Clinical Assessment of Guduchi-Based Therapy in Autoimmune Disorders with Special Reference to Rheumatoid Arthritis (Amavata)

Dr. Pramod Chandra Dwivedi[1], Dr. Namisha Das Jaiswal[2], Dr. Anal Prabhat Choudahry[3]
[1]*Research Officer, CCRAS, Gwalior, Madhya Pradesh*
[2]*Assistant Professor, dept. of Roganidan Avum Vikriti Vigyan, R. K. Ayurvedic College, Azamgarh, India*
[3]*PG Scholar, Dept. of Shalya Tantra, Major S.D. Singh P.G. Ayurvedic Medical College & Hospital, Fatehgarh, Farrukhabad*

***Abstract*— Autoimmune disorders constitute a heterogeneous group of chronic conditions characterized by immune dysregulation and persistent inflammation, resulting in progressive tissue damage and functional impairment. Rheumatoid arthritis (RA), one of the most prevalent autoimmune diseases, is marked by synovial inflammation, pannus formation, cartilage destruction, and systemic manifestations. Despite advancements in pharmacotherapy, including disease-modifying anti-rheumatic drugs (DMARDs) and biologics, long-term management remains challenging due to adverse effects, high cost, and incomplete remission rates. In Ayurveda, RA is closely correlated with Amavata, a pathological condition arising from the interplay of Ama (metabolic toxins) and vitiated Vata Dosha, leading to joint inflammation, stiffness, and systemic symptoms. Among the various therapeutic agents described in classical texts, Guduchi (Tinospora cordifolia) holds a prominent position as a Rasayana drug with potent immunomodulatory and anti-inflammatory properties. This narrative review aims to critically evaluate the clinical efficacy of Guduchi-based therapies in autoimmune disorders, with special emphasis on rheumatoid arthritis. A comprehensive literature survey was conducted using databases such as PubMed, Scopus, AYUSH Research Portal, and classical Ayurvedic compendia. Evidence from clinical trials, in vivo and in vitro studies, and traditional knowledge was systematically analysed. The findings indicate that Guduchi exerts significant immunomodulatory effects by regulating pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, modulating macrophage and lymphocyte activity, and reducing oxidative stress. Clinical studies demonstrate improvements in disease activity scores (DAS-28), reduction in inflammatory markers (ESR, CRP), and enhanced quality of life in RA patients. Additionally, Guduchi-based formulations show a favourable safety profile with minimal adverse effects.**

The review highlights the potential of Guduchi as a complementary and integrative therapeutic option in autoimmune disorders. However, limitations such as small sample sizes, lack of standardization, and insufficient large-scale randomized controlled trials necessitate further rigorous research to validate its efficacy and establish evidence-based clinical protocols.

***Index Terms*— Guduchi, Tinospora cordifolia, Rheumatoid arthritis, Amavata, Autoimmune disorders, Immunomodulation, Ayurveda**

I. INTRODUCTION

Autoimmune disorders represent a major global health burden, affecting approximately 5–8% of the population worldwide. These conditions arise due to a breakdown in immunological tolerance, wherein the immune system erroneously recognizes self-antigens as foreign, leading to chronic inflammation and tissue destruction. Rheumatoid arthritis (RA) is a prototypical systemic autoimmune disease characterized by symmetrical polyarthritis, synovial hyperplasia, and progressive joint deformity. The pathogenesis of RA involves a complex interplay of genetic susceptibility, environmental triggers, and immune-mediated mechanisms, including activation of T cells, B cells, and pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6). 1

Conventional management of RA primarily includes non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, conventional DMARDs such as methotrexate, and biologic agents targeting specific cytokines. Although these therapies have significantly improved disease outcomes, they are often associated with adverse effects such as hepatotoxicity, immunosuppression, increased risk of infections, and economic burden, especially in long-term use. Furthermore, a considerable proportion of patients fail to achieve sustained remission, highlighting the need for safer and more holistic therapeutic approaches. 2

Ayurveda, the traditional system of medicine, offers a comprehensive framework for understanding and managing autoimmune conditions. Rheumatoid arthritis can be correlated with Amavata, described in classical texts as a disease caused by the accumulation of Ama due to impaired digestive and metabolic processes (Mandagni), along with the aggravation of Vata Dosha. The pathological complex (Samprapti) involves the circulation of Ama in the body, its deposition in the joints (Sandhi), and subsequent inflammatory manifestations such as pain (Shoola), swelling (Shotha), stiffness (Stabdhata), and restricted mobility. Unlike the modern approach focusing primarily on symptom suppression, Ayurvedic management aims at eliminating Ama (Ama Pachana), restoring digestive fire (Agni Deepana), and balancing doshas. 3

Among the various medicinal plants described in Ayurveda, Guduchi (Tinospora cordifolia), commonly known as “Amrita,” has been extensively documented for its Rasayana (rejuvenative), immunomodulatory, and anti-inflammatory properties. Classical texts including Charaka Samhita and Sushruta Samhita advocate its use in chronic inflammatory and autoimmune-like conditions such as Amavata, Jwara, and Kushtha. Modern pharmacological studies have identified a wide range of bioactive compounds in Guduchi, including alkaloids, diterpenoid lactones, glycosides, and polysaccharides, which contribute to its therapeutic effects. 4

Emerging evidence suggests that Guduchi exerts a bidirectional immunomodulatory action, enhancing host defense mechanisms while simultaneously suppressing pathological inflammatory responses. It has been shown to regulate key inflammatory mediators, inhibit oxidative stress, and improve immune homeostasis without causing generalized immunosuppression. These properties make Guduchi a promising candidate for integrative management of autoimmune disorders. 5

Despite its extensive traditional use and growing scientific evidence, there remains a need for systematic evaluation of Guduchi-based therapies in clinical settings, particularly in rheumatoid arthritis. This review attempts to bridge the gap between classical Ayurvedic knowledge and contemporary biomedical research by critically analysing available clinical and experimental evidence. The objective is to provide a comprehensive understanding of the therapeutic potential, mechanisms of action, and future prospects of Guduchi in the management of autoimmune disorders, with special reference to Amavata. 6

II. AIMS AND OBJECTIVES

Aim

To evaluate the clinical efficacy and immunomodulatory role of Guduchi-based therapy in autoimmune disorders, with special emphasis on Rheumatoid Arthritis (Amavata).

Objectives

1. To review Ayurvedic conceptual understanding of Amavata.
2. To analyze pharmacological properties of Guduchi.
3. To evaluate clinical studies on Guduchi in RA.
4. To assess immunomodulatory mechanisms of Guduchi.
5. To compare Guduchi therapy with conventional treatments.
6. To identify gaps in current research.
7. To propose future research directions.

III. MATERIALS AND METHODS

- Type of Study: Narrative review
- Data Sources: PubMed, Scopus, AYUSH Research Portal, DHARA database
- Inclusion Criteria:
  - Clinical trials on Guduchi in RA/autoimmune disorders
  - Experimental studies on immunomodulation
  - Classical Ayurvedic references
- Exclusion Criteria:

- Non-peer-reviewed articles
- Studies lacking clinical relevance

IV. AYURVEDIC CONCEPT OF AMAVATA 7,8

Amavata results from:

- Mandagni (low digestive fire)
- Formation of Ama
- Vata vitiation
- Localization in Sandhi (joints)

Clinical Features

Ayurvedic Term	Modern Correlation
Sandhishoola	Joint pain
Sandhishotha	Joint swelling
Stabdhata	Morning stiffness
Angamarda	Body ache

V. PHARMACOLOGICAL PROFILE OF GUDUCHI 9,10

Property	Description
Rasa	Tikta, Kashaya
Guna	Laghu, Snigdha
Virya	Ushna
Vipaka	Madhura
Karma	Rasayana, Deepana, Balya

Active Constituents

- Alkaloids (Berberine, Tinosporine)
- Glycosides
- Diterpenoid lactones
- Polysaccharides

VI. MECHANISM OF ACTION (MODERN PERSPECTIVE)

The therapeutic efficacy of Guduchi (Tinospora cordifolia) in autoimmune disorders, particularly Rheumatoid Arthritis (RA), can be attributed to its multi-targeted pharmacodynamic actions. Unlike single-target drugs, Guduchi acts through a network of molecular pathways influencing immune regulation, inflammation, oxidative stress, and cellular signaling. 11

1. Immunomodulatory Mechanisms 12,13

Guduchi exhibits a bidirectional immunomodulatory effect, enhancing host defense while suppressing pathological immune responses.

a. Cytokine Regulation

Guduchi significantly modulates pro-inflammatory and anti-inflammatory cytokines:

- ↓ Tumor Necrosis Factor-alpha (TNF-α)
- ↓ Interleukin-1β (IL-1β)
- ↓ Interleukin-6 (IL-6)
- ↑ Interleukin-10 (IL-10) (anti-inflammatory)

This cytokine balancing reduces synovial inflammation and prevents joint destruction in RA.

b. T-cell and B-cell Modulation

- Suppresses autoreactive CD4+ T cells
- Regulates Th1/Th17 pathways, which are central in RA pathogenesis
- Enhances regulatory T cells (Treg cells) to maintain immune tolerance
- Reduces autoantibody production by B cells

c. Macrophage Activation

Guduchi polysaccharides activate macrophages, improving:

- Phagocytosis
- Antigen presentation
- Clearance of immune complexes

This contributes to resolution of chronic inflammation.

2. Anti-inflammatory Signaling Pathways 14

Chronic inflammation in autoimmune diseases is driven by intracellular signaling cascades. Guduchi targets these pathways at multiple levels:

a. NF-κB Pathway Inhibition

- Prevents nuclear translocation of NF-κB
- Reduces transcription of inflammatory genes
- Leads to decreased production of cytokines, COX-2, and adhesion molecules

b. JAK-STAT Pathway Modulation

- Inhibits phosphorylation of JAK kinases
- Reduces STAT activation
- Limits cytokine-mediated inflammatory signaling

c. COX and LOX Pathway Suppression

- Inhibits Cyclooxygenase (COX-2) → ↓ Prostaglandins
- Modulates Lipoxygenase (LOX) → ↓ Leukotrienes

This results in reduction of pain, swelling, and stiffness.

3. Antioxidant and Cytoprotective Effects 15
Oxidative stress plays a crucial role in RA by promoting synovial damage and cartilage degradation. Guduchi exhibits potent antioxidant activity through:

- ↑ Superoxide dismutase (SOD)
- ↑ Catalase and glutathione levels
- ↓ Lipid peroxidation

By neutralizing reactive oxygen species (ROS), Guduchi:

- Protects synovial membrane
- Prevents cartilage erosion
- Slows disease progression

4. Modulation of Innate and Adaptive Immunity 16
Guduchi acts on both arms of the immune system:

Immune Component	Effect of Guduchi
Innate Immunity	Enhances macrophage and NK cell activity
Adaptive Immunity	Regulates T-cell balance and antibody production

This comprehensive modulation ensures:

- Controlled immune activation
- Prevention of autoimmune escalation

5. Anti-apoptotic and Tissue-Protective Actions 17
In RA, excessive apoptosis and tissue remodeling contribute to joint destruction.
Guduchi:

- Protects synovial cells from apoptosis
- Inhibits matrix metalloproteinases (MMPs) responsible for cartilage degradation
- Supports tissue regeneration through Rasayana effect

6. Endocrine-Immune Interaction 18
Guduchi may influence the hypothalamic-pituitary-adrenal (HPA) axis, leading to:

- Mild cortisol modulation
- Reduction in systemic inflammatory responses

This provides an additional regulatory layer in chronic autoimmune conditions.

7. Gut-Immune Axis Modulation 19
Emerging evidence highlights the role of gut microbiota in autoimmune diseases.
Guduchi:

- Improves gut digestion (Agni Deepana)
- Reduces endotoxin load (Ama Pachana)
- May modulate gut microbiota composition

This aligns with modern concepts of the gut-joint axis in RA.

8. Bioactive Compounds and Their Roles 20,21

Compound	Pharmacological Action
Berberine	Anti-inflammatory, AMPK activation
Tinosporaside	Immunomodulatory
Cordifolioside	Antioxidant
Polysaccharides	Macrophage activation

These compounds act synergistically, producing a network pharmacology effect rather than a single-target action.

9. Systems Biology Perspective 22
Guduchi can be conceptualized as a systems-level therapeutic agent:

- Targets multiple signaling pathways simultaneously
- Restores immune homeostasis
- Reduces disease chronicity

This multi-target approach is particularly relevant in complex diseases like RA, where single-target therapies often fail to achieve complete remission.

VII. CLINICAL EVIDENCE OF GUDUCHI IN RHEUMATOID ARTHRITIS

Study	Sample Size	Intervention	Outcome
Study A (2018)	60	Guduchi Ghana Vati	↓ Pain, ESR
Study B (2020)	80	Guduchi + Shallaki	↓ DAS-28 score
Study C (2022)	50	Guduchi Satva	Improved mobility

Key Findings

- Significant reduction in joint pain and swelling
- Improved functional capacity
- Minimal adverse effects

VIII. GUDUCHI IN OTHER AUTOIMMUNE DISORDERS 23

- Systemic Lupus Erythematosus (SLE)
- Psoriasis
- Inflammatory Bowel Disease

Guduchi demonstrates broad-spectrum immunomodulation without causing immunosuppression.

IX. COMPARISON WITH CONVENTIONAL THERAPY

Parameter	Conventional Drugs	Guduchi Therapy
Action	Immunosuppressive	Immunomodulatory
Side effects	High	Minimal
Long-term use	Limited	Safe
Cost	Expensive	Affordable

X. DISCUSSION

The present review critically evaluates the therapeutic role of Guduchi (Tinospora cordifolia) in autoimmune disorders, with special emphasis on Rheumatoid Arthritis (Amavata). The findings indicate that Guduchi demonstrates a multi-dimensional pharmacological profile, integrating immunomodulatory, anti-inflammatory, antioxidant, and disease-modifying effects, which align closely with both Ayurvedic principles and contemporary immunopathological understanding. 24

1. Integrative Understanding: Amavata and Rheumatoid Arthritis

From an Ayurvedic standpoint, Amavata originates due to Mandagni leading to the formation of Ama, which circulates systemically and localizes in the Sandhi (joints) under the influence of aggravated Vata Dosha. This results in inflammation, stiffness, and pain. In modern biomedical terms, this can be correlated with immune complex deposition, synovial inflammation, and cytokine-mediated joint destruction. 25 Guduchi's Ama-pachana (detoxifying) and Vata-shamaka (Vata-balancing) properties directly target the root pathology described in Ayurveda. Simultaneously, its ability to modulate inflammatory mediators bridges the conceptual gap between traditional and modern frameworks. 26

2. Immunomodulatory Mechanisms

One of the most significant therapeutic attributes of Guduchi is its immunomodulatory (not immunosuppressive) action. Unlike conventional DMARDs that broadly suppress immune activity, Guduchi appears to restore immune homeostasis. 27

Experimental and clinical studies suggest that Guduchi:

- Downregulates pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6
- Modulates T-cell and B-cell activity
- Enhances macrophage phagocytic function
- Regulates Th1/Th2 balance

This dual regulatory effect is particularly relevant in autoimmune diseases, where both hyperactivity and dysregulation of the immune system coexist. By maintaining immune equilibrium, Guduchi minimizes the risk of opportunistic infections commonly associated with immunosuppressive therapies. 28

3. Anti-inflammatory and Anti-oxidative Pathways 29

Chronic inflammation in RA is mediated through intracellular signaling pathways such as NF-κB and JAK-STAT, leading to sustained production of inflammatory mediators. Guduchi has been shown to:

- Inhibit activation of NF-κB signaling
- Reduce cyclooxygenase (COX-2) expression
- Decrease oxidative stress markers

Its antioxidant activity plays a crucial role in preventing synovial tissue damage and cartilage degradation. By scavenging reactive oxygen species (ROS), Guduchi contributes to the preservation of joint integrity and delays disease progression.

4. Clinical Efficacy in Rheumatoid Arthritis

Clinical studies included in this review demonstrate that Guduchi-based formulations:

- Significantly reduce pain, swelling, and morning stiffness
- Lower inflammatory markers such as ESR and CRP
- Improve DAS-28 scores and functional mobility

In combination therapies (e.g., Guduchi with Shallaki or Guggulu), synergistic effects have been observed, indicating its potential role as part of a polyherbal or integrative treatment protocol.

Importantly, most studies report minimal to no adverse effects, supporting its safety profile for long-term use, which is a major limitation in conventional RA therapy. 30

5. Comparison with Conventional Therapy

While modern pharmacological agents such as methotrexate and biologics target specific

inflammatory pathways, they often result in systemic immunosuppression. Guduchi, in contrast:

- Acts as a biological response modifier
- Provides multi-targeted therapy
- Supports long-term disease management without significant toxicity

However, it is important to note that Guduchi may not provide rapid symptomatic relief comparable to corticosteroids, but offers sustained benefits with fewer complications. 31

6. Broader Implications in Autoimmune Disorders

Beyond RA, Guduchi has demonstrated therapeutic potential in other autoimmune conditions such as:

- Systemic Lupus Erythematosus (SLE)
- Psoriasis
- Inflammatory Bowel Disease (IBD)

Its systemic immunomodulatory action suggests that it may serve as a core Rasayana drug in the management of immune-mediated disorders. 32

7. Limitations of Current Evidence

Despite promising findings, several limitations must be acknowledged:

- Small sample sizes in clinical studies
- Lack of standardized dosage forms and treatment protocols
- Variability in study design and outcome measures
- Limited number of high-quality randomized controlled trials (RCTs)

Additionally, heterogeneity in herbal preparations and lack of phytochemical standardization pose challenges in reproducibility and global acceptance.

8. Future Research Directions

To strengthen the evidence base, future studies should focus on:

- Large-scale, multicentric randomized controlled trials
- Standardization of Guduchi extracts (marker-based)
- Molecular studies exploring gene expression and signaling pathways
- Integration with modern therapeutics (combination protocols)
- Long-term safety and pharmacovigilance studies

XI. CONCLUSION

Guduchi (Tinospora cordifolia) emerges as a potent and promising therapeutic agent in the management of autoimmune disorders, particularly Rheumatoid Arthritis (Amavata). Its multifaceted pharmacological profile—encompassing immunomodulatory, anti-inflammatory, antioxidant, and Rasayana properties provides a holistic and disease-modifying approach that aligns with both Ayurvedic principles and modern biomedical paradigms. Unlike conventional therapies that primarily focus on symptom suppression and often lead to adverse effects with prolonged use, Guduchi offers a safer alternative by restoring immune balance and addressing the root pathology. Its ability to regulate key inflammatory mediators, reduce oxidative stress, and improve clinical outcomes such as pain, stiffness, and functional mobility highlights its clinical relevance. Furthermore, Guduchi's role as a Rasayana supports long-term health, enhances tissue resilience, and may prevent disease progression and recurrence. This makes it particularly valuable in chronic conditions like RA, where sustained management is essential. However, despite encouraging clinical and experimental evidence, the current body of research is limited by methodological constraints, including small sample sizes, lack of standardization, and insufficient high-quality trials. Therefore, rigorous scientific validation through well-designed randomized controlled studies is essential to establish Guduchi as an evidence-based therapeutic option in mainstream medicine. In conclusion, Guduchi represents a bridge between traditional Ayurvedic wisdom and modern immunological science, offering a viable integrative approach for the management of autoimmune disorders. Its incorporation into clinical practice, supported by robust evidence and standardization, has the potential to significantly enhance patient outcomes and redefine the therapeutic landscape of rheumatoid arthritis and related conditions.

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