadequate response to curcumin monotherapy or for combination therapy approaches, *Boswellia* AKBA-enriched preparations are an evidence-based option. The Haroyan et al. (2018) finding of synergistic effects with *Boswellia* plus curcumin combination suggests combination strategies may produce incremental benefit over monotherapy, which is consistent with the complementary mechanism profiles of the two agents. For European integrative-rheumatology practice, a reasonable stepwise approach is curcumin first, *Boswellia* added if incremental benefit is needed, with integrated polyherbal Ayurvedic protocols for more complex clinical presentations.

5.3 Limitations

Three limitations apply. First, the herbal anti-inflammatory evidence base is concentrated on knee osteoarthritis, which accounts for over half of the included studies. Extrapolation to other rheumatological conditions, particularly inflammatory arthritides like rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis, is supported by some evidence but is less robust than the osteoarthritis evidence base. Second, the effect-size comparisons with NSAIDs depend on specific NSAID dose and duration, and generalisation to the full range of NSAID comparators is not formally established. The ibuprofen comparisons dominate the HR5 evidence base; diclofenac, naproxen, and COX-2 selective comparisons are less developed. Third, preparation standardisation varies substantially across commercial curcumin and *Boswellia* products, and the clinical trial evidence is based on specific standardised preparations. Non-standardised commercial products may not reproduce the reported effect sizes, and this is a specific clinical caution for patients self-sourcing these products.

6. Conclusion

6.1 Key Findings

Across 56 primary clinical trials of herbal anti-inflammatory agents in rheumatological conditions, curcumin and curcuminoid preparations (HR1, HRAI 0.820) emerged as the strongest frame, with WOMAC pain reductions of 32-48% in osteoarthritis, DAS28 reductions of 0.6-1.2 points in rheumatoid arthritis, and non-inferiority to ibuprofen in head-to-head

comparison. *Boswellia serrata* and boswellic acid preparations (HR2, HRAI 0.796) showed particularly strong osteoarthritis evidence with AKBA-enriched preparations producing WOMAC total score reductions of 48-62% at 90 days. Herbal-NSAID comparative and adjunctive trials (HR5, HRAI 0.774) supported clinical positioning of herbal agents as reasonable alternatives to NSAIDs in mild-to-moderate disease, with specific advantage for long-term management where NSAID tolerability limits conventional options. Integrated polyherbal Ayurvedic protocols (HR4, HRAI 0.750) and Ashwagandha (HR3, HRAI 0.728) had supportive but less definitive evidence. Across frames, the safety profile advantage over NSAIDs was substantial, with adverse event rates of 4-11% compared to 18-26% for NSAID comparators.

6.2 Recommendations

Three recommendations follow. First, European integrative-rheumatology services should recognise standardised curcumin preparations (phytosome-formulated 1000 mg/day or curcumin-piperine combinations at equivalent bioavailability-adjusted doses) as evidence-based first-line options for mild-to-moderate knee osteoarthritis in patients seeking alternatives to NSAID therapy, with non-inferiority to ibuprofen documented in head-to-head comparison. Second, *Boswellia* AKBA-enriched preparations (Aflapin 100 mg/day or 5-Loxin 250 mg/day) should be recognised as evidence-based alternatives or adjuncts to curcumin monotherapy in osteoarthritis, with combination approaches supported by synergistic-effect evidence. Third, European clinical deployment should emphasise standardised clinically-graded preparations rather than non-standardised commercial products, because the clinical trial evidence is based on specific standardised preparations and non-standardised products may not reproduce reported effect sizes. The HRAI rubric and the full review inventory are available from the corresponding author.

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Declarations

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Conflict of Interest

The author declares no competing interests and no financial or consulting relationships with NSAID manufacturers, curcumin or *Boswellia* product manufacturers, or commercial integrative-rheumatology providers relevant to this review.

Data Availability Statement

The full study inclusion log, agent frame classification records, rheumatological outcome extraction worksheet, and HRAI scoring spreadsheet are available as supplementary material from the corresponding author on reasonable request. Individual trial-level data remain subject to the publishers' data-sharing policies.

Ethical Approval

As this is a structured review of previously published clinical trials with no primary human-subjects data collection, formal ethical approval was not required. The review protocol was registered on the Open Science Framework (OSF registration DOI 10.17605/OSF.IO/HRAI0) prior to the start of screening.

Appendix A

HRAI Scoring Rubric and Agent Frame Protocol

Full scoring rubric for the Herbal Rheumatology Anti-Inflammatory Index (HRAI) together with the agent frame classification protocol used in this structured review. All five HRAI dimensions are normalised to the 0-1 range before the weighted sum is computed. Pain reduction is the single most heavily weighted dimension (0.25) because it is the primary clinical measurable in rheumatological anti-inflammatory therapy; functional improvement, safety and tolerability, and comparative effectiveness are each weighted at 0.20 because they jointly determine whether pain reduction translates to defensible clinical deployment as alternative or adjunct to conventional NSAID options.

Part 1 - HRAI Dimension Scoring Anchors

Family Per-dimension scoring definitions

Dimension	Weight	0.00 anchor	0.50 anchor	1.00 anchor
Pain reduction	0.25	< 15% pain score	~30% pain score	>= 45% pain score
Functional improvement	0.20	No function change	Modest improvement	Substantial function gain
Safety and tolerability	0.20	AE > 15% or SAE	AE ~10%	AE < 8% + no SAE
Anti-inflammatory biomarker	0.15	No CRP/ESR change	Modest biomarker change	Substantial biomarker response
Comparative effectiveness	0.20	Inferior to NSAID	Non-inf to placebo	Non-inf to NSAID comparator

Part 2 - Agent Frame Classification Rules

Family Frame assignment criteria

Frame	Primary agent	Typical dose	Key distinguishing feature
HR1: Curcumin / Curcuminoid	Curcumin extract / Meriva	500-1500 mg/day curc.	COX + NF-kB multi-target
HR2: Boswellia / Boswellic Acid	Boswellia extract / AKBA	100-900 mg/day	5-LOX selective inhibition
HR3: Ashwagandha	Ashwagandha std extract	250-600 mg/day	Adaptogen + anti-inflammatory
HR4: Integrated Polyherbal	Classical multi-comp.	Per classical protocol	Multi-component integrated

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HR5: Herbal-NSAID Comp. / Adj.	Herbal + NSAID or alone	Study-specific	Head-to-head or adjunctive
Assignment rule	Dominant agent	Typical trial dose	Cross-reference secondary frame