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EVIDENCE-BASED SIDDHA HERBO-MINERAL/METALLIC FORMULATIONS FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS (UTHIRAVATHA SURONITHAM): A SYSTEMATIC REVIEW

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ABSTRACT

Background: Rheumatoid Arthritis (RA), known as Uthiravatha Suronitham in Siddha medicine, is a chronic autoimmune inflammatory disorder affecting synovial joints. Despite advancements in modern medicine, RA management often faces challenges related to efficacy, side effects, and patient compliance, leading to a growing interest in traditional therapeutic approaches like Siddha medicine. Siddha formulations, particularly herbo-mineral/metallic preparations, are traditionally used for their anti-inflammatory, immunomodulatory, and analgesic properties in various chronic conditions. **Objective:** This systematic review aims to summarize and critically evaluate the available classical Siddha evidence and modern scientific studies on herbo-mineral/metallic formulations used for the management of Rheumatoid Arthritis (Uthiravatha Suronitham). **Methods:** A systematic literature search was conducted across databases including PubMed and Google Scholar. The search terms "Rheumatoid arthritis," "Herbo-mineral/metallic Siddha formulations," "Uthiravatha suronitham," were used with Boolean operators (AND, OR). Inclusion criteria comprised published journals exploring pre-clinical studies, clinical studies, and standardization studies of Siddha herbo-mineral/metallic drugs against rheumatoid arthritis. Exclusion criteria included narratives, letters, conference papers, dissertations, and articles in languages other than English. The study selection process followed PRISMA 2020 guidelines, involving identification, screening, eligibility, and inclusion phases. Data extraction focused on study characteristics, interventions, outcomes, and findings. Risk of bias was assessed using appropriate tools where applicable, and data were synthesized qualitatively. **Results:** A total of 68 records were identified (43 from database searching, 25 from other sources like classic literary texts and Materia medica). After screening, 57 records were assessed, and 11 were excluded. Sixteen full-text articles were included in the review, comprising 7 clinical studies, 3 preclinical studies, 5 standardization studies, and 1 literature evidence. Clinical studies demonstrated reductions in RA factors, CRP, DAS 28, HAQ-DI, VAS scores, pain, and swelling, alongside improvements in ROM with formulations like Amirdha Gandhi Kukkil Vallathy, Rasa chenduram, Thirikadugu choornam, Karpoora Chindhamani Mathirai, Seenthil chooranam, Serankottai Nei, Meghasaanthi Chooranam, Amirtharasa Mathirai, Suronitha vatha ennai, and Chandamarutha Chenduram. Preclinical animal studies showed reductions in arthritic swelling, score, joint swelling, and reversal of bone and tissue morphology, with evidence of down-regulation of pro-inflammatory cytokines (TNF-α, IL-1β) and extracellular matrix degradation. Standardized drugs for RA were identified, including Keel Vayu Nivarana Chooranam, Chanthirothaya Tablet, Amirdha Gandhi Kukkil Vallathy, Ratthi Naagara Rasa Mezhugu, and Sanda Marutha Chendooram, among others. **Conclusion:** The available evidence suggests that Siddha herbo-mineral/metallic formulations hold promising therapeutic potential for the management of Rheumatoid Arthritis (Uthiravatha Suronitham), exhibiting anti-inflammatory, immunomodulatory, and pain-relieving effects. While traditional wisdom and preliminary modern studies support their efficacy, there is a significant lacuna in robust, evidence-based data, particularly large-scale clinical trials. Further rigorous research is warranted to validate their safety, efficacy, and mechanisms of action, paving the way for their integration into broader healthcare.

KEYWORDS: Rheumatoid arthritis, Herbo-mineral/metallic Siddha formulations, Uthiravatha suronitham, Literature review.

1. INTRODUCTION

Rheumatoid Arthritis (RA) is a systemic, chronic inflammatory autoimmune disease primarily affecting the synovial lining of joints, leading to pain, swelling, stiffness, and progressive joint destruction. It significantly impacts patients' quality of life, leading to disability and increased mortality if left untreated. In Siddha medicine, one of the oldest traditional medical systems, RA is correlated with the condition known as Uthiravatha Suronitham. This condition is characterized by an imbalance of the three humors (Vata, Pitta, Kapha) and is often associated with pain, swelling of ankle, knee & smaller joints of hand, depression, and fever. Current modern treatments for RA include NSAIDs, corticosteroids, and disease-modifying anti-rheumatic drugs (DMARDs), including biological agents. While effective, these treatments often come with significant side effects and may not be suitable for all patients, highlighting treatment gaps and the need for alternative or complementary therapies. Traditional systems of medicine like Siddha offer a rich repository of formulations derived from herbs, minerals, and metals, which have been used for centuries to manage various chronic ailments. The purification process, termed "SUTHIMURAI" in Siddha, is critical for detoxifying drugs, minimizing side effects, and improving therapeutic efficacy. This systematic review aims to comprehensively summarize and critically evaluate both classical Siddha evidence and modern scientific studies on herbo-mineral/metallic formulations specifically used for the management of Rheumatoid Arthritis (Uthiravatha Suronitham). The objective is to provide an evidence-based perspective on their therapeutic potential, mechanisms of action, and areas requiring further scientific validation.

2. Methods

2.1. Study Design: This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.

2.2. Objective: The primary objective was to review Siddha herbo-mineral/metallic formulations for the management of Rheumatoid Arthritis (Uthiravatha Suronitham).

2.3. Search Strategy and Information Sources: A systematic literature search was performed using electronic databases, including PubMed and Google Scholar. Additionally, "other sources" such as classic literary texts and Materia medica from Siddha tradition were consulted to capture traditional evidence. The search was conducted using a combination of keywords and Boolean operators (AND, OR).

2.4. Search Terms: The following keywords were used: "Rheumatoid arthritis," "Herbo-mineral/metallic Siddha formulations," "Uthiravatha suronitham," and "Literature review".

2.5. Eligibility Criteria

- **Inclusion Criteria:** Published journals exploring pre-clinical studies, clinical studies, and standardization studies of Siddha herbo-mineral/metallic drugs against rheumatoid arthritis.
- **Exclusion Criteria:** Narratives, letters, conference papers, dissertations, and articles in languages other than English.

2.6. Study Selection Process (PRISMA Flow): The study selection process involved four phases:

- **Identification:** Records were identified through database searching and other sources.
- **Screening:** Titles and abstracts of identified records were screened against the inclusion and exclusion criteria.

- **Eligibility:** Full-text articles of potentially relevant records were assessed for eligibility.
- **Included:** Final records meeting all eligibility criteria were included in the review.

Figure 1 illustrates the PRISMA flow diagram for the study selection process.

2.7. Data Extraction: Data were independently extracted from the included studies by two reviewers. Discrepancies were resolved through discussion or by consulting a third reviewer. Extracted data included: author(s), year of publication, source, title of study, specific Siddha medicine/formulation used, dosage/duration, study design (clinical, preclinical, standardization), and key results/outcomes.

2.8. Risk of Bias in Individual Studies: For clinical and preclinical studies, the risk of bias was intended to be assessed using appropriate tools (e.g., Cochrane Risk of Bias tool for clinical trials, SYRCLE's Risk of Bias tool for animal studies). However, given the nature and details provided in the PowerPoint, a formal quantitative assessment of bias was not feasible. A qualitative assessment based on reported methodologies was considered.

2.9. Data Synthesis: A qualitative synthesis approach was adopted due to the heterogeneity of the included studies in terms of interventions, outcomes, and study designs. Findings were grouped based on study type (clinical, preclinical, standardization) and presented descriptively, highlighting common trends and significant results.

3. RESULTS

3.1. PRISMA Flow Summary: As depicted in Figure 1 (PRISMA Flowchart placeholder), a total of 68 records were identified. This included 43 records from database searching and 25 from other sources such as classic literary texts and Materia medica. After initial screening, 57 records were assessed for eligibility, and 11 records were excluded. Consequently, 16 full-text articles were included in this systematic review.

- Clinical studies: n=7
- Preclinical studies: n=3
- Standardization studies: n=5
- Literature evidence: n=1

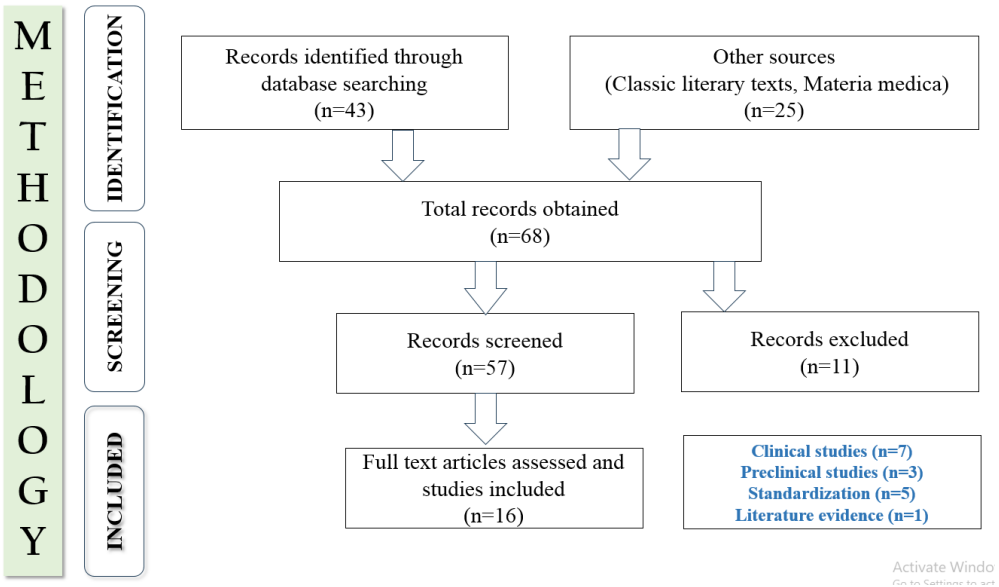

Figure 1: PRISMA flow diagram for the study selection process.

3.2. Characteristics of Included Studies: Tables 1 and 2 provide a summary of the characteristics and outcomes of the included clinical and preclinical studies.

Table 1: Characteristics and Outcomes of Clinical Studies

Author (Year)	Title	Medicine	Results
Juliet L et al., 2023	Management of Uthiravathasuronitham (rheumatoid arthritis) by Siddha Traditional Formulation Amirdha Gandhi Kukkil Vallathy – A Case Series	Amirdha Gandhi Kukkil Vallathy 2 gm BD × 48 days	RA Factor↓, CRP↓, Reduction in RAPS score and clinical symptoms
Bhavani Subramani et al., 2021	Management of Rheumatoid Arthritis in Siddha System of Medicine - A Case report	Rasa chenduram (100mg) - BD; Thirikadugu choornam (1 gm) - BD; Pinda thailam (ext) × 3 Weeks	DAS 28 (ESR) ↓, HAQ-DI ↓, VAS SCORE (cm) ↓, RA Factor ↓, CRP ↓
Meena R, 2015	Treatment of Uthiravatha Suronitham (Rheumatoid Arthritis) with a Siddha Compound Formulation - A Case Study	Karpoora Chindhamani Mathirai 130 mg – BD × 45 days; Mannennai Kalavai Thylam (ext)	RA factor-negative, CRP-negative ESR ↓, ROM ↑, Pain ↓
Kingsley J et al., 2018	A Pilot Study on "Combination of Siddha Formulation" In the treatment of "Vali Azhal Keel Vayu" (Rheumatoid Arthritis)	Seenthil chooranam - 2 gm BD; Serankottai Nei – 10 drops BD × 45 days	Pain and swelling ↓, ROM ↑, DAS 28 score ↓
Kiruthika R	Clinical Evaluation of Meghasaanthi Chooranam in the treatment of Uthiravaathasuronitham (Rheumatoid Arthritis) - Single case study.	Meghasaanthi chooranam – 3g BD × 45 days	RA factor-negative, CRP-negative ESR ↓, ROM ↑, Pain ↓
Kumar S, 2018	Combined Efficacy Of Amirtharasa Mathirai And Suronitha Vatha Ennai In The Management Of Uthiravatha Suronitham - A Open Clinical Trial	Amirtharasa mathirai (130 mg) BD; Suronitha vatha ennai (ext) × 48 days	ROM ↑, Pain ↓
Radhika Madhavan, 2012	The influence of the Siddha Formulation Chandamarutha Chenduram on Serum Rheumatoid Factor in Uthiravatha Suronitham (Rheumatoid Arthritis)	Chandamarutha Chenduram -65 mg with palm jaggery BD (after food) × 48 days	Serum RA factor – negative for 5 patients; Serum RA factor ↓ for 15 patients

Table 2: Characteristics and Outcomes of Preclinical Animal Studies (Based on PPT pages 8-9)

Author (Year)	Title	Medicine	Results
R. Naveen Kumar et al., 2021	Pharmacological Evaluation of Anti-Arthritic Potential of Siddha formulation Theer Andhaskhan Mathirai on Freund's Adjuvant Induced Arthritis in Wistar Rats	Theer Andhaskhan MATHIRAI – 200 mg/kg & 400 mg/kg × 21 days	Arthritic swelling (paw volume and thickness) ↓, reduction in arthritic score, Radiological changes, joint swelling ↓, reversal in bone and tissue morphology
Ramamurthy et al., 2020	Anti arthritic activity of herbo mineral Siddha preparation Arumuga Chendhuram against type ii collagen induced arthritis in experimental rats.	Arumuga Chendhuram 24mg/kg & 48mg/kg × 42 days	Paw volume ↓, arthritic score ↓, RA Factor ↓, CRP ↓ in par with Leflunomide (10mg/kg)
Rajendran Mythilypriyaa, 2009	Ameliorating effect of kalpaamruthaa, a Siddha preparation in adjuvant induced arthritis in rats with reference to changes in proinflammatory cytokines and acute phase proteins	Kalpaamruthaa 150 mg/kg × 14 Days	↓ extracellular matrix degradation and cartilage and bone destruction (down regulating the levels of TNF- and IL-1B), KA showed enhanced lowering effect of these immunoglobulins than SA (Standard Anti-inflammatory drug, likely)

3.3. Pharmacological and Clinical Evidence

The clinical studies consistently reported improvements in various RA markers and symptoms. Key outcomes observed include:

- **Reduced Inflammatory Markers:** Significant decreases in RA Factor and C-Reactive Protein (CRP), as well as Erythrocyte Sedimentation Rate (ESR), were noted across multiple studies (Juliet L et al., 2023; Bhavani Subramani et al., 2021; Meena R, 2015; Kiruthika R; Radhika Madhavan, 2012).
- **Improved Clinical Symptoms:** Patients experienced reduction in pain, swelling, and overall disease activity, as indicated by decreased RAPS scores, DAS 28 scores, HAQ-DI, and VAS scores (Juliet L et al., 2023; Bhavani Subramani et al., 2021; Kingsley J et al., 2018).
- **Enhanced Joint Mobility:** Several studies reported an increase in Range of Motion (ROM) (Meena R, 2015; Kingsley J et al., 2018; Kiruthika R; Kumar S, 2018).

Preclinical animal studies further substantiated these findings by demonstrating direct anti-arthritic activities:

- **Anti-inflammatory and Immunomodulatory Effects:** Formulations like Theer Andhaskhan Mathirai and Arumuga Chendhuram reduced arthritic swelling, paw volume, and arthritic scores in induced arthritis models. Kalpaamruthaa specifically showed a reduction in pro-inflammatory cytokines (TNF-α and IL-1β) and extracellular matrix degradation (R. Naveen Kumar et al., 2021; Ramamurthy et al., 2020; Rajendran Mythilypriyaa, 2009).
- **Tissue Protection and Regeneration:** Radiological changes indicated reversal in bone and tissue morphology, suggesting a protective or regenerative potential of these Siddha formulations on affected joints (R. Naveen Kumar et al., 2021).

3.4. Standardized Siddha Formulations for RA: The review identified a list of documented Siddha herbo-mineral/metallic drugs that have been standardized for Rheumatoid Arthritis (Uthiravatha Suronitham). These include:

- KEEL VAYU NIVARANA CHOORANAM
- CHANTHIROTHAYA TABLET
- AMIRDHA GANDHI KUKKIL VALLATHY
- RATTHI NAAGARA RASA MEZHUGU
- SANDA MARUTHA CHENDOORAM

Additionally, a comprehensive list of Siddha herbal preparations documented for Rheumatoid Arthritis in classical texts includes: Aya Chendooram, Ayaveera Chendooram, Gandhagaparpaam, Gandhagarasayanam, Kaalamega Naarayana Chendooram, Nandhi Mezhugu, Navauppu Mezhugu, Pachaikarpoora Mathirai, Panchasootha Mezhugu, Poora Kattu, Koushigar Kulambu, Vatha Rakshanan, Velvanga Chunnam, Linga Chendooram, Linga Pathangam, Mahaveera Mezhugu, Mehanaatha Kuligai, Muthuchippi Parpam, Rasa Mezhugu, Sivanar Amirtham, Thalaga Parpam, Thanga Parpam, Ulogamandoora Chendooram, Muthu Parpam, Velli Chendooram, and Viresana Poobathi.

4. DISCUSSION

The findings of this systematic review indicate a promising role for Siddha herbo-mineral/metallic formulations in the management of Rheumatoid Arthritis (Uthiravatha Suronitham). The observed reductions in inflammatory markers, improvements in clinical symptoms, and enhanced joint mobility align with the traditional Siddha understanding of

Uthiravatha Suronitham as a condition requiring therapies that balance humoral derangements and reduce inflammation. The preclinical studies provide insights into the potential mechanisms of action, highlighting anti-inflammatory and immunomodulatory properties through the reduction of pro-inflammatory cytokines like TNF-α and IL-1β. This suggests that some Siddha formulations may operate via pathways similar to conventional DMARDs or biological agents by targeting key inflammatory mediators. The evidence of reduced extracellular matrix degradation and reversal in bone/tissue morphology further underscores the potential for disease modification, rather than just symptomatic relief. A significant strength of Siddha medicine lies in its emphasis on "SUTHIMURAI" or purification processes, which are believed to detoxify potentially harmful components in herbo-mineral/metallic preparations, thereby minimizing side effects and enhancing therapeutic efficacy. This traditional wisdom about processing is crucial for ensuring the safety and potency of these complex formulations. However, the review also highlights several limitations in the existing literature. The included clinical studies are predominantly case series, case reports, or pilot studies, with a lack of large-scale, randomized controlled trials. This limits the generalizability of the findings and the ability to draw definitive conclusions about efficacy and safety compared to modern treatments. Furthermore, detailed information on adverse events, precise standardization protocols for all formulations, and robust risk of bias assessments were often not explicitly reported in the summarized data. Comparing these Siddha treatments with modern pharmacological approaches, it appears that while modern medicine focuses on single molecular targets, Siddha formulations often offer a multi-component approach, potentially modulating several pathways simultaneously. This holistic action could contribute to their efficacy and perhaps a better side-effect profile, though more rigorous research is needed to substantiate these claims. The emphasis on safety and standardization cannot be overstated for herbo-mineral/metallic preparations. Given the metallic components, concerns about heavy metal toxicity are often raised. Therefore, robust standardization studies, including detailed chemical characterization, quality control, and long-term toxicity assessments, are imperative to ensure patient safety and build confidence in these traditional medicines. The identification of standardized drugs is a positive step, but this effort needs to be expanded and validated scientifically.

5. CONCLUSION

This systematic review provides evidence suggesting that various Siddha herbo-mineral/metallic formulations possess therapeutic potential for the management of Rheumatoid Arthritis (Uthiravatha Suronitham). Both traditional classical texts and preliminary modern scientific studies (clinical and preclinical) indicate their efficacy in reducing inflammatory markers, alleviating symptoms, and potentially modifying disease progression. The mechanistic insights from preclinical studies point towards anti-inflammatory and immunomodulatory actions. Despite these promising findings, there is a clear and urgent need for large-scale, well-designed, randomized controlled clinical trials to validate the safety, efficacy, and optimal dosage of these formulations. Further research should also focus on elucidating their precise mechanisms of action, conducting comprehensive standardization and quality control assessments, and performing long-term safety evaluations. Such rigorous validation will be crucial to integrate these valuable traditional Siddha therapies into contemporary evidence-based healthcare for chronic autoimmune diseases like Rheumatoid Arthritis.

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