SAFETY AND EFFICACY OF GUGGULU FORMULATIONS IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS - A SYSTEMIC REVIEW

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ABSTRACT

Background: Rheumatoid arthritis (RA) is widely prevalent throughout the world. The lifetime risk of developing RA is 3.6% for women and 1.7% for men. Material and Method: Subjected related published research article from journals were searched through online search engines google Scholar, Pubmed, AYUSH Research Portal Online, Ayu Journals. The data of Articles were analyzed to confirm their Safety and efficacy in management of RA. Total 138 review articles are found in the management of RA. Among these articles Shamana Yoga 62, Shamana and Shodhana chikitsa yoga 35 and Shodhana yoga 34 and Yogika chikitsa, Satvavajaya chikitsa were also given. Results and Discussion: Total 5 Clinical Studies on management of RA with Guggulu Formulation are selected for the study. 4 studies were Randomized Controlled Trials (RCTs), 1 open Random trial. Among 4 RCTs, 2 RCTs studies were suggested Shodhana and Shamana Chikitsa both were given, and the obtained results was showing more effectiveness than only Shamana Chikitsa. Maximum Guggulu preparations were given in management of RA. Conclusion: It is revealed that all therapies were found to be significantly effective. This systemic review investigates the evidence regarding safety and efficacy of Guggulu formulation in RA. No ADR was noticed.

Keywords: Amavata, Rheumatoid Arthritis (RA), Guggulu formulations

INTRODUCTION

Rheumatoid Arthritis (RA) is a joint disorder that involves inflammation and possible weakening of the lining of different body joints. The affected joints may lose their shape that leads to loss of normal mobility and the body attacks its own tissue including joints. In severe cases, it attacks internal organs. RA is widely prevalent throughout the world. RA is generally starting between the ages of 30 and 60 in women and somewhat later in life in men. The lifetime risk of developing RA is 3.6% for women and 1.7% for men. However, RA can strike at any age even small children can get it. Out of every 1,00,000 people 41 are diagnosed with RA every year. About 1.3 million Americans have RA. Women are about two to three times more likely to get RA than men.¹
**Amavata** is made up of a combination of two words, *Ama* and *Vata*. The disease is mainly due to derangement of *Agni*, resulting in the production of *Ama* which circulates in the body and gets located in the *Sandhisa* causing pain, stiffness, and swelling over the joints. According to modern medicine, it can be correlated with RA, which is a chronic Auto immune disease that causes inflammation of the joint.

Ayurved, an Indian system of medicine, is well known for its unique therapeutic techniques. *Guggulu* is an established anti-inflammatory and anti-arthritis drug and used in the treatment of *Amavata*. *Guggulu* formulations are drug of choice them for the treatment of RA. These formulations are more popular in therapeutics because of its smaller dose, palatability, shelf life and efficacy. *Guggulu* formulations are prepared from processed herbal drugs, *Guggulu* etc. Herbal drugs are used in pharmaceutical process which act as a chelating agent and provide large number of trace elements. Ayurvedic classics have described some basic rules for all formulations regarding their preparation and prescription such as dose, duration, adjuvant and diet restriction.

In Rheumatoid Arthritis disease some *Guggulu* formulations have also found in routine practice such as *Simhanada Guggulu*, *Vatari Guggulu*. These formulations are widely prescribed by Ayurvedic physicians since ancient age and they are safe and effective in RA. Present work is a humble effort to collect and highlight some evidences regarding safety and efficacy of the *Guggulu* formulations in RA.

**Materials and Methods:** Subject related published research articles from reputed journals were searched through four online search engines - Google scholar, Pubmed, Ayush research portal and Ayu journals. Articles published in English language were included in the review. Full text of these studies is available in pdf format through the related publishing websites.

**Objective** - To evaluate the safety and efficacy of *Guggulu* formulations in the management of RA.

**Search strategy:** Published literatures on recent advancements in assessing the safety and efficacy of *Guggulu* formulations on Rheumatoid Arthritis which includes original articles and research papers in databases such as Google scholar, Pubmed, AYUSH research portal, Ayu journals were taken into the study for review.

A literature search to collect relevant data was performed using the Mesh terms - clinical trials on *Amavata* by Ayurvedic drugs - *Amavata* disease - Management of RA in Ayurved - *Guggulu* formulations in the management of RA - Ayurvedic management in RA

A total of 138 abstracts appeared with this combination. Total of 5 articles were retrieved for review.

**Search engine**
- Google Scholar
- PubMed
- AYUSH Research portal
- Ayu journals

**Types of studies:** Only clinical trials described in proper scientific manner were included in this review. Randomized trial, open label, single and double blind-trials and the trials evaluated safety and efficacy of Ayurvedic *Guggulu* formulations in management of RA is included in the review. Case reports, case series, pharmacological studies, and observation studies were excluded from the review. *Vamana*, *Virechana Karma* in management of RA were also excluded.

**Types of interventions:** Studies designed to treat RA by Ayurvedic *Guggulu* formulations were included in the review. In all studies *Guggulu* formulations as interventions were given by oral route and some of them *Basti* was given. *Guggulu* formulations were prescribed in proper dose along with proper adjuvant.

**Types of outcome measurement:** For the outcome’s measurement, assessment of before and after intervention and a follow up period were essential for the review. Hematological and Biochemical investigations have been taken as a safety measure.

**Quality of evidence:** Studies that were nonrandomized, limited, indirect or imprecise or exhibited publication bias were considered as a low-quality evidence. studies that were randomized trial were consider for medium to high quality evidence and based of randomization, blinding, reliability, and external validity were applied on them.
**Data extraction:** Standard proforma was prepared for data analyzing that comprised the following items: author, study design, participants, disease, age, intervention, safety measures and results. (Efficacy)

**Study selection and exclusion:** In Google scholar 69, Pubmed 9, AYUSH research portal 47, Ayu journals 11 articles clinical trials on RA were found. Total 138 clinical trials through Ayurvedic treatment in RA were found, respectively.

**Results**

**Figure 1:** Flow diagram showing the number of studies identified, screened, assessed for eligibility, excluded and included in the systemic review.

- Records identified through database total 138
  - Google Scholar (n=69)
  - Pubmed (n=9)
  - AYUSH Research Portal (n=47)
  - Ayu journals (n=11)

- Duplicate article removed (n = 17)

- Records after duplication removed (n=121)

- Not full texts article available (n=17) excluded

- Record screened (n=104)

- Articles excluded (n=90)
  1. Only *Shodhana* treatments were given (n=34)
  2. *Shodhana* and *Shamana* (other than *guggulu kalpana*) were given (n=35)
  3. In *Shamana Chikitsa* other than *Guggulu kalpana* are excluded (n=17)
  4. Only mineral drugs formulations (n=4)

- Total Articles (n=14)

- Articles finally selected for review (n=5)

- Total excluded articles (n=9)
  1. External applications excluded (n=4)
  2. *Shamana chikitsa* after *Shodhana chikitsa* excluded (n=1)
  3. Equally effective both interventions excluded (n=1)
  4. not given a formulations name excluded (n=2)
  5. Not Randomized trials (n=1)
Table 1: Shows the characteristics of the interventions in the included studies.

<table>
<thead>
<tr>
<th>Method</th>
<th>Design: Randomized Control Trials</th>
<th>Duration: 45 days follow up 1 month after completion of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Number randomized: 113 patients</td>
<td>Group A (50 pt) Group B (53 pt)</td>
</tr>
<tr>
<td></td>
<td>Age of Participants: 16-60 years</td>
<td>Inclusion criteria of the study: Morning stiffness Arthritis of three or more joints and hand joints Symmetrical arthritis Presence of RA factor - Diagnostic criteria is made with four or more criteria. RA factor: Hematological investigation Urine analysis Exclusion criteria of the study: Chronicity for more than 10 years Having severe crippling deformity Patients suffering with cardiac disease, pulmonary TB, DM etc.</td>
</tr>
<tr>
<td>Interventions</td>
<td>Group - A Matra Basti and Vatari guggulu</td>
<td>Vatari guggulu - 2vati(500mg) thrice a day with lukewarm water Matra Basti - 60 ml of Brihat saindhavadi taila Group - B Vatari guggulu 2vati(500mg) thrice a day with lukewarm water</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Group A patients had better relief in most of the cardinal signs and symptoms of the disease</td>
<td></td>
</tr>
</tbody>
</table>

2. Shweta et al - 2012

<table>
<thead>
<tr>
<th>Method</th>
<th>Design: Randomized Control Trials</th>
<th>Duration: 8 weeks and follow up for 8 weeks after completion of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Number randomized: 24 patients (12 pt in Both Group)</td>
<td>Age of Participants: Age 18-60 yrs</td>
</tr>
<tr>
<td></td>
<td>Inclusion criteria of the study: Morning stiffness Arthritis of three or more joints and hand joints Symmetrical arthritis Presence of RA factor - Diagnostic criteria is made with four or more criteria. RA factor: Hematological investigation Urine analysis Exclusion criteria of the study: Chronicity for more than 10 years Having severe crippling deformity Patients suffering with cardiac disease, pulmonary TB, DM etc.</td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>Group - A Shiva Guggulu 6gm/day with lukewarm water</td>
<td></td>
</tr>
</tbody>
</table>
3. **Shashikant s. Nikam et al - 2015**

<table>
<thead>
<tr>
<th>Method</th>
<th>Design:</th>
<th>open Randomized Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of Participants:</strong></td>
<td>20-70 years</td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>Patients of RA fulfilling the criteria of clinical symptoms of RA.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Diagnostic criteria based on clinical features of the diseases.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RA factor</td>
<td></td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td>All complicated cases having any adverse deformity of RA.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cardiac disease, pulmonary and pregnant woman.</td>
<td></td>
</tr>
</tbody>
</table>

**Interventions**

- **Group A**: Bhallathaka Churna with guda 2.5 gm twicw a day
- **Group B**: Bhallataka Guggulu 500mg TDS

**Outcomes**

Group B showed faster and better improvement. Highly significant result found.

4. **Shiv shankar shukla et al - 2017**

<table>
<thead>
<tr>
<th>Method</th>
<th>Design:</th>
<th>Double blind Randomized interventional Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration:</strong></td>
<td>3 months follow up at every 15 days</td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>Number randomized: 60 patients (30 pt in Both Group)</td>
<td></td>
</tr>
<tr>
<td><strong>Age of Participants:</strong></td>
<td>20-60 years</td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>Patients of RA fulfilling the criteria of clinical symptoms of RA.</td>
<td></td>
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<td></td>
<td>- Diagnostic criteria based on clinical features of the diseases.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RA factor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CRP less than 1</td>
<td></td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td>All complicated cases having any adverse deformity of RA.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cardiac disease, pulmonary and pregnant woman.</td>
<td></td>
</tr>
</tbody>
</table>

**Interventions**

- **Group A**: Bhallathaka Churna
- **Group B**: Bhallataka Guggulu

**Outcomes**

Group B showed faster and better improvement. Highly significant result found.

5. **Valiparambil c Deep et al - 2017**

<table>
<thead>
<tr>
<th>Method</th>
<th>Design:</th>
<th>open label</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration:</strong></td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>Number randomized: 111 pt</td>
<td></td>
</tr>
<tr>
<td><strong>Age of Participants:</strong></td>
<td>20-60 yrs</td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>Morning stiffness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arthritis of three or more joints and hand joints</td>
<td></td>
</tr>
</tbody>
</table>
Symmetrical arthritis
Presence of RA factor
- Diagnostic criteria based on clinical features of the diseases.
RA factor
Reduction in DAS-28
Exclusion criteria of the study
All complicated cases having any adverse deformity of RA.
Cardiac disease, pulmonary and pregnant woman.

Interventions
Internal: Simhanada Guggulu-1.5 gm (3 tabs of 500mg each) Lukewarm water
External: Saindhavadi taila local application

Outcomes
The statistical analysis reveals that there was significant relief of symptoms (p<0.05) at 5% level of significance.

DISCUSSION
Rheumatoid Arthritis is a joint disorder that involves inflammation and possible weakening of the lining of different body joints. Arthritis means inflammation of one or more joints. Inflammation of joints brings lot of pain, stiffness and even swelling. It can be correlated with Amavata in view of its clinical features. Guggulu formulation are used in treatment of RA. Guggulu is Katu Vipaka, Ushna Veerya, Vedahara Guna. so that used in RA. Basti therapy is considered as prime among all the therapeutic, especially for management of Vatavyadhies. Basti dravyas can act as Vatahara, Shulahara, Shothahara, Stratoshodhaka, Yogavahi, Agnideepaka and Rasayana.

1) Rita Khagram et al
Group A- Matra basti with Brihat saindhavadi taila along with Vatari guggulu
Group B- Vatari guggulu
All the patients responded favorably to the treatment in both the groups: however, patients treated with Matra basti had better relief in most of the cardinal signs and symptoms of the disease. Effect of therapies in the Matra basti group that most of the patients (52%) showed marked improvement, while in the Vatari guggulu group most of the patients (54.72%) showed mild improvement. Thus, both therapies provided significant relief of the cardinal symptoms as well as general symptoms of RA. However, there was better relief in Matra Basti group than in the Vatari guggulu group.

2) Shweta Pandey et al
Group A- Shiva guggulu
Group B- Simhanada guggulu
on analysis of the results, it was found that simhanada guggulu provided better results as compared to Shiva guggulu in management of RA. In Group A, marked improvement in 30% and moderate improvement in 70% of patients was observed, whereas in group B, 40% of patients showed marked improvement and moderate improvement was seen in 60%.

3) Shashikanta nikam et al
Rasanadyo guggulu:- The mean symptoms significantly reduced after the treatment. The statistical analysis reveals that was significant relief of symptoms (p<0.05) at 5% level of significance. Rasanadyo guggulu was significantly effective in symptoms of RA.

4) Shiv Shankar Shukla et al
Group A- Bhallathaka churna with guda 2.5 gm twice a day.
Group - B Bhallataka guggulu 500mg TDS
Present study reflects that both regimes have given very good relief in sign and symptoms of Amavata but in Group B who received Bhallataka guggulu showed faster and better improvement. Bhalltaka Guggulu is safe, beneficial and very effective in management of Amavata and in RA.

5) Valiparambil C Deep: Internal -Simhanada Guggulu-1.5 gm (3 tabs of 500mg each) Lukewarm water
External- Saindhavadi taila local application. Simhanada Guggulu and Brihata Saindhavadi taila administered together in the above-mentioned dose were found effective, safe and tolerable in patients with RA.
CONCLUSION

There is strong conclusion evidence that Guggulu formulations can be used in management of RA.

There was a systemic review investigating the evidence regarding safety and efficacy of Ayurvedic Guggulu formulations RA. In this review Ayurvedic Guggulu formulations are found quite safe to the use in RA with proper dose and adjuvant. Basti treatment followed by Shamana Aushadha with Pathya Aahara was found as a suitable treatment plan to manage RA

Among the Shamana Aushadhas usage of Guggulu formulations proved to have a significant effect on the recovery of RA. It also revealed the fact that all the therapies were found to be significantly effective and clinically safe as no adverse drug reaction were reported during treatment period among any of the screened studies.

ACKNOWLEDGMENT

Author duly acknowledge the authorities of the PG Department of Rasashastra and Bhaishajya Kalpana, Government Ayurved College Vadodara for their support and also Rita Khagram et al, Shweta A. Pandey et al, Dr. Shashikant s. Nikam et al, Dr. Shashikant s. Nikam et al, Valliparambil c Deep et al for their Research paper publication, which is used for the Review Study.

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Source of Support: Nil
Conflict of Interest: None Declared