

# **FINAL REPORT OF THE STUDY**

## ***EVALUATION OF THE CLINICAL EFFICACY OF ARTHPLUS CAPSULE AND ARTH OIL IN PATIENTS SUFFERING FROM “OSTEOARTHRITIS” OF THE KNEEJOINT***

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## **INTRODUCTION**

“Arthritis” is one of the most common medical problem affecting joints of the knees, hips, spine and hands. The aetiology of osteoarthritis is not clear and differs according to the age, sex, genetic factors, lifestyle changes and obesity. Industrialization, speedy lifestyle and repeated trauma are known to be associated with a higher incidence of osteoarthritis.<sup>1</sup>

The common symptoms of “osteoarthritis” include pain in the joint during or after movement, discomfort in the joint before or during a change in the weather, swelling and stiffness in the joint particularly after using it and bony lumps on the middle or distal end of the joints of the fingers or base of the thumb. No single test can diagnose osteoarthritis as diagnosis is based on a combination of clinical history, physical examination, radiological examination of the joint and if required aspiration of synovial fluid for confirmatory diagnosis.<sup>2</sup>

Osteoarthritis (OA) is a major public health problem, and there are only a few effective remedies available for its management. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed agents for OA; however, the use of NSAIDs is causally associated with numerous Short- and long-term adverse events (ranging from esophagitis, gastritis, Peptic ulceration, hematopoietic disturbances, to renal failure). Similarly, prolonged use of acetaminophen for the symptomatic Management of OA can lead to hepato toxicity or nephro-toxicity.<sup>3,4</sup> In this context the use of herbal formulations get popularity in the management of OA, but only a few comparative clinical trials have been conducted to generate the required evidence establishing their efficacy. “*Arthplus Capsule*” and “*Arth Oil*” are poly herbal formulation recommended for the management of OA.

## Prevalence:

About 13% of women and 10% of men aged 60 years and older have symptomatic knee OA. The proportions of people affected with symptomatic knee OA is likely to increase due to the aging of the population and the rate of obesity or overweight in the general population. During a one year period, 25% of people over 55 years may demonstrate persistent episode of knee pain, in which about one in six have to consult their general practitioner about it in the same time period. About 10% of people aged over 55 years have painful disabling knee OA of whom one quarter is severely disabled. Prevalence of knee OA in men is lower compared with women. This was shown in a Meta analysis of males and females in which the incidence of knee OA in males aged <55 years was lower than females.<sup>5,6</sup>

## Drug Review

The trial drug is a combo of Arthplus capsule and arth oil manufactured by Good Care Pharma Pvt. Ltd., Bagi Mouza, Bishnupur, 24 Parganas and approved by Directorate of ISM Drugs control, Deptt. Of Health & F.W. Govt. of West Bengal and supplied by Goodcare Pharma Pvt. Ltd. 1, Gupta lane, Kolkata-700006.

### Each Arthplus capsule contain-<sup>7,8,9,10</sup>

- |   |  |
|---|--|
| 1. Yogaraj Guggulu –                          | 100 mg. Ref- Bhaishajyaratnavali, Pg-844 |
| 2. Singhanad Guggulu -                        | 200 mg. Ref- Ay. Sarasamgraha, Pg-523    |
| 3. Khurasani Ajwain ( <i>Hyocymus niger</i> ) | 25 mg. Ref- Bhabaprakash, pg-23          |

- |  |                                    |
|--|------------------------------------|
| 4. Shallaki ( <i>Boswellia serrata</i> ) | 100 mg. Ref- Bhabaprakash, Pg.-242 |
| 5. Nirgundi ( <i>Vitex nirgundo</i> )    | 25 mg. Ref- Bhabaprakash, Pg-90    |
| 6. Methi ( <i>Trigonelia foenum</i> )    | 50mg. Ref- Bhabaprakash, Pg-28     |

All these drugs are processed in :-

- |   |                                |
|---|--------------------------------|
| 1. Bala ( <i>Cida cordifolia</i> )          | q.s. Ref- Bhabaprakash, Pg-202 |
| 2. Eranda moola ( <i>Ricinus communis</i> ) | q.s. Ref-Bhabaprakash, Pg- 261 |

### Each 5 ml. of Arth oil contains

Aquas extract of:

- |  |                                     |
|--|-------------------------------------|
| 1. Eranda moola ( <i>Ricinus communis</i> )  | 0.12 gm, Ref-Bhabaprakash, Pg-261   |
| 2. Dhatura panchang ( <i>Dhatura metal</i> ) | 0.125 gm. Ref- Bhabaprakash, Pg-174 |
| 3. Aswagandha ( <i>Withania somnifera</i> )  | 0.125 gm. Ref- Bhabaprakash, pg-219 |
| 4. Satavari ( <i>Asparagus racemosa</i> )    | 0.125 gm. Ref- Bhabaprakash, pg-218 |
| 5. Amra haldi ( <i>Curcuma amada</i> )       | 0.125 gm. Ref- Bhabaprakash, Pg.-70 |
| 6. Vatsanabha ( <i>Aconitum ferox</i> )      | 0.125 gm. Ref- Bhabaprakash, Pg-287 |
| 7. Prasarani ( <i>Paederia foetida</i> )     | 0.125 gm. Ref- Bhabaprakash, Pg-246 |
| 8. Karpoora ( <i>Cinamomum camphora</i> )    | 0.25 gm. Ref- Bhabaprakash, Pg-94   |
| 9. Gandhapuri Taila                          | 0.35 ml. Ref-Adarsh Nighantu,Pg-795 |
| 10. Tarpeen Taila                            | 0.5 gm. Ref- Bhabaprakash, Pg-558   |
| 11. Liquid paraffin (as base)                | q.s. Ref- Indian pharmacopia        |

All the drugs present in Arthplus capsule are having *Vedanahara* (Analgesic), *Sothara* (Anti-inflammatory), *Vatahara* (Nurvine) and nutritive properties and after triturating with the specified decoction its properties enhances.

Apart from these the drugs like *Shallaki*, *Bala* and *Guggulu* present in the capsule enhance the regeneration power of joint capsule and repair the joint cartilages.

The constituent of Arth oil are also having the analgesic, anti-inflammatory and nutritive properties and by applying it locally it reduces the pain and inflammation of the joint.

## CLINICAL STUDY

### MATERIALS AND METHOD

Patients attending the OPD or IPD of Gopabandhu Ayurveda Mahavidyalaya & Hospital, Puri, and Odisha were screened for Osteoarthritis irrespective of their sex, religion, cast etc. Only those patients who fulfilled the inclusion criteria and were ready to give informed consent for the study were registered for the trial in between the age group of 30 to 65 year. A specially designed research case sheet was used for collecting and maintaining different data. 20 patients were randomly allocated to Group-A and were treated with the trial drug Arthplus Capsule for a period of 3 months, 20 patients were also randomly allocated to the Group-B and were treated with Arth oil and another 20 patients were selected randomly and allocated to the Group-C and treated with both Arthplus capsule and Arth oil. Randomization was done by computerized Random number generator. The entire study was completed in a span of six months (November-2015 to April-2016).

### SELECTION CRITERIA

## **A. INCLUSION CRITERIA**

1. Ambulatory patients of both sexes in the age group of 30-65 years.
2. Clinical diagnosis of primary OA of the knee (tibio-femoral joint) based on clinical and radiographic criteria i.e. patients at the time of enrolment in this study had moderate to severe knee pain with or without morning stiffness of <30 minutes duration and radiographic osteophytes with one or more of the following: <sup>11,12,13</sup>
  - a. Marginal lipping
  - b. Narrowing of joint space
  - c. Sharpened articular margin
  - d. Sclerosis i.e. damaged thickened or eburnated sub-chondral bone
3. Clinical symptoms of OA for at least 2 months prior to study entry.

## **B. EXCLUSION CRITERIA**

- Age below 30 years and above 65 years
- Patients with established hypertension, renal, hepatic or cardiac failure.
- On long-term steroid treatment, with biochemical and clinical evidence of RA or gout.
- Grade-II & Grade-III obesity.

## **CONCOMITANT MEDICATION**

Concomitant medications were monitored throughout the study and recorded in the research case sheet. 50 patients took no other drugs, 4 took laxatives, 5 took antacids, and 1 took antibiotics. Most of these medications were taken for very short periods. None of the patients took any known arthritis related medication other than trial drug.

## **INVESTIGATION**

All patients were investigated for their Complete Blood Count (CBC) and X-Ray of the Knee joints before starting and after the completion of the trial. All the tests were performed in NABL accredited laboratory.

## **STUDY DESIGN**

The current study was design in three groups Gr-A (Arthplus Casule) and Gr-B (Arth Oil) and Gr-C (Both Arthplus capsule and Arth Oil). The study was started after obtaining the approval of the Institutional Ethical Committee (IEC). Informed written consent was obtained from every patient before registering them in to the trial.

## **DRUGS AND POSOLOGY**

**Trial group-A:** Arthplus Capsule was orally administered to the patients in the trial group-A in a dose of 2 capsules twice in a day after principal meal followed by Luke warm water for a period of 3 months.

**Trial group-B:** Arth oil was locally applied to the affected joint to the patients in the trial group-B in a dose of 10 ml. in a day for a period of 3 months.

**Trial group-C:** Arthplus Capsule was orally administered to the patients in the trial group-B in a dose of 2 capsules twice in a day after principal meal followed by lukewarm water for a period of 3 months and also Arth Oil is applied locally to the affected joint in a dose of 10 ml twice daily.

## **ASSESSMENT OF THE STUDY**

### **Criteria of Assessment**

The following objective and subjective criteria were follows to assess the improvement of the cases before and after treatments.

Six point Osteoarthritis rating scale<sup>14,15</sup> and X-Ray of the involve knee was done for every patient included in the trial before starting and after completion of the study. Change in these parameters were analysed to get the outcome of the study by using suitable statistical method.

### **STATISTICAL ANALYSIS**

The values of Osteoarthritis rating scale before and after treatment and radiological change before and after were compared using Students Paired t-test. If the p – value was found to be < .05 the result was interpreted as insignificant. If the p – value was found to be < .01 the result was interpreted as significant. If the p – value was found to be < .001 the result was interpreted as extremely significant. All the calculations were done by using Graph pad statistical software.<sup>16</sup>

The overall benefit of the drug was assessed by a specially designed scoring system. A percentage reduction in overall score after treatment (AT) was calculated for every patient. The percentage reduction in overall score was interpreted as per the following grid.

Scores > 80% – Excellent Result

Scores between 56% to 80% – Good Result

Scores between 31% to 56% – Moderate Results

Scores between 6% to 30% – Mild Results

Scores ≤ 5% – Unsatisfactory Result

### **OBSERVATION & RESULT**

20 patients were registered in each treatment group. But there was a drop out of 1 patient from Group-A and 2 patients from Group-B due to different reasons and all patients of Group-C completed their treatments. Therefore total 57 patients have completed the trial.

### **DEMOGRAPHIC DATA**

#### **1. Sex Wise Distribution of Subject**

Sex	No.	%
Male	30	52.63
Female	27	47.37

#### **2. Age group wise distribution of Subject**

Age	No.	%
31-40	4	7.02
41-50	16	28.10
51-60	26	45.61
61-70	10	17.54

#### **3. Addiction Wise Distribution of Subject**

Addiction	No.	%
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No	25	43.86
Alcohol	3	5.26
Tobacco	23	40.35
Others	6	10.53

4. **Occupation Wise Distribution of Subject**

Occupation	No	%
Labourer	12	21.05
Executive	16	28.07
Housework	25	43.86
Business	4	7.02

5. **Socio-economic status Wise Distribution of Subject**

Socio-economic Status	No	%
High	7	12.28
Medium	28	49.12
Low	22	38.60

6. **Habitat**

Habitat	No.	%
Urban	30	52.63
Rural	27	47.37

7. **Body Built**

Body Built	No.	%
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Normal	21	36.84
Over weight	19	33.33
Obese	17	29.83

## EFFECTIVENESS OF TRIAL DRUG

### Group-A

Parameter	Frequency (N)	Degree of Freedom (df)	Mean		Standard Deviation (SD)		↑	↓	t-value	P-value	Interpretation
			B.T.	A.T.	B.T.	A.T.					
Pain	19	18	3.05	1.11	± 0.23	± 0.32		↓	37.00	< 0.0001	Extremely significant
Swelling	19	18	2.68	0.95	± 0.48	± 0.52		↓	16.73	< 0.0001	Extremely significant
Stiffness	19	18	2.74	0.68	± 0.56	± 0.58		↓	17.06	< 0.0001	Extremely significant
Crepitation	14	13	2.50	0.79	± 0.65	± 0.43		↓	13.68	< 0.0001	Extremely significant
Pain during Extention and Flexion	19	18	2.84	1.05	± 0.37	± 0.40		↓	18.62	< 0.0001	Extremely significant
Tenderness	19	18	2.79	0.89	± 0.63	± 0.46		↓	14.56	< 0.0001	Extremely significant
Over all	19	18	15.95	5.26	± 2.07	± 1.41		↓	28.48	< 0.0001	Extremely significant

### Group-B

Parameter	Frequency (N)	Degree of Freedom (df)	Mean		Standard Deviation (SD)		↑	↓	t-value	P-value	Interpretation
			B.T.	A.T.	B.T.	A.T.					
Pain	18	17	3.05	1.17	± 0.24	± 0.38		↓	24.78	< 0.0001	Extremely significant
Swelling	18	17	2.94	1.00	± 0.24	± 0.34		↓	35.00	< 0.0001	Extremely significant
Stiffness	18	17	2.67	1.00	± 0.49	± 0.59		↓	14.57	< 0.0001	Extremely significant
Crepitation	13	12	2.77	1.15	± 0.44	± 0.55		↓	11.50	< 0.0001	Extremely significant
Pain during Extention and Flexion	18	17	2.78	0.94	± 0.43	± 0.24		↓	20.28	< 0.0001	Extremely significant
Tenderness	18	17	2.56	0.89	± 0.51	± 0.32		↓	14.57	< 0.0001	Extremely significant
Over all	18	17	16.00	5.83	± 1.68	± 0.92		↓	26.08	< 0.0001	Extremely significant

### Group-C

Parameter	Frequency (N)	Degree of Freedom (df)	Mean		Standard Deviation (SD)		↑	↓	t-value	P-value	Interpretation
			B.T.	A.T.	B.T.	A.T.					
Pain	20	19	3.20	0.50	± 0.52	± 0.51		↓	25.68	< 0.0001	Extremely significant
Swelling	20	19	2.54	0.20	± 0.83	± 0.41		↓	12.79	< 0.0001	Extremely significant
Stiffness	20	19	3.05	0.75	± 0.51	± 0.55		↓	18.00	< 0.0001	Extremely significant
Crepitation	13	12	2.40	0.92	± 0.52	± 0.28		↓	10.69	< 0.0001	Extremely significant
Pain during Extention & Flexion	20	19	2.95	0.55	± 0.83	± 0.60		↓	15.77	< 0.0001	Extremely significant
Tenderness	20	19	2.85	0.65	± 0.49	± 0.49		↓	18.80	< 0.0001	Extremely significant
Over all	20	19	16.10	3.25	± 1.77	± 1.16		↓	29.40	< 0.0001	Extremely significant

### (Graph showing overall improvement assessment in 3 treatment groups) Performance Grid in 3 different treatment groups

Performance Grid	Criteria	Group-A		Group-B		Group-C	
		No.	%	No.	%	No.	%
Excellent	> 80%	0	0.00	0	0.00	11	55
Good	56% - 80%	17	89.47	16	88.89	9	45
Moderate	31% - 55%	2	10.53	2	11.11	0	0
Mild	6% - 30%	0	0.00	0	0.00	0	0



Unsatisfactory	< 5%	0	0.00	0	0.00	0	0
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## ASSESSMENT OF ADVERSE EFFECT OF TRIAL DRUG

2 patients in Group-A and 3 patients in Group-C were reported mild occasional gastric irritation.

## OBSERVATION HIGHLIGHTS

- The study included both male (30 nos.) and female (27 nos.) patients. But males are more than female patients.
- The Study included patients in the age limit of 30 to 65 years (both inclusive). Patients in the age group of 51 – 60 years were maximum (27) and in the age group of 31 – 40 years were minimum (4).
- Osteoarthritis was found to be well distributed among different occupation. However patients with house work were found to be maximum (25 nos.) & people with business were found to be minimum (4 nos.).
- Osteoarthritis affects all types of Socio-economic classes from society. Medium class being the maximum (49.12%) followed by low and high classes.
- Out of the total registered patients 56.14 % reported some or the other kind of addiction. However tobacco users were maximum among them (40.35 %).
- Osteoarthritis affects both urban (52.63%) and rural (47.37%) population nearly in equal proportion.
- Among 57 nos. of patients 36.84% were normal, 33.33% were overweight and 29.83% were obese.
- Arthplus capsule (Group-A) was found effective in improving all the sign and symptoms OA. The mean scores of pain was reduced from 3.05 to 1.11, swelling reduced from 2.68 to 0.95, stiffness reduced from 2.74 to 0.68, crepitation reduced from 2.50 to 0.79, pain during extension & flexion reduced from 2.84 to 1.05 and tenderness reduced from 2.79 to 0.89. The mean overall score reduced from 15.95 to 5.26. All the above mentioned changes were found to be extremely significant statistically ( $p < 0.0001$ ).
- Arth Oil (Group-B) was found effective in improving all the sign and symptoms of OA. The mean score of pain reduced from 3.05 to 1.17, Swelling reduced from 2.94 to 1.00, stiffness reduced from 2.67 to 1.00, crepitation reduced from 2.77 to 1.15, pain during extension & flexion reduced from 2.78 to 0.94 and tenderness reduced from 2.56 to 0.89. The mean overall score reduced from 16.00 to 5.83 and all the results were found to be extremely statistically significant ( $p < 0.0001$ ).
- The combined use of Arthplus capsule & Arth oil (Group-C) was also found effective in reducing all the sign and symptoms of OA. The mean sores of pain reduced from 3.20 to 0.50, swelling reduced from 2.54 to 0.20, stiffness reduced from 3.05 to 0.75, crepitation reduced from 2.46 to 0.92, pain during extension & flexion reduced from 2.95 to 0.55 and tenderness reduced from 2.85 to 0.65. The overall score reduced from 16.10 to 3.25. Statistically, all these changes were found to be extremely significant ( $p < 0.0001$ ).
- On overall rating of the effectiveness of Arthplus capsule only in OA (Group – A) we got Good results in 89.47 % cases and Moderate result in 10.53 % cases. Arth oil only (Group –B) gave Good result in 88.89% cases and moderate result in 11.11% cases. But the combined use of both Arthplus capsule and Arth oil gave Excellent result in 55% cases and Good result in 45% cases. Therefore in terms of efficacy in the management of OA the combined use of both Arthplus capsule and Arth oil has clear advantage over the single use of either capsule or oil.

- On analysing the incidence of adverse effects we got, only 2 patients in group-A and 3 patients in Group-C having mild occasional gastric irritation but no one has reported adverse effect of any other type.

## DISCUSSION

In the present study we observed that patients in the age group 51- 60 years were highest in number. This may be due to the fact that in this period of life degenerative and senile changes start taking their toll. Females also reach menopause by this age leading to osteoporosis which is a potential risk factor for OA.

Patients with Executive work and House hold works (particularly females) mostly have a sedentary life style which leads to weight gain. We also observed that approximately 63 % of patients were either overweight or obese. This further proves a positive co-relation between body weight and risk of developing OA.

It was further observed that OA is well distributed among all socio-economic groups and urban/rural population.

We observed highly significant result in improving the different sign and symptoms of OA in Group – A in which patients were given oral Arthplus capsule which is a combination of *Yogaraj Guggulu*, *Singhanad Guggulu* and other herbs like *Shallaki*, *Khurashani Ajwain*, *Nirgundi* and *Methi*. The formulation is further processed in decoction of *Bala* and *Eranda Mula*. Both *Yogaraj Guggulu* and *Singhanad Guggulu* are two proven antiarthritic preparations from Ayurvedic Pharmacopia. Their efficacy has been proven beyond doubt in multiple clinical trials. *Methi* and *Khurashani Ajwain* are having agnidipaka action (enhancing effect on both *kosthagni* and *dhatwagni*). *Shallaki*, *Nirgundi*, *Eranda Mula* and *Vala* are important *Vata shamak* (pacifying action on Vata dosha) drugs as described in Ayurvedic texts. Modern science has also proved the analgesic, anti-inflammatory, anti-oxidant and anti-artritic effect of these drugs.<sup>17,18,19,20</sup>

Highly significant result was also observed in Group – B where patients were given Arth oil for local application with gentle massage. According Ayurvedic principles *Taila* (Oil) is the best remedy for *Vatic* Disorders. Maharshi Charak has also advised both external and internal oleation therapy (*snehana*) in the management of *Asthi* and *Sandhigata Vata*.<sup>21</sup> Arth oil is a poly herbal oil formulation containing *Eranda moola*, *Dhatura panchang*, *Aswagandha*, *Satavari*, *Vatsanabha*, *Prasarani* & *Karpura*. Out of these *Karpura* has local counter irritant effect and all others are potential *vata shamak* (analgesic, anti-inflammatory and anti –arthritic) drugs.

The most impressive result was observed in Group – C where patients were given the combination of Arthplus capsule (orally) and Arth oil (locally). The different symptoms of OA not only improved significantly but also the overall improvement was found to be better in comparison to the other two groups. In this group we got Excellent result in 55 % cases and Good Result in 45 % cases which outnumbered the results of other two groups. This is obviously because of the synergistic action of both Arthplus capsule and Arth oil in the comprehensive management of OA.

No adverse effect was noticed in any group except few cases of mild occasional gastric irritation which subsided on its own in due course. Therefore Arthplus capsule and Arth oil are found safe for long term use in the management of OA.

## CONCLUSION

The investigators are quite sure on the efficacy of Arthplus capsule and Arth oil in the management of OA basing on the outcomes of the present study. Both Arthplus capsule and Arth oil are individually capable for improving the sign and symptoms along with the overall wellbeing of patient suffering from OA. However the combined use of Arthplus capsule and Arth Oil can yield much better result. Therefore only mild cases should be prescribed either oil or capsule as per the suitability of patient and disease

condition. But moderate, severe and chronic cases should be prescribed both Arthplus capsule and Arth oil simultaneously for predictable results. Moreover the therapy was found safe in long term use which is an essential condition in the management of OA requiring long term treatment.

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