

**PJN**

ISSN 1680-5194

PAKISTAN JOURNAL OF  
**NUTRITION**

**ANSI***net*

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## Clinical Evaluation of Herbal Medicines for the Treatment of Rheumatoid Arthritis

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**Abstract:** Present research work was conducted to study the clinical efficacy of coded herbal medicine Arthritin in comparison with Methotrexate for treatment of rheumatoid arthritis. One hundred patients with rheumatoid arthritis were randomly assigned into two groups, 50 in each group. Test group was treated with Arthritin and control group was treated with Methotrexate. The effect of both drugs for treatment of rheumatoid arthritis was observed before and after treatment. Comparison of data recorded by physician relating to these variables showed significant differences between test and control groups ( $p < 0.05$ ). The efficacy of the test treated medication (Arthritin) was superior as  $p = 0.03$ . Arthritin is more effective than the Methotrexate in the treatment of rheumatoid arthritis.

**Key words:** Rheumatoid arthritis, arthritin, methotrexate, efficacy

### INTRODUCTION

Rheumatoid arthritis is a chronic multi systemic inflammatory disease of unknown etiology characterized by symmetrical polyarthritis, synovitis and joint erosion usually involving peripheral joints. Extra articular manifestations including ocular pulmonary vascular hematologic neurological cardiovascular changes may also be seen (Inai *et al.*, 1999). Rheumatoid arthritis affects all ages and is quite prevalent in all the countries of the world. Methotrexate is utilized to treat rheumatoid arthritis. This medication works by suppressing the immune system. Treatment of rheumatoid arthritis with methotrexate helps to reduce joint damage but it exerts side effects like nausea, vomiting, stomach pain, drowsiness. However, the alternate therapy such as herbal treatment could be another option and may be effective in rheumatoid arthritis. Herbal medicines have been described in traditional texts and used to treat rheumatoid arthritis (Miao *et al.*, 2008). This article describes the currently available scientific evidence that regarding the safety and efficacy and toxic effects, if known, of *Apium graveolens*, *Nigella Sativa L.*, *Smilax China*, *Trigonella foenum graecum L.*, *Zingiber officinale*, *Withania somnifera dunal* and *Colchicum autumnale L.* since these are most commonly used as medicinal agents for the treatment of rheumatoid arthritis or the action of these medicine is likewise Disease Modifying Anti Rheumatic Drugs (DMARD).

### MATERIALS AND METHODS

**Study design:** This case controll examination based study was conducted at Shifa-ul-Mulk Memorial Hospital

for Eastern Medicine on the patient living in the rural areas of 70 villages surrounding Madinat-ul-Hikmah Hamdard University, Karachi. The study has been conducted according to the principles of good clinical practice i.e., a written informed consent was obtained from the patients before enrollment and proper history and clinical examination were recorded at base line and on each follow up. The study was carried out from September 2006 to August 2008. The patients 50 in number were treated with Arthritin and 50 of Methotrexate for twenty four weeks based on randomized clinical trial. Chi-square test and exact fisher test were used to analyze the statistical difference.

**Patients and dosage form design:** The study was carried out on the patients of ages between 25-75 years. The trial was conducted on 100 patients irrespective of socio economic status at outpatient department in Shifaul-Mulk-Memorial Hospital. The patients were divided in control and test group. Control group received Methotrexate (2.5 mg x 3 per week) and the test group received herbal medicine Arthritin Tab. 500 mg (three times per day). Each 500 mg Arthritin tablet contains Each 500 mg Arthritin capsule contains, *Nigella sativa* 75 mg, *Withania somnifera* 75 mg, *Smilax china* 75 mg, *Apium graveolens* 75 mg, *Trigonella foenum graecum* 90 mg, *Zingiber officinale* 90 mg, *Colchicum autumnale* 20 mg. The Arthritin as such comprises of seven different types of botanical drugs the quantity of which were considered on the basis of ethnomedical information as well as pointed out in Hamdard Pharmacopoeia and Tibbi Pharmacopoeia (Said, 1969).

Furthermore Methotrexate 2.5 mg x 3 per week is the recommended dosage form as given in Pharma guide (Ahmed and Mahmood, 2003). The patients suffering from diabetes, hypertension, renal impairment and other musculoskeletal disorders were excluded from this study. As such it was monitored that patients were not suffering from any other serious disease or ailment. The literature search very clearly displayed that Methotrexate is not involved in any way with the food interaction such as vegetables and meat (chicken and fish). The patients were also directed not to consume red meat of any sort.

**Setting:** The therapeutic evaluations of these medicines were conducted after the diagnoses of rheumatoid arthritis on clinical and biochemical evaluation at Shifa-ul-Mulk Memorial Hospital, for Eastern Medicine, Hamdard University. The patients were registered from the general OPD and hospitalized to the clinical ward of the hospital. All the patients selected for the study, were thoroughly examined and clinical history was recorded.

**Sample selection:** The sample was selected from the out patient enrolled in Shifa ul Mulk Memorial Hospital and on the basis of preliminary clinical examination the patients who were suffering from rheumatoid arthritis were referred to the project physician and upon the basis of inclusion and exclusion criteria the patient marked as candidates were selected. The study period include 2 years time from September 2006 to August 2008. Among this population all the patient suffering from rheumatoid arthritis were interviewed immediately and upon their consent to participate they were grouped as case and control groups.

**Data collection:** Data collected for this research work included filling of clinical trial proforma through personal interview, personal observation and use of case record, file and documents. The designed clinical trial proforma specified the clinical feature and information to be filled by the physician for record and utilized in statistical assessment.

**Statistical analysis:** Statistical analysis were performed using SPSS and excel software, the Chi Square Test was determined. All differences were considered statistically significant by generating a 'p-value' from test statistics. The significant result with 'p-value' less than 0.05 was considered as statistically significant.

**Inclusion criteria:** The cases suffering from rheumatoid arthritis were selected on the following lines:

- The patients suffering from rheumatoid arthritis
- Patients between age group of 25-75 years
- Patient having no obvious pathological findings on routine examination
- Patients living in Karachi, Pakistan
- All socio-economical classes including lower, middle and upper

**Exclusion criteria:** The cases suffering from rheumatoid arthritis were excluded on the following lines:

- Patient with concurrent physical illness example uncontrolled hypertension and diabetes
- Patient with hepatic or renal impairment.
- Patient belonging to area outside Karachi because of inherent difficulty in follow up

**Patient characteristics:** These data was collected from September 2006 - August 2008, which completed the clinical trial protocol at baseline. The collected data of 50 patients, the frequency of male patients were 26 (percentage of male 26%) while, 74 were of female patients (percentage of female 74%) were enrolled into the study. These patients have been selected after the adjustment made in all patients according to exclusion and inclusion decisive factor but the completely responding patients as well as shown in Table 1.

All of the patients recruited in this study were categorized in different class interval ranging from 25 years of age to 75 years of age as shown in Table 2. All patients had sign symptoms of rheumatoid arthritis such as joint pain, swelling, stiffness, tenderness, functional disability, night pain.

Table 1: Total No. of patients

Diseases	Treatment group	Sex	Number (n)
Rheumatoid arthritis	Test drug (Arthritin)	Male	16
		Female	34
		Total	50
	Control drug (Methotrexate)	Male	10
		Female	40
		Total	50

Table 2: Distribution of age group in total patients

	Rheumatoid arthritis		Total (n)
	Test (n)	Control (n)	
25-33 Years	10	12	22
33-41 Years	14	18	32
41-49 Years	10	6	16
49-57 Years	8	4	12
57-65 Years	6	8	14
65-73 Years	2	2	4
Total	50	50	100

## RESULTS

Arthritin and Methotrexate were prescribed to 100 patients with rheumatoid arthritis. The primary criteria in evaluating the efficacy was the degree of relief of pain, swelling, stiffness and tenderness how the patients felt after taking the medication. After six months study of patients taking the herbal formulation orally, three times per day, patients reported improved range of motion in their joints and decreased pain, swelling, tenderness, in hands elbows, knees, ankles joints. This study very clearly reveals that in case of rheumatoid arthritis when treated with Arthritin and Methotrexate, the result on the efficacy display that Arthritin is more effective for treatment of rheumatoid arthritis.

Rheumatoid arthritis			
Sign symptoms		After applying test of significance with chi square	p-value (p<0.05)
<b>Joint pain</b>	At base line	No significant difference between test and control groups	0.91
	After treatment	Slight significant difference between test and control drugs	0.045
<b>Swelling</b>	At base line	Slight significant difference between test and control groups	0.036
	After treatment	Significant difference between test and control drugs	0.01
<b>Morning stiffness</b>	At base line	No significant difference between test and control groups	0.177
	After treatment	No significant difference between test and control drugs	1.00
<b>Tenderness</b>	At base line	No significant difference between test and control groups	0.102
	After treatment	No significant difference between test and control drugs	0.75
<b>Functional disability</b>	At base line	Significant difference between test and control groups	0.005
	After treatment	No significant difference between test and control drugs	0.206
<b>Night pain</b>	At base line	No significant difference between test and control groups	1.00
	After treatment	Slight significant difference between test and control drugs	0.015

## DISCUSSION

Methotrexate is commonly used in patient with rheumatoid arthritis but it exerts side effects. In order to overcome this problem, there is a great need to find new medicinal agents, which have good efficacy and less adverse effects. The different medicinal herbs used in this study were selected on the basis of their traditional use in Unani system of medicine. For example *Colchicum autumnale* and *Smilax chinensis* are used to treat rheumatoid arthritis but in addition supplementary herbal drug such as *Withania somnifera* is utilized in immunity, *Zingiber officinale* is anti-inflammatory and *Apium graveolens* is also anti-inflammatory and uricosuric (Chopra *et al.*, 1956). This unicenter trial has been conducted, for comparing the efficacy and safety of two different treatment modalities showed the greater efficacy of coded herbal formulation Arthritin as test drug and Methotrexate administered as control drug for the treatment of rheumatoid arthritis. This study was conducted at Shifa-ul-Mulk Memorial Hospital, for Eastern Medicine, Hamdard University. The primary criteria in evaluating the efficacy was the degree of relief of pain, swelling, stiffness and tenderness how the patients felt after taking the medication. After six months study of patients taking the herbal formulation orally, three times per day, patients reported improved range of motion in their joints and decreased pain, swelling, tenderness, in hands elbows, knees, ankles joints.

The herbal formulation of Arthritin contains ingredients derived from seven herbs and indirect evidences exhibit that it influence various immune functions, such as curtailing inflammatory responses, improving cellular functions and curtailing the production of pro-inflammatory cytokines. With these immunological changes, a patient with arthritis is expected to physically improve in terms of pain and joint swelling within days of an oral medicinal regimen. Reduction of pain and swelling and increased range of joint motion are expected over prolonged daily use of the formulation.

A comparative study was conducted for Arthritin with Methotrexate. Altogether 100 patients who had fulfilled the exclusion and inclusion criteria were administered the test and control drug and similarly were monitored

for follow up. The patients' gender, age and baseline clinical features at the time of enrolment were recorded in both groups. Half of the patients were treated with coded herbal formulation Arthritin and remaining half with Methotrexate administered orally. The effect was evaluated in both groups who took the drug as part of their regular treatment. The degree of pain reduction and other parameters before, during and after the treatment were measured, as well as creatinine clearance before and during the treatment. A disease modifying effect of arthritin was found in all the patients, regardless of age, sex.

**Conclusion:** Arthritin is more effective than the Methotrexate in the treatment of rheumatoid arthritis as determined by p value <0.03. Therefore, control drug showed lesser efficacy than the test drug in its compliance to treat rheumatoid arthritis. The control drug exhibited side effects like gastrointestinal intolerance nausea and vomiting, where the test drug did not display or show any untoward manifestation associated with the use of this medication and found acceptability by all treated patients.

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