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Original Research Article

Efficacy and safety of Amrith Noni Arthoplus in osteoarthritis: a double-blinded, randomized clinical trial

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ABSTRACT

Background: Osteoarthritis (OA) is a chronic, degenerative joint disorder marked by pain, inflammation, and impaired mobility, significantly affecting quality of life. Current treatments often provide limited relief and may have adverse effects with long-term use. This study aimed to evaluate the efficacy and safety of Amrith Noni Arthoplus in individuals with OA through a double-blinded, randomized clinical trial.
Methods: This double-blind, randomized, placebo-controlled study evaluated the efficacy and safety of Amrith Noni Arthoplus, an herbal formulation containing *Morinda citrifolia* (Noni) as the primary ingredient, in 40 patients with osteoarthritis (OA). Efficacy was evaluated using the visual analog scale (VAS) for pain intensity, 6-minute walk test, stair climb test, physician and subject global assessments (PGA/SGA), serum biomarkers (hs-CRP, calcium, phosphorus, magnesium, vitamin D_3), and bone mineral density (BMD) via DEXA scans. Safety was assessed through vital signs, haematology, liver and kidney function tests, and adverse event monitoring.
Results: The active group demonstrated significant improvements in pain intensity (33.82% reduction in VAS scores, $p<0.0001$), physical function (14.17% increase in walking distance, $p<0.0001$), and stair climb time (12.75% reduction, $p<0.0001$) compared to the placebo group. Serum biomarkers, including hs-CRP (31.33% reduction, $p<0.0001$) and bone health markers (calcium, phosphorus, magnesium, vitamin D_3), showed significant improvements. BMD increased by 25.48% in the active group ($p<0.0001$), while the placebo group experienced an 18.10% decline ($p=0.002$). No adverse events were reported, and all safety parameters remained within normal limits.
Conclusions: Amrith Noni Arthoplus significantly alleviates OA symptoms, improves physical function, and enhances bone health, demonstrating its potential as a safe and effective complementary therapy for OA management.

Keywords: Bone mineral density, *Morinda citrifolia*, Noni, Osteoarthritis, Pain management

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease and the most common chronic musculoskeletal disorder worldwide, affecting millions of people, especially the elderly population.[1] It is described as a degenerative process with deterioration of articular cartilage, synovial inflammation, and alteration of underlying subchondral bone affecting joint pain, stiffness, and functional impairment.[2] The burden of OA extends beyond decreased physical and functional capacities; it also negatively impacts patients' quality of life and imposes a significant cost burden on health services.[3] It is important to note that although medical science has developed advanced techniques, controlling osteoarthritis remains challenging. Existing therapeutics are primarily focused on symptom relief rather than disease amelioration.[4]

Current management strategies for OA consist of both non-pharmacological therapies, such as physical therapy,

weight control, and lifestyle changes, with pharmacological treatment (e.g., nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, intra-articular corticosteroids).[5] However, due to limited efficacy and adverse effects, particularly in the long term, these treatments are often poorly controlled.[6] For example, NSAIDs help to reduce pain and inflammation but are associated with complications in the gastrointestinal, cardiovascular, and renal systems.[7] Similarly, the use of opioids for pain management raises concerns due to the risk of dependency and other associated complications.[8] These factors have spurred interest in exploring herbal and natural alternative and complementary therapies, which are perceived to offer safer options for managing OA symptoms.

Amrith Noni Arthoplus, a polyherbal formulation, has emerged as a potential therapeutic option for OA. At the core of this formulation is *Morinda citrifolia*, commonly known as Noni, a plant traditionally used for its anti-inflammatory, analgesic, and antioxidant properties.[9] *M. citrifolia* is rich in bioactive compounds such as iridoids, flavonoids, and polysaccharides, which have been shown to modulate inflammatory pathways, reduce oxidative stress, and promote tissue repair.[10] The anti-inflammatory effects of Noni are thought to be mediated through the inhibition of pro-inflammatory cytokines such as TNF-α and IL-1β, as well as the suppression of cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, which play a key role in the pathogenesis of OA.[9,11] Additionally, *M. citrifolia* has demonstrated antioxidant activity, which may help mitigate oxidative stress associated with cartilage degradation in OA.[12] Preclinical studies have also suggested that *M. citrifolia* extracts can reduce pain sensitivity and improve joint function in animal models of arthritis, further supporting its potential therapeutic benefits.[13] Despite the promising pharmacological properties of *M. citrifolia*, clinical evidence evaluating its efficacy and safety as part of the Amrith Noni Arthoplus formulation in OA patients remains limited. While preliminary studies and anecdotal reports suggest potential benefits, randomized controlled trials are essential to establish its therapeutic value and safety profile. This study aimed to address this gap by conducting a double-blinded, randomized clinical study to assess the efficacy and safety of Amrith Noni Arthoplus in managing OA symptoms.

METHODS

Study design

This study was a double-blinded, randomized clinical trial designed to assess the efficacy and safety of Amrith Noni Arthoplus in patients with OA. Subjects were selected based on predefined inclusion and exclusion criteria. The study included four visits: screening visit (1-2 days prior to randomization), randomization visit (day 0), follow-up visit at week 12, and final visit at week 24. The study protocol and informed consent procedures were approved by the institutional ethics committee (IEC) prior to subject enrolment. Eligible participants were randomized into either the active or placebo group at day 0. The study protocol and informed consent procedures were approved by the Vatsalya Ethics Committee on August 8, 2023. The study adhered to ethical guidelines, including the Declaration of Helsinki, ICMR Ethical Guidelines for Biomedical Research 2006, ICH-GCP, and ASU-GCP. Written informed consent was obtained from all participants before enrolment. The study is registered with CTRI (CTRI/2023/10/058700) dated October 16, 2023.

Study population and sample size

Participants with OA were recruited from the outpatient department (OPD) of Shivnath Hospital, Varanasi, during their routine visits. Participants were selected based on predefined inclusion and exclusion criteria, and eligible subjects were enrolled in the study. The sample size was determined based on practical considerations, with a pre-planned total of 40 evaluable subjects, evenly divided into two groups of 20 participants each.

Inclusion criteria

The study included male and female participants aged between 45-70 years who had been diagnosed with OA in at least one knee. Participants were required to have experienced knee pain for a minimum of 3 months, with a visual analog scale (VAS) score exceeding 4 in the past week. Participants were included if they had no intention of initiating new treatments during the study period, did not use anti-inflammatory or analgesic medications on a regular basis, or were dissatisfied with their current treatments and desired to explore alternative options. Lastly, all participants were required to provide written informed consent and demonstrate willingness to comply with the study protocol.

Exclusion criteria

Participants were excluded from the study if they exhibited rapidly worsening knee symptoms accompanied by a hot, swollen knee, had a history of knee replacement, or had undergone significant trauma, joint injection, or arthroscopy within the past six months. Those who had major surgery in the previous year were also excluded. Additional exclusion criteria included the use of anticoagulants or pain relievers in the past three months and the presence of conditions such as rheumatoid arthritis, septic arthritis, gout, pseudogout, malignancy, severe immobility, or uncontrolled medical issues (e.g., diabetes, hypertension, cardiovascular disease). Furthermore, participants with a history of peptic ulcer disease, gastrointestinal bleeding, or long-term corticosteroid or immunosuppressant use were excluded. Individuals currently enrolled in other clinical trials within the past 30 days, those with known allergies to study drugs, or those with planned surgeries were not eligible. Women

who were pregnant, lactating, or of childbearing potential without adequate contraception were also excluded.

Randomization and blinding

Eligible subjects were randomly assigned to either the placebo group or the test group using a pre-determined randomization code, with a 1:1 allocation ratio. The randomization process was conducted in a double-blinded manner, ensuring that neither the participants nor the study personnel were aware of the group assignments. Both the Amrith Noni Arthoplus and placebo were identical in appearance, taste, and packaging. The randomization codes were securely maintained by an independent biostatistician and remained concealed until the completion of the data analysis phase.

Intervention and dosage

Amrith Noni Arthoplus is a herbal formulation designed to support joint health and alleviate symptoms of OA. It consists of traditional herbs, including noni fruit juice (*Morinda citrifolia*), known for their anti-inflammatory, antioxidant, and analgesic properties. The dosing regimen was designed to gradually increase tolerance and efficacy: during the first week, subjects took 5 ml of Amrith Noni Arthoplus mixed with 50 ml of lukewarm water twice daily on an empty stomach. In the second week, the dosage was increased to 10 ml mixed with 100 ml of lukewarm water twice daily. From the third week onward, subjects received 15 ml mixed with 150 ml of lukewarm water twice daily. All doses were administered half an hour before meals to optimize absorption and effectiveness.

Follow ups

The study involved 4 scheduled visits: screening, randomization, follow-up and final visits. Screening visit (1-2 days prior to randomization) involved obtaining informed consent, assessing eligibility through medical history, physical examinations, vital signs, and laboratory tests (hematology and serum biochemistry). Eligible participants were assigned a unique identifier and scheduled for randomization visit (day 0), where they were randomized into either the study or placebo group. Baseline assessments, including physical examination, vital signs, and efficacy parameters, were recorded. Follow-up visit (week 12), included reassessment through physical examinations, vital signs, adverse event documentation, and efficacy evaluations. Finally, the final visit (week 24), involved a comprehensive assessment of physical health, adverse events, concomitant medications, symptomatic improvement, and laboratory tests (haematology and serum biochemistry) to evaluate both efficacy and safety outcomes.

Assessment of efficacy and safety

The efficacy of Amrith Noni Arthoplus was assessed using multiple parameters across the study visits. The VAS score, 6-minute walk test, stair climb test, and subject/physician global assessment (SGA/PGA) were evaluated at randomization visit, follow-up visit, and end-of-study. Additionally, serum biomarkers such as hs-CRP, vitamin D_3, calcium, phosphorous, and magnesium were measured at these visits, alongside Dexa scans for bone thickness.

Safety assessments included physical examinations and vital signs at all visits, while haematology (routine blood counts) and serum biochemistry (creatinine, BUN, uric acid, bilirubin, AST, ALT, and albumin) were performed at screening and end-of-study. Adverse events were monitored and documented from randomization visit through follow-up visit and end-of-study.

Primary outcomes

The primary outcome measure was the change in pain levels, assessed using the VAS score, from baseline to the end of the treatment period. The VAS score provided a quantitative measure of pain intensity.

Secondary outcomes

Secondary outcomes included a range of measures to evaluate the efficacy of the intervention. Changes in physical endurance were assessed using the 6-minute walk test, while lower limb function was evaluated through the stair climb test. The overall health status and treatment effectiveness were captured using SGA and PGA scores. Additionally, changes in serum levels of hs-CRP were monitored to assess inflammation, and biochemical markers such as vitamin D_3, serum calcium, phosphorus, and magnesium were analyzed to evaluate metabolic and nutritional status. Bone mineral density (bone thickness) was measured using DEXA scans, and structural changes in the knee joints were assessed via x-ray imaging at specified intervals. Finally, the incidence of adverse events related to the study interventions was recorded throughout the study period to ensure the safety and tolerability of the treatment.

Statistical analysis

Data were analyzed on a per-protocol (PP) basis. Descriptive statistics, including numbers, percentages, means, and standard deviations (SD), were used to characterize the study population. Efficacy and safety variables were summarized using descriptive statistics, such as arithmetic means, SDs, and percentages for quantitative variables, and frequencies for qualitative variables.

Within the group comparisons were performed using paired t-test and between groups comparison were performed using analysis of covariance (ANCOVA). Statistical analysis was performed SPSS software (version 10.0) and a p value of <0.05 was considered statistically significant.

RESULTS

Demographics and baseline characteristics

In this study, demographic and baseline characteristics were analyzed using standard descriptive statistical methods (Table 1). Numerical variables, such as age, height, weight, and BMI, were summarized using mean values and standard deviations (SD), while categorical variables, such as gender, were represented by frequency counts and percentages. Out of 42 participants screened, 2 were failures and 40 participants were successfully enrolled in this study. These participants were evenly divided into two groups: a placebo group (n=20) and an active group (n=20). The placebo group had a higher proportion of females (57.10%) compared to the active group (42.90%), though this difference was not statistically significant (p=0.342). The mean age of participants in the active group (60.35±6.63 years) was significantly higher than that of the placebo group (55.25±6.77 years, p=0.021). No significant differences were observed in height, weight, or BMI between the two groups (p>0.05).

Efficacy assessment

Pain intensity

The pain intensity results, as measured by visual analog scale (VAS) scores, demonstrated significant differences both within and between the placebo and active groups across the study visits (Table 2). At day 0, both groups had comparable VAS scores (placebo: 6.89±0.56; active: 6.8 ±0.49, p>0.05). At week 12, the active group showed a significant reduction in pain intensity (5.49±0.60, p<0.0001), representing 19.62% decrease from baseline, while the placebo group exhibited minimal change (6.84±0.40, p=0.515), with only 0.73% reduction. At week 24, the active group further improved, with VAS scores decreased to 4.52±0.71 (p<0.0001), reflecting 33.82% reduction from baseline. In contrast, the placebo group showed modest decline to 6.61±0.53 (p=0.033), representing 4.06% reduction. These results indicate that the Amrith Noni Arthoplus was significantly more effective in reducing pain intensity compared to the placebo.

Physician and subject global assessment (PGA and SGA)

The PGA and SGA scores showed significant improvements in the active group compared to the placebo group (Table 3). At day 0, both groups had similar PGA and SGA scores. At week 12, the active group demonstrated greater reductions in PGA (28.28% improvement) and SGA (30.28% improvement) compared to the placebo group (PGA: 9.18%; SGA: 15.24%). At week 24, the active group further improved, with PGA and SGA scores decreasing by 45.45% and 49.54%, respectively, while the placebo group showed smaller improvements (PGA: 14.29%; SGA: 22.86%). Between-group comparisons at both week 12 and week 24 demonstrated statistically significant (p<0.0001) improvements in PGA and SGA scores in the active group, indicating that the Amrith Noni Arthoplus was more effective than the placebo.

Table 1: Summary of demographics and baseline characteristics.

Variables	Placebo group (n=20)	Active group (n=20)	P value
Female, N (%)	12 (57.10%)	9 (42.90%)	0.342^
Male, N (%)	8 (42.10%)	11(57.90%)	
Age (years), mean, SD	55.25±6.77	60.35±6.63	0.021*
Height (cm), mean, SD	163.35±7.0	160.85±6.04	0.234*
Weight (kg), mean, SD	65.88±5.20	63.55±5.45	0.176*
BMI (kg/m^2), mean, SD	24.67±1.18	24.54±1.24	0.725*

p$^{\$}$: Between groups comparison analysed using independent t-test p^: P value is for chi-square test.

Table 2: Within and between groups comparison of VAS scores at different assessment points.

	VAS scores		P value$^{\$}$
	Placebo group, n=20 (mean±SD)	**Active group, n=20 (mean±SD)**	
Day 0	6.89±0.56	6.83±0.49	-
Week 12	6.84±0.40	5.49±0.60	<0.0001
%change	-0.73%	-19.62%	-
P value*	0.515	<0.0001	
Week 24	6.61±0.53	4.52±0.71	<0.0001
%change	-4.06%	-33.82%	-
P value*	0.0330	<0.0001	

p*: Within the group comparisons performed using paired t test; and p$^{\$}$: Between groups comparison performed using ANCOVA with considering baseline variable (day 0) as a covariate.

Table 3: Within and between groups comparison of SGA and PGA scores at different assessment points.

	Score		P value$
	Placebo group, n=20 (mean±SD)	Active group, n=20 (mean±SD)	
PGA			
Day 0	4.9±0.55	4.95±0.39	-
Week 12	4.45±0.61	3.55±0.61	<0.0001
% change	-9.18%	-28.28%	-
P value*	0.004	<0.0001	
Week 24	4.2±0.70	2.7±0.57	<0.0001
% change	-14.29%	-45.45%	-
P value*	0.0047	<0.0001	
SGA			
Day 0	5.25±0.72	5.45±0.61	-
Week 12	4.45±0.61	3.8±0.52	<0.0001
%change	-15.24%	-30.28%	-
P value*	<0.0001	<0.0001	
Week 24	4.05±0.76	2.75±0.64	<0.0001
% change	-22.86%	-49.54%	-
P value*	<0.0001	<0.0001	

p*: Within the group comparisons performed using paired t test; and p$: Between groups comparison performed using ANCOVA with considering baseline variable (day 0) as a covariate.

Table 4: Within and between groups comparison of distance walked in 6 minutes at different assessment points.

	6-minute walk distance (m)		P value$
	Placebo group, n=20 (mean±SD)	Active group, n=20 (mean±SD)	
Day 0	363.40±21.72	364.15±22.68	-
Week 12	375.90±20.79	391.80±22.32	<0.0001
% change	3.44%	7.59%	-
P value*	<0.0001	<0.0001	
Week 24	380±20.0	415.75±22.77	<0.0001
% change	4.57%	14.17%	-
P value*	<0.0001	<0.0001	

p*: Within the group comparisons performed using paired t test; and p$: Between groups comparison performed using ANCOVA with considering baseline (day 0) variable as a covariate.

Table 5: Within and between groups comparison of stair climb time at different assessment points.

	Stair climb time (seconds)		P value$
	Placebo group, n=20 (mean±SD)	Active group, n=20 (mean±SD)	
Day 0	14.79±1.27	15.77±0.84	-
Week 12	14.49±1.17	14.69±1.35	0.0003
% change	-2.03%	-6.85%	-
P value*	<0.0001	<0.0001	
Week 24	14.54±1.16	13.76±1.46	<0.0001
% change	-1.69%	-12.75%	-
P value*	0.012	<0.0001	

p*: Within the group comparisons performed using paired t test; and p$: Between groups comparison performed using ANCOVA with considering baseline (day 0) variable as a covariate.

6-minute walk distance

6-minute walk distance measured by SMWT demonstrated significant differences between the placebo and active groups across various assessment points (Table 4). At day 0, both groups had similar mean walking distances, with the placebo group covering 363.40±21.72 meters and the active group covering 364.15±22.68 meters. After 12 weeks of treatment, the active group showed a significant improvement with mean walking distance 391.80±22.32

meters (7.59% increase, p<0.0001) compared to 375.90±20.79 meters (3.44% increase, p<0.0001) in the placebo group. After 24 weeks of treatment, the active group further improved to achieve mean walking distance 415.75±22.77 meters (14.17% increase, p<0.0001), while the placebo group reached 380±20.0 meters (4.57% increase, p<0.0001). These findings suggest that Amrith Noni Arthoplus significantly improved walking distance, demonstrating its superior effectiveness in enhancing functional capacity of OA patients compared to the placebo.

Stair climb time

The stair climb test results demonstrated significant improvements in stair climb time for both the placebo and active groups, with the active group showing greater reductions over the study period (Table 5). At baseline (day 0), the placebo group had mean stair climb time 14.79±1.27 seconds, while the active group took slightly longer time 15.77±0.84 seconds. After 12 weeks of treatment, the active group showed 6.85% improvement in stair climb time (14.69±1.35 secs, p<0.0001), compared to 2.03% improvement in the placebo group (14.49±1.17 secs, p<0.0001). After 24 weeks, the active group showed further improvement with 12.75% reduction in stair climb time (13.76±1.46 secs, p<0.0001), while the placebo group showed minimal 1.69% improvement (14.54±1.16 secs, p=0.012). Between-group comparisons at week 12 and week 24 revealed statistically significant differences (p=0.0003 and p<0.0001, respectively), indicating that the Amrith Noni Arthoplus was more effective in reducing stair climb time compared to the placebo.

Serum biochemicals

The serum biochemical test results showed significant improvements in the active group compared to the placebo group. For hs-CRP, the active group showed 22.09% reduction after 12 weeks of treatment and 31.33% reduction after 24 weeks (p<0.0001), while the placebo group showed minimal changes (-3.10%, p>0.05). Magnesium levels increased significantly in the active group by 11.30% at 12 weeks and 20.43% at 24 weeks (p<0.0001), whereas the placebo group experienced slight declines (-1.25% and -2.92%, respectively). Similarly, serum calcium levels rose by 3.74% and 7.05% in the active group (p<0.0001), with negligible changes in the placebo group (0.22% and 0.54%). Phosphorus levels increased by 8.56% and 15.75% in the active group (p<0.0001), while the placebo group showed minor declines (-1.01% and -2.02%). Vitamin D_3 levels improved by 9.85% and 14.94% in the active group (p<0.0001), compared to minimal changes in the placebo group (0.54% and 1.52%). Between-group comparisons using ANCOVA, adjusted for baseline values, revealed statistically significant improvements in the active group for all biomarkers (p<0.05) at both 12 and 24 weeks of treatment (Figure 1). These findings suggest that Amrith Noni Arthoplus significantly improved serum biochemical parameters in OA patients compared to the placebo.

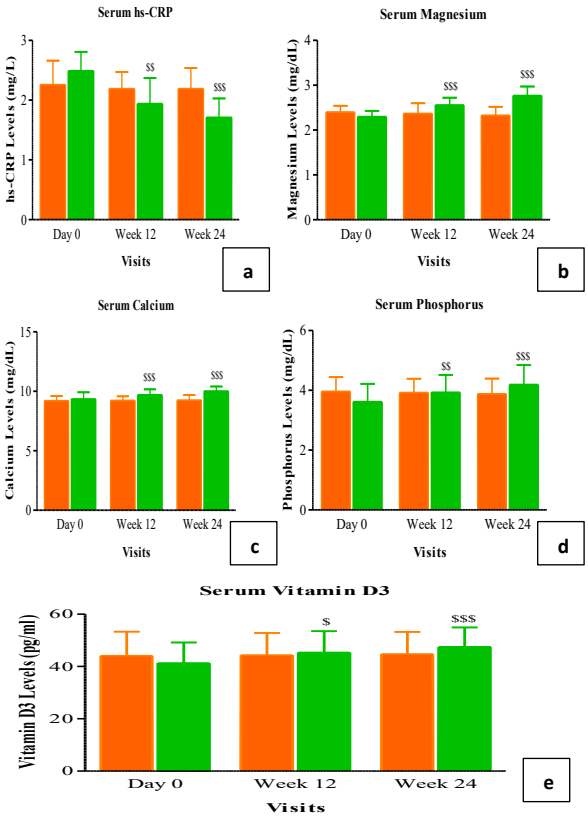

Figure 1: (a-e) Between groups comparison of mean change in serum biochemicals throughout the study period.

Between group comparisons were performed using ANCOVA with considering baseline variable as a covariate. $^{\$}$p<0.05, $^{\$}$p<0.01 and $^{\$\$\$}$p<0.001.

Bone mineral density

The bone mineral density (BMD) results demonstrated significant improvements in the active group compared to the placebo group over the study period (Table 6). At baseline (day 0), both groups had similar BMD values (placebo: -2.1±0.53 g/cm^2; active: -2.08±0.55 g/cm^2). By week 12, the active group showed a 15.87% improvement in BMD (-1.75±0.44 g/cm^2, p<0.0001), while the placebo group experienced a 7.14% decline (-2.25±0.5 g/cm^2, p=0.111). At week 24, the active group further improved, with a 25.48% increase in BMD (-1.55±0.54 g/cm^2, p<0.0001), whereas the placebo group showed an 18.10% decline (-2.48±0.66 g/cm^2, p=0.002). Between-group comparisons revealed statistically significant differences at both week 12 and week 24 (p<0.0001). These findings indicate that Amrith Noni Arthoplus was significantly more effective in improving bone mineral density compared to the placebo.

Table 6: Within and between groups mean change in bone mineral density throughout the study period.

	Bone mineral density (gm/cm²)		P value$
	Placebo group, n=20 (mean±SD)	Active group, n=20 (mean±SD)	
Day 0	-2.1±0.53	-2.08±0.55	-
Week 12	-2.25±0.5	-1.75±0.44	<0.0001
% Change	7.14%	-15.87%	
P value*	0.111	<0.0001	
Week 24	-2.48±0.66	-1.55±0.54	<0.0001
% Change	18.10%	-25.48%	
P value*	0.002	<0.0001	

p*: Within the group comparisons performed using paired t test; and p$: Between groups comparison performed using ANCOVA with considering baseline (day 0) variable as a covariate.

Table 7: Between groups comparison of mean change in hematological parameters at baseline and end of the study.

Parameters	Visit	Placebo group (n=20, mean±SD)	Active group (n=20, mean±SD)	P value$
Hb (gm/dl)	Screening	13.17±0.886	13.27±0.579	-
	End of study	13.46±0.76	13.55±0.59	0.891
Platelet (10^3/mm^3)	Screening	222.6±38.74	215.05±26.71	-
	End of study	222.9±35.71	219.7±26.90	0.156
TLC (10^3/mm^3)	Screening	6.6±1.15	6.33±1.05	-
	End of study	6.59±0.96	6.51±1.38	0.950
RBC (10^6/mm^3)	Screening	4.59±0.43	4.57±0.35	-
	End of study	4.65±0.55	4.63±0.45	0.971
ESR (mm/hour)	Screening	9.4±1.76	10.15±1.98	-
	End of study	9.1±2.13	8.85±1.87	0.238
Neutrophils (%)	Screening	57.55±2.48	57.65±3.22	-
	End of study	62.85±5.94	62.25±5.56	0.7532
Lymphocytes (%)	Screening	33.5±2.91	32.6±4.06	-
	End of study	28.40±5.66	29.3±4.67	0.642
Eosinophils (%)	Screening	2.8±0.89	3.1±1.07	-
	End of study	2.9±1.12	3.15±0.81	0.425
Monocytes (%)	Screening	6.1±1.33	6.1±1.25	-
	End of study	5.9±1.21	5.85±1.31	0.898
Basophils (%)	Screening	0±0	0±0	-
	End of study	0±0	0±0	-

p$: Between groups comparison performed using ANCOVA with considering screening variable as a covariate.

Table 8: Between groups comparison of mean change in liver and kidney function parameters at baseline and end of the study.

Parameters	Visit	Placebo group (n=20, mean±SD)	Active group (n=20, mean±SD)	P value$
Serum creatinine (mg/dl)	Screening	0.87±0.15	0.88±0.11	-
	End of study	0.85±0.12	0.88±0.11	0.207
Uric acid (mg/dl)	Screening	4.62±0.83	4.48±0.60	-
	End of study	4.6±0.64	4.46±0.60	0.683
BUN (mg/dl)	Screening	13.64±2.07	13.17±1.519	-
	End of study	13.75±1.85	13.39±1.38	0.707
Serum bilirubin (mg/dl)	Screening	0.57±0.22	0.55±0.21	-
	End of study	0.58±0.15	0.57±0.22	0.916
AST (IU/l)	Screening	26.8±4.61	27.01±2.81	-
	End of study	26.92±4.49	27.08±3.15	0.866
ALT (IU/l)	Screening	32.32±9.36	33.47±6.62	-
	End of study	32.95±7.89	34.7±5.40	0.160
	Screening	4.25±0.35	4.28±0.38	-

Continued.

Parameters	Visit	Placebo group (n=20, mean±SD)	Active group (n=20, mean±SD)	P value[$]
Serum albumin (gm/dl)	End of study	4.31±0.30	4.22±0.36	0.345

Safety assessment

Vital signs

All vital sign parameters, including pulse rate, blood pressure (systolic and diastolic), respiratory rate, and body temperature, remained within the normal range throughout the study for both the placebo and active groups. At week 12, pulse rate showed slight decreases in both groups (placebo: -3.00%; active: -2.03%) and remained stable by week 24, with no significant between-group differences. Systolic and diastolic blood pressure exhibited minor fluctuations, with a marginal between-group difference in diastolic pressure by week 24. Respiratory rate and body temperature remained consistent, with negligible changes. Overall, the treatment had no clinically significant impact on vital signs, and all values remained within normal limits.

Hematology

The hematology results showed no significant differences between the placebo and active groups at the end of the study. All hematological parameters such as Hb, platelet count, TLC, RBC, ESR, and differential leukocyte counts (neutrophils, lymphocytes, eosinophils, monocytes, and basophils) remained stable and within normal ranges for both groups (Table 7). Small fluctuations were observed in some parameters, such as a slight increase in neutrophils and a decrease in lymphocytes in both groups, but these changes were not statistically significant.

Liver and kidney functions

The liver and kidney function parameters remained stable and within normal ranges for both the placebo and active groups throughout the study. Parameters such as serum creatinine, uric acid, blood urea nitrogen (BUN), serum bilirubin, AST, ALT, and serum albumin showed minimal fluctuations from baseline to the end of the study. For example, serum creatinine slightly decreased in the placebo group (0.87±0.15 to 0.85±0.12 mg/dl) but remained unchanged in the active group (0.88±0.11 mg/dl). Similarly, AST and ALT levels showed negligible changes in both groups (Table 8).

Adverse effects

Based on data collected from all 40 subjects who completed the study, no adverse events were reported or observed throughout the study period. These findings indicate that the study intervention is safe and well-tolerated for clinical use.

DISCUSSION

The findings of this study demonstrate that Amrith Noni Arthoplus significantly improves pain, physical function, and biochemical markers in patients with OA, while also enhancing BMD. These results align with existing literature on the therapeutic potential of *M. citrifolia* and other herbal ingredients in managing OA symptoms. *M. citrifolia* has been widely studied for its anti-inflammatory, antioxidant, and analgesic properties, which are attributed to its bioactive compounds such as iridoids, flavonoids, and polysaccharides.[9,10] The observed reduction in pain intensity, as measured by the VAS, and improvements in physical endurance, as assessed by the 6-MWT and SCT, are consistent with previous studies highlighting the efficacy of *M. citrifolia* in alleviating joint pain and improving mobility.[11,13]

The significant reduction in hs-CRP levels in the active group highlights the anti-inflammatory effects of Amrith Noni Arthoplus. Elevated hs-CRP is a marker of systemic inflammation, commonly associated with OA progression.[14] The 31.33% reduction in hs-CRP levels by week 24 suggests that Amrith Noni Arthoplus may help mitigate inflammation, thereby slowing disease progression. Additionally, the improvements in serum calcium, phosphorus, magnesium, and vitamin D_3 levels highlight the potential of Amrith Noni Arthoplus in supporting bone and joint health. These findings are consistent with studies demonstrating the role of these nutrients in maintaining bone density and reducing OA-related complications.[15,16]

The improvement in BMD observed in the active group is particularly noteworthy. OA is often associated with subchondral bone changes, and interventions that improve BMD can potentially delay disease progression.[17] The 25.48% improvement in BMD in the active group, compared to an 18.10% decline in the placebo group, suggests that Amrith Noni Arthoplus may have a protective effect on bone health. This is supported by preclinical studies indicating that *M. citrifolia* enhances bone formation and reduces bone resorption.[18]

The clinical significance of Amrith Noni Arthoplus lies in its potential to offer a safe and effective alternative or adjunct to conventional OA treatments, which are often associated with adverse effects and limited long-term efficacy. For instance, NSAIDs, while effective in reducing pain and inflammation, are linked to gastrointestinal, cardiovascular, and renal complications.[7] The absence of adverse events in this study further underscores the safety profile of the formulation, making it a viable option for long-term use in OA management.

One of the key strengths of this study is its rigorous double-blind, randomized, placebo-controlled design, which minimizes bias and enhances the validity of the findings. The inclusion of multiple efficacy parameters, including pain intensity, physical function, biochemical markers, and BMD, provides a comprehensive assessment of the intervention's impact.

Additionally, the study's focus on *M. citrifolia* as the central component of the formulation adds to the growing body of evidence supporting its therapeutic potential.

CONCLUSION

In conclusion, this study demonstrates that Amrith Noni Arthoplus is a safe and effective intervention for managing OA symptoms. The formulation significantly reduces pain, improves physical function, enhances biochemical markers, and increases bone mineral density, with no reported adverse events. These findings highlight the potential of Amrith Noni Arthoplus as a complementary therapy for OA, offering a holistic approach to symptom management and disease modification.

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