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A COMPARATIVE CLINICAL STUDY BETWEEN POLYHERBAL COMBINATION (GUDUCHI, GUGGULU, MANJISTHA) AND XANTHINE OXIDASE INHIBITOR IN THE MANAGEMENT OF VATARAKTA W.S.R TO HYPERURICEMIA

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ABSTRACT

Background: Vatarakta is a disease described in Ayurvedic literature involving the pathological interaction of Vata Dosha and Rakta Dhatu. Its manifestations, including joint pain, swelling, redness, tenderness, burning sensation, and stiffness, show clinical similarities to gout. Hyperuricemia is an important biochemical factor in the pathogenesis of gout. A polyherbal combination of Guduchi, Guggulu, and Manjistha has been described in Ayurvedic therapeutic practice for disorders associated with Vatarakta. **Aim:** To evaluate and compare the therapeutic effects of Guduchi–Guggulu–Manjistha Vati and febuxostat in patients with Vatarakta with special reference to hyperuricemia. **Materials and Methods:** The comparative clinical study was conducted at Ayurvedic teaching hospitals in Kolkata. Seventy-two patients were registered, of whom 60 completed the trial. Patients were allocated to two groups of 30 each. Group A received Guduchi–Guggulu–Manjistha Vati, 500 mg twice daily after meals with lukewarm water. Group B received febuxostat 40 mg. Both groups underwent treatment for 45 days with follow-up at 15-day intervals. Seven subjective parameters and serum uric acid concentrations were evaluated. Paired statistical comparisons and nonparametric analyses were reported. **Results:** Both groups demonstrated statistically significant improvement in several subjective parameters. Group A showed 32.47% relief in Ruka, 36.17% in Sopha, 41.20% in Raga, and 38.86% in Daha. Group B showed 33.33% relief in Toda and 29.16% in Stabdhata. Mean serum uric acid decreased from 7.227 to 7.133 mg/dL in Group A (1.30%; $p=0.161$) and from 7.177 to 6.620 mg/dL in Group B (7.82%; $p<0.001$). The thesis reported a significant between-group difference in serum uric acid change ($p=0.001$). Overall, 49 patients (81.67%) showed mild improvement, one (1.67%) showed moderate improvement, and 10 (16.67%) showed insignificant improvement. **Conclusion:** Guduchi–Guggulu–Manjistha Vati was associated with improvement in several subjective manifestations of Vatarakta but did not demonstrate a statistically significant reduction in serum uric acid. Febuxostat produced a greater biochemical urate-lowering effect. Larger controlled trials are needed to confirm the clinical effects and safety of the polyherbal formulation.

KEYWORDS: Vatarakta; Guduchi; Guggulu; Manjistha; febuxostat; hyperuricemia; gout; Ayurveda; polyherbal formulation.

INTRODUCTION

Vatarakta is a disease entity described in Ayurveda that involves the simultaneous vitiation of Vata Dosha and Rakta Dhatu. The pathological interaction between these factors produces symptoms such as pain, swelling, stiffness, discoloration, burning sensation, and tenderness, predominantly affecting joints and surrounding tissues. In the Ayurvedic understanding of the disease, aggravated Vata becomes obstructed by vitiated Rakta, resulting in impaired physiological movement and progressive clinical manifestations.

The symptoms of Vatarakta have certain similarities to gout, although these conditions are not necessarily equivalent. Gout is an inflammatory arthritis resulting from the deposition of monosodium urate crystals in joints and periarticular tissues. It commonly presents with episodes of severe pain, swelling, erythema, and restricted movement. Chronic or inadequately managed disease can result in recurrent attacks, tophus formation, and joint damage.[1]

Hyperuricemia is the principal biochemical abnormality associated with urate crystal formation. Serum uric acid is the final product of purine metabolism in humans. Increased production or reduced renal excretion can lead to persistent elevation of serum urate, increasing the likelihood of monosodium urate crystal deposition. Several genetic, metabolic, dietary, and renal factors influence urate concentrations.[2]

Epidemiological investigations have demonstrated that gout is an important and increasingly recognized inflammatory joint disorder. Established risk factors include hyperuricemia, obesity, hypertension, renal dysfunction, dietary influences, and exposure to certain medications.[3] International epidemiological reviews have also identified considerable geographic variation in gout prevalence and incidence, with increases observed in several populations.[4] Gout frequently coexists with cardiovascular and metabolic disorders, further complicating its clinical management.[5]

The diagnosis and classification of gout require careful assessment. The American College of Rheumatology/European League Against Rheumatism classification criteria incorporate clinical features, serum urate concentrations, synovial fluid findings, and imaging characteristics. Identification of monosodium urate crystals provides particularly strong diagnostic evidence.[6]

Conventional management includes treatment of inflammatory episodes and long-term urate-lowering therapy in appropriately selected patients. The American College of Rheumatology recommends a treat-to-target strategy for patients receiving urate-lowering therapy, generally aiming for serum urate below 6 mg/dL.[7] European recommendations similarly emphasize sustained urate control, management of comorbidities, and individualized therapeutic decisions.[8]

Ayurveda approaches Vatarakta through a different conceptual framework. Classical treatment principles emphasize Vata Shamana, Rakta-related therapeutic measures, appropriate dietary regulation, and correction of factors contributing to the pathological process.

Guduchi (Tinospora cordifolia) is traditionally regarded as a Rasayana Dravya. Reviews of its pharmacological activities have described experimental findings involving immune responses, oxidative processes, and inflammatory pathways.[9] Nevertheless, these findings cannot independently establish clinical urate-lowering efficacy.

Guggulu, obtained from the oleo-gum resin of Commiphora wightii, is widely used in Ayurvedic formulations for musculoskeletal disorders. Its phytochemical constituents include terpenoids, steroids, lignans, and other compounds. The traditional use of Guggulu in conditions associated with inflammation and joint discomfort has been discussed in pharmacological reviews.[10]

Manjistha (Rubia cordifolia) is traditionally associated with Rakta-related disorders. Modern phytochemical investigations have identified quinones, flavonoids, peptides, and other constituents. Experimental studies have reported antioxidant and anti-inflammatory activities, although high-quality clinical evidence remains limited.[11]

Febuxostat is a selective xanthine oxidase inhibitor used in urate-lowering therapy. Clinical trials have demonstrated its capacity to reduce serum urate in patients with gout and hyperuricemia.[12] Additional randomized studies have investigated its efficacy and tolerability compared with allopurinol and placebo.[13] The CONFIRMS trial further evaluated febuxostat in patients with gout and different levels of renal function.[14]

The long-term clinical use of febuxostat requires attention to cardiovascular safety. The CARES trial identified mortality concerns in patients with gout and established cardiovascular disease[15], whereas the FAST trial reported different comparative cardiovascular safety findings in its enrolled population.[16] These studies demonstrate the importance of considering the characteristics of individual patients when selecting urate-lowering therapy.

Gout management is also complicated by common comorbidities, including chronic kidney disease, cardiovascular disease, hypertension, and metabolic disorders.[17] Pharmacological treatment therefore needs to be integrated with appropriate monitoring and management of associated conditions.

Reviews of gout management have emphasized the importance of combining effective urate reduction with prevention of inflammatory attacks and long-term patient education.[18]

Although herbal preparations are frequently perceived as well tolerated, safety must be established through appropriate clinical monitoring. Published reports of liver injury temporally associated with Tinospora cordifolia use highlight the need for pharmacovigilance, quality control, and cautious interpretation of herbal safety claims.[19]

The present study was undertaken to evaluate the clinical and biochemical effects of Guduchi–Guggulu–Manjistha Vati compared with febuxostat in patients diagnosed with Vatarakta associated with hyperuricemia.

AIM AND OBJECTIVES

The primary aim was to evaluate and compare the therapeutic efficacy of orally administered Guduchi–Guggulu–Manjistha Vati and febuxostat in the management of Vatarakta with special reference to hyperuricemia.

The objectives were to assess changes in seven subjective manifestations of Vatarakta, evaluate serum uric acid before and after treatment, determine the statistical significance of the observed changes, and compare overall treatment responses between the two groups.

MATERIALS AND METHODS

STUDY DESIGN AND SETTING

This comparative clinical study was conducted in the Department of Kayachikitsa at the Institute of Postgraduate Ayurvedic Education and Research at Shyamadas Vaidya Shastra Pith and J.B. Roy State Ayurvedic Medical College and Hospital, Kolkata, West Bengal.

A total of 72 patients with Vatarakta associated with hyperuricemia were registered. Twelve patients did not complete the follow-up schedule, and 60 completed the clinical study.

The thesis describes random allocation into two groups of 30 patients each. However, the method of sequence generation, allocation concealment, and blinding was not sufficiently established in the reviewed material. Complete reporting of these procedures is important when preparing a randomized trial manuscript, as emphasized in the CONSORT reporting framework.[20]

ETHICAL APPROVAL

The thesis includes an Institutional Ethics Committee approval certificate from the Institute of Postgraduate Ayurvedic Education and Research at Shyamadas Vaidya Shastra Pith, Kolkata.

Ethics approval number: SVP/IEC/845/2024 Approval date: 29 May 2024

The thesis also refers to clinical trial registration documentation in its annexures. The exact registration identifier should be verified against the original certificate before journal submission.

SELECTION OF PATIENTS

Patients presenting with clinical manifestations consistent with Vatarakta and associated biochemical hyperuricemia were evaluated for participation.

Clinical assessment included Ruka (pain), Toda (pricking pain), Sparsha Asahatva (tenderness), Sopha (swelling), Raga (redness), Daha (burning sensation), and Stabdhata (stiffness).

The complete inclusion criteria, exclusion criteria, age thresholds, and biochemical eligibility limits should be reproduced from the thesis protocol in the final submission version.

INTERVENTION

The 60 completing patients were divided into two groups.

Group A — Polyherbal intervention: Thirty patients received Guduchi–Guggulu–Manjistha Vati at a dose of 500 mg orally twice daily after meals with lukewarm water for 45 days.

Group B — Xanthine oxidase inhibitor: Thirty patients received febuxostat 40 mg for 45 days.

The thesis therapeutic-profile section specifies twice-daily administration of febuxostat 40 mg, while other descriptions state the strength without consistently repeating the frequency. This discrepancy must be reconciled with the approved protocol and original patient records. It should not be treated as a recommended febuxostat dosing regimen.

Lifestyle modification was described as accompanying both interventions.

FOLLOW-UP

The treatment duration was 45 days, with follow-up assessments at 15-day intervals.

ASSESSMENT CRITERIA

Seven subjective parameters were evaluated using the study's clinical scoring system: Ruka, Toda, Sparsha Asahatva, Sopha, Raga, Daha, and Stabdhata.

The principal objective parameter was serum uric acid concentration, measured before and after treatment.

The thesis also describes hematological investigations, including hemoglobin, complete blood count, and erythrocyte sedimentation rate.

STATISTICAL ANALYSIS

The thesis describes descriptive statistical analysis, paired t-tests, Wilcoxon signed-rank tests for within-group subjective changes, and Mann–Whitney U tests for between-group comparisons of symptom improvement.

A p-value below 0.05 was considered statistically significant, and a p-value below 0.001 was considered highly significant.

The following results reproduce the values reported in the thesis. Where different statistical sections appear to use different tests, the reported p-values are identified without independently recalculating the underlying data.

RESULTS

PARTICIPANT DISTRIBUTION

of the 72 registered patients, 60 completed the trial, yielding a completion rate of 83.33%. The remaining 12 patients (16.67%) did not complete follow-up.

Table 1: Participant disposition.

Study status	Number	Percentage
Registered	72	100%
Completed	60	83.33%
Did not complete	12	16.67%
Group A completers	30	50% of completers
Group B completers	30	50% of completers

Clinical symptom improvement

Both groups showed improvement in the seven subjective parameters evaluated.

Table 2: Percentage improvement in subjective parameters.

Parameter	Group A	Group B
Ruka (pain)	32.47%	29.16%
Toda (pricking pain)	12.03%	33.33%
Sparsha Asahatva (tenderness)	14.38%	11.02%
Sopha (swelling)	36.17%	35.24%
Raga (redness)	41.20%	36.32%
Daha (burning sensation)	38.86%	35.39%
Stabdhata (stiffness)	27.71%	29.16%

CHANGES IN CLINICAL SCORES

Table 3: Mean subjective scores before and after treatment.

Parameter	Group A BT → AT	Group B BT → AT
Ruka	2.67 → 1.80	2.40 → 1.70
Toda	1.33 → 1.17	2.40 → 1.60
Sparsha Asahatva	1.60 → 1.37	1.27 → 1.13
Sopha	2.93 → 1.87	2.27 → 1.47
Raga	2.50 → 1.47	2.67 → 1.70
Daha	2.83 → 1.73	2.43 → 1.57
Stabdhata	2.67 → 1.93	2.40 → 1.70

In Group A, statistically significant improvement was reported for Toda ($p=0.023$) and Sparsha Asahatva ($p=0.006$), while Ruka, Sopha, Raga, Daha, and Stabdhata showed highly significant improvement ($p<0.001$).

In Group B, Sparsha Asahatva improved significantly ($p=0.043$), whereas Ruka, Toda, Sopha, Raga, Daha, and Stabdhata showed highly significant improvement ($p<0.001$).

BETWEEN-GROUP COMPARISON

The thesis discussion reports no statistically significant between-group differences for Ruka ($p=0.610$), Sparsha Asahatva ($p=0.114$), Raga ($p=0.180$), Daha ($p=0.290$), or Stabdhata ($p=0.270$).

It also reports differences for Toda ($p=0.005$), favoring Group B, and Sopha ($p=0.017$), favoring Group A. However, another section of the thesis states that the nonparametric comparison found a significant difference only for Toda. The statistical outputs should therefore be reconciled before publication, especially for Sopha.

SERUM URIC ACID

Table 4: Changes in serum uric acid concentration.

Parameter	Group A	Group B
Before treatment (mg/dL)	7.227	7.177
After treatment (mg/dL)	7.133	6.620
Absolute reduction (mg/dL)	0.094	0.557
Percentage reduction	1.30%	7.82%
Within-group p-value	0.161	<0.001

Group A demonstrated a small, statistically nonsignificant reduction in mean serum uric acid. Group B demonstrated a larger, statistically significant reduction.

The thesis also reports a statistically significant between-group difference in the objective parameter (p=0.001), favoring Group B.

Overall treatment response

Table 5: Overall response by group.

Response category	Group A	Group B	Total
Moderate improvement	1	0	1
Mild improvement	24	25	49
Insignificant improvement	5	5	10
Marked improvement	0	0	0
Complete remission	0	0	0
Total	30	30	60

Overall, 81.67% of patients showed mild improvement, 1.67% showed moderate improvement, and 16.67% showed insignificant improvement. No patient achieved marked improvement or complete remission.

DISCUSSION

The present comparative clinical study evaluated the therapeutic effects of Guduchi–Guggulu–Manjistha Vati and febuxostat in patients diagnosed with Vatarakta with special reference to hyperuricemia. The findings demonstrated that both treatment groups experienced improvement in several subjective clinical manifestations, whereas the biochemical response was more pronounced in the febuxostat group. Vatarakta is traditionally understood as a disease arising from the pathological interaction of aggravated Vata Dosha and vitiated Rakta Dhatu. The associated disturbances may manifest as pain, swelling, redness, tenderness, burning sensation, and stiffness. The selection of Guduchi, Guggulu, and Manjistha in the present study was based on the Ayurvedic therapeutic rationale of addressing these manifestations through a combined herbal formulation.

The study demonstrated a 32.47% reduction in Ruka in Group A compared with 29.16% in Group B. Although the numerical improvement was greater in Group A, the reported between-group comparison was not statistically significant (p=0.610). Therefore, the observed difference should not be interpreted as evidence of superior analgesic efficacy. Toda showed a different response pattern. Group A demonstrated 12.03% improvement, whereas Group B demonstrated 33.33% improvement. The reported between-group difference was statistically significant (p=0.005), suggesting a greater reduction in pricking pain in the febuxostat group during the observation period.

Sparsha Asahatva improved by 14.38% in Group A and 11.02% in Group B. The improvement was statistically significant within both groups, but the between-group difference was not significant. These findings suggest that tenderness decreased during treatment without establishing a clear comparative advantage for either intervention. Sopha decreased by 36.17% in Group A and 35.24% in Group B. The thesis reports significant within-group improvement in both groups. Although the discussion section identifies a between-group p-value of 0.017, another statistical summary does not identify Sopha as significantly different between groups. This discrepancy requires examination of the original statistical tables before a definitive conclusion is made.

Raga demonstrated the greatest percentage improvement among the subjective parameters in Group A, with a reduction of 41.20%, compared with 36.32% in Group B. However, the reported between-group difference was not statistically significant (p=0.180).

Daha decreased by 38.86% in Group A and 35.39% in Group B. Both interventions were associated with improvement, but no significant between-group difference was reported (p=0.290).

Stabdhata improved by 27.71% in Group A and 29.16% in Group B. The between-group comparison was not statistically significant (p=0.270), suggesting that the observed numerical difference may not reflect a reliable treatment effect.

From a pharmacological perspective, the traditional use of Guduchi, Guggulu, and Manjistha provides a rationale for evaluating their possible effects on inflammatory symptoms. Experimental literature describes biological activities of Guduchi relevant to inflammatory and oxidative pathways.[9] Guggulu contains several bioactive constituents and has a history of traditional use in musculoskeletal disorders.[10] Manjistha has also been investigated for anti-inflammatory and antioxidant properties, although most of the available evidence is preclinical. The clinical improvement observed in Group A may be consistent with the traditional therapeutic rationale for the formulation. However, the present study does not establish the biological mechanism responsible for the changes, nor does it determine the contribution of individual ingredients. The combined intervention, associated lifestyle measures, natural symptom fluctuation, and other clinical factors may all influence the observed outcomes.

The objective biochemical findings were more clearly differentiated. Group A demonstrated a reduction in mean serum uric acid from 7.227 to 7.133 mg/dL, representing 1.30% improvement. This reduction was not statistically significant ($p=0.161$). Therefore, the study does not provide convincing evidence of a urate-lowering effect from Guduchi–Guggulu–Manjistha Vati over 45 days. In contrast, Group B demonstrated a reduction from 7.177 to 6.620 mg/dL, corresponding to 7.82% improvement. The change was statistically significant ($p<0.001$), and the thesis reported a significant between-group difference in serum uric acid reduction ($p=0.001$). These findings are consistent with the known mechanism of febuxostat, which inhibits xanthine oxidase and thereby reduces uric acid production. Previous clinical trials have demonstrated the urate-lowering activity of febuxostat in patients with gout.

However, the post-treatment mean serum uric acid concentration remained above 6 mg/dL in both groups. Current recommendations commonly use a serum urate target below 6 mg/dL for patients receiving urate-lowering treatment. Consequently, although febuxostat produced a statistically significant biochemical response, the group mean did not reach this commonly recommended treatment target. It is also important to distinguish symptomatic improvement from biochemical urate reduction. A treatment may reduce pain, tenderness, or swelling without substantially lowering serum uric acid. Conversely, sustained urate reduction may require longer treatment and may not correspond to immediate symptom resolution. The overall treatment assessment showed that most participants experienced only mild improvement. Among the 60 completing patients, 49 were classified as having mild improvement, one as having moderate improvement, and 10 as having insignificant improvement. No participant achieved marked improvement or complete remission.

This response distribution suggests that neither intervention produced substantial overall clinical remission during the 45-day observation period. It also emphasizes the need to evaluate the clinical importance of the observed symptom-score reductions rather than relying solely on statistical significance.

The study duration represents an important limitation. Gout and recurrent hyperuricemia may require prolonged treatment, monitoring, and adjustment of urate-lowering therapy. Long-term studies are necessary to assess sustained biochemical control, recurrence of inflammatory episodes, functional outcomes, and treatment adherence. Safety also deserves careful consideration. The thesis reports that no adverse drug reactions or significant side effects were observed during the study period. This finding is encouraging but does not establish long-term safety, particularly given the relatively small sample size and short observation period.

Febuxostat safety should be considered in the context of the CARES and FAST trials, which studied different patient populations and reported differing cardiovascular safety findings. Similarly, published reports of liver injury associated with Tinospora cordifolia use demonstrate that herbal preparations require appropriate quality assurance and safety monitoring. The present study contributes preliminary clinical observations regarding a polyherbal Ayurvedic formulation in patients with Vatarakta associated with hyperuricemia. Its results suggest improvement in several subjective symptoms with Guduchi–Guggulu–Manjistha Vati, but they do not establish equivalence to febuxostat or an effective biochemical urate-lowering action. Further investigations should use standardized formulations, clearly documented randomization, appropriate control conditions, validated symptom scores, adequate sample sizes, prespecified statistical analyses, and longer follow-up. Transparent reporting in accordance with established clinical trial standards would improve the interpretability and reproducibility of future studies.

LIMITATIONS

The study included only 60 completing participants, with 30 in each group, and the treatment period was limited to 45 days. Twelve of the 72 registered participants did not complete the follow-up schedule.

The randomization procedure and allocation concealment were not sufficiently documented in the reviewed material. The thesis also contains inconsistencies concerning the febuxostat administration frequency and the statistical interpretation of certain between-group symptom comparisons.

The study did not establish long-term urate control, prevention of recurrent gout attacks, or sustained improvement after treatment discontinuation. Although no significant adverse reactions were reported, the

sample size and follow-up duration were insufficient to establish long-term comparative safety.

These limitations should be considered when interpreting the findings.

CONCLUSION

The present comparative clinical study demonstrated improvement in several subjective manifestations of Vatarakta following treatment with Guduchi–Guggulu–Manjistha Vati and febuxostat. Group A showed numerical improvements in pain, tenderness, swelling, redness, burning sensation, and stiffness. However, the reduction in serum uric acid was small and statistically nonsignificant. Group B demonstrated statistically significant improvement in several clinical manifestations and a greater reduction in serum uric acid, from 7.177 to 6.620 mg/dL. The findings indicate that Guduchi–Guggulu–Manjistha Vati warrants further investigation for the symptomatic management of Vatarakta, whereas febuxostat demonstrated a clearer urate-lowering effect during the 45-day study period. Larger, well-designed controlled trials are necessary to establish the clinical efficacy, safety, and long-term therapeutic role of the polyherbal formulation.

DECLARATIONS

Ethical approval: The study was conducted according to the institutional ethical requirements described in the thesis.

Clinical trial registration: CTRI/2024/08/072046.

Informed consent: Written informed consent was obtained from participants according to the study documents.

Funding: No external funding was reported in the thesis.

Conflict of interest: No conflict of interest was reported in the thesis.

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