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Research Article

Clinical Efficacy of Pankajakasthuri Orthoherb Tablets in Managing Various Signs and Symptoms Associated with Patients Diagnosed with Osteoarthritis: Open Clinical Trial

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Abstract

Osteoarthritis is a severe regenerative and inflammatory disease that is common among the aging population worldwide. The current techniques to manage osteoarthritis focus on relieving pain and slowing the progression of the disease. Today, public interest in the use of complementary medicine, especially traditional herbal medicines, has increased. The present study was designed to investigate the efficacy of Pankajakasthuri orthoherb tablets on patients in managing signs and symptoms associated with osteoarthritis. A total of 500 patients were recruited for the study. On the baseline visit, patients were enrolled in the study based on inclusion and exclusion criteria. All enrolled patients were assigned to a single group and were administered with Pankajakasthuri orthoherb tablets, a polyherbal formulation, in a dose of 2 tablets trice daily, orally after meals, for 180 days. The patients were then scheduled for follow-up visits at the second, fourth, and sixth months. On each follow-up visit, the patient's general and systemic physical examinations were performed. Analysis of the data obtained during the baseline and follow-up visits clearly demonstrated that the treatment with Pankajakasthuri orthoherb tablets significantly improved the pain, oedema, stiffness, tenderness and pain with movement associated with osteoarthritis patients. Moreover, our data also clearly demonstrated that prolonged usage of orthoherb tablets at the prescribed dose significantly improved the various symptoms associated with osteoarthritis.

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Keywords: Efficacy; Osteoarthritis; Pain; Oedema; Pankajakasthuri orthoherb tablets

Introduction

Osteoarthritis (OA) is a slowly evolving degenerative and inflammatory disease, highly prevalent, limits health and well-being (especially in the elderly population) and is one of the most common causes of physical incapacity in the world. OA commonly falls under the umbrella term of "degenerative diseases" that are associated with aging. OA is the most common form of arthritis, affecting around 250 million people globally and is one of the leading causes of disability that affects the joints [1]. The prevalence of knee osteoarthritis is about 22–39% in India, and an estimated 32.5 million Americans are affected by it each year [2, 3].

The main symptoms and signs are joint pain, stiffness, limitation on motion, joint deformity, and different degrees of joint inflammation [4]. Various modalities to manage knee joint pain range from conservative management, such as exercise, oral medication, including nonsteroidal anti-inflammatory agents, and joint injections, to surgical treatment. All medications for osteoarthritis have the potential for side effects [5-7] depending on the type of drug or individual involved.

Therefore, to overcome all these issues and find a more harmless and equally efficacious therapeutic option, researchers are considering plants as a source of medicine. Initially, these plant-based medicinal systems formed the foundation of folk or ethno medicines, practiced in India. Concerns regarding the safety and costs of conventional arthritis therapies have sparked interest in natural remedies. In addition, difficulty with chronic pain management in arthritis has led to the investigation of herbal therapies. Herbs may offer a complementary or alternative method for effective and safe treatment.

Pankajakasthuri Herbals India Pvt. Ltd. formulated Orthoherb Tablets, a polyherbal Ayurvedic formulation, that was proven to have a significant role in managing the pain and inflammation in joints due to various etiologies and pathophysiologies like osteoarthritis, polyarthritis, rheumatoid arthritis and other chronic degenerative disorders. This polyherbal formulation contains active herbal ingredients like *Ricinus communis, Adathoda vasica, Aegle marmelos, Azadirecta indica, Sida retusa, Tragia involucrata, Abrus precatorius, Cyclea peltata, Scoparia dulcis* etc.

The present study was designed to investigate the efficacy of Pankajakasthuri Orthoherb Tablets, which has been claimed to be effective in managing the various signs and symptoms associated with osteoarthritis.

Materials and Methods

Study Drug

Pankajakasthuri orthoherb tablets (500 mg tablets) were manufactured on the Pankajakasthuri Herbals India Pvt. Ltd. production line in Poovachal, Kattakada, Trivandrum, Kerala, India.

Study Design

This study was conducted as an open label clinical study at Pankajakasthuri Ayurveda Medical College Hospital, Killy, Kattakada, Trivandrum, Kerala, India.

Ethics Approval and Consent to Participate

The study was approved by the institutional ethical committee. The study was performed in accordance with the protocol, and all subjects provided written, informed consent. The study protocol was approved by the institutional ethical committee and registered with the Clinical Trials Registry, India (CTRI registration number: CTRI/2018/02/012189).

Selection and Inclusion Criteria

The following are the inclusion criteria: Subjects of either gender, aged 18 to 70 years, with OA symptoms for a minimum of 6 months and a maximum of 5 years; Classical Signs and Symptoms of Osteoarthritis - Pain during movement and weight bearing, Swelling, Stiffness. Also fulfilling the classical criteria of Sandhigatavata mentioned in Ayurvedic texts- Shoola i.e., Akunchana prasarana vedana, Shotha and Sthambha; Diagnosed case of OA Knee based on the Kellegren-Lawerence grading scale (Grade-1 & 2); and subjects willing to sign the informed consent form.

Exclusion Criteria

The major exclusion criteria include: Secondary Arthritic conditions, Fractures, Ligament tear, Dislocation, Osteomyelitis, SLE; Tumors Bone density disorders; Anatomical joint deformities, NSAID/Analgesic/steroid treatment for Osteoarthritis; Patients who have undergone major surgery in the affected joint.

Participants who met the inclusion criteria were recruited to the trial.

Interventions and Dosage

The intervention used in this clinical trial was Pankajakasthuri orthoherb. The dosage fixed for Pankajakasthuri orthoherb tablets in the study was 2×500 mg three times daily for a period of six months.

Study Procedures

On the screening visit, the patient's voluntary, written, informed consent was taken and general and systemic examinations were performed. The diagnosis of OA of the knee joint was confirmed by clinical evaluation and radiographs of the knee joint (ACR Diagnostic Criteria for the Diagnosis of OA of the Knee).

On the baseline visit, 500 patients were enrolled who met the inclusion and exclusion criteria. All enrolled subjects were assigned to a single group and were given 'Pankajakasthuri orthoherb tablets' a polyherbal formulation, in a dose of 2 tablets trice daily, orally after meals, for 180 days. Recruited patients were advised to continue their daily activities and exercises that they had been doing before the enrollment and to continue the same until the end of the study period.

Follow-up Assessment

Follow-up visits were scheduled for patients at the second, fourth, and sixth months. On each follow-up visit, the patient's general and systemic physical examinations were performed. Assessment of the symptoms of OA was done on the VAS-OA Index. A global assessment of the overall efficacy of the study treatment was also done by the investigator and the patient on every follow-up visit.

Statistical Analysis

A paired t-test was used to assess changes from baseline measurements for both the primary and secondary outcomes between each treatment group. Student's t-test was used to compare differences between the treatment groups in the change from baseline for continuous outcome measures. $P \leq 0.05$ was used as the level of significance for all analyses. All analyses were performed using PASW Statistics 18 (SPSS Inc., Chicago, IL, USA)

Results

Distribution of Patients According to their Age

Table 1 showed that, according to age, out of 500 patients, 0% were in the age group of 0–16 years. 2.8% were in the age group of 16–30 years. 19.4% were in the age group of 31–45 years. 43.2% were in the age group of 46-60 years. 34.6% were in the age group of 61 or older

Table 1: Distribution of Participants According to Age

Age group	No. of patients	Percentage
00-16	0	0%
16-30	14	2.8%
31-45	97	19.4%
46-60	216	43.2%
61 and above	173	34.6%

Effect of Treatment with Pankajakasthuri Orthoherb Tablets on Signs and Symptoms

The effect of treatment with Pankajakasthuri orthoherb tablets on signs and symptoms associated with osteoarthritis is given below (Tables 2-6). The results of this study clearly demonstrated that Pankajakasthuri orthoherb tablets significantly improved various signs and symptoms associated with OA.

Effect of Pankajakasthuri Orthoherb Tablets on Pain in Osteoarthritis Patients

The mean score of the symptoms was 3.410 before treatment, and it was reduced to 2.436 with a mean difference of 0.974±0.574 on the second month after treatment, and it was further reduced to 0.102 (a mean difference of 3.308±0.605) during the 6th month follow-up period **(Table 2)**. This data showed that 6-month treatment with Pankajakasthuri orthoherb tablets on patients resulted in significant progression of osteoarthritic pain.

Table 2: Effect of Pankajakasthuri Orthoherb Tablets on Pain

Mean of BT	Mean of		Mean difference	%	Paired t test			
					S. D	S. E	t value	p value
3.410	AT-1	2.436	0.974	29%	0.574	0.0281	37.914	<0.001
3.410	AT-2	1.436	1.974	58%	0.734	0.0328	60.156	<0.001
3.410	FU-1	0.102	3.308	97%	0.605	0.0271	122.289	<0.001

Effect of Pankajakasthuri Orthoherb Tablets on Oedema in Osteoarthritis Patients

The mean score of the oedema symptoms before treatment was 2.460, which was reduced to 1.562 with a mean difference of 0.898±0.303 on the second month after treatment, and further reduced to 0.000 (a mean difference of 2.460±0.711) during the sixth month follow-up **(Table 3)**. Thus, it was clear that 6-month treatment with Pankajakasthuri orthoherb tablets on patients resulted in significant progression of osteoarthritic oedema.

Table 3: Effect of Pankajakasthuri Orthoherb Tablets on Oedema

Mean of BT	Mean of		Mean difference	%	Paired t test			
					S. D	S. E	t value	p value
2.460	AT-1	1.562	0.898	37%	0.303	0.0318	66.281	<0.001
2.460	AT-2	0.564	1.896	77%	0.592	0.0265	71.674	<0.001
2.460	FU-1	0.000	2.460	100%	0.711	0.0318	77.374	<0.001

Effect of Pankajakasthuri Orthoherb Tablets on Stiffness in Osteoarthritis Patients

The mean score of the stiffness symptoms before treatment was 3.208, which was reduced to 2.208 with a mean difference of 1.000±0.506 on the second month after treatment, and further reduced to 0.102 (a mean difference of 3.106±0.746) during the sixth month follow-up **(Table 4)**. Thus, it was clear that 6-month treatment with Pankajakasthuri orthoherb tablets on patients resulted in significant progression of osteoarthritic oedema.

Table 4: Effect of Pankajakasthuri Orthoherb Tablets on Stiffness

Mean of BT	Mean of		Mean difference	%	Paired t test			
					S. D	S. E	t value	p value
3.208	AT-1	2.208	1.000	31%	0.506	0.0227	44.150	<0.001
3.208	AT-2	1.358	1.850	58%	0.770	0.0344	53.733	<0.001
3.208	FU-1	0.102	3.106	97%	0.746	0.0333	93.153	<0.001

Effect of Pankajakasthuri Orthoherb Tablets on Tenderness in Osteoarthritis Patients

The mean score of the tenderness symptoms, which was 2.616 before treatment, reduced to 1.490 with a mean difference of 1.126±0.565 on the 2nd month after the treatment, which further reduced to 0.000 (mean difference of 2.616±0.487) during the 6th month follow-up **(Table 5)**. As a result, it was clear that 6-month treatment with Pankajakasthuri orthoherb tablets on patients resulted in significant progression of OA tenderness.

Table 5: Effect of Pankajakasthuri Orthoherb Tablets on Tenderness

Mean of BT	Mean of		Mean difference	%	Paired t test			
					S. D	S. E	t value	p value
2.616	AT-1	1.490	1.126	43%	0.565	0.0252	44.595	<0.001
2.616	AT-2	1.076	1.540	58%	0.499	0.0223	69.023	<0.001
2.616	AT-3	0.000	2.616	100%	0.487	0.0218	120.152	<0.001

Effect of Pankajakasthuri Orthoherb Tablets on Pain on Movement in Osteoarthritis Patients

The mean score of the symptoms, which was 3.336 before treatment, was reduced to 2.360 with a mean difference of 0.976±0.482 on the second month after treatment, and then to 0.102 (a mean difference of 3.234±0.767) on the sixth month follow-up **(Table 6)**.

Table 6: Effect of Pankajakasthuri Orthoherb Tablets on Pain on Movement

Mean of BT	Mean of		Mean difference	%	Paired t test			
					S. D	S. E	t value	p value
3.336	AT-1	2.360	0.976	43%	0.482	0.0215	45.321	<0.001
3.336	AT-2	1.282	2.054	58%	0.783	0.0350	58.695	<0.001
3.336	AT-3	0.102	3.234	100%	0.767	0.0343	94.272	<0.001

Hence it can be concluded that the treatment with Pankajakasthuri orthoherb tablets significantly cured the signs and symptoms associated with OA **(Fig. 1)**

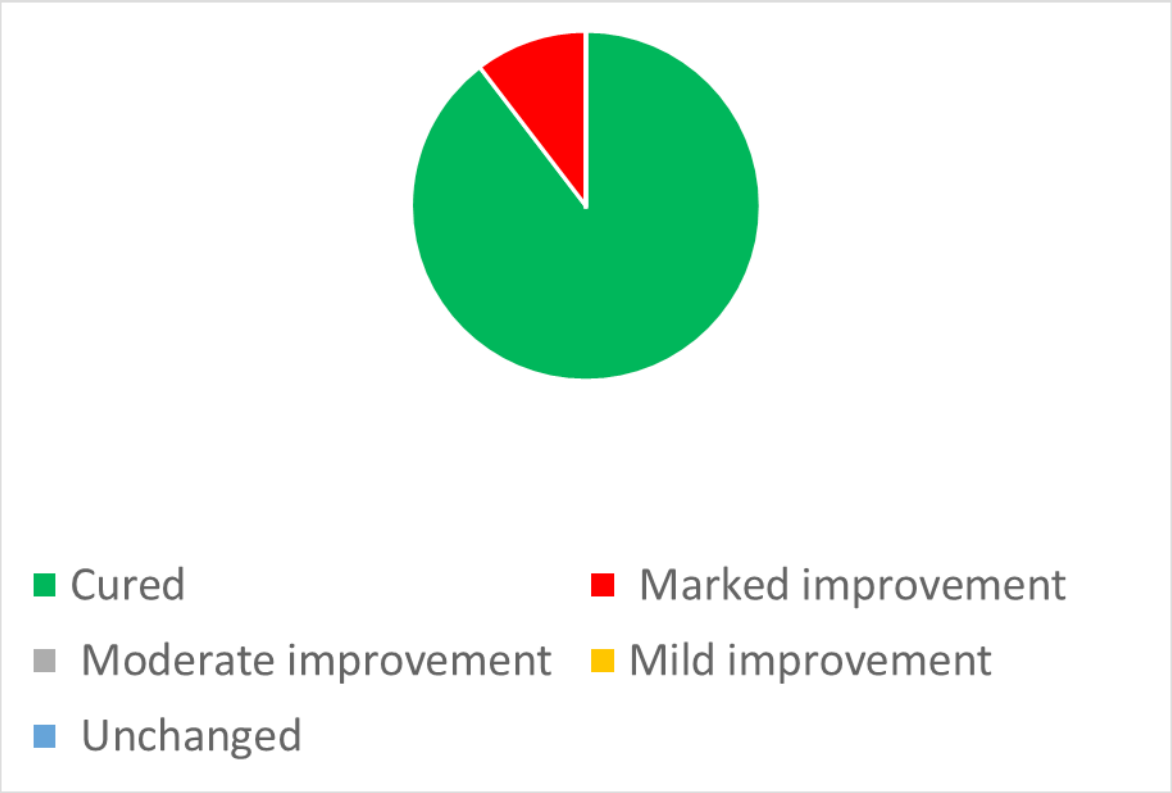

Figure 1: Effect of Prolonged Treatment of Pankajakasthuri Orthoherb Tablets on OA Patients

Discussion

Arthritis is the most common inflammatory disease in elderly individuals. The symptoms are characterized by inflammation, pain, and stiffness mainly in the musculoskeletal system [8]. Pain is the most important symptom of this disease. Many medications for osteoarthritis have the potential for side effects [4-7]. Because of the side effects of oral painkillers, public interest in the use of complementary medicine, especially traditional herbal medicines, has increased [9]. Many herbal remedies are recommended for joint

pain in traditional medical treatises [9, 10]. Therefore, demands for the development of safer medications have increased during the last few decades. As a result, we developed Pankajakasthuri orthoherb tablets, which contain 22 herbs that have previously been shown to be effective in the treatment of rheumatoid arthritis. This study found that Pankajakasthuri orthoherb tablets significantly reduced OA-related knee pain and increased joint mobility.

The improvement in knee mobility could be due to the supplement's effects on reducing inflammation and initiating tissue repair. The increase in joint space width seen is an interesting finding. This suggests that, over and beyond pain reduction, some physiological changes could be contributing to the improvement experienced by the patient. The physiological changes could include-repair or regeneration of connective tissue (collagen/ cartilage) and/or an increase in the secretion of lubricating synovial fluid or changes in the synovial fluid characteristics.

Guggulu (*Commiphora wightii*), one of the major ingredients used for the manufacture of Pankajakasthuri orthoherb tablets, possesses anti-inflammatory and analgesic actions. It helps in the prevention of degenerative changes that may occur in bones and joints due to arthritis. Guggulu reduces inflammation and joint stiffness as well as pain associated with arthritis, and increases joint mobility [11]. Earlier pharmacological studies on Guggulu have established its anti-inflammatory and anti- arthritic activities in formaldehyde-induced arthritis, in albino rats [12]. Significant anti-inflammatory and anti-arthritic activities of oleo-gum resin have been reported against carrageenan-induced rat paw edema, granuloma pouch, as well as adjuvant arthritis [13]. There are several studies that report decreased inflammation and joint swelling after administration of the extracts of Guggulu resin.

Nirgundi (*Vitex nigundo*) possesses analgesic and anti-inflammatory actions [14]. It has been used to treat disorders characterized by shopha (swelling) and shula (pain) in the majority of the nighantus [15]. Its preventive effect on the development of formaldehyde induced experimental arthritis has been observed [16]. The present study supports these earlier observations and recommendations by the Nighantus.

Aegle marmelos (L.) Correa (AM) commonly known as Beal or Bilva belongs to the family Rutaceae has been widely used in Ayurveda for the treatment of Sandhigata vata. The anti-arthritic activity of various *Aegle marmelos* extracts was tested in vitro against protein denaturation against bovine serum albumin and egg albumin. The fruit extract of *Aegle marmelos* showed significantly higher anti-arthritic activity with increasing concentration. The flavonoids and triterpenoids present in *Aegle marmelos* may be the reason for this anti-arthritic activity. Hence, *Aegle marmelos* can be used as an anti-arthritic agent [17].

Eranda (*Ricinus communis*) leaf extract shows a significant antiarthritic effect at the 200mg/kg and 400mg/kg dose levels. It is possible that this is due to the presence of phytochemicals such as flavonoids and saponins.10 The results of an 80% methanolic extract (500 mg/kg) and total flavonoid fractions (50 mg/kg) were on par with diclofenac sodium (20 mg/kg). *Ricinus communis* leaves have anti-inflammatory potentials, and flavonoids dominate this activity in the extract [18].

Pashanabheda (*Curculiginis orchioides*) curculigoside exhibited significant anti-arthritic activity in vivo and in vitro. This may be mediated by inhibition of pro-inflammatory cytokine release and downregulation of JAK/STAT pathway proteins, as well as an increase in NF-κB and IκB expression. According to the findings of this study, curculigoside could be considered a potential candidate drug for arthritis treatment [19].

The extract of Punarnava (*Boerhaavia diffusa*) possesses potentially useful anti-arthritic activity in Complete Freunds Adjuvant model. Study has shown that 1000 mg petroleum ether extract of roots of *B. diffusa* shown 81.58 % response as comparable to standard drug (Indomethcin) and 500 mg petroleum ether extract of roots of *B. diffusa* shown 41.92 % as comparable to standard [20].

Conclusion

This study demonstrated that Pankajakasthuri orthoherb tablets improve OA symptoms and can be an effective treatment option for patients with OA. Since this formulation consists of herbs, it can be taken long-term, without the side effects associated with other pain medications.

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