



RESEARCH ARTICLE

Clinical Safety of Selected Ayurvedic Formulations in Rheumatoid Arthritis

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease which mainly affects the small joints leading to erosion of cartilage and bone associated with irreversible joint damage, joint deformity, and systemic complications. The symptoms of RA resemble with the signs and symptoms mentioned in *Amavata* described in different texts of Ayurveda. *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* are commonly used in the management of this disease. However, the safety data are not collected on these formulations till now.

Objective: Critical analysis and presentation of clinical safety outcomes of classical Ayurvedic formulations *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* in patients of RA generated

through multicenter open label studies at different Central Council for Research in Ayurvedic Sciences (CCRAS) centers.

Materials and methods: Data were collected from three different clinical studies executed in peripheral institutes of CCRAS and were critically evaluated to assay the safety profile of five formulations. Safety assessments were done through analyzing liver function tests (LFTs) and kidney function tests (KFTs) before and after the study trial period.

Conclusion: The findings in the three different clinical studies clearly indicate that *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* are clinically safe and tolerable in the participants belonging to different age groups, gender, geographical area, and different *prakrti*.

Keywords: *Amavata*, *Brihat Saindhavadya Taila*, *Hingvashtaka Churna*, *Rasna Saptaka Kashaya*, Rheumatoid arthritis, Safety, *Simhanada Guggulu*, *Vatari Guggulu*.

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INTRODUCTION

Rheumatoid arthritis is an autoimmune disease with a worldwide prevalence of approximately 0.5 to 1% among adults,¹ and two to three times more common in women compared with men. In India, the prevalence in adults has been estimated to be 0.75%² mainly affecting articular and extra-articular structures resulting in pain, disability, and mortality³ leading to erosive joint damage and functional impairment.⁴

The signs and symptoms of RA can be correlated with sign and symptoms of *Amavata*. The pathogenesis of *Amavata* revolves around *Ama* and *Vata*. *Ama* is formed due to malfunctioning of the digestive and metabolic mechanisms, initiated by *Viruddha Ahara-Vihar* with pre-existence of *Mandagni*.⁵ The manifestation of the symptoms in *Amavata* is due to *Vata* and *Ama*, but *Kapha*

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and *Pitta* may also invariably be involved in its *samprapti* (pathogenesis).⁶

Ayurveda, an ancient traditional medicine system, is widely practiced throughout the country. It is reported that 60 to 90% of persons with arthritic conditions use complementary and alternative medicines.⁷ People from all over world are also developing interest in traditional herbal practices. The concern about safety, ADRs, and drug–drug interactions with these traditional health care systems is rising.⁸ This set of studies was done to analyze the safety of *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* in patients with RA.

DRUG PROFILE

The different formulations are chosen as per the etiology and hence the ingredients of these indicated formulations have multifarious actions. The major ingredients reduce the *Amavastha* to *Niramavastha* by improving *Agni* (digestive fire) and pacifying the vitiated *Vata dosha*. Major ingredients of these indicated formulations are *Vatashamaka* (pacifying Vata), *Amapachaka* (eliminating undigested metabolic products), *Ama Shoshaka* (drying undigested metabolic products), *Deepniya* (potentiating digestive activity), and possess *Ushna* (hot) *Virya* and *Katu* (*pungent*) *Vipaka* properties (Table 1).

OBJECTIVE

Critical analysis and presentation of clinical safety outcomes of classical Ayurvedic formulations *Simhanada Guggulu*, *Brihat Saindhavadi Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* in patients of RA were generated through multicenter open label studies at different CCRAS institutes.

MATERIALS AND METHODS

The formulations fulfilling the physicochemical standards and quality parameters were prepared as per standard operating procedures and procured from good manufacturing practice-certified companies for all the studies. These three different clinical studies were approved by institutional ethics committee of all the participating centers and done in accordance with World Health Organization Good Clinical Practice Guidelines. The data obtained from the completed clinical studies were analyzed retrospectively to assess the safety profile of *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* through liver function test (LFTs) and kidney function tests (KFTs) (Table 1).

Open label multicenter clinical trials were done in selected peripheral institutes of CCRAS to evaluate the safety and efficacy of *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* in RA and the details are briefed in Table 2. Follow-up was done every 2 weeks to record the onset of any ADRs during the intervention. The data thus generated were analyzed to evaluate the safety of these formulations in patients with RA.

Statistical Analysis

Laboratory parameters at the beginning and at the end of the trial period were compared using paired t-test. A p-value of <0.05 was considered significant. All statistical analyses were performed using Statistical Package for Social Sciences, version 15.0.

OBSERVATION

Study I: Effect of *Simhanada Guggulu* and *Brihat Saindhavadya Taila*

Total 111 subjects completed the trial. The majority of the subjects were females, i.e., 96 (86.5%). Total 28 (25.2%) were illiterate and 83 (74.8%) know how to read and write. Thirty-one (27.9%) belonged to below poverty line, and 11 (9.9%) were vegetarian and 100 (90.1%) were nonvegetarian. It was also observed that maximum number of subjects 48 (43.2%) were of *Vata-Pittaja prakriti* followed by 24 (21.6%) *Pitta-Kaphaja prakriti*. Table 3 shows the basic information and demographic profile of the subjects. The combination of *Simhanada Guggulu* and *Brihat Saindhavadya Taila* has been found effective in the management of RA. Pain in joints, swelling in joints, morning stiffness and tenderness, along with malaise and fever were the major symptoms seen, which were assessed on disease activity score (DAS) and Disability Index. The clinical improvement was significant. The DAS and Disability Index baseline mean was 6.8162 and it reduced to 5.0715 on 84th day. Serum bilirubin, serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), serum alkaline phosphatase, serum protein, albumin, globulin, blood urea, and serum creatinine were within normal limits during the entire period and the values were compared with paired t-test after the trial and there was no detectable change in these parameters (Table 4 and Graphs 1 to 4).

Study II: Effect of *Vatari Guggulu*, *Rasna Saptaka Kashaya* and *Brihat Saindhavadya Taila*

Total 225 subjects completed the trial. The majority of the subjects were females, i.e., 182 (80.88%). Total 35

Table 1: Components of Simhanada Guggulu, Brihat Saindhavadya Taila, Vatari Guggulu, Rasna Saptaka Kashaya, and Hingvashtaka Churna

Sanskrit name	Botanical name	Part used
Simhanada Guggulu⁹		
Haritaki	<i>Terminalia chebula</i> Retz.	Dried fruit
Bibhitaki	<i>Terminalia bellirica</i> (Gaertn.) Roxb.	Dried fruit
Amalaki	<i>Emblica officinalis</i> Gaertn.	Dried fruit
Jala	Water	
Shuddha gandhaka	Sulfur	
Guggulu	<i>Commiphora mukul</i> (Hook. ex Stocks) Engl.	Resin
Eranda Taila	Castor oil	Oil
Brihat Saindhavadya Taila¹⁰		
Saindhava lavana	Rock salt	
Gajpipali	<i>Scindapsus officinalis</i> (Roxb.) Schott	Fruit
Rasna	<i>Pluchea lanceolata</i> (DC.) C.B. Clarke	Leaf
Shatapushpa	<i>Anethum sowa</i> Roxb. ex Fleming	Fruit
Yamanika	<i>Trachyspermum ammi</i> (L.) Sprague	Fruit
Sarjika kshara	Potassium nitrate	Alkali
Maricha	<i>Piper nigrum</i> L.	Dried fruit
Kustha	<i>Saussurea lappa</i> (Decne.) Sch.Bip.	Root
Shunthi	<i>Zingiber officinale</i> Roscoe	Dried rhizome
Sauvarcala lavana	Salt	
Vida lavana	Salt	
Vacha	<i>Acorus calamus</i> L.	Rhizome
Ajamoda	<i>Apium graveolens</i> L.	Fruit
Madhuka	<i>Glycyrrhiza glabra</i> L.	Root
Jiraka	<i>Cuminum cyminum</i> L.	Fruit
Paushkaramula	<i>Inula racemosa</i> Hook.f.	Root
Pippali	<i>Piper longum</i> L.	Fruit
Eranda taila	Castor oil	Oil
Shatapushpa	<i>Anethum sowa</i> Roxb. ex Fleming	Fruit
Kaanjika	Fermented medicinal gruel	
Mastu (godadhi)	Curd	
Vatari Guggulu¹¹		
Eranda	Castor oil	Oil
Gandhaka	Sulfur	
Guggulu	<i>Commiphora mukul</i> (Hook. ex Stocks) Engl.	Resin
Haritaki	<i>Terminalia chebula</i> Retz.	Fruit
Bibhitaki	<i>Terminalia bellirica</i> (Gaertn.) Roxb.	Fruit
Amalaki	<i>Emblica officinalis</i> Gaertn.	Fruit
Rasna Saptaka Kashaya¹²		
Rasna	<i>Pluchea lanceolata</i> (DC.) C.B. Clarke	Rhizome
Amrita	<i>Tinospora cordifolia</i> (Willd.) Miers	Stem
Aragvadha	<i>Cassia fistula</i> L.	Stem bark
Devadaru	<i>Cedrus deodara</i> (Roxb. ex D. Don) G. Don	Heart wood
Punarnava	<i>Boerhavia diffusa</i> L. nom. cons.	Root
Eranda	<i>Ricinus communis</i> L.	Seed
Trikantaka	<i>Tribulus terrestris</i> L.	Fruit
Hingvashtaka Churna¹³		
Shunthi	<i>Zingiber officinale</i> Roscoe	Rhizome
Maricha	<i>Piper nigrum</i> L.	Fruit
Pippali	<i>Piper longum</i> L.	Fruit
Ajamoda	<i>Apium graveolens</i> L.	Fruit
Saindhava lavana	Rock salt	
Shwet jiraka	<i>Cuminum cyminum</i> L.	Fruit
Krishna jiraka	<i>Carum carvi</i> L.	Fruit
Hingu	<i>Ferula narthex</i> Boiss.	Oleo-resin

Table 2: Brief description of studies conducted in the management of RA

Name of study	Study period	Study design	No of centers	Current names	Sample size	Study interventions	Dosage schedule	Intervention period
Clinical evaluation of <i>Simhanada Guggulu</i> and <i>Brihat Saindhavadya Taila</i> in the management of rheumatoid arthritis CTRI/2012/03/002534	2010–2011	Open label multicenter study	2	1. NARIP, Cheruthuruthy 2. RARIGID, Guwahati	111	<i>Simhanada Guggulu</i> <i>Brihat Saindhavadya Taila</i>	1.5 gm (3 tablets of 500 mg each) BD after food with lukewarm water 2.0 mL twice a day for local application	12 weeks
Clinical evaluation of <i>Vatari Guggulu</i> , <i>Rasna Saptaka</i> , <i>Kashaya</i> and <i>Brihat Saindhavadya Taila</i> in the management of rheumatoid arthritis CTRI/2013/12/006087	2010–2011	Open label multicenter study	4	1. CSMRADDI, Chennai 2. CARICD, Delhi 3. MSRARIED, Jaipur 4. RARISD, Vijayawada	225	<i>Vatari Guggulu</i> <i>Rasna Saptaka</i> <i>Kashaya</i> <i>Brihat Saindhavadya Taila</i>	1.5 gm (3 tablets of 500 mg each) BD after food with lukewarm water 15 mL BD empty stomach twice a day 20 mL twice a day for local application	12 weeks
Clinical evaluation of <i>Vatari Guggulu</i> , <i>Hingvashtaka Churna</i> and <i>Brihat Saindhavadya Taila</i> in the management of rheumatoid arthritis CTRI/2014/12/005242	2012–2013	Open label multicenter study	3	1. RARIGID, Guwahati 2. CARIHD, Bhubaneswar 3. RARIID, Patna	179	<i>Vatari Guggulu</i> <i>Hingvashtaka Churna</i> <i>Brihat Saindhavadya Taila</i>	1 gm (2 tablets of 500 mg each) TDS after food with lukewarm water 3 gm twice a day along with first bolus of food mixed with ghee 20 mL twice a day for local application	12 weeks

NARIP: National Ayurveda Research Institute for Panchakarma, Cheruthuruthy; RARIGID: Research Ayurveda Regional Institute for Gastro-Intestinal Disorders, Guwahati; CSMRADDI: Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute, Chennai; CARICD: Central Ayurveda Research Institute for Cardiovascular Diseases, New Delhi; MSRARIED: M.S. Regional Ayurveda Research Institute for Endocrine Disorders, Jaipur; RARISD: Regional Ayurveda Research Institute for Skin disorders, Vijayawada; RARIID: Regional Ayurveda Research Institute for Infectious Diseases, Patna

Table 3: Demographic profile of the patients in three clinical trials

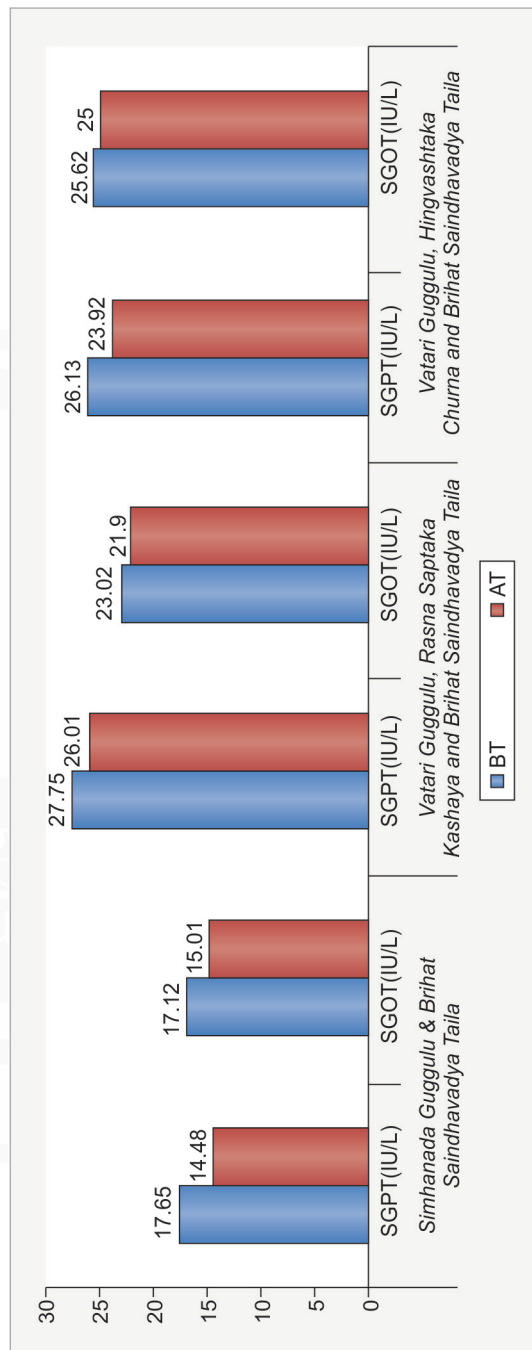
Demographic profile	<i>Simhanada Guggulu</i> and <i>Brihat Saindhavadya Taila</i> (n = 111)	<i>Vatari Guggulu</i> , <i>Rasna Saptaka</i> , <i>Kashaya</i> , and <i>Brihat Saindhavadya Taila</i> (n = 225)	<i>Vatari Guggulu</i> , <i>Hingvashtaka Churna</i> , and <i>Brihat Saindhavadya Taila</i> (n = 179)
Sex			23 (12.8%)
Male	15 (13.5%)	43 (19.12%)	156 (87.2%)
Female	96 (86.5%)	182 (80.88%)	
Education			30 (16.8%)
Illiterate	28 (25.2%)	35 (15.56%)	149 (83.2%)
Literate	83 (74.8%)	190 (84.44%)	
Socioeconomic status			36 (20.1%)
Below poverty line	31 (27.9%)	66 (29.34%)	143 (79.9%)
Above poverty line	80 (72.1%)	159 (70.66%)	
Diet			32 (17.9%)
Vegetarian	11 (9.9%)	105 (46.67%)	147 (82.1%)
Nonvegetarian	100 (90.1%)	120 (53.33%)	
Prakriti			8 (4.5%)
Vataja	6 (5.4%)	3 (0.01%)	11 (6.1%)
Pittaja	13 (11.7%)	1 (0.004%)	2 (1.1%)
Kaphaja	2 (1.8%)	1 (0.004%)	64 (35.8%)
Vata-Pittaja	48 (43.2%)	70 (31.12%)	85 (47.5%)
Pitta-Kaphaja	24 (21.6%)	69 (30.67%)	1 (0.6%)
Vata-Kaphaja	5 (4.5%)	70 (31.12%)	8 (4.5%)
Sannipataja	13 (11.7%)	11 (0.048%)	
Patients completing the trial from different geographical locations			
Kerala (Cheruthuruthy)	58 (52.2%)	New Delhi	47 (20.8%)
Assam (Guwahati)	53 (47.8%)	Rajasthan (Jaipur)	60 (26.8%)
		Andhra Pradesh (Vijayawada)	59 (26.2%)
		Tamil Nadu (Chennai)	59 (26.2%)
Total	111		225
			179

Values are expressed as n (%)

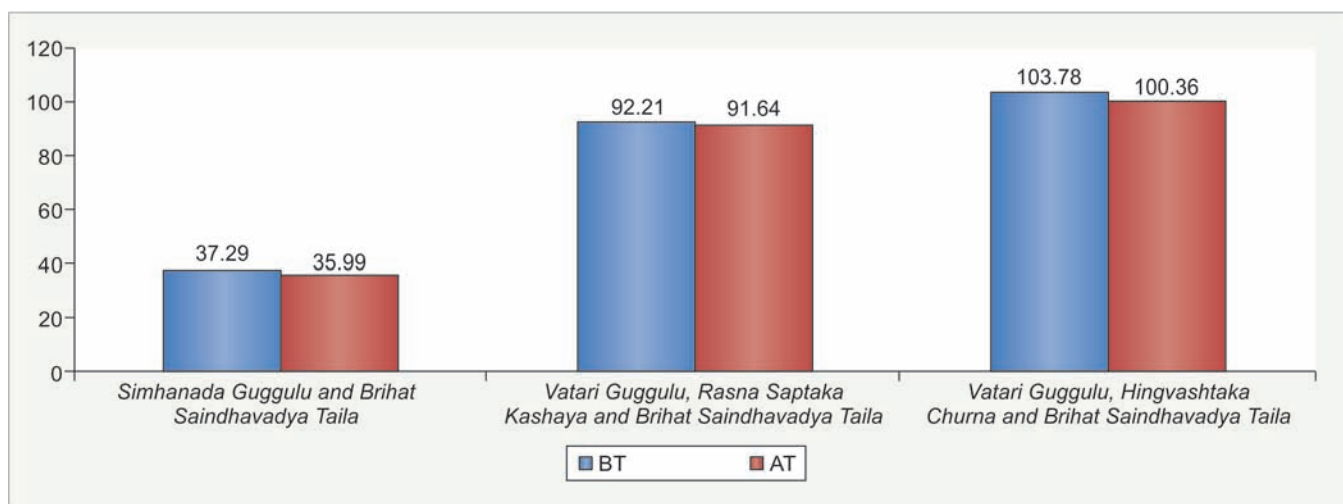
Table 4: Safety profile of the patients in three clinical trials

Parameters	Simhanada Guggulu and Brihat Saindhavadya Taila			Vatari Guggulu, Rasna Saptaka Kashaya, and Brihat Saindhavadya Taila			Vatari Guggulu, Hingvashtaka Churna, and Brihat Saindhavadya Taila		
	BT	AT	p-value	BT	AT	p-value	BT	AT	p-value
LFT									
Serum bilirubin (conjugated) (mg/dL)	0.26 (0.20)	0.30 (0.24)	0.162	0.17 (0.10)	0.16 (0.07)	0.550	0.44 (1.47)	0.30 (0.13)	0.209
Serum bilirubin (unconjugated) (mg/dL)	0.49 (0.24)	0.53 (0.2)	0.085	0.44 (0.22)	1.42 (10.49)	0.324	0.42 (1.48)	0.30 (0.13)	0.268
SGPT (IU/L)	17.65 (18.66)	14.48 (14.62)	0.011	27.75 (15.72)	26.01 (15.69)	0.039	26.13 (9.96)	23.92 (8.6)	0.004
SGOT (IU/L)	17.12 (14.75)	15.01 (12.43)	0.056	23.02 (7.08)	21.90 (6.01)	0.060	25.62 (9.44)	25.00 (8.42)	0.409
Serum alkaline phosphate (IU/L)	37.29 (29.41)	35.99 (31.86)	0.176	92.21 (26.35)	91.64 (25.69)	0.786	103.78 (35.37)	100.36 (36.26)	0.108
Total protein	7.63 (5.71)	7.11 (0.64)	0.342	7.24 (0.54)	7.20 (0.54)	0.402	7.67 (0.47)	7.61 (0.48)	0.065
Serum albumin (gm/dL)	4.08 (0.34)	4.18 (0.50)	0.114	3.93 (0.37)	3.91 (0.38)	0.297	4.25 (0.28)	4.19 (0.27)	0.004
Serum globulin (gm/dL)	3.01 (0.61)	2.91 (0.73)	0.233	3.30 (0.58)	3.28 (0.54)	0.624	3.41 (0.43)	3.42 (0.46)	0.737
KFT									
Blood urea (mg/dL)	24.91 (11.85)	24.18 (12.69)	0.516	22.53 (7.51)	22.48 (7.87)	0.658	21.78 (5.72)	21.64 (5.29)	0.717
Serum creatinine (mg/dL)	0.82 (0.16)	0.85 (0.17)	0.260	0.75 (0.20)	0.74 (0.21)	0.478	0.77 (0.13)	0.81 (0.56)	0.303
Serum uric acid (mg/dL)	4.67 (4.67)	4.75 (4.75)	0.440	4.31 (1.03)	4.28 (1.05)	0.680	4.41 (1.04)	4.46 (1.06)	0.361

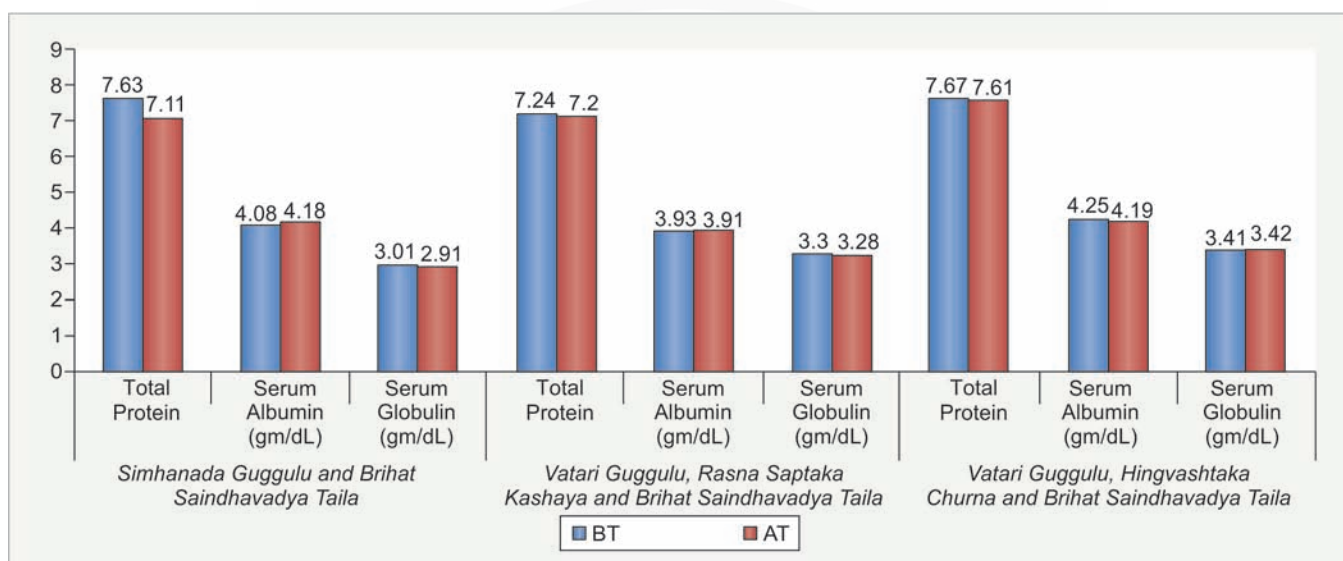
Values are expressed as mean (standard deviation). *p-value of <0.05 has been considered as significant



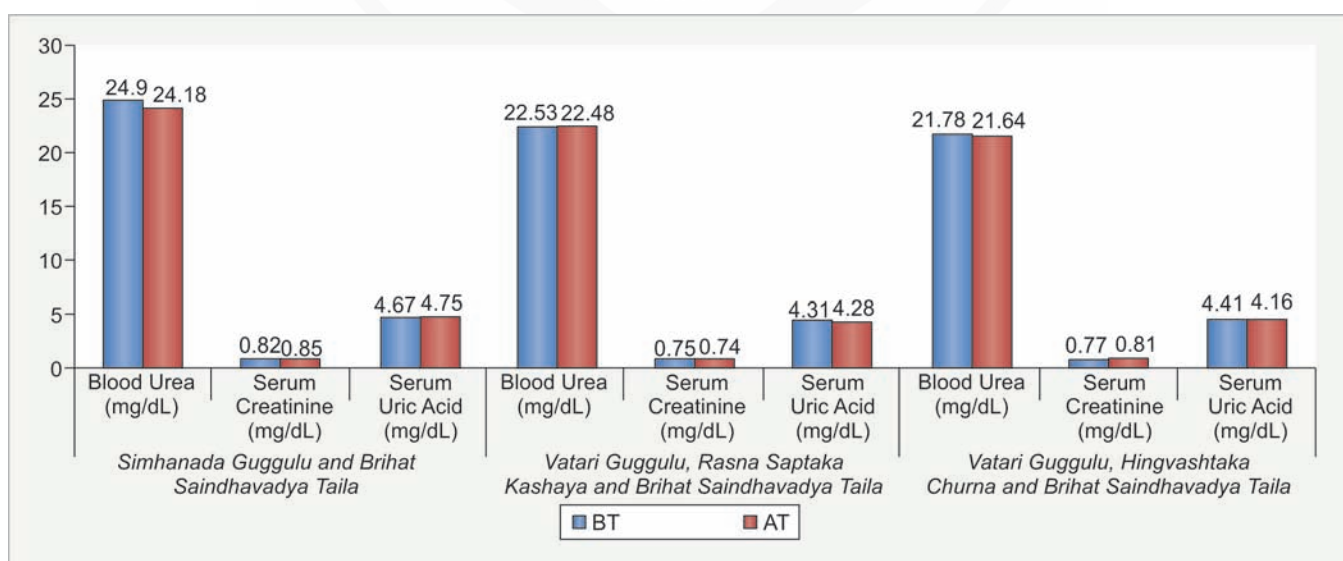
Graph 1: Comparison of LFTs [SGOT (IU/L) and SGPT (IU/L)] before and after the trial in three studies



Graph 2: Comparison of LFTs (serum alkaline phosphatase) before and after the trial in three studies



Graph 3: Comparison of LFT (total protein, globulin, and albumin) before and after trial in the three studies



Graph 4: Comparison of KFT (blood urea and serum creatinine) before and after the trial in the three studies

(15.56%) were illiterate and 190 (84.44%) are literate. Sixty-six (29.34%) belonged to below poverty line and 159 (70.66%) belonged to above poverty line. Total 105 (46.67%) were vegetarian and 120 (53.33%) were non-vegetarian. It was also observed that maximum number of subjects (70 (31.12%)) were of *Vata-Pittaja prakriti* and 70 (31.12%) were of *Vata Kaphaja prakriti*. Table 3 shows the basic information and demographic profile of the subjects. The combination of *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Brihat Saindhavadya Taila* has been found effective in the management of RA. Pain in joints, swelling in joints, morning stiffness and tenderness, along with malaise and fever were the major symptoms seen, which were assessed on DAS and Disability Index. The clinical improvement was significant. The effect of this treatment on LFTs and KFTs was assessed at baseline and at 84th day. The values were within range during the entire trial period (Table 4 and Graphs 1 to 4). These observations validate that these classical drugs are safe for human use. Further, no adverse drug effect or AEs were reported during the treatment period.

Study 3: Effect of *Vatari Guggulu*, *Hingvashtaka Churna*, and *Brihat Saindhavadya Taila*

Total 179 subjects completed the trial. The majority of the subjects were females, i.e., 156 (87.2%). Thirty (16.8%) were illiterate and 149 (83.2%) were literate. Thirty-six (20.1%) belonged to below poverty line and 143 (79.9%) belonged to above poverty line. About 32 (17.9%) were vegetarian and 147 (82.1%) were nonvegetarian. It was also observed that maximum number of subjects (85 (47.5%)) were of *Pitta-Kaphaja prakriti* and 64 (35.8%) were of *Vata Pittaja prakriti*. Table 3 shows the basic information and demographic profile of the subjects. The combination of *Vatari Guggulu*, *Hingvashtaka Churna*, and *Brihat Saindhavadya Taila* has been found effective in the management of RA. Pain in joints, swelling in joints, morning stiffness and tenderness, along with malaise and fever were the major symptom seen which were assessed on DAS and Disability Index. The clinical improvement was significant. The effect of this treatment on LFTs and KFTs was assessed at baseline and at 84th day. The values were within range during the entire trial period (Table 4 and Graphs 1 to 4). These observations validate that these classical drugs are safe for human use. Further, no adverse drug effect or AEs were reported during the treatment period.

The data regarding demographic profile, efficacy, and safety obtained from the all three studies are given in Tables 3, 4 and Graphs 1 to 4.

DISCUSSION

The main purpose was to collect the data from three different clinical studies executed in peripheral institutes of CCRAS to assess the safety profile of 5 formulations viz., *Simhanada Guggulu*, *Vatari Guggulu*, *Hingvashtaka Churna*, *Rasna Saptaka Kashaya* and *Brihat-Saindhavadya Taila* through liver function tests and kidney function tests. In these studies though there was change in LFT and KFT before and after the Ayurvedic interventions but the change was not to that extent that could cross the normal limit. During these studies none of the patients complained of any adverse reaction or side effects. *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* have been studied in the management of RA. Joint pain, swelling, tenderness, morning stiffness, fever, malaise, fatigue, and weakness are the major clinical manifestations in this disease. The aforementioned clinical studies demonstrate that the scheduled Ayurvedic treatment has potential effects to manage these signs and symptoms without any adverse effect. There is highly significant progress in DAS-28, Disability Index score, 36-item Short Form Health Survey (SF-36) survey compared with the baseline and 84th day as well as 112th day of follow-up in statistical analysis. All parameters show statistically highly significant results.

These symptoms resemble with the symptoms of *Amavata* mentioned in different Ayurveda classics. *Vata* associated with *Ama* is the main causative factor in *Amavata*. The drugs which are having *Vatashamaka*, *Amapachaka*, *Ama Shoshaka*, and *Deepniya* properties can be used in the treatment of this disease. Most of the ingredients of above formulations are *Ushna Virya*, *Katu Vipaka*, and having *Snigdha* and *Ruksha* properties. *Ushna Virya* drugs are helpful in digesting and absorbing the vitiated *Ama* by its *Shoshana Karma*. The *Deepniya* property of these drugs also slows down the *Ama* formation. The *Eranda Taila* and *Triphala* also have *Anulomana* (purgative) action and reduce the *Vibandha* (constipation) and *Anaha* (tympanitis). Similarly, internal administration of *Hingvashtaka Churna* reduces the *Vata dosha* within the abdomen by its *Agnideepana* property and *Vatanulomana* by this way pacify *Amadosha*. *Brihat Saindhavadya Taila* together may reduce the aggravated *Vata Dosha*. Charaka has stated *Rasna* as "*Shreshtha Vataharanam*."¹⁴ *Shunthi* is considered as best *Aampachaka* having *Deepana* and *Pachana* properties, which is helpful in improving *Jatharagni*.¹⁵ It is also proved by latest researches that ginger has anti-inflammatory activity and some of the constituents are potent inhibitors of prostaglandin synthesis and leukotriene synthesis.¹⁶ *Simhanada Guggulu* and *Vatari*

Guggulu have *Guggulu* as main ingredient. Both formulations are used as antiinflammatory drugs. This effect is probably due to guggulsterones present in both drugs. Guggulsterone is reported to inhibit significantly lipopolysaccharide-induced upregulation of tumor necrosis factor-alpha expression and cyclooxygenase-2 production.¹⁷ When *Brihat Saindhavadya Taila* was applied locally the local counter irritant effect occurred and diluted the accumulated *Doshas*. Due to *Ushna Tikshna* property, it acts as *Shamaka* of vitiated *Ama* and *Vata*.

All these three studies scheduled for Ayurvedic treatment have potential effects to manage signs and symptoms of RA. Statistical analysis shows that there is highly significant increase in DAS-28, Disability Index score, SF-36 survey compared with the baseline and 84th day as well as 112th day of follow-up. Serum bilirubin, SGPT, SGOT, serum alkaline phosphatase, serum protein, albumin, globulin, blood urea, and serum creatinine were within normal limits during the entire period and the values were compared with paired t-test after the trial and there was no detectable change in these parameters. This study revealed that all the parameters were within the specified limits during the entire period.

CONCLUSION

The study to evaluate the safety and efficacy of *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* was conducted at peripheral institutes of CCRAS spread throughout various bio-geographical areas of India. The analysis of outcome of these scientifically planned studies demonstrates that in spite of the differences in gender, socioeconomic status, age group, *prakrati*, and geographic region *Simhanada Guggulu*, *Brihat Saindhavadya Taila*, *Vatari Guggulu*, *Rasna Saptaka Kashaya*, and *Hingvashtaka Churna* proved to be very safe, effective, and tolerable in the management of RA. No ADRs or AEs pertaining to drug interaction were noticed during the trial period. This study ascertains that the classical *Ayurvedic* formulations are safer as far as liver and renal functions are concerned. The data collected from these three studies provide a positive conclusion about the safety of these *Ayurvedic* medicines. Further exploration with larger samples can be taken to establish the safety concern.

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हिंदी सारांश

“रुमेटाइड अर्थराइटिस रोग में चयनित आयुर्वेदिक योगों की चिकित्सकीय सुरक्षा—एक फार्मको एपिडेमोलॉजिकल परिपेक्ष्य अध्ययन”

¹सुनीता, ²श्रुति खंडूड़ी, ³बबीता यादव, ⁴प्रदीप दुआ, ⁵वी सी दीप, ⁶बिकरतन दास, ⁷एस संगविकर
⁸शशि घोष, ⁹ए के जैन, ¹⁰जी के स्वामी, ¹¹टी महेश्वर, ¹²साईप्रसाद, ¹³आलोक श्रीवास्तव
¹⁴दीप सुंदर साहू, ¹⁵तापसी बोरा, ¹⁶एमएम राव, ¹⁷रेणू माखीजा, ¹⁸वी एम कुमावत
¹⁹पिप्पट्टा श्रीनिवास, ²⁰के के सिंह, ²¹एस के मेहर, ²²दिनेश बरुआ, ²³राजेश कुमारी, ²⁴राकेश राणा
²⁵रिचा सिंघल, ²⁶नारायणम श्रीकांत

परिचय: रुमेटाइड अर्थराइटिस एक जीर्ण, प्रणालीगत आटोइम्यून शोथीय व्याधि है, जो मुख्य रूप से हाथ व पैर के छोटे जोड़ों को प्रभावित करती है जिससे उपास्थि व सम्बंधित अस्थि में क्षरण अपरिवर्तनीय संधिक्षति, संधि विकलता, प्रणालीगत उपद्रव होते हैं। रुमेटाइड अर्थराइटिस रोग के लक्षणों की तुलना आयुर्वेद के विभिन्न ग्रंथों में वर्णित ‘आमवात’ रोग के लक्षणों से की जा सकती है। सिंहनाद गुग्गुलु, बृहद सैधवादि तैल, वातारि गुग्गुलु, रास्नासप्तक कषाय एवं हिंवाष्टक चूर्ण सामान्य रूप से इस रोग की चिकित्सा में प्रयुक्त होते हैं।

उद्देश्य: शास्त्रीय आयुर्वेदीय योगों यथा सिंहनाद गुग्गुलु, बृहद सैधवादि तैल, वातारि गुग्गुलु रास्नासप्तक कषाय एवं हिंवाष्टक चूर्ण का रुमेटाइड अर्थराइटिस के रोगियों में चिकित्सकीय सुरक्षात्मक एवं प्रभावकारिता परिणामों का महत्वपूर्ण विश्लेषण एक बहुकेंद्रीय, खुले स्तरीय सीसीआरएस के विभिन्न परिधीय केंद्रों पर अध्ययन करना है।

सामग्री व विधि: रुमेटाइड अर्थराइटिस रोग प्रबंधन की पांच औषधियों तथा सिंहनाद गुग्गुलु, बृहद सैधवादि तैल, वातारि गुग्गुलु, रास्नासप्तक कषाय एवं हिंवाष्टक चूर्ण का विशिष्ट रूप से सुरक्षामक प्रोफाइल जांच करने के लिए सीसीआरएस के विभिन्न परिधीय संस्थानों में पूर्ण किये गये तीन विभिन्न चिकित्सकीय अध्ययनों से एकत्रित किये गये आंकड़ों के पूर्वव्यापी विश्लेषण से किया गया है यह सुरक्षात्मक आंकलन यकृत कार्य परीक्षण) एलएफटी (यथा एल्नाइन एमिनो ट्रांसफारेज, एस्पार्टेट एमिनो ट्रांसफरेज, एल्कलीन फास्टफोटेज, सीरम प्रोटीन, एल्ब्युमिन, ग्लोब्यूलिन, बिलीरुबिन एवं वृक्क कार्य परीक्षण) केएफटी (यथा सीरम यूरिया व सीरम क्रिएटिनिन के परीक्षण अवधि से पूर्व व पश्चात किये गये आंकड़ों से किया गया है। आधारभूत दिवस से अध्ययन अवधि पूर्णन पर औसत परिवर्तन में तुलना करने के लिये युग्मित नमूना टी-परीक्षण प्रयुक्त किया गया। इस अध्ययन से यह ज्ञात हुआ कि सभी मापदंड पूरी अध्ययन अवधि के दौरान निर्दिष्ट सीमाओं के भीतर थे। <0.05 का पी-मान महत्वपूर्ण माना जाता है। औषध अनुपालना, प्रतिकूल औषध प्रतिक्रिया या प्रतिकूल घटनायें नहीं पाई हैं।

निष्कर्ष: तीन विभिन्न नैदानिक/चिकित्सकीय अध्ययनों का निष्कर्ष स्पष्ट रूप से इंगित करता है कि सिंहनाद गुग्गुलु बृहद सैधवादि तैल, वातारि गुग्गुलु, रास्नासप्तक कषाय व हिंवाष्टक चूर्ण चिकित्सकीय रूप से सुरक्षित, प्रभावी व सहनशील है। यह विभिन्न आयु समूहों, लिंग, भौगोलिक क्षेत्र व प्रकृति से जुड़े प्रतिभागियों के अच्छी तरह से नियोजित अनुसंधान अध्ययनों के परिणामों के माध्यम से समझा जा सकता है कि परीक्षण औषध ने समान रूप से सभी में अच्छा परिणाम दिया।

मुख्य शब्द: रुमेटाइड अर्थराइटिस, आमवात, सिंहनाद गुग्गुलु, बृहद सैधवादि तैल, वातारि गुग्गुलु रास्नासप्तक काषाय, हिंवाष्टक चूर्ण, सुरक्षा।