

# Management of *Amavata*/Rheumatoid Arthritis with *Langhan* (Fasting), *Sunthi* (dried ginger) and *Trikatu* - an Ayurvedic Polyherbal Formulation

## Research Article

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### Abstract

*Amavata*, a progressively debilitating, disabling condition, is similar to rheumatoid arthritis that occurs in nearly 1% of the population. Rheumatoid arthritis is generally treated with anti-inflammatory drugs to slow down its progression and save joints and tissues from permanent damage. However, these drugs have side effects. In Ayurveda, *Langhan* / modified fasting and use of ginger or *Trikatu*, a three herbal formulation is recommended. In the present study, a combination of *Langhan* plus a decoction prepared from either Ginger powder/*Sunthi* or *Trikatu* was studied. Patients were randomly assigned to the *Sunthi* group (n=32) or *Trikatu* (n=36). Functionality was assessed using the HAQ disability index, Ritchie's articular index and grip strength. Symptoms like pain, fever, and gastrointestinal problems were assessed on Days 0, 7 and 14. The HAQ-DI assessed the amount/level of difficulty experienced in performing common daily activities. Ritchie's Articular Index assessed six joints of fingers, wrist, elbow, shoulder, knee and ankle on the left and the right side as a single unit for pain, swelling, warmth, and limitation of motion. Both treatments were effective but benefits were better and side effects were less with *Sunthi*. Also, benefits with *Sunthi* were seen in the first week of treatment. The duration of this study was only 14 days, as patients found it difficult to adhere to the diet particularly because wheat was restricted completely, resulting in a high number of dropouts. Further study on modification of diets for patients with RA/ *Amavata* to obtain maximum benefits would be worthwhile.

**Keywords:** Rheumatoid Arthritis; *Amavata*; Ginger; *Trikatu*; Functionality; Disability Index

### Abbreviations

Rheumatoid Arthritis - RA; Gastrointestinal - GI; HAQ-DI - Health Assessment Questionnaire-Disability Index; RAI - Ritchie's Articular Index; BMI - Body Mass Index; WHO - World Health Organization, RDA - Recommended Dietary Allowances, IL-6 - Interleukin-6; CRP - C-Reactive Protein; IgM - Immunoglobulin M; TNF- $\alpha$  - Tumour Necrotic Factor- $\alpha$ ; GLP-1 - Glucagon-like Peptide-1.

### Introduction

*Amavata* is a chronic, progressive disease that clinically resembles

rheumatoid arthritis (RA) and is characterized by inflammation of joints and surrounding tissues, swelling, pain in ankles, knees, hips, elbows, shoulders, as well as joint deformity. Ayurveda considers *Amavata* to be a manifestation of the vitiation of *Vatadosha* and localization and accumulation of *Ama* in the joints, resulting in pain, stiffness, swelling and tenderness in the joints [1]. *Ama* is believed to be cellular and metabolic waste/toxic material generated in the gastrointestinal (GI) system and cells due to improper diet and impaired metabolism.

Modern medicine generally relies upon anti-inflammatory drugs

i.e., Analgesics, Steroids and disease-modifying drugs for treating RA. However, there is not much to offer in terms of dietary management. In Ayurveda however, treatment is multi-faceted in which *Deepana* i.e., selected plant materials like ginger (*Zingiber officinale*), pepper (*Piper nigrum*), long pepper (*Piperlongum*) are used and dietary measures are advised depending on whether *Amavata* is chronic or acute. These include *Langhan*/ abstinence from food totally or consuming light and easily digestible foods, while some foods are not permitted [1]. The treatment aims to remove the accumulated *Ama*, keep further production in check, cleanse the circulatory channels and pacify the vitiated *dosha*. Furst et al., (2011) conducted one of the first randomized, double-blind controlled study comparing methotrexate with ayurvedic treatment and their combination [2]. While efficacy was similar in all three treatment groups, the Ayurveda only group had fewer side effects. In this context, we undertook a clinic-based study of *Amavata* involving *Langhan* along with dry ginger/*Sunthi*, or *Trikatu* a combination of *Sunthi*, pepper and long pepper.

## Methodology

**Sample selection:** Outdoor patients attending the Seth Tarachand Ramnath Hospital, Pune were recruited after obtaining permission from the hospital and informed written consent, based on the following inclusion and exclusion criteria.

**Inclusion criteria:** Patients between 20 and 70 years of age, diagnosed with *Amavata* by the Ayurvedic physician, at least 4 weeks prior to the start of the study, who were not concurrently taking medications from other systems of medicine and any other medications. Patients should satisfy at least four of the American College of Rheumatism criteria: morning stiffness, arthritis of three or more joints, arthritis of hands, symmetric arthritis, rheumatoid nodules, positive rheumatoid factor and /or radiographic changes.

**Exclusion criteria:** Patients concurrently taking allopathic and/or homeopathic treatment, pregnant and lactating women, those clinically not advised *langhan* e.g., diabetes mellitus or tuberculosis or serious complications associated with any other systemic disease.

**Sample size:** Initially 68 patients were enrolled and 32 were randomly assigned to the *Sunthi* group and 36 to the *Trikatu* group, irrespective of their *prakriti* or chronicity and severity of the disease. Weekly follow up was done.

At the first follow up on Day 7, 17 patients from the *Sunthi* group did not return. On Day 14, another 10 patients in this group had dropped out. In the *Trikatu* group, from the 36 patients initially assigned, 19 patients did not return for the first follow up and 12 more had dropped out by Day 14. Due to a lack of sufficient subjects, the study was discontinued on Day 14.

**Intervention:** After baseline measurements, each participant in the *Sunthi* group was given 14 packets, each containing 6 grams of *Sunthi*. Similarly, the *Trikatu* group participants received 14 packets of *Trikatu* (6 g/packet). Each packet of *Trikatu* contained 2g each of the three constituents dried ginger powder (*Sunthi*), powdered long pepper (*Pippali*) and powdered black pepper (*Marich*).

Patients were instructed to prepare a decoction as follows, using one packet per day. The *Sunthi* or *Trikatu* was to be boiled with 1 cup

(150 ml) of milk and 2 cups (300 ml) of water on a low flame until the volume was reduced to 1 cup. Besides this, they were advised to consume warm water throughout the day and observe *langhan* as part of the intervention.

**Langhan:** This was a modified dietary regimen. Patients were allowed to consume *ad libitum*: rice, moong dal (decorticated *Vigna radiata*), tur dal (decorticated *Cajanus cajan*), spinach, *shepu* (*Anethum graveolens* L), drumstick (*Moringa oleifera*), *parwar*/ pointed gourd (*Trichosanthes dioica* Roxb), pumpkin (*Cucurbita pepo*), and onion. They were allowed to use only salt, cumin seeds, ginger, garlic, and asafoetida.

**Pilot study:** A pilot trial was carried out on six patients who were not part of the main study, to finalize the amount of *Sunthi* and *Trikatu*, to determine whether there were any side effects and finalize the instructions to be given to patients. Acceptance of the dose and reactions were monitored. Two doses - 4g and 6g of the *Sunthi* and *Trikatu* were used. Six grams of the daily dose of each was well tolerated, none of the patients experienced any side effects and the degree of relief from pain was better with the 6g dose than with 4g. Hence, the dose of 6 grams was finalized.

**Data collection:** A) Baseline data included family history, *prakriti*, personal habits such as chewing tobacco/*paan*, smoking, duration of disease in terms of years from the onset of disease, and previous treatments underwent. *Prakriti* was assessed as per *Ashtanga Hridayam* and was confirmed for each patient by a Senior Ayurvedic Physician in the hospital.

B) Severity of morning stiffness, pain at rest and while moving, digestive impairment, presence of fever, anorexia, and bowel habits were recorded at baseline and the follow-up visits. Each symptom was given a score as follows: 0 - no pain/ no symptom, 1 - for mild, 2 - for moderate and 3 - for severe. The maximum possible score was 21.

**Functionality:** This was assessed using the disability index that examines the difficulty in performing daily activities and a visual analogue scale.

The HAQ-Disability Index (HAQ-DI) given by Bruce and Fries was used to record the amount/level of difficulty experienced in performing eight items/ activities [3], namely dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. The level of difficulty experienced was scored as: '0' - can perform without any difficulty, '1' - with some difficulty, '2' - with much difficulty and '3' - unable to do and need someone to help with the task. The total disability index score was calculated as per Fries et al., [3].

**Pain Faces Scale:** The Pain Faces Scale, a visual analogue scale developed by Wong et al., was used for self-assessment of the intensity of pain [4]. The scale consists of six different faces to express the degree of pain. The scores ranged from 1 - very happy, 2 - pains a little bit, 3 - pains even more, 4 - pains much more, 5 - pains a lot, to 6 - hurts as much as you can imagine. Subjects were asked to choose the face that best described how he/she was feeling.

Ritchie's Articular Index (RAI) was used to assess joints of fingers, wrist, elbow, shoulder, knee and ankle on the left and the right side

as a single unit [5]. These joints were assessed for pain, swelling, warmth, and limitation of motion.

**Grip strength:** Grip strength and time required to walk a specified distance were measured at each weekly follow-up. This was measured using the Grip-D dynamometer with 0.1 kg force accuracy. Each patient was asked to stand straight with arms extended downwards. He/she was asked to grip the handle and exert full force without letting the hand touch any part of the body. Grip strength was measured for both arms separately, to the nearest 0.1 kg force. The test was repeated thrice for each arm and the average was calculated.

The time required to walk was used to determine whether there was any improvement in the lower limbs. Patients were asked to walk a distance of 110 feet (33.5 meters) at their normal pace and the time required was recorded using a digital stopwatch (Race make) with an accuracy of 1/100 seconds.

**Dietary assessment:** A 24-hour diet recall was done for the day prior to the hospital visit. Dietary intake was recorded in terms of household measures and wherever applicable, the number of food items e.g., biscuits, *chapatis* were recorded. Household measures were then converted to raw weights and intakes of energy, protein, carbohydrate, fat, iron and calcium were calculated using the nutritive value tables [6].

**Anthropometric measurements:** Height was measured using a standardized, flexible non-stretchable, plasticized tape with 1mm accuracy using standard techniques. Weight was measured using a weighing balance (Kohinoor make) and recorded to the nearest 0.1 kg using standard techniques. Before every measurement, the instrument was calibrated to zero. Three readings were taken and the average of three readings was calculated. Body Mass Index (BMI) was calculated and subjects were classified using the WHO standards for Asians [7].

**Data Analysis:** Data was analyzed for only those subjects who participated until Day 14 of the study (15 in *Sunthi* group and 17 in *Trikatu* group). Data was analyzed using Graph pad instat and SPSS version 17. Paired t-test was applied to determine whether there were significant differences between pre- and post-intervention status. Unpaired t-test was used to compare the *Sunthi* and *Trikatu* groups. Pearson's and Spearman's chi-square test and correlation coefficients were calculated to determine associations between different variables.

## Results

### Baseline Profile of subjects:

**Age and BMI:** Subjects' ages varied from 24 years to 65 years (Table 1), the mean age in the two groups being fairly similar. A little more than one-third of the subjects (37.5%) were 40-49 years old and 28.1% were 30 to 39 years of age. Thirteen of the 15 subjects in the *Sunthi* group and 15 of the 17 subjects in the *Trikatu* group were female. Mean BMI did not differ significantly between the two groups. In the *Sunthi* group, 60% of the subjects (n= 9) had normal BMI compared to only 46.8% (n=7) in the *Trikatu* group. In the *Sunthi* group, 19.9% (n=3) were in different grades of obesity compared to 28% (n=9) in the *Trikatu* group. Eighteen percent of the subjects chewed *paan* or tobacco, 36% had chewed *supari* and 27% smoked.

**Table 1:** Baseline Profile of Subjects in *Sunthi* and *Trikatu* groups.

	Sunthi (n=15)	Trikatu(n=17)
Age (years)	45.1±11.4 <sup>1</sup> 27-65 <sup>2</sup>	42.5±11.9 24-65
Symptom score	12.7±3.9 4-19	12.6±2.9 8-19
Pain related symptoms		
Morning stiffness	2.2±0.6 1-3	2.4±0.5 2-3
Pain on rest	2.1±0.8 1-3	2.2±0.5 1-3
Pain on motion	2.2±0.7 0-3	2.4±0.6 1-3
Distribution according to HAQ Disability Index		
Mild: 0.0-1.0 1.1-1.5	6.7(1) 13.2(2)	11.8(2) 52.9(9)
Moderate: 1.6-2.0 2.1-2.5	46.7(7) 26.7(4)	52.9 (9) 23.5(4)
Severe: 2.6-3.0	6.7(1)	11.8(2)
Grip Strength		
Right hand	14.8±6.9 5.0-32.2	13.2±5.8 0-23.4
Left hand	13.8±6.6 4.8-29.6	14.2±9.3 5.3-36.7
Time required to walk 33.5 meters	46.9±26.2 26.1-132.2	37.7±17.5 21.5-100.2
Ritchie's articular index		
Right side	0.55±0.55 0.15-0.75	0.53±0.55 0.25-0.72
Left side	0.56±0.54 0.14-0.87	0.57±0.57 0.28-0.78

<sup>1</sup>Mean±SD, <sup>2</sup>Minimum-Maximum

**Prakriti:** *Vata prakriti* was predominant 60% of the subjects overall, with subdominant *kapha* or predominance of *kapha* followed by *vata*, and only 18% of subjects had *pitta* predominant *prakriti*. There was a significant difference between the two groups ( $\chi^2=30.693$ ,  $p=0.0001$ ). In the *Sunthi* group, one third of the patients had *kapha-pitta prakriti* and 20% had *vata -kapha and prakriti*. In the *Trikatu* group, 28.5% had *vata-kapha prakriti* and 32.1% had *kapha-vata prakriti*.

**Disease duration:** Duration of disease varied from 1 month to 384 months, although the majority in both treatment groups (60.0% in *Sunthi* group and 64.7% in *Trikatu* group) had suffered from the disease for less than 2 years. In the *Sunthi* group, the maximum duration was 96 months whereas, in the *Trikatu* group, the duration was longer, 3 patients reported a duration of more than 97 months. Almost all the subjects (90.6%, n=29) had been on allopathic medication alone or along with Ayurvedic treatment. Only 9.3% (n=3) were new cases seeking Ayurveda as the first line of treatment.

**Family history:** Eight subjects (25%) had a family history, and for 87.5% of patients the mother had the same problem. None had a father or paternal relative with RA or *Amavata*.

**Symptoms:** Mean total scores for symptoms did not differ significantly between the two groups (Table 1). For the Pain Faces Visual Analogue scale, 46.6% (n=7) in the *Sunthi* group and 47.0% (n=8) in the *Trikatu* group marked 'pains much more'. Eight patients in all, six from the *Sunthi* group and two from the *Trikatu* group,

marked 'hurts as much as you can imagine'. These patients suffered so much pain and joint stiffness that they were unable to perform their daily activities, even if they were helped by other family members. One-fourth reported having 'considerable pain' and needed help in every activity.

Twenty four of the 32 patients (75%) had gastric upsets, with 37.5% experiencing problems frequently. Six patients (18.8%) had fever frequently and 68.8% sometimes had elevated body temperature.

**Functionality:** Functional ability was compromised as the majority (75%) of the subjects had a moderate disability and 9.1% had a severe disability, although there was no significant difference between the two groups. The mean grip strength for the left hand, as well as right hand, did not differ between the two groups, although women (right hand - 22.9±6.9kgf, left hand - 12.6±5.2 kgf) had less grip strength than men (Right hand -30.7±5.8 kgf, left hand -11.5±4.4 kgf). The time required to walk did not differ significantly between the two treatment groups. The time required for walking was significantly and positively correlated with the disability index score ( $r=-0.489$ ,  $p=0.004$ ).

**Assessment of joints:** There was no significant difference between the two groups and between the left side and the right side, respectively, in the number of joints affected as judged by mean RAI values (Table 1).

**Nutritional Status and Dietary Intakes:** Most subjects ( $n=25$ , 78.1%) did not eat breakfast regularly, and 81.3% ( $n=26$ ) ate dinner late. Approximately two-fifths (46.9%) of the subjects had a habit of drinking cold water. Two-thirds of the subjects (62.5%) consumed stale foods, with 50% doing so regularly. Also, 62% ( $n=20$ ) reported that they had a low to moderate degree of anorexia-53.3% in the *Sunthi* group and 76.4% in the *Trikatu* group. One subject suffered from severe anorexia. Nutrient intakes calculated from the 24-hour diet recall did not differ significantly between the two intervention groups at baseline (Table 2). The majority of patients met more than 50% of the recommended dietary allowances (RDA) for energy, protein, fat and calcium. However, iron intakes particularly among women were less than 50% of the RDA. Anorexia was significantly and negatively correlated with total energy intakes ( $r=-0.456$ ,  $p=0.015$ ).

### Effect of intervention- Day 7

**Nutrient Intakes:** The modified diet along with consumption of

the decoction of either *Sunthi* or *Trikatu*, resulted in a considerable reduction in the intakes of energy, and carbohydrates with a small decrease in the protein and fat intakes, while calcium intakes increased in both groups. Iron intake did not decrease much in the *Sunthi* group but reduced more in the *Trikatu* group (Table 2).

**Body weight and BMI:** *Langhan* resulted in a significant loss in body weight in both groups Day 7 and Day 14 (*Sunthi* group:  $t=8.56$ ,  $p=0.0001$ ; *Trikatu* group:  $t=4.58$ ,  $p=0.0003$ ) (Table 2). Only one patient in the *Trikatu* group gained 0.6 kg. BMI also reduced significantly (*Sunthi* group:  $t=4.9$ ,  $p=0.0002$ , *Trikatu* group:  $t=4.374$ ,  $p=0.0005$ ). The mean decrease in BMI was slightly more in the *Sunthi* than the *Trikatu* group, although, the difference was not statistically significant.

**Symptoms:** Symptom score reduced significantly ( $t=2.54$ ,  $p=0.01$ ), more in the *Sunthi* group ( $t=8.569$ ,  $p=0.0001$ ) than in the *Trikatu* group ( $t=2.840$ ,  $p=0.01$ ), (Table 3). Mean scores reduced significantly-  $1.0\pm0.4$  for the *Sunthi* group ( $t=9.025$ ,  $p=0.0001$ ) and  $0.7\pm0.4$  ( $t=6.197$ ,  $p=0.0001$ ) for the *Trikatu* group. Patients reported a significant reduction in morning stiffness after treatment, *Sunthi* being more effective in reducing morning stiffness ( $t=2.196$ ,  $p=0.035$ ) (Table 3). Similarly, the score for pain on rest decreased (*Sunthi* group  $1\pm0.5$  ( $t=7.2$ ,  $p=0.0001$ ) compared to only  $0.4\pm0.6$  ( $t=3.1$ ,  $p=0.0068$ ) for the *Trikatu* group. Reduction in scores for morning stiffness significantly correlated with the score for pain on rest ( $r=0.563$ ,  $p=0.045$ ). In both groups, the percentage of patients experiencing severe pain on movement decreased to nil and the percentage of subjects experiencing pain of mild intensity increased to 33.3%. The mean reduction in scores for pain on movement was  $0.7\pm0.7$  for the *Sunthi* group ( $t=4.036$ ,  $p=0.001$ ) and  $0.7\pm0.8$  ( $t=3.4$ ,  $p=0.003$ ), for the *Trikatu* group, with no significant difference between the two groups. The number of patients experiencing GI upsets was also reduced.

The number of patients who experienced burning sensation while urinating was greater on Day 7 as compared to baseline, particularly in the *Trikatu* group ( $t=2.7$ ,  $p=0.01$ ). In the *Sunthi* group, also the number of patients experiencing burning sensation increased, but this increase was not statistically significant.

The number of patients reporting the presence of blood in stools decreased in both groups (Table 3), although the number of patients suffering from fever, a sign of *Amavata*, did not change

**Table 2:** Mean Body Weight, BMI, and Nutrient Intakes between Baseline and Day 7 of Interventions.

	Sunthi group (n=15) Mean $\pm$ SD			Trikatu group (n=17) Mean $\pm$ SD		
	Baseline	Post intervention	Difference	Baseline	Post intervention	Difference
Anthropometric measurements						
Weight (kg)	58.9 $\pm$ 8.7	58.1 $\pm$ 8.7	0.8 $\pm$ 0.3	60.1 $\pm$ 8.9	59.2 $\pm$ 8.7	0.7 $\pm$ 0.1
BMI (kg/m <sup>2</sup> )	23.9 $\pm$ 3.6	23.4 $\pm$ 3.7	0.4 $\pm$ 0.3	24.2 $\pm$ 4.8	23.9 $\pm$ 4.7	0.2 $\pm$ 0.2
Nutrient Intakes						
Energy (kcal)	1425 $\pm$ 393	1099 $\pm$ 257	-325 $\pm$ 213	1340 $\pm$ 357	1119 $\pm$ 388	-220 $\pm$ 269
Protein(g)	29.6 $\pm$ 8.1	25.7 $\pm$ 4.7	-3.8 $\pm$ 5.6	29.0 $\pm$ 8.8	24.6 $\pm$ 4.2	-4.4 $\pm$ 5.9
Carbo-hydrates(g)	237 $\pm$ 32	206 $\pm$ 19	-32 $\pm$ 21	259 $\pm$ 37	238 $\pm$ 34	-20 $\pm$ 38
Total Fat (g)	25.7 $\pm$ 7.1	22.5 $\pm$ 4.3	-3.2 $\pm$ 4.4	26.9 $\pm$ 6.3	23.0 $\pm$ 5.4	-3.9 $\pm$ 7.2
Calcium (mg)	299 $\pm$ 94	641 $\pm$ 107	342 $\pm$ 101	278 $\pm$ 101	636 $\pm$ 115	359 $\pm$ 127
Iron (mg)	12.8 $\pm$ 6.0	11.9 $\pm$ 4.3	-0.4 $\pm$ 4.7	12.3 $\pm$ 6.3	10.2 $\pm$ 5.5	-2.3 $\pm$ 6.0

**Table 3:** Number of Patients experiencing various symptoms at Baseline and Days 7 and 14 after intervention.

Symptom	Sunthi group		Trikatu group	
	Baseline (n=15)	Day 7 (n=15)	Baseline (n=17)	Day 7 (n=17)
Score (Mean± SD)	12.7±3.9	7.8±3.2	12.6±2.9	10.3±3.8
Min-Max	4-19	1-14	8-19	8-17
Morning Stiffness				
Severe	4	0	8	3
Moderate	10	12	9	10
Mild	1	3	0	4
Pain on rest				
Severe	6	0	7	6
Moderate	5	5	9	8
Mild	4	10	1	5
Gastrointestinal upsets				
Severe	7	0	9	2
Moderate	5	8	7	4
Mild	3	7	1	11
Dysuria (Burning sensation during urination)				
Severe	0	0	1	1
Moderate	2	3	0	2
Mild	1	5	4	5
Blood in stools				
Occasionally	1	2	5	0
Frequently	0	0	1	0
Regularly	1	0	0	0
Fever				
Severe	4	4	4	5
Moderate	7	9	7	7
Mild	3	1	6	4

**Table 4:** Mean decrease in Ritchie's Articular Index for Right and Left sides (Baseline minus Day 7 scores).

	Sunthi (n=15)		Trikatu (n=17)	
Pain	-4.0±1.1	-5.0±1.9	-3.2±3.1	-3.8±2.4
Swelling	-3.4±2.6	-2.6±3.7	-3.3±3.6	-3.4±3.8
Warmth	-3.8±1.6	-3.9±2.0	-3.4±3.3	-3.6±2.0
Limitation of motion	-3.6±1.0	-4.0±1.1	-3.1±3.4	-3.0±1.9

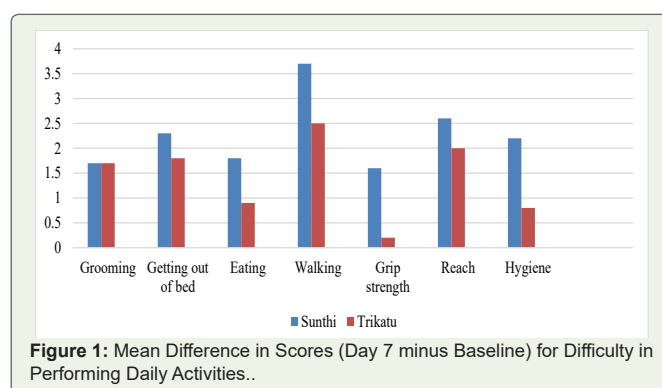
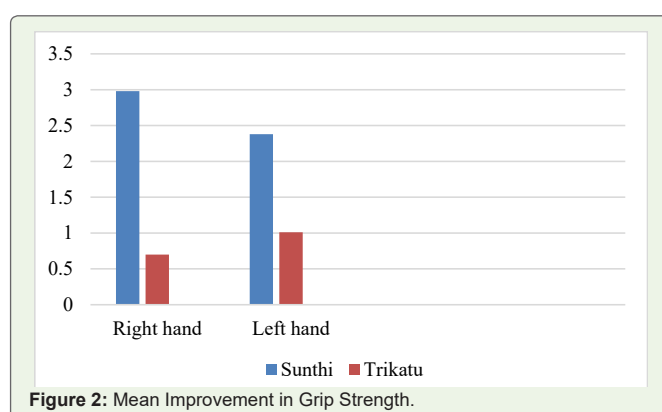
much. Anorexia was experienced at baseline by 53.3% of patients in the *Sunthi* group, which reduced to 33.7% on Day 7 of intervention. In the *Trikatu* group also, the percentage of patients reduced from 76.4% at baseline to 58.8% on Day 7.

**Functionality:** The HAQ-DI scores between baseline and Day 7 showed a significant reduction in all components in the *Sunthi* group whereas (Figure 1), in the *Trikatu* group, the reduction was comparatively less. Grip strength increased with both treatments (Figure 2), for both the right hand and left hand (scores- for right hand,  $t=2.839$ ,  $p=0.0085$ ; for left hand,  $t=20.7$ ,  $p=0.048$ ).

There was a considerable reduction in RAI on Day 7 for both sides (Table 4), particularly in the reduction of scores for pain and swelling. There was no significant difference between the *Sunthi*- and *Trikatu* - treated groups.

#### Effect of Intervention - Day 14

Only five patients in both groups reported for follow-up. There

**Figure 1:** Mean Difference in Scores (Day 7 minus Baseline) for Difficulty in Performing Daily Activities..**Figure 2:** Mean Improvement in Grip Strength.

was a reduction in symptoms from Day 0, to Days 7 and 14 of treatment, respectively in the mean scores for different symptoms, functionality and disability index for these five patients were lower and in the difference between these scores during follow up (Tables 5 and 6). In the *Sunthi* group, the symptom scores decreased progressively between baseline and Day 14 when the trial was terminated. In contrast for the *Trikatu* group, a significant decrease in the symptom score was seen only between Days 7 and 14. Dysuria was an exception as it was experienced in both groups as reflected by the increase in the score.

The functional ability scores of the patients improved as indicated by the lower scores and the mean differences in scores on Days 7 and 14 as compared to the baseline scores (Table 7). On Day 14, there was not much difference between the *Sunthi* and *Trikatu* groups. The mean scores at the three time points and the mean differences in scores for RAI between baseline, Days 7 and 14, respectively; indicated that for all five patients in pain, swelling, warmth and limitation of motion reduced.

#### Discussion

Treatment of RA and preventing its aggravation and the consequent disability requires attention, as it affects approximately 0.92% of the adult population in India, with an annual increase of 20-40 new cases per 100000 populations [8].

*Amavata* often considered to be equivalent to RA is attributed to *ama* formation due to weakened *agni* i.e., digestive capacity,

**Table 5:** Mean Scores and Mean Difference in Scores for Symptoms at Baseline and on Days 7 and 14.

Symptom	Sunthi (n=5)			Trikatu (n=5)		
	Baseline	Day 7	Day 14	Baseline	Day 7	Day 14
Mean Scores						
Morning stiffness	2.4±0.5	1.4±0.5	0.4±0.5	2.4±0.5	1.8±0.5	0.8±0.5
Pain on rest	2.0±0.7	1.0±0.4	0.2±0.4	2.4±0.5	1.8±0.8	0.8±0.8
Pain during movements	2.4±0.5	1.0±0.5	1.0±0.7	2.8±0.4	1.06±0.5	1.0±0.0
Gastric upsets	2.2±0.8	1.4±0.5	0.6±0.5	1.6±0.5	1.2±0.4	0.6±0.5
Fever	2.0±0.7	1.0±0.7	0.8±0.4	1.8±1.3	1.0±1.0	0.4±0.5
Anorexia	1.2±1.3	1.2±1.3	0.8±0.9	2.0±0.0	1.2±0.4	0.4±0.5
Dysuria	0	0.8±0.8	0.8±0.8	0	0.4±0.5	1.2±1.2
Blood in stools	0	0.2±0.4	0	0.2±0.4	0	0
Differences in Mean Scores						
	Baseline - Day 7	Day 7-Day 14	Baseline - Day 14	Baseline - Day 7	Day 7-Day 14	Baseline - Day 14
Morning stiffness	-0.8±0.8	-0.6±0.2	-1.8±0.2	-0.6±0.5	-0.4±0.1	-1.6±0.5
Pain on rest	-0.8±0.8	-0.6±0.5	-1.4±0.5	-0.2±0.5	-0.6±0.2	-1.6±0.5
Pain during movements	-0.8±0.4	-0.8±0.4	-1.6±0.8	-0.6±0.5	-1.2±0.8	-1.8±0.4
Gastric upsets	+0.8±0.8	+0.2±0.4	+0.8±0.8	-0.4±0.8	-0.6±0.5	-1.0±1.0
Fever	-0.4±0.6	-0.2±0.4	-1.2±0.4	-0.8±0.4	-0.6±1.5	-1.4±0.4
Anorexia	-0.6±0.5	-0.2±1.0	-0.6±0.4	-0.8±0.4	-0.8±0.4	-1.6±0.5
Dysuria	+0.8±0.8	0	+0.8±0.8	+0.4±0.5	+0.8±0.4	+1.2±0.4
Blood in stools	+0.2±0.4	+0.2±0.1	+0.2±0.1	+0.2±0.4	0	-0.2±0.4

**Table 6:** Mean Scores and Mean Difference in Scores for Difficulty in Functionality at Baseline and on Days 7 and 14.

Activities	Sunthi (n=5)			Trikatu (n=5)		
	Baseline	Day 7	Day 14	Baseline	Day 7	Day 14
Mean Scores						
Grooming	3.8±1.0	2.0±1.2	0.4±0.5	3.4±0.5	2.8±0.5	1.2±0.8
Arising	8.2±2.5	4.8±2.5	3.4±1.5	8.8±0.8	6.6±2.8	2.8±2.6
Eating	2.8±3.1	1.2±1.6	0.6±0.8	4.2±1.0	2.4±1.8	1.2±0.8
Walking	16.4±2.6	11.8±0.5	7.6±1.6	15.4±1.8	11.6±5.1	5.4±3.1
Grip	3.2±2.8	1.8±1.6	0.4±0.8	4.0±2.0	2.8±1.7	0.4±0.5
Reach	9.8±1.3	6.8±0.8	5.0±0.7	11.2±0.4	8.6±2.3	4.6±1.8
Hygiene	7.2±1.7	4.6±2.0	2.6±0.8	8.0±2.5	7.2±3.0	3.8±2.6
Disability index	2.4±0.4	1.3±0.4	0.8±0.2	2.2±0.2	1.7±0.7	0.8±0.4
Differences in Mean Scores						
	Baseline - Day 7	Day 7-Day 14	Baseline - Day 14	Baseline - Day 7	Day 7-Day 14	Baseline - Day 14
Grooming	-1.8±0.4	-1.6±1.1	-3.4±0.8	-0.6±0.8	-1.6±0.8	-2.2±0.4
Arising	-3.4±0.8	-1.4±1.5	-4.8±1.6	-2.2±3.3	-3.8±0.8	-6.0±3.0
Eating	-1.6±1.5	-0.6±0.8	-2.2±0.8	-1.8±2.1	-1.2±1.7	-3.0±0.4
Walking	-4.6±1.8	-4.2±1.7	-8.8±2.7	-3.8±0.6	-6.2±2.4	-10.0±4.2
Grip	-1.4±1.3	-1.4±1.1	-2.8±2.2	-1.2±1.4	-2.4±1.3	-3.6±1.8
Reach	-3.0±1.2	-1.8±0.8	-4.8±1.6	-2.6±2.1	-4.0±0.4	-6.6±1.6
Hygiene	-2.6±1.3	-2.0±1.5	-4.6±1.6	-0.8±2.6	-3.4±1.3	-4.2±1.9
Disability index	-0.7±0.2	-0.5±0.2	-1.3±0.3	-0.5±0.7	-0.9±0.3	-1.4±0.4

**Table 7:** Mean Scores and Mean Difference in Scores for Ritchie's Articular Index at Baseline and on Days 7 and 14.

Activities	Sunthi (n=5)			Trikatu (n=5)		
	Baseline	Day 7	Day 14	Baseline	Day 7	Day 14
Mean Scores						
Pain	12.8±2.3	7.8±3.7	3.6±1.3	11.8±2.6	8.0±4.1	3.6±2.4
Swelling	9.4±3.2	8.8±3.8	4.4±2.8	10.0±2.4	7.4±5.0	2.8±2.1
Warmth	13.2±2.5	7.8±2.2	3.0±2.5	12.8±3.8	9.4±4.2	4.2±1.9
Restriction in movements	11.6±2.1	7.6±1.8	4.2±2.1	11.2±2.1	7.8±3.1	3.4±2.7
RAI	0.69±0.1	0.4±0.1	0.2±0.1	0.6±0.1	0.4±0.2	0.2±0.1
Differences in Mean Scores						
	Baseline - Day 7	Day 7-Day 14	Baseline - Day 14	Baseline - Day 7	Day 7-Day 14	Baseline - Day 14
Pain	-5.0±2.3	-4.2±2.8	-9.2±2.1	-3.8±3.5	-4.4±2.3	-8.2±3.3
Swelling	-0.6±4.1	-4.4±1.5	-5.0±4.3	-2.6±5.3	-4.6±3.0	-7.2±3.5
Warmth	-5.4±1.5	-4.8±1.3	-10.2±2.2	-3.4±2.7	-5.2±3.1	-8.6±2.0
Restriction in movements	-4.0±0.7	-3.4±1.5	-7.4±1.8	-3.4±2.7	-4.4±0.5	-7.8±2.4
RAI	-0.2±0.0	-0.2±0.0	-0.4±0.1	-0.1±0.1	-0.2±0.1	-0.4±0.1

consumption of inappropriate diet and foods, as well as disequilibrium in the three *doshas* (*Vata*, *Kapha* and *Pitta*), resulting in improperly formed *Anna rasa*. This is considered as the initiating factor is vitiated and propelled throughout the body and lodges in *Sandhisthana* (joints) [1].

Ayurvedic literature indicates that *Langhan* and *tikta-katu ahara* i.e., modified diet with hot and pungent potency, with use of *aushadhi dravyas*, generally *Sunthi* and *Trikatu* help in treating *Amavata* [1]. Therefore, in the present study, we explored the effect of *Langhan* with *Sunthi* or *trikatu* on patients with *Amavata*. *Langhan* i.e., fasting or consumption of a light diet is considered the first line of treatment in Ayurveda. Restriction or elimination of food breaks the vicious cycle of improper digestion and *ama* production, contributes to the digestion of already formed *ama* besides enhancing digestive and metabolic capacities [1]. Charaka stated that consuming heavy, cold and/or excess food, and impure diets contribute to *Ama* formation, resulting in inflammation typically seen in *Amavata*/RA and the obstructive processes that are said to occur in *Amavata*.

Fasting and reduced caloric intake have been associated with improved outcomes for metabolic, autoimmune and inflammatory diseases including RA [9]. Inflammation is a crucial event in the complex chain of events involved in the development of RA. Inflammatory cytokines stimulate fibroblasts and chondrocytes, resulting in inflammation. And there is the degradation of peptidoglycans and cartilage [10]. Anti-inflammatory medications in modern medicine help to reduce pain and stiffness, however, with long-term use; they can have adverse effects on the bone marrow, kidneys and liver. Inflammatory arthritis presents with dysregulation of cell metabolism and dysfunctional lymphocytes. Alterations in CD4 T cell metabolism, particularly in glucose metabolism could increase the severity of joint inflammation [10]. Fasting alters cellular metabolic pathways, immune function, erythrocyte sedimentation rate and expression of pro-inflammatory cytokines, IL-6, CRP [9]. A subtotal fast for seven days resulted in decreased CD4+ lymphocyte number and function, Relief from pain and reduced disease activity score. However, there are indications that when fasting ceases, symptoms reappear or flare-up.

In a single-blind study of 53 patients with RA; participants in the experimental group fasted for 7-10 days and then followed a vegan diet for 3.5 months (doctors were blinded about the allocation to fasting and control groups). After this, milk and dairy products were introduced singly but were withdrawn if symptoms were aggravated. Thirteen months of this regimen brought about significant improvement [9]. Other benefits include lower duration of morning stiffness, articular index, increase in hemoglobin and reduced release of lysozyme associated with inflammation and joint destruction, leukotriene B4 that is pro-inflammatory and involved in activation of neutrophils that mediate tissue damage [11,12].

Recently, Rose and Strombom reported that vegan or vegetarian diets improved the leukocyte count [13], levels of rheumatoid factor, IgM, C3 and C4 and symptoms. Jordan and co-workers observed that fasting decreased the size of the circulating monocyte pool [14], a favorable effect as monocytes produce pro-inflammatory cytokines. Metabolic activity and gene expression patterns were modified.

Also, short-term and intermittent fasting did not compromise tissue regeneration.

From the Ayurvedic perspective, further production of *Ama* needs to be controlled, generally using foods and/or drugs having *katu*, *tikta* rasa and *deepana* properties. Among the food items that have this capacity with was *Sunthi*/ginger, turmeric, garlic, pepper. All three are well known for their anti-inflammatory effects. Ginger provided relief from pain and swelling with no side effects when it was consumed over a long duration from 3 months to as long as 2.5 years [15]. Prakash and Dwivedi reported that *Sunthi* reduced stiffness of joints, anorexia, heaviness and changes in taste [16].

In an animal model, Funk et al., observed that a crude ginger extract prevented both joint inflammation and bone destruction [17]. The crude extract that contained both polar compounds and essential oils has more therapeutic potency than did gingerol and its derivatives. Shrivastava and coworkers reported a reduction of pain upon treatment with ginger powder [15]. Phan et al., demonstrated that in human synoviocytes, the ginger extract significantly inhibited cytokine expression [18].

In the present study, we demonstrated the beneficial effects of ginger and *Trikatu* for their ability to mitigate the symptoms. *Trikatu* possessed immunomodulatory, and anti-inflammatory potential at a dose <1 g/day, and was found to be safe to use [19]. Active principles in *Trikatu* like piperine, 6-shogaol and 6-gingerol have an anti-inflammatory effect in RA and acute gouty arthritis [19]. Studies on paw edema in animal models have shown that *Trikatu* reduced edema, levels of circulating immune complexes and the inflammatory mediators TNF -  $\alpha$  and Interleukin-1 $\beta$  [20,21]. Piperine in pepper and long pepper in *Trikatu* has anti-inflammatory activity.

However, a common side effect of *Trikatu* is heartburn and acidity. In the present study, we found that more patients given *Trikatu* experienced side effects than those who were given *Sunthi*. A lower number of patients experiencing side effects with ginger could be attributed to the analgesic effect of gingerol and gingerdione, in addition to their anti-inflammatory effect. In a rat model of human RA, a blend of turmeric and ginger was effective against the extra-articular complications of RA [22].

Diets that are typically calorically rich, particularly containing processed foods that are low in micronutrients, 'phytobioactives' and fiber can result in chronic low-grade inflammation and increase the risk of chronic diseases. Nutrients and dietary constituents can modulate immune-metabolic homeostasis [23]. *Sunthi*, milk, *pippali*/long pepper and foods like mung gruel that were used in the present study, have been recommended for use in RA. Consumption of stale foods, irregular meals and/or long gaps between consecutive meals is considered to increase susceptibility to *ama* formation. Ayurveda recommends the inclusion of certain food items such as barley (*yava*), horsegram (*kulith/kulatha*) sama millet (*shyamaka*), red rice (*raktashali*), drumstick, bitter melon, brinjal, pointed gourd among vegetables, consumption of lukewarm water (*ushnaja*), and to avoid consumption of curd, milk, fish, jaggery and *pishtanna* i.e., foods made out of flour [1].

In the present study, our patients were allowed to consume *ad libitum* - rice, mung dal or tur dal; among vegetables, spinach, *shepu*

(*Anethum graveolens*) drumstick, *parwar*/pointed gourd, pumpkin and onion, but no other vegetables. They were allowed to add salt, *jeera* (*Cuminum cyminum*), ginger, garlic and asafoetida to flavor the preparations but to try and avoid other foods and spices/condiments. This restricted diet along with the use of decoctions made with either ginger/*Sunthi* or *Trikatu* was beneficial. Khanna, Jaiswal and Gupta reported that subtotal fasting with limited consumption of carbohydrates [24], vegetable juices, and limited vitamin and mineral supplements reduced the CD4+ number and lymphocyte activation. There was transient immunosuppression that contributed to the suppression of RA. Intake of vegetable broth, juice and controlled energy intake was associated with a decrease in swollen and tender joints, pain, erythrocyte sedimentation rate and CRP levels. Also, vegan diets have been shown to be clinically beneficial in terms of decreased immune reactivity to certain food antigens in the diet and allergenic foods can increase inflammatory mediators like TNF- $\alpha$  and interleukin-1 [14,20,21,25].

Patients with RA generally have gastrointestinal problems such as bloating, postprandial fullness, nausea, epigastric pain, burning, belching, constipation or diarrhoea and early satiety [26]. In our study, before the intervention, 75% of the participants experienced varying degrees of gastric problems, with 46.8% having them frequently. We observed that the use of *Sunthi* particularly reduced GI problems such as GI upsets, burning sensation and blood in stools. Nanda et al., reported that intestinal mobility was strengthened in 111 patients given 3g of *Sunthi* powder thrice daily with warm water for one month [27]. In a randomized, double-blind controlled trial with 11 dyspeptic patients, Hu et al., [28] observed that ginger stimulated gastric emptying and antral contractions, although fundus dimensions, serum concentrations of GLP-1, motilin and ghrelin were not affected.

In the present study, morning stiffness, pain on rest and during motion, fever and anorexia were reduced. At the end of the study, the number of patients who had severe pain on movement reduced to nil, while there was an increase in the percentage that experienced mild pain. This may be attributed to the digestion of Ama by *Sunthi*/*Trikatu* and mobilization of *vata* from the joints. However, dysuria and digestive upsets increased after treatment, particularly in the *Trikatu* group. This may be attributed to the 'hot' potency of *Trikatu*. As per Ayurveda, *Sunthi* has better *Vata* pacifying action and can be taken for a longer duration.

Diet also influences gut microflora. Recently, an *in vitro* simulated digestion and fermentation model, showed that ginger extract had a prebiotic effect, with the growth of beneficial organisms such as *Bifidobacterium* and *Enterococcus*. Ginger, black pepper and *pipali* (*Piper longum*) all increased the relative abundance of *Bifidobacteriaceae*. Ginger was observed to strongly select for *Coriobacteriaceae* that are involved in isoflavone bio-transformation, bile acid conversion, and generation of cholesterol-derived compounds, while black pepper and *pipali* (the latter having a greater impact) induced *Bacteroidaceae*, modulated the relative abundance of taxa that produce butyrate and propionate taxa, and reduced the relative numbers of pathogenic and opportunistic organisms. The authors attributed these effects to the diverse glycans present in these spices that serve as substrates for the microflora [29].

These studies support the use of both *Trikatu* and *Sunthi* in Ayurveda for improving digestive function. *Trikatu* is often used to treat *Agnimandya*/ decreased digestive ability and, ginger is said to strengthen intestinal motility [30]. In our study, the number of patients experiencing digestive disturbances/upsets decreased after treatment. However, *Trikatu* consumption resulted in patients experiencing more severe symptoms than those consuming *Sunthi*. Gogate stated that *Trikatu* can cause stomach ache, abdominal cramping and increase stool frequency [30]. In the present study, none of the patients from the *Trikatu* group had severe digestive problems at baseline, however on Day 7, two patients reported having severe gastric upsets, that may be attributed to '*ushna veerya*' of *Trikatu*.

Fever is considered to be an important sign of *amavata* because the *ama* blocks perspiration channels leading to elevation of body temperature, which is considered to be a defence mechanism of digesting *ama*. After treatment, the percentage of patients having fever reduced, which may be attributed to a reduction of *ama* in the body. Also, the percentage of patients experiencing anorexia reduced, with both *Sunthi* and *Trikatu* being equally effective.

The HAQ-DI scores were considerably lower after the intervention. The *Sunthi* group showed a significant reduction in all indicators *i.e.*, grooming, arising, eating, walking, grip, reach and hygiene-related activities whereas, in the *Trikatu* group, significant improvement was observed for only three activities- grooming, arising and reach. Mishra and Pandya in their review of various treatments reported that *Shunthi kwath* used alone or in combination with castor oil showed significant beneficial effects on subjective criteria like *Sandhishoola* (joint pain), *Sandhishotha* (swelling of joints), *Sandhigraha* (stiffness), *Sparshasahatva* (extreme tenderness in the afflicted joints) as well as in objective criteria such as improvement in handgrip [31], walking time and foot pressure. The modified dietary regime used in the present study may also have contributed to improvement in functionality.

*Sunthi* is generally used more often than *Trikatu* in all formulations for *Amavata*. The present study also showed that *Sunthi* was more effective and was accompanied by fewer side effects than was *Trikatu*. *Trikatu* was tested in the present study because conceptually it was expected that it would have an effect sooner than would *Sunthi*. However, with *Trikatu*, the benefits were seen only between Days 7 and 14, whereas *Sunthi* showed beneficial effects by Day 7 itself. This suggests that there may be a time lag before *Trikatu* exerts its effects and/or the mechanism(s) of action of *Sunthi* and *Trikatu* may differ. In *Trikatu*, piperine is the bioactive substance in both pepper and long pepper.

In conclusion, the results of the present study indicated the effectiveness of *Sunthi* alone or in combination with pepper and long pepper in *Trikatu*. However, a major limitation of the study was the small number of subjects and the high number of dropouts, probably because of the restrictive diet. Subjects who dropped out were asked why they dropped out when they presented to the treating Ayurveda Physician after the study was completed. They all stated that they were not given any medications or *Panchakarma* treatment in contrast to other patients who had received treatment earlier at the hospital and on whose recommendation, they had sought treatment. They

also felt that the diet was too challenging to adhere to, especially because wheat was eliminated. It must be pointed out that all the study participants were habitual wheat eaters who missed consuming *chapati* at both meals. Thus, recommendations for inclusion of the foods advised in the present study need to be considered in modern dietetic practice, the limited food choices may limit adherence to such diets, particularly since RA is a chronic health problem. It would be worthwhile to determine how to modify the diets and make them more consumer-friendly, particularly in the present-day context of easy availability of processed foods. Integrating Ayurveda with a modern system of medicine and modern dietetics for better management of RA/*Amavata* would be worthwhile as there are limitations to treatment with modern medicine.

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