

A REPORT OF RANDOMIZED OPEN LABELED NON CONTROLLED COMPARATIVE STUDY TO ASSESS THE EFFICACY OF THE HOMOEOPATHIC MEDICINE SIMAROUBA GLAUCA IN TREATING RHEUMATOID ARTHRITIS PATIENTS

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Abstract

Rheumatoid arthritis (RA) is the most common inflammatory arthritis and autoimmune disease that is associated with progressive disability, systemic complications, early death and socioeconomic costs. It occurs in 0.5-1.0% of the adult population worldwide and is more common in women. Its Indian prevalence is ranging between 0.19-2.50%. The peak incidence is between the ages of 20 and 40, the most productive years of adulthood. Complex aetiological factors like genotype (50%), environment, age, gender, family history, smoking, etc., can cause RA. These triggers entail several inflammatory cascades leading to persistent synovial inflammation and associated damage to articular cartilages. The efficiency of its treatment can be assessed by the modulation of Erythrocyte Sedimentation Rate (ESR), Rheumatoid Arthritis Factor (RF) and C-Reactive Protein (CRP). In the Review of Homoeopathic Literature it is found that many Homoeopathic Medicines are having such an anti-inflammatory effect. So to prove such effects of the rarely used Homoeopathic Medicine Simarouba Glauca, its different potencies were compared for their effectiveness in controlling the inflammation of Rheumatoid Arthritis Patients. Pre and Post Treatment Investigation results were analyzed statistically. The modulation of ESR and CRP levels were Highly Statistically Significant in both the Treatment Groups A & B with the P Values < 0.00001. The Pre and Post treatment 'Rheumatoid Arthritis Impact of Disease (RAID) Questionnaire Scores' of the patients were independently compared and analyzed. The Results were also Statistically Significant in both the Treatment Groups A & B with the P Values < 0.00001. By the end of the study it was found that both the 2 Potencies of the medicine Simarouba Glauca viz. 6 CH and 30 CH have shown good Anti-inflammatory effect and improved the Quality of Life of the Patients by relieving pain, stiffness, etc.,

Keywords: C-Reactive Protein, Erythrocyte Sedimentation Rate, Homoeopathic Medicines, Rheumatoid Arthritis, Rheumatoid Arthritis Factor, Rheumatoid Arthritis Impact of Disease Questionnaire, Simarouba Glauca 6 CH, Simarouba Glauca 30 CH.

INTRODUCTION

Rheumatoid arthritis (RA) is the most common inflammatory arthritis and autoimmune disease that is associated with progressive disability, systemic complications, early death and socioeconomic costs.[1]

RA occurs in 0.5-1.0% of the adult population worldwide and is more common in women.[2,3] Its Indian prevalence is ranging between 0.19-2.50%. The peak incidence is between the ages of 20 and 40, the most productive years of adulthood.[3,4]

Complex aetiological factors like genotype (50%), environment, age, gender, family history, smoking, etc., can cause RA. These triggers entail several inflammatory cascades leading to persistent synovial inflammation and associated damage to articular cartilages.[5] About 80% of RA patients are Seropositive for Rheumatoid

Factor (Normal range: 0-20 U/ml) and its presence predicts a more aggressive & destructive course.[6]

Patients often complain of pain & early morning joint stiffness lasting >1 hour. Typically the small joints of hands and feet are affected with a polyarticular (>5 joints) symmetric distribution. Later it may affect the large joints.[7] The classical Extra-articular manifestations of RA are also extensive.

The confirmative diagnosis may be done with '2010 American College of Rheumatology / European League against Rheumatism Classification Criteria for RA'.[8]

RA has a significant negative impact on the ability to perform daily activities, including work & household tasks, and health related quality of life. The goal of treatment in RA patients is to eliminate symptoms, slow disease progression and optimize quality of life.

Simarouba galuca (Lakshmi Taru) is a herb well known for its medicinal uses including Rheumatoid Arthritis.[10,11] Recent In-vitro studies have evidenced the anti-inflammatory activity of its extracts in Arthritis Models.[12,13] But no evidence is available for its Human Use. This information intended me to do a Comparative Experimental Study of this medicine in different Homoeopathic potencies, to check its Effectiveness and Anti-inflammatory property in RA patients.

Project Abstract:

- The Project titled “Randomized Open labelled Non Controlled Experimental Study to Assess the Efficacy of the Homoeopathic Medicine Simarouba glauca 6CH and 30CH in the Treatment of Rheumatoid Arthritis Patients” has been shortlisted under “Seed Money Research Project Funding by Vinayaka Mission’s Research Foundation – Deemed to be University, Salem” on the month of August 2021.
- **Institutional Ethics Committee Approval** for the same was **issued on 19.10.2021**.
- This study was also registered under ‘**Clinical Trial Registry of India**’ with the Reference Number: **CTRI/2021/12/038982 on 28/12/2021**.
- The said project was **commenced on 15.02.2022** by getting permission from the Head of the Institution.
- As per the protocol of the study **30 Rheumatoid patients** were selected randomly from Medical Unit IV of the College Hospital and treated between the period from February 2022 to June 2022.
- All the patients were explained in detail about the study and treatment procedures in the beginning itself. ‘Informed Patient Consent’ in English / in their local language was also obtained from each patient.
- The project was **completed on 27.06.2022**.
- No adverse effects were noticed during the study.

Aim:

- To Assess the Efficacy of the Homoeopathic Medicine Simarouba glauca in the treatment of Rheumatoid arthritis.

Objectives:

- To show the efficacy of the Homoeopathic Medicine Simarouba glauca in Acute Pain Management of Rheumatoid Arthritis.
- To show the Positive Modulation (Reduction) of the Erythrocyte Sedimentation Rate (ESR), Rheumatoid Factor (RF) and C-Reactive Protein (CRP) levels of Rheumatoid Arthritis patients after Treated with the Homoeopathic Medicine Simarouba glauca.

MATERIALS & METHODS

Methodology: Randomized Open labelled Non Controlled Experimental Study design of 2 parallel groups.

Patient Selection & Sample design: According to the inclusion, exclusion criteria 30 patients were selected by Random Sampling Method.

Inclusion Criteria

- Patients fulfilling the 2010 American College of Rheumatology / European League Against Rheumatism Classification Criteria for Rheumatoid Arthritis.[8]
- Both Male and Female adult patients were included.
- Patients in the age group of 25 - 75 yrs.[7]

Exclusion Criteria

- Patients with Systemic Complications and Deformities.
- Patients with Extra-articular manifestations.[7,14]
- Patients under Chronic medication for Rheumatoid Arthritis.

Sample Allocation Design: 15 patients were randomly allocated to each Treatment group by 'Pre-coded Concealed Identical Envelops'. [**Group: A** - Simarouba glauca 6CH, **Group: B** - Simarouba glauca 30CH]

Medicines Used: Simarouba galuca

Potency Selection: 6th Centesimal Potency (6CH) & 30th Centesimal Potency (30CH) were selected as this can be prescribed on the basis of 'Pathological Prescription' and in Acute Phase of the Disease.

Prognostic Tool: Pre & Post Treatment Serum ESR, CRP and RF.

Questionnaire used : 'Rheumatoid Arthritis Impact of Disease (RAID) Questionnaire Score' developed by the 'European League against Rheumatism (EULAR)' and Visual Analogue pain Scale Score.

Data Collection: Case taking, investigatory findings, past history & reports of patients from outpatient, inpatient, peripheral center and medical camps of Vinayaka Missions Homoeopathic Medical College were taken.

Operational Design:

- Initial Screening was done by the 'Screening Tool for Inflammatory Joint Disease - An Eight point Questionnaire'. [15] Patients having 3 or more Positive Answers were considered for Diagnostic Criteria Assessment.
- The selected patients were subjected to '2010 - American College of Rheumatology / European League against Rheumatism Classification Criteria for Rheumatoid Arthritis'[8] and those with Criteria Score ≥ 6 were diagnosed as Rheumatoid Arthritis.
- According to the Inclusion & Exclusion Criteria, 30 Diagnosed Patients were selected as Study Samples.
- A general Case taking in a Standard format was taken to evaluate the patients and to rule out any Extra-articular manifestations, Co-morbid diseases or complications.
- The Serum Rheumatoid Factor & Erythrocyte Sedimentation Rate levels of all the 30 Patients were investigated prior to the initiation of treatment. Anti-citrullinated protein antibodies & C-reactive protein were investigated only for those needed.
- Each Patient was assessed by the 'Rheumatoid Arthritis Impact of Disease (RAID) Questionnaire Score'[16] developed by the 'European League against Rheumatism (EULAR)' prior to the initiation of treatment.
- The patients who were already under short term medication for Rheumatoid Arthritis, they were given placebo treatment for 1 month and then included in the study.
- All the patients were explained about the nature of this Study and 'Informed Patient Consent' was obtained from each patient in their Local Language.
- 15 patients were randomly allocated to each Treatment group by 'Pre-coded Concealed Identical Envelops'. [Group-A: Simarouba glauca 6CH, Group-B: Simarouba glauca 30CH]
- 5 Medicated Globules of 30 Size of respective Medicine soaked Pills were prescribed orally in morning & night every day before food to each patient.
- All the patients were followed up at least once a month during the study Period.
- This treatment was given for at least 3 months (90 days) to each patient.
- The patients were explained and educated about Rheumatoid Arthritis and the needed diet & regimen for the same.
- The Prognosis of Patients were assessed by the Serum RF, ESR CRP levels and RAID Questionnaire Scores after the completion of treatment.
- Some Sample Characters like Age Distribution, Gender Distribution, Stimulating Factors, Family History, Clinical manifestations, etc., were also analyzed.

OBSERVATIONS & RESULTS

Table 1a: ESR levels @ 1hr of Patients of Treatment Group-A (Simarouba glauca 6CH)

SI.No.	Before Treatment		After Treatment		Actual Modulation in mm	
	Date	Value/	Date	Value		
1	15.02.2022	44	30.05.2022	18	26	↓
2	17.02.2022	60	01.06.2022	22	38	↓
3	18.02.2022	46	01.06.2022	14	32	↓
4	22.02.2022	48	07.06.2022	18	30	↓
5	24.02.2022	34	13.06.2022	20	14	↓
6	25.02.2022	48	13.06.2022	24	24	↓
7	26.02.2022	54	13.06.2022	20	34	↓
8	28.02.2022	42	13.06.2022	18	24	↓
9	02.03.2022	36	14.06.2022	12	24	↓
10	04.03.2022	36	16.06.2022	22	14	↓
11	14.03.2022	46	17.06.2022	18	28	↓
12	16.03.2022	44	24.06.2022	12	32	↓
13	18.03.2022	46	24.06.2022	08	38	↓
14	19.03.2022	38	24.06.2022	12	26	↓
15	21.03.2022	54	27.06.2022	16	38	↓

Table 1b: ESR levels @ 1hr of Patients of Treatment Group-B (Simarouba glauca 30CH)

SI.No.	Before Treatment		After Treatment		Actual Modulation in mm	
	Date	Value	Date	Value		
1	15.02.2022	40	30.05.2022	22	18	↓
2	16.02.2022	80	30.05.2022	24	56	↓
3	21.02.2022	76	01.06.2022	26	50	↓
4	23.02.2022	44	07.06.2022	14	30	↓
5	23.02.2022	50	07.06.2022	20	30	↓
6	25.02.2022	36	13.06.2022	18	18	↓
7	26.02.2022	40	13.06.2022	14	26	↓
8	01.03.2022	42	14.06.2022	22	20	↓
9	02.03.2022	46	14.06.2022	12	34	↓
10	03.03.2022	48	14.06.2022	16	32	↓
11	14.03.2022	40	17.06.2022	20	20	↓
12	16.03.2022	38	24.06.2022	18	20	↓
13	18.03.2022	38	24.06.2022	14	24	↓
14	19.03.2022	52	24.06.2022	16	36	↓
15	21.03.2022	44	27.06.2022	22	22	↓

Table 2a: Serum RF levels of Patients of Treatment Group-A (Simarouba glauca 6CH)

SI.No.	Before Treatment		After Treatment		Actual Modulation	
	Date	Value	Date	Value		
1	15.02.2022	++	30.05.2022	+	↓	
2	17.02.2022	+	01.06.2022	-	↓	
3	18.02.2022	+++	01.06.2022	++	↓	
4	22.02.2022	+++	07.06.2022	+	↓	
5	24.02.2022	++	13.06.2022	+	↓	
6	25.02.2022	+	13.06.2022	-	↓	
7	26.02.2022	++	13.06.2022	+	↓	
8	28.02.2022	++	13.06.2022	++	↔	
9	02.03.2022	+	14.06.2022	-	↓	
10	04.03.2022	+++	16.06.2022	++	↓	
11	14.03.2022	++	17.06.2022	+	↓	
12	16.03.2022	+	24.06.2022	-	↓	
13	18.03.2022	+++	24.06.2022	+	↓	
14	19.03.2022	++	24.06.2022	-	↓	
15	21.03.2022	+	27.06.2022	+	↔	

Table 2b: Serum RF levels of Patients of Treatment Group-B (Simarouba glauca 30CH)

Sl.No.	Before Treatment		After Treatment		Actual Modulation	
	Date	Value	Date	Value		
1	15.02.2022	++	30.05.2022	++	↓	
2	16.02.2022	+++	30.05.2022	+++	↔	
3	21.02.2022	+	01.06.2022	-	↓	
4	23.02.2022	++	07.06.2022	+	↓	
5	23.02.2022	++	07.06.2022	++	↔	
6	25.02.2022	+	13.06.2022	-	↓	
7	26.02.2022	++	13.06.2022	+	↓	
8	01.03.2022	++	14.06.2022	++	↔	
9	02.03.2022	+++	14.06.2022	+++	↔	
10	03.03.2022	+	14.06.2022	-	↓	
11	14.03.2022	+	17.06.2022	+	↔	
12	16.03.2022	++	24.06.2022	+	↓	
13	18.03.2022	+++	24.06.2022	++	↓	
14	19.03.2022	++	24.06.2022	+	↓	
15	21.03.2022	+	27.06.2022	-	↓	

Table 3a: Serum CRP levels of Patients of Treatment Group-A (Simarouba glauca 6CH)

Sl.No.	Before Treatment		After Treatment		Actual Modulation	
	Date	Value	Date	Value		
1	15.02.2022	16.6	30.05.2022	11.8	↓	4.8
2	17.02.2022	14.0	01.06.2022	7.2	↓	6.8
3	18.02.2022	11.7	01.06.2022	5.5	↓	6.2
4	22.02.2022	9.8	07.06.2022	4.3	↓	5.5
5	24.02.2022	12.0	13.06.2022	8.0	↓	4
6	25.02.2022	15.4	13.06.2022	10.7	↓	4.7
7	26.02.2022	10.9	13.06.2022	3.9	↓	7
8	28.02.2022	7.9	13.06.2022	2.5	↓	5.4
9	02.03.2022	13.2	14.06.2022	7.7	↓	5.5
10	04.03.2022	10.1	16.06.2022	5.9	↓	4.2
11	14.03.2022	11.6	17.06.2022	12.8	↑	-1.2
12	16.03.2022	12.2	24.06.2022	5.1	↓	7.1
13	18.03.2022	19.1	24.06.2022	10.4	↓	8.7
14	19.03.2022	17.0	24.06.2022	11.6	↓	5.4
15	21.03.2022	13.3	27.06.2022	5.7	↓	7.6

Table 3b: Serum CRP levels of Patients of Treatment Group-B (Simarouba glauca 30CH)

Sl.No.	Before Treatment		After Treatment		Actual Modulation	
	Date	Value	Date	Value		
1	15.02.2022	13.9	30.05.2022	7.1	↓	6.8
2	16.02.2022	15.2	30.05.2022	9.0	↓	6.2
3	21.02.2022	8.5	01.06.2022	3.9	↓	4.6
4	23.02.2022	11.4	07.06.2022	4.7	↓	6.7
5	23.02.2022	7.9	07.06.2022	8.0	↔	-0.1
6	25.02.2022	16.2	13.06.2022	10.1	↓	6.1
7	26.02.2022	17.1	13.06.2022	11.2	↓	5.9
8	01.03.2022	9.3	14.06.2022	3.9	↓	5.4
9	02.03.2022	10.2	14.06.2022	6.0	↓	4.2
10	03.03.2022	9.7	14.06.2022	4.8	↓	4.9
11	14.03.2022	19.0	17.06.2022	10.2	↓	8.8
12	16.03.2022	6.7	24.06.2022	2.4	↓	4.3
13	18.03.2022	10.1	24.06.2022	3.7	↓	6.4
14	19.03.2022	12.2	24.06.2022	6.7	↓	5.5
15	21.03.2022	11.4	27.06.2022	7.9	↓	3.5

Table 4a: Questionnaire Scores' of Treatment Group-A (Simarouba glauca 6CH)

Sl.No.	Before Treatment		After Treatment		Actual Modulation	
	Date	Value	Date	Value		
1	15.02.2022	5.68	30.05.2022	1.31	4.37	↓
2	17.02.2022	7.77	01.06.2022	1.37	6.4	↓
3	18.02.2022	7.37	01.06.2022	1.55	5.82	↓
4	22.02.2022	6.77	07.06.2022	0.85	5.92	↓
5	24.02.2022	7.44	13.06.2022	1.34	6.1	↓
6	25.02.2022	8.00	13.06.2022	0.64	7.36	↓
7	26.02.2022	7.13	13.06.2022	1.67	5.46	↓
8	28.02.2022	7.25	13.06.2022	0.45	6.8	↓
9	02.03.2022	6.36	14.06.2022	1.00	5.36	↓
10	04.03.2022	6.23	16.06.2022	0.67	5.56	↓
11	14.03.2022	6.5	17.06.2022	2.37	4.13	↓
12	16.03.2022	5.38	24.06.2022	2.55	2.83	↓
13	18.03.2022	7.73	24.06.2022	2.32	5.41	↓
14	19.03.2022	6.61	24.06.2022	2.38	4.23	↓
15	21.03.2022	6.65	27.06.2022	1.01	5.64	↓

Table 4b: Questionnaire Scores' of Treatment Group-A (Simarouba glauca 30CH)

Sl.No.	Before Treatment		After Treatment		Actual Modulation	
	Date	Value	Date	Value		
1	15.02.2022	4.40	30.05.2022	3.41	0.99	↓
2	16.02.2022	6.89	30.05.2022	2.25	4.64	↓
3	21.02.2022	7.61	01.06.2022	1.84	5.77	↓
4	23.02.2022	8.19	07.06.2022	1.92	6.27	↓
5	23.02.2022	8.24	07.06.2022	4.37	3.87	↓
6	25.02.2022	7.55	13.06.2022	2.65	4.9	↓
7	26.02.2022	7.17	13.06.2022	0.96	6.21	↓
8	01.03.2022	7.13	14.06.2022	2.28	4.85	↓
9	02.03.2022	6.70	14.06.2022	0.80	5.9	↓
10	03.03.2022	6.86	14.06.2022	3.64	3.22	↓
11	14.03.2022	6.89	17.06.2022	1.99	4.9	↓
12	16.03.2022	8.13	24.06.2022	2.65	5.48	↓
13	18.03.2022	7.37	24.06.2022	3.41	3.96	↓
14	19.03.2022	7.25	24.06.2022	1.61	5.64	↓
15	21.03.2022	6.47	27.06.2022	2.06	4.41	↓

Summary of Results:

The Mean Modulation of ESR Levels @ 1hr observed are 28mm and 29mm reduction in Group A & B Respectively. Serum CRP Values have been decreased by 5.4 Units and 5.3 Units respectively in Group A & B. There observed a reduction in RAID Questionnaire Scores by 5.4 in Group A and 4.7 in Group B.

By Statistical Analysis of Variance the modulation of ESR and CRP levels were seen Highly Significant in both the Treatment Groups A & B with the P Values < 0.00001. The RAID Questionnaire Scores were seen also Statistically Significant in both the Treatment Groups A & B with the P Values < 0.00001.

CONCLUSION

This 'Randomized Open labeled Non Controlled Experimental Study to Assess the Efficacy of Simarouba Glauca 6C And 30C in the Treatment of Rheumatoid Arthritis Patients' has proved that the different potencies of Simarouba Glauca had shown a Good Anti-inflammatory effect on Rheumatoid Arthritis patients.

Bibliography

- 1) McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. *New England Journal of Medicine*. 2011-Dec 8;365(23):2205-19.
- 2) Smolen JS, Aletaha D, et.al. Rheumatoid arthritis. *Lancet*[Internet]. 2016; 388 (10055):2023-2038.
- 3) Handa R, et.al. Literature review of rheumatoid arthritis in India. *International journal of rheumatic diseases*. 2016-May;19(5):440-51.
- 4) Carmona L, et.al. (2010). Rheumatoid arthritis. *Best Practice & Research Clinical Rheumatology*, 24(6):733-45.
- 5) Scott DL, et.al. (2010). Rheumatoid arthritis. *The Lancet*, 376(9746):1094-1108.
- 6) Firestein GS. Evolving concepts of rheumatoid arthritis. *Nature*. 2003-May;423(6937):356-61.
- 7) Ankoor S. et.al. Rheumatoid Arthritis. *Harrison's Principles of Internal Medicine*. 19th Edition. McGraw Hill. 2015:2136-37.
- 8) Aletaha D, et al. 2010 Rheumatoid arthritis classification criteria: American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis & rheumatism*. 2010-Sep;62(9): 2569-81.
- 9) <https://www.medassignments.com/rheumatoid-arthritis-7111> (Last accesses 05.07.2021)
- 10) Sharanya VK, et.al. A pharmacological review on simarouba glauca. *Int.J.Pharma.Res.Rev*. 2016-Jun;5:32-6.
- 11) Bhattacharyya RK, Debbarma N, et.al. Medicinal plants-Simarouba glauca and Dillenia indica. *Int.J. Minor Fruits, Medicinal and Aromatic Plants*. 2018;4(2):42-5.
- 12) Jibi Antony, et.al. In vitro anti-arthritic activity on leaves of Simarouba glauca by bovine serum albumin method, *Asian Journal of Phytomedicine and Clinical Research*, 5(1),2017:20-4.
- 13) Sandya S, Biochemical Investigations on anti-arthritic and Matrix metallo-proteinase modulator effect of Simarouba glauca, *International Conference on Homoeopathy and Phytomedicine*, Jan-2020.
- 14) Ralston SH, McInnes IB. Rheumatology and bone disease. *Davidson's Principles and Practice of Medicine*. 22nd edition. Elsevier Churchill Livingstone. 2014:1098.
- 15) Barbour JA, et.al. Evaluation of a screening tool for inflammatory joint disease. *Annals of the rheumatic diseases*. 2003-Feb-1;62(2):187-8.
- 16) Dougados M, et.al. Defining cut-off values for disease activity states and improvement scores for patient-reported outcomes: the example of the Rheumatoid Arthritis Impact of Disease (RAID). *Arthritis research & therapy*. 2012-Jun-1;14(3):R129.