Original Article

A clinical study to evaluate efficacy and safety of AHPL/AYTAB/0313 tablet in subjects suffering from osteoarthritis of knee(s)

Sanjay U. Nipanikar[1], Shailesh Deshpande[2], Ashutosh H. Bhosale[3], Mayura V. Jadhav-Shinde[4]

[1]Medical Services Department, Head R and D, Ari Healthcare Pvt. Lt, Unit No.-401, International Biotech Park, BTS 2 Building, Chrysalis Enclave, 4th Floor, Plot No. 2A, MIDC, PhaseII, Hinjewadi, Departments of [2]Kayachikitsa, [3]Orthopedic Surgery, and [4]Panchakarma, Pune District Education Association's, College of Ayurved and Research Centre and Hospital, Sector No. 25, Pradhikaran, Nigdi, Pune, Maharashtra, India

Abstract

Background: Osteoarthritis (OA) is the most common form of arthritis with unsatisfactory treatment outcomes. **Objectives:** To evaluate efficacy and safety of AHPL/AYTAB/0313 tablet in subjects with OA of knee joint. **Study Design:** Prospective, open-label, single-arm clinical study conducted in daily clinical practice setting. **Method:** Subjects were advised to take 2 AHPL/AYTAB/0313 tablets twice daily orally after meals for 180 days. 48 subjects completed the study. The primary endpoints were changes in mean visual analogue scale (VAS) pain score and WOMAC score. Secondary endpoints were quality of life, time to walk 50 feet, knee joint swelling, use of analgesic drug as rescue medicine, and safety parameters. **Results:** At baseline visit, the mean index knee joint pain (VAS) score was 82.29 ± 15.19, which reduced significantly to 19.38 ± 13.75 on day 180. The mean WOMAC combined score at baseline was 39.94 ± 11.67, which reduced significantly to 09.58 ± 05.77 (76.0%) on day 180. The mean WOMAC pain score at baseline was 09.65 ± 02.91, which reduced significantly to 02.06 ± 01.46 on day 180. The mean WOMAC stiffness score at baseline was 03.48 ± 01.58, which reduced significantly to 00.63 ± 01.08 on day 180. The mean WOMAC difficulty score at baseline was 26.81 ± 09.63, which reduced significantly to 06.90 ± 04.78 on day 180. The mean walking time to walk 50 feet reduced significantly by 40% on day 180. Not a single subject was known to have knee joint swelling from 150 days onwards. Only 5 subjects were using analgesic as rescue medicine on day 180. Twenty-six subjects had adverse events (AEs). Most of the AEs were not associated with the study medication. Vitals and all the safety laboratory parameters were within normal limits both at baseline and on day 180. **Conclusion:** "AHPL/AYTOP/0113" tablet is safe and significantly effective in reducing pain, swelling, and stiffness of knee joints and improving mobility of knee joints in patients with OA. CTRI registration No. is CTRI/2015/09/006177.

Keywords: AHPL/AYTAB/0313, clinical study, mobility, osteoarthritis of knee, VAS, WOMAC

Introduction

Osteoarthritis (OA) is a chronic degenerative joint disease characterized by loss or injury of articular cartilage, subchondral thickening, hypertrophy of bone, and alterations of the synovial membrane and joint capsule.[1] OA is estimated to be the eighth leading cause of disability in the world.[2] It is more common in

Address for correspondence: Dr. Sanjay U. Nipanikar, Medical Services Department, Head R and D, Ari Healthcare Pvt. Lt, Unit No.401, International Biotech Park, BTS 2 Building, Chrysalis Enclave, 4th Floor, Plot No.2A, MIDC, PhaseII, Hinjewadi, Pune, Maharashtra - 411 057, India.
E-mail: sanjay.n@arihealthcare.in

Received: 09-10-2018 **Revised:** 13-12-2019
Accepted: 16-12-2019 **Published:** 28-01-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_321_18

How to cite this article: Nipanikar SU, Deshpande S, Bhosale AH, Jadhav-Shinde MV. A clinical study to evaluate efficacy and safety of AHPL/AYTAB/0313 tablet in subjects suffering from osteoarthritis of knee(s). J Family Med Prim Care 2020;9:61-8.

women than men. According to a report in year 2010, all over the world, 100 million people suffered from OA. In India, OA is the most frequent joint disease with prevalence of 17% to 60.6%.[2] In addition, it is the second most common rheumatological problem in India.[1]

Presently very few underlying factors are known to cause OA. But, some common factors such as age, sex, obesity, genetics, bone density, smoking, and local factors including trauma are contributors in the pathogenesis of OA. These factors initiate alterations in the equilibrium of cartilage formation and enhance degenerative cascade, thus cause OA.[1,3]

NSAIDs, analgesics, and paracetamol are considered to be the first-line therapy in the management of OA. COX-2 inhibitor is one of the commonly used treatment methods for OA. In addition, the symptomatic slow-acting drugs for OA (SYSADOA) such as diacerein, hyaluronic acid (HA), and chondroitin sulfate are useful in OA management.[4] Intra-articular corticosteroid injections are believed to be the most effective in patients with evidence of inflammation, effusion, or both. Currently, though pharmacological, mechanical, and surgical interventions are used, there is no known cure for OA. Also, long term use of NSAIDS and steroids may lead to many side effects. Thus, physicians and patients tend to move toward alternative treatment methods.[4-6]

Sandhigat Vata in Ayurveda can be correlated to OA. According to Ayurveda, *Sandhigat Vata* starts with pain in one joint but subsequently spreads to other joints. In Ayurveda, various local as well as oral treatment methodologies have been used in the management of *Sandhigat Vata*. Several plants such as *Shallaki*, *Ashvagandha*, *Guggulu, Rasna, Nirgundi, Eranda*, *Guduchi*, *Shunthi*, etc., have been commonly used to treat OA.[7-9]

Keeping in mind the basic concept of Ayurveda, Ari Healthcare Pvt. Ltd., has developed "AHPL/AYTAB/0313" tablet (Marketed as Ariflex Tablet) for effective management of various types of arthritis. AHPL/AYTAB/0313 tablet is a unique, safe, and effective formulation for the treatment of arthritis of varied etiology such as osteoarthritis, rheumatoid arthritis, gouty arthritis, lumbago, sciatica, and spondylosis. The ingredients of AHPL/AYTAB/0313 tablet possess anti-inflammatory, analgesic, antipyretic, chondroprotective, anti-osteoporotic, immunomodulator, anti-oxidant, rejuvenating, and anti-stress activities. These multiple activities of the ingredients present in the formulation help to reduce inflammation and pain in arthritis of varied etiology.[10-14]

Looking at the activities of the ingredients present in AHPL/AYTAB/0313 tablet, a hypothesis was postulated that AHPL/AYTAB/0313 tablet would be helpful in the management of OA. Hence, to test this hypothesis, a clinical study titled "A Clinical study to evaluate efficacy and safety of AHPL/AYTAB/0313 tablet in subjects suffering from Osteoarthritis of Knee(s)" was planned.

Materials and Methods

This study was approved by Institutional ethics committee (IEC) of Ayurved College and Research Center, Nigdi, Pune on 01.09.2015. The study was conducted between Jan 2016 and Jan 2017 in accordance with GCP guidelines (AYUSH). The CTRI registration No. is CTRI/2015/09/006177 [Registered on: 11/09/2015]. Male and female participants of age between 30 and 65 years (both inclusive) with confirmed diagnosis of OA by radiograph and ACR diagnostic criteria for the osteoarthritis of the knee (s) were recruited in the study.

Subjects suffering from rheumatoid arthritis, gout, pseudogout, inflammatory arthritis, Paget's disease of bone, chronic pain syndrome, fibromyalgia, or another major joint disease were excluded from the trial. Subjects with the history of surgery, including arthroscopy, or major trauma to the study joint in the previous 6 months before the screening visit, and subjects requiring knee arthroplasty within 6 months of screening or anticipating any need for a surgical procedure on the index joint during the study were excluded from the study. Subjects with signs of clinically important active inflammation of the study knee joint including redness, warmth and/or a large, bulging effusion with the loss of normal contour at the screening and/or baseline visits, subjects using systemic corticosteroids within 2 months of screening or intraarticular visco-supplementation within the past 3 months, subjects who used any other investigational drug within 1 month prior to randomization, subjects with known major medical or surgical disease, known hypersensitivity to ingredients used in study drug, subjects with significant abnormal laboratory parameters, diabetes mellitus, tuberculosis, HIV, ischemic heart disease, and ECG demonstrating any signs of uncontrolled arrhythmia/acute ischemia were excluded from the trial. Pregnant and lactating women were also excluded from the trial.

Sample size calculation was based on the assumption that a sample size of 46 evaluable cases provides 80% power to estimate the reduction of mean change in knee joint pain on visual analogue scale (VAS) and WOMAC Index at 5% level of significance. Considering 20% dropout rate, we planned to enroll 56 subjects to get 46 completers at the end of the study.

The study included a washout period of 7 days from screening visit (day-7) followed by baseline visit (Day 0), visit 1 (Day 30), visit 2 (Day 60), visit 3 (Day 90), visit 4 (Day 120), visit 5 (Day 150), and visit 6 (Day 180).

On screening visit, subject's written informed consent was obtained, demographic data were recorded. *Dosha Prakriti Parikshan*, general and systemic examinations were done. History of any concomitant medical illness, medications, and surgery during last 6 months was recorded. Subjects underwent investigations such as RA test, serum uric acid, and X-Ray (AP and lateral view) of index/selected knee. Subject's knee joint (s) pain was assessed on VAS. Knee joint swelling was assessed on graded scale. 50 feet walk test was conducted and recorded in the CRF. Subjects

underwent investigations, namely, ECG, fasting blood sugar, CBC, ESR, Hb%, liver function tests, renal function tests, lipid profile, urine routine and microscopic, urine pregnancy test (only if the subject was female of childbearing potential), and HIV test.

During washout period and the whole study period, subjects were advised to refrain from NSAID'S or any other local or systemic analgesics, steroids, Ayurvedic, Homeopathy, Unani, Siddha Medicine, Nutraceutical, and food supplements for OA of Knee except tab Paracetamol (up to 2 gm/day) or any standard analgesic drug as a rescue medication in case of severe joint pain.

On baseline visit and on every follow-up visit, subjects underwent general and systemic examinations. Subjects were assessed for knee joint (s) pain on VAS. Subject's joint pain, stiffness, and physical function were assessed on WOMAC Index. Subject's knee joint swelling (grade: 0 = none, 1 = mild, 2 = moderate, 3 = severe.), quality of life (SF-36 questionnaires), and 50 feet walk test were assessed. Two HDPE containers each containing 60 AHPL/AYTAB/0313 tablets (composition details are provided in Table 1) were provided to subjects every month for 6 months and advised to take 2 tablets twice daily orally after meals with water for 180 days. On every follow-up visit, empty containers were collected and drug compliance was checked. Use of paracetamol or any standard analgesic drug as a rescue medicine was recorded in the CRF. Subjects were closely monitored for any adverse event. Subject's and Investigator's global evaluation for overall improvement was done. Tolerability of the study drug was assessed by the investigator and subjects at the end of study. All the safety investigations were repeated at the end of the study.

The primary efficacy endpoints were to assess the change in knee joint pain on VAS scale, and to assess the changes in WOMAC Index. Secondary endpoints included change in quality of life on SF-36 questionnaire, time to walk 50 feet on even surface, knee joint swelling on graded scale, global assessment for overall improvement by subjects and by physician at the end of the study, use of analgesic drug as rescue medicine, drug tolerability by subjects and by physician, assessment of adverse events, and laboratory investigations.

Summary statistics were used to analyze the demographic and baseline data. Demographic variables such as age, weight, and height were assessed by one way of ANOVA. The efficacy and safety parameters were analyzed by using Student *t*-test and Chi-square test. All *P* values were reported based on two-sided significance test and all the statistical tests were interpreted at 5% level of significance.

Results

A total of 82 subjects were screened for recruitment, out of which 69 were found eligible and recruited in the study. Forty-eight (48) subjects completed the study, out of which, 9 (18.8%) were males and 39 (81.2%) were females. The mean age was 53.88 ± 7.85 years and the mean weight was 66.35 ± 10.99 Kg.

Table 1: Ariflex (AHPL/AYTAB/0313) tablet composition

Ingredients	Botanical name	Quantity
Shallaki Gum Resin Extract	*Boswellia serrata*	110 mg
Guggulu Gum Resin Extract	*Commiphora mukul*	100 mg
Rasna Leaf Extract	*Pluchea lanceolata*	65 mg
Ashvagandha Root Extract	*Withania somnifera*	65 mg
Nirgundi Leaf Extract	*Vitex negundo*	60 mg
Guduchi Stem Extract	*Tinospora cordifolia*	55 mg
Eranda Root Extract	*Ricinus communis*	50 mg
Shunthi Rhizome Extract	*Zingiber officinale*	20 mg

Table 2: Changes in mean VAS pain score

Duration in days	Mean VAS pain score ($\bar{X}$±SD) (*n*=48)
Baseline	82.29±15.19
30	71.46±15.71
60	60.42±18.56
90	51.98±21.16
120	43.75±19.75
150	30.00±17.14
180	19.38±13.75
Mean Diff.(Baseline-30) (*P*)	*-10.83±09.42 (0.001)
Mean Diff.(Baseline-60) (*P*)	*-21.87±14.54 (0.001)
Mean Diff.(Baseline-90) (*P*)	*-30.31±15.99 (0.001)
Mean Diff.(Baseline-120) (*P*)	*-38.54±16.37 (0.001)
Mean Diff.(Baseline-150) (*P*)	*-52.29±16.66 (0.001)
Mean Diff.(Baseline-180) (*P*)	*-62.91±17.86 (0.001)

By student *t*-test, *Significant

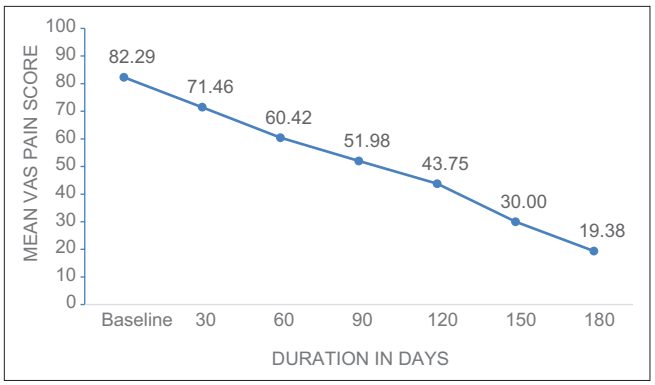

Figure 1: Effect of trial drug on mean VAS pain score

At baseline, mean pain score (VAS) of Index knee was 82.29 ± 15.19. The mean pain score reduced significantly ($P = 0.001$) by 13.2%, 26.6%, 36.8%, 46.8%, 63.5%, and 76.4% on day 30, day 60, day 90, day 120, day 150, and day 180, respectively. The details are presented in Table 2 and Figure 1.

The mean WOMAC combined score at baseline was 39.94 ± 11.67. The mean WOMAC combined score reduced significantly by 20.2%, 38%, 41.7%, 54.9%, 67.4%,

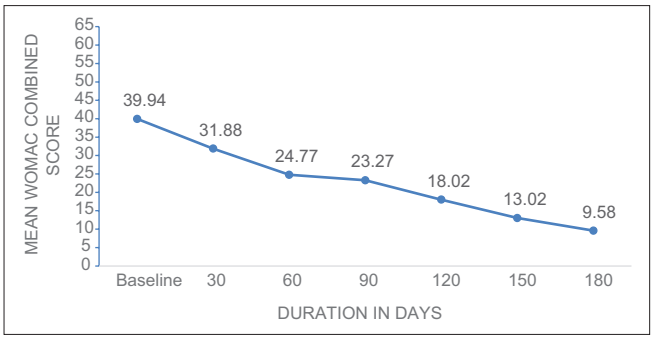

Figure 2: Effect of trial drug on mean WOMAC combined score

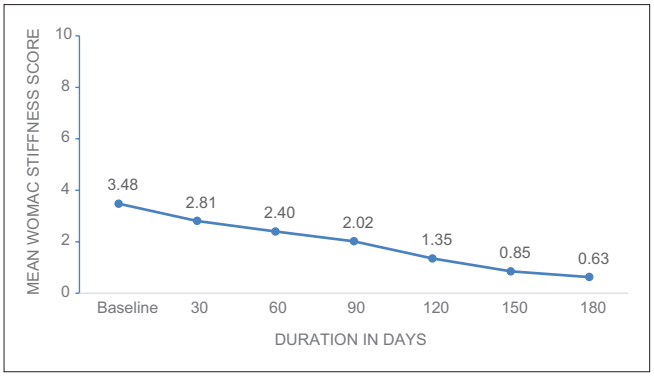

Figure 4: Effect of trial drug on mean WOMAC stiffness score

and 76.0% on day 30, day 60, day 90, day 120, day 150, and day 180, respectively. The details are presented in Table 3 and Figure 2.

The mean WOMAC pain score at baseline was 09.65 ± 02.91. The mean WOMAC pain score reduced significantly by 18.6%, 35.2%, 42.2%, 54.0%, 67.3%, and 78.6% on day 30, day 60, day 90, day 120, day 150, and day 180, respectively. The details are presented in Table 4 and Figure 3.

The mean WOMAC stiffness score at baseline was 03.48 ± 01.58. The mean WOMAC stiffness score reduced significantly by 19.2%, 31.0%, 41.9%, 61.2%, 75.6%, and 81.9% on day 30, day 60, day 90, day 120, day 150, and day 180, respectively. The details are presented in Table 5 and Figure 4.

The mean WOMAC difficulty score at baseline was 26.81 ± 09.63. The mean WOMAC difficulty score reduced significantly by 20.9%, 39.8%, 41.5%, 54.4%, 66.3%, and 74.3% on day 30, day 60, day 90, day 120, day 150, and day 180, respectively. The details are presented in Table 6 and Figure 5.

Quality of life of recruited subjects was assessed using SF-36 Questionnaire. After completion of the study, significant improvement in limitation of activities, problems faced during daily activities due to physical health or emotional health, interference by pain perceived in normal work, social activities, energy, and emotions were observed. These parameters altogether were considered to reflect the overall quality of life of the individual.

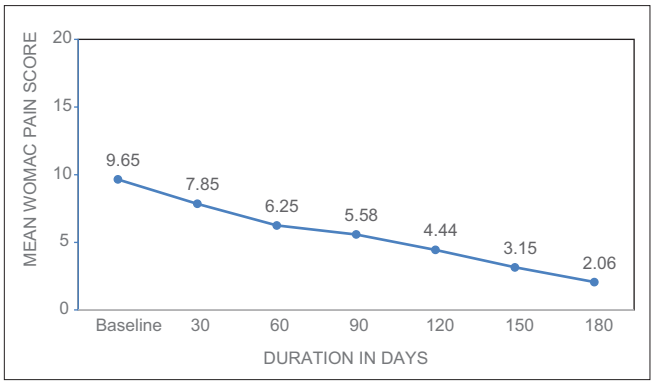

Figure 3: Effect of trial drug on mean WOMAC pain score

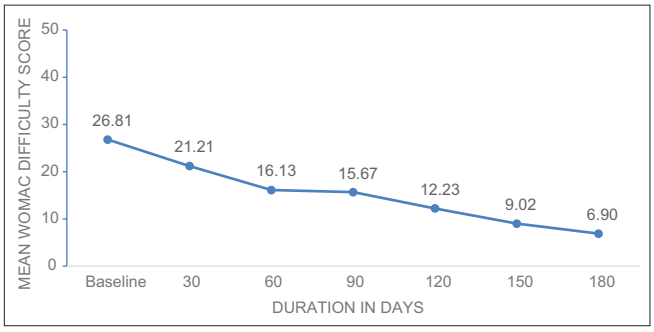

Figure 5: Effect of trial drug on mean WOMAC difficulty score

Table 3: Changes in mean WOMAC Combined score

Duration in Days	Mean WOMAC combined score ($\bar{X}$± SD), (*n*=48)
Baseline	39.94±11.67
30	31.88±11.23
60	24.77±10.28
90	23.27±11.25
120	18.02±08.60
150	13.02±06.94
180	09.58±05.77
Mean Diff.(Baseline-30) (*P*)	*-08.06±09.67 (0.001)
Mean Diff.(Baseline-60) (*P*)	*-15.17±12.53 (0.001)
Mean Diff.(Baseline-90) (*P*)	*-16.67±12.31 (0.001)
Mean Diff.(Baseline-120) (*P*)	*-21.92±11.47 (0.001)
Mean Diff.(Baseline-150) (*P*)	*-26.92±12.02 (0.001)
Mean Diff.(Baseline-180) (*P*)	*-30.36±11.61 (0.001)

By student *t*-test, $P<0.05$, *Significant

The mean walking time to walk 50 feet on flat surface at baseline was 28.40 ± 08.99 s. The mean walking time to walk 50 feet on flat surface reduced significantly by 8%, 14%, 20%, 27%, 33%, and 40% on day 30, day 60, day 90, day 120, day 150, and day 180, respectively.

At baseline visit, 2.1%, 22.9%, 56.2%, and 18.8% subjects had severe, moderate, mild, and no knee joint swelling, respectively. Significant change in the proportion of subjects having knee joint swelling was observed from day 30 onwards and after 150 days, not a single subject was known to have knee joint swelling. The details are presented in Table 7.

Table 4: Effect of trial drug on mean WOMAC pain score

Duration in Days	Mean WOMAC pain score ($\bar{X}$±SD), (*n*=48)
Baseline	09.65±02.91
30	07.85±03.24
60	06.25±02.79
90	05.58±02.70
120	04.44±02.37
150	03.15±01.96
180	02.06±01.46
Mean Diff.(Baseline-30) (*P*)	*-01.80±01.98 (0.001)
Mean Diff.(Baseline-60) (*P*)	*-03.40±02.46 (0.001)
Mean Diff.(Baseline-90) (*P*)	*-04.07±02.68 (0.001)
Mean Diff.(Baseline-120) (*P*)	*-05.21±02.70 (0.001)
Mean Diff.(Baseline-150) (*P*)	*-06.50±03.00 (0.001)
Mean Diff.(Baseline-180) (*P*)	*-07.59±02.87 (0.001)

By Student *t*-test, *Significant

Table 5: Effect of trial drug on mean WOMAC stiffness score

Duration in Days	Mean WOMAC stiffness score ($\bar{X}$±SD), (*n*=48)
Baseline	03.48±01.58
30	02.81±01.51
60	02.40±01.45
90	02.02±01.48
120	01.35±01.04
150	00.85±00.92
180	00.63±01.08
Mean Diff.(Baseline-30) (*P*)	*-00.67±01.43 (0.002)
Mean Diff.(Baseline-60) (*P*)	*-01.08±01.81 (0.001)
Mean Diff.(Baseline-90) (*P*)	*-01.46±02.02 (0.001)
Mean Diff.(Baseline-120) (*P*)	*-02.13±01.71 (0.001)
Mean Diff.(Baseline-150) (*P*)	*-02.63±01.68 (0.001)
Mean Diff.(Baseline-180) (*P*)	*-02.85±01.92 (0.001)

By Student *t*-test, *Significant

Table 6: Effect of trial drug on mean WOMAC difficulty score

Duration in Days	Mean WOMAC difficulty score ($\bar{X}$±SD) (*n*=48)
Baseline	26.81±09.63
30	21.21±08.51
60	16.13±07.63
90	15.67±08.91
120	12.23±06.91
150	09.02±05.71
180	06.90±04.78
Mean Diff.(Baseline-30) (*P*)	*-05.60±08.46 (0.001)
Mean Diff.(Baseline-60) (*P*)	*-10.68±10.63 (0.001)
Mean Diff.(Baseline-90) (*P*)	*-11.14±09.89 (0.001)
Mean Diff.(Baseline-120) (*P*)	*-14.58±09.61 (0.001)
Mean Diff.(Baseline-150) (*P*)	*-17.79±09.55 (0.001)
Mean Diff.(Baseline-180) (*P*)	*-19.91±09.09 (0.001)

By Student *t*-test, *Significant

At baseline visit, 87.5% subjects were using analgesic drug as rescue medicine. Proportion of cases requiring use of analgesic drug reduced significantly to 22.9%, 25.0%, 18.8%, 16.7%, 18.8%, and 10.4% on day 30, day 60, day 90, day 120, day 150, and day 180 of treatment, respectively.

As per investigator's as well as subject's assessment, a total of 87.3% of subjects had excellent to good improvement in terms of remission of signs and symptoms of OA at the end of the study.

As per the investigator's as well as the subject's evaluation, 95.8% subjects reported to have excellent drug tolerability at the end of the study.

Among 69 subjects enrolled in the study, 26 subjects had at least one adverse event. Total 48 adverse events were recorded throughout the study period. Among 48 adverse events, two subjects who suffered from rashes and hyperacidity were reported to have probable association with study medication as per the investigator and they were dropped out from the study prematurely after due course of treatment. One subject suffered from serious adverse event (auto-immune hepatitis) and had to discontinue the treatment. However, as per the investigator, the serious adverse event was not associated with the study medication. The details are presented in Table 8.

No significant change from baseline to end of therapy in values of any of the vital signs (pulse rate, body temperature, respiratory rate, and systolic and diastolic blood pressure) and body weight was observed.

Significant change in mean hemoglobin, RBC count, differential leucocytes count was observed on day 180 when compared to the baseline values. However, all the values were within normal limits. No significant change in lipid profile, liver function tests, and renal function tests was observed with 180 days of treatment with AHPL/AYTAB/0313 tablets.

Discussion

Significant reduction in the knee joint pain (on VAS) was seen right from day 30 and continued till the end of the treatment. There was 76.4% reduction in the knee joint pain (on VAS) at the end of the study. The results observed on VAS are in line with the results assessed on WOMAC pain score, wherein significant reduction in pain started from day 30 and continued till the end of the study. There was 78.6% reduction in the knee joint pain (WOMAC) at the end of the study. Both these results can be verified by assessing the intake of analgesic medication used by subjects for breakthrough knee joint pain management. Initially, almost all the subjects used analgesic medication for breakthrough knee joint pain management. After one month, only 11 subjects needed analgesic medication and at the end of the study, only 5 subjects required analgesic medication. Among these cases, most of the subjects required rescue medicine to alleviate the pain, which was seen arising due to some unusual or heavy exercise or traveling that occurred in addition to subjects' daily activities.

Table 7: Changes in proportion of subjects with knee joint swelling

Grade	% of Cases with swelling (*n*=48)													
	Baseline		Day 30		Day 60		Day 90		Day 120		Day 150		Day 180	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%
None (0)	9	18.8	*18	37.5	*30	62.5	*39	81.2	*46	95.8	*48	100.0	*48	100.0
Mild (1)	27	56.2	26	54.2	17	35.4	8	16.7	2	4.2	-	-	-	-
Moderate (2)	11	22.9	3	6.2	1	2.1	1	2.1	-	-	-	-	-	-
Severe (3)	1	2.1	1	2.1	-	-	-	-	-	-	-	-	-	-

By Chi-square test, P<0.05, *Significant

Table 8: Adverse events during the trial

Events	No. of subjects (*n*=69)
No of Patients with at least one event	26
Total No. of Events	48
Fever	7
Cough and Cold	4
Constipation	2
Stye on left eye	1
Fullness of Abdomen	2
Pain in Abdomen,	1
Headache	3
Hyperacidity	7
Loose motions	1
Rt. shoulder pain	1
Rt. Breast abscess	1
Rashes	3
Hemorrhoidectomy	1
Polyuria	1
Diarrhea	1
Multiple boils over bowel	1
Eczema over both legs	1
Toothache	3
Boil on left foot	1
Pain	4
Swelling	1
Gall stones	1

Statistically significant reduction in WOMAC stiffness score was observed from day 30 onwards and the reduction continued to be significant till the end of the study. There was 81.9% reduction in WOMAC stiffness score at the end of the study. There were 39 subjects, who had swelling at the beginning of the study. No subject had swelling after 150 days of treatment with AHPL/AYTAB/0313 tablet. Significant reduction in swelling and stiffness of knee joint led to ease in movements of knee joint. The increase in mobility of knee joints leads to a significant reduction in difficulty score. There was 74.3% reduction in WOMAC difficulty score at the end of the study. Combined WOMAC score also reduced significantly from day 30 onwards and there was 76% reduction in combined WOMAC score at the end of the study.

Significant improvement was also seen in the mean walking time to walk 50 feet on flat surface, which reduced from 28.40 ± 08.99 s on baseline to 17.06 ± 05.24 s on day 180. Since the pain, swelling, stiffness, and difficulty in movement of joint reduced with the treatment, resistance offered by the joint during walking could also have minimized, leading to ease in walking reflected by decrease in the walking time.

Improvement in overall quality of life of osteoarthritis subjects was observed after 180 days of treatment with AHPL/AYTAB/0313 tablet. Reduction in suffering from various signs and symptoms of OA like pain, swelling, and difficulty in movements could have led to the improvement in quality of life.

In the present study, no post-treatment significant change in vital parameters (pulse rate, body temperature, respiratory rate, and systolic and diastolic blood pressure) and body weight was seen when compared to baseline visit. Significant change in mean hemoglobin, RBC count, differential leucocytes count was observed on day 180 when compared to the baseline values. However, all the values were within normal limits. No significant change in lipid profile, liver function tests, and renal function tests was observed with 180 days of treatment with AHPL/AYTAB/0313 tablets.

Adverse events such as fever, cough and cold, constipation, hyperacidity, hepatitis (autoimmune) etc., were recorded in 26 subjects. Only 2 subjects had allergic rash and abdominal discomfort, which were reported to have probable association with study medication and were dropped out from the study prematurely after treating the symptoms.

Ingredients[15-24] of AHPL/AYTAB/0313 tablet inhibit COX enzyme and thereby reduce inflammation. *Shallaki* (*Boswellia serrata*) works on lypooxygenase pathway,[25] *Commiphora mukul* inhibits NF-kB activation and decreases the expression of inflammatory cascade in arthritis.[10,26] *W. somnifera* possesses chondroprotective, anti-inflammatory, immunomodulatory and, immunosuppression activities[11,27,28] *Vitex negundo* and *Tinospora cordifolia* reported to possess anti-osteoporotic activity.[29,30] Nirgundi (*Vitex negundo*),[31,32] Shunthi (*Zingiber officinale*),[22,23,33] and Shallaki (*Boswellia serrata*)[24] possess analgesic activity. Thus, the observed significant analgesic and anti-inflammatory activities of AHPL/AYTAB/0313 tablet could be the results of synergetic activities of the herbs present in the formulation.

Conclusion

In the present study, 6 months of use of "AHPL/AYTOP/0113" tablet in subjects suffering from OA is proved to be safe. "AHPL/

AYTOP/0113" tablet is significantly effective in reducing pain, swelling, and stiffness of knee joint in OA subjects. "AHPL/AYTOP/0113" tablet is also significantly effective in improving mobility of knee joints. "AHPL/AYTOP/0113" tablet improves overall quality of life of OA subjects. Thus, "AHPL/AYTOP/0113" tablet is safe and effective in the management of osteoarthritis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Mahajan A, Verma S, Tandon V. Osteoarthritis. JAPI 2005;53:634-41.
2. Radha MS, Gangadhar MR. Prevalence of knee osteoarthritis patients in Mysore city, Karnataka. Int J Recent Sci Res 2015;6:3316-20.
3. Tallheden T, Bengtsson C, Brantsing C, Sjogren-Jansson E, Carlsson L, Peterson L, *et al.* Proliferation and differentiation potential of chondrocytes from osteoarthritic patients. Arthritis Res Ther 2005;7:R560-8.
4. Scheinfeld N. A comprehensive review and evaluation of the side effects of the tumor necrosis factor alpha blockers etanercept, infliximab and adalimumab. J Dermatol Treat 2004;15:280-94.
5. Kongtharvonskul J, Anothaisintawee T, Mcevoy M, Attia J, Woratanarat P, Thakkinstian A. Efficacy and safety of glucosamine, diacerein, and NSAIDs in osteoarthritis knee: A systematic review and network meta-analysis. Eur J Med Res 2015;20:24.
6. Tascioglu F, Armagan O, Tabak Y, Corapci I, Oner C. Low power laser treatment in patients with knee osteoarthritis. Swiss Medical Weekly 2004;134:254-8.
7. Long L, Soeken K, Ernst E. Herbal medicines for the treatment of osteoarthritis: A systematic review. Rheumatology 2001;40:779-93.
8. Sawarkar GR, Suple YV. Prevention and management of osteoarthritis. Int J Res Ayurveda Pharm 2013;4:454-8.
9. Akhtar B, Mahto RR, Dave AR, Shukla VD. Clinical study on Sandhigata Vata w.s.r. to osteoarthritis and its management by Panchatikta Ghrita Guggulu. AYU 2010;31:53-7.
10. Sharma JN. Comparison of the anti-inflammatory activity of Commiphora Mukul (an indigenous drug with those of phenylbutazone and ibuprofen in experimental arthritis induced by mycobacterial adjuvant. Arzneimittelforschung 1977;27:1455-7.
11. Sumantran VN, Kulkarni A, Boddul S, Chinchwade T, Koppikar SJ, Harsulkar A, *et al.* Chondroprotective potential of root extracts of Withania somnifera in osteoarthritis. J Biosci 2007;32:299-307.
12. Singh A, Malhotra S, Subban R. Anti-inflammatory and analgesic agents from Indian medicinal plants. Int J Integr Biol 2008;3:57-72.
13. Subramoniam A, Madhavachandran V, Gangaprasad A. Medicinal plants in the treatment of arthritis. Ann Phytomed 2013;2:3-36.
14. Patel D, Kaur G, Sawant MG, Deshmukh P. Herbal medicine – A natural cure to arthritis. Int J Nurs Res 2013;4:27-35.
15. Cao H, Yu R, Choi Y, Ma ZZ, Zhang H, Xiang W, *et al.* Discovery of cyclooxygenase inhibitors from medicinal plants used to treat inflammation. Pharmacol Res 2010;61:519-24.
16. Alam M, Khan H, Samiullah L, Siddique KM. A review on phytochemical and pharmacological studies of Kundur (Boswellia serrata Roxb ex Colebr.)-A Unani drug. J Appl Pharm Sci 2012;2:148-56.
17. Srivastava P. Chemical standardization of some Anti-inflammatory Rasayana plants used in Indian System of Medicine, Department of Chemistry University of Lucknow, Lucknow, 2013. p. 2-10.
18. Gacche R, Shaikh R, Pund M, Deshmukh R. Cyclooxygenase inhibitory, cytotoxicity and free radical scavenging activities of selected medicinal plants used in Indian traditional medicine. Pharmacogn J 2011;3:57-64.
19. Chattopadhyay P, Hazarika S, Dhiman S, Upadhyay A, Pandey A, Karmakar S, *et al.* Vitex negundo inhibits cyclooxygenase-2 inflammatory cytokine-mediated inflammation on carrageenan-induced rat hind paw edema. Pharmacogn Res 2012;4:134-7.
20. Kumar V, Modi PK, Sharma S. Evaluation of anti-inflammatory activity of Tinospora cordifolia: Role in arthritis. Int J Pharm Res Biosci 20121:193-204.
21. Luseba D, Elgorashi EE, Ntloedibe DT, Van Staden J. Antibacterial, anti-inflammatory and mutagenic effects of some medicinal plants used in South Africa for the treatment of wounds and retained placenta in livestock. South Afr J Botany 2007;73:378-83.
22. Van Breemen RB, Tao Y, Li W. Cyclooxygenase-2 inhibitors in ginger (*Zingiber officinale*). Fitoterapia 2011;82:38-43.
23. Ojewole JA. Analgesic, anti-inflammatory and hypoglycemic effects of ethanol extract of Zingiber officinale (Roscoe) rhizomes (ZIngibiraceae) in mice and rats. Phytother Res 2006;20:764-72.
24. Singh GB, Bani S, Singh S. Toxicity and safety evaluation of boswellic acids. Phytomedicine 1996;3:87-90.
25. Siddiqui MZ. *Boswellia serrata*, A potential antiinflammatory agent: An overview. Indian J Pharm Sci 2011;73:255-61.
26. Singh BB, Mishra LC, Vinjamury SP, Aquilina N, Singh VJ, Shepard N. The effectiveness of Commiphora mukul for Osteoarthritis of the knee an outcome study. Altern Ther Health Med 2003;9:74-9.
27. Rassol M, Varalakshmi P. Immunomodulatory effects of Withania Somnifera root powder on experimental induced inflammation: An *in vivo* and *in vitro* study. Vasc Pharmacol 2001;44:406-10.
28. Singh D, Aggarwal A, Maurya R, Naik S. Withania somnifera inhibits NF-kappa B and AP-1 transcription factors in human peripheral blood and synovial fluid mononuclear cells. Phytother Res 2007;21:905-13.
29. Upadhyay AK, Kumar K, Kumar A, Mishra HS. Tinospora cordifolia (Willd.) Hook. F. and Thoms. (Guduchi) – Validation of the Ayurvedic pharmacology through experimental and clinical studies. Int J Ayurveda Res 2010;1:112-21.
30. Vishwanathan AS, Basavaraju R. A review on Vitex negundo L.-A medicinally important plant. Eur J Biolog Sci 2010;3:30-42.
31. Dharmasiri MG, Jayakody JR, Galhena G, Liyanage SS,

Ratnasooriya WD. Anti- inflammatory and analgesic activities of mature fresh leaves of Vitex negundo. J Ethnopharmacol 2003;87:199-206.

32. Gupta M, Mazumder UK, Bhawal SR. CNS activity of Vitex negundo Linn., in Mice. Indian J exp Biol 1999;37:143-6.
33. Srivastava KC, Mustafa T. Ginger (Zingiber officinale) in rheumatism and musculoskeletal disorders. Med Hypotheses 1992;39:342-8.