



EVALUATING THE EFFECT OF CINNAMON ON PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS: A DOUBLE-BLIND RANDOMIZED CLINICAL TRIAL

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Abstract

Objective: This study aimed to evaluate the effect of cinnamon supplementation, compared with a control intervention, on reducing pain in patients with rheumatoid arthritis attending Dr. Sedigheh Ravanshad Clinic in Isfahan.

Methods: A double-blind, randomized clinical trial with a pre-test, post-test, and follow-up design was conducted on 91 patients selected through convenience sampling. Participants were randomly assigned to either the cinnamon group or the placebo group. Pain intensity was measured at baseline, immediately after the intervention, and at follow-up using the Visual Analogue Scale (VAS). Data were analyzed using SPSS version 26.

Results: At baseline, no significant difference was observed in mean pain scores between the cinnamon and placebo groups ($P > 0.05$). However, post-intervention and at follow-up, patients receiving cinnamon reported significantly lower pain scores compared with the placebo group ($P < 0.05$).

Conclusion: The findings suggest that cinnamon supplementation may serve as an effective adjunctive approach for reducing pain in patients with rheumatoid arthritis.

Keywords: Cinnamon, Rheumatoid Arthritis, Pain

The term *rheumatism* encompasses a wide range of inflammatory (1) and non-inflammatory conditions that can affect the bones (2), muscles (3), and connective tissues (4) of the body (5). Since connective tissue constitutes the majority of the body's structural composition(6), patients with rheumatic disorders often experience the greatest range and severity of symptoms within these tissues(7). Rheumatoid arthritis (RA) is a chronic autoimmune disease (8) characterized by persistent inflammation and pain in the

synovial tissue. Over time, this ongoing inflammatory process leads to progressive joint destruction and eventual loss of joint function (9, 10, 11). The disease damages the musculoskeletal system, resulting in irreversible deterioration of bone and cartilage (12, 13).

Several factors have been identified as possible contributors to RA development, including obesity, advancing age, genetic predisposition, and joint trauma (14–18). Global epidemiological data from 1980 to 2019 estimate the prevalence of RA at approximately 0.46%(19), with the condition occurring two to three times more frequently in women than in men(20, 21).

Despite advances in medical science, there is currently no fully curative treatment for RA (22–24). Existing therapeutic approaches primarily aim to stabilize disease activity and alleviate disabling symptoms (23). Common manifestations include joint pain, swelling, stiffness, tenderness, warmth, muscle pain, paresthesia (“pins and needles” sensation) in the joints, and fatigue (25–28). Management strategies may involve csDMARDs, tsDMARDs, and bDMARDs, as well as agents targeting interleukin-1, interleukin-6, and tumor necrosis factor-alpha, alongside various herbal medicines (29–33). Among these symptoms, muscle pain is particularly common and distressing in RA, making the search for complementary therapies—such as cinnamon—especially relevant due to its potential analgesic benefits and lower side-effect profile.

Cinnamon is derived from the dried bark of trees in the genus *Cinnamomum*, belonging to the laurel family (*Lauraceae*) (34–36). Traditionally used both as a culinary spice and a medicinal agent, cinnamon trees grow naturally in Sri Lanka and southern India, and are now cultivated worldwide. Historically, cinnamon has been used to treat ailments including nausea, indigestion, cough, diarrhea, malaria, gastric disorders, diabetes, Parkinson’s disease, inflammation, and pain (35, 38–41).

Phytochemical analyses have identified several bioactive components in cinnamon, including cinnamaldehyde, cinnamic alcohol, cinnamic acid, eugenol, and cinnamate(42–46). In the present study, the focus is on two of these compounds—cinnamaldehyde and eugenol—due to their documented biological activity (43, 47–50). Cinnamaldehyde, a bioactive phytochemical found in cinnamon bark (51), has the chemical formula C_9H_8O (52) and exhibits both anti-inflammatory and antioxidant properties, partly through its effects on the central nervous system (53). Eugenol ($C_{10}H_{12}O_2$)(54) also has central analgesic activity, which involves inhibition of calcium influx into cells, suppression of neurotransmitter release associated with pain signaling, and blockade of voltage-gated sodium channels in the dorsal horn of the spinal cord(55, 56).

Although research in this specific area remains limited, several studies support the potential therapeutic effects of cinnamon in RA: The study by Letarouilly et al., a review examining the effects of spices on RA, demonstrated that supplements containing cinnamon can significantly reduce RA symptoms such as joint inflammation and pain (57). In a double-blind randomized clinical trial conducted by Shishehbor et al. to investigate the effects of cinnamon on disease activity, inflammatory markers, and cardiovascular risk factors in 36 women with rheumatoid arthritis (RA), it was found that taking 500 mg cinnamon capsules four times daily significantly decreased serum levels of C-reactive protein (CRP) and tumor necrosis factor- α (TNF- α), as well as reduced diastolic blood pressure in the intervention group (58). Another review by Almatroodi et al., which examined the impact of cinnamon on overall health, indicated that cinnamon may improve RA symptoms through its antioxidant effects (41). A further review by Pahan et al., analyzing the potential of cinnamon supplements in managing autoimmune disorders through evidence of anti-autoimmune mechanisms and modulation of autoimmune pathways, showed that cinnamon, via its metabolite sodium benzoate, can regulate autoimmune pathways and provide protection against autoimmune disorders, highlighting its therapeutic potential (59). In a study by Gunawardena et al. investigating the anti-inflammatory properties of cinnamon polyphenols and their monomeric precursors, it was shown that cinnamon can reduce inflammation associated with aging and middle-aged diseases and alleviate symptoms of inflammation-related conditions (60). In another study by Gunawardena et al., which evaluated the anti-inflammatory activity of *C. zeylanicum* and *C. cassia* extracts and identified their primary phytochemical compounds, the most potent bioactive compounds were found to be E-cinnamaldehyde and o-methoxy cinnamaldehyde, exhibiting significant anti-

inflammatory activity and potential for treating age-related inflammatory conditions (61). A meta-analysis by Zhu et al. investigating the effects of cinnamon supplementation on inflammation and oxidative stress biomarkers indicated that cinnamon supplementation may help reduce inflammation and oxidative stress in humans (62). Given that most studies have focused on the effects of cinnamon on inflammation and general osteoarthritis symptoms, and research specifically addressing the impact of cinnamon on rheumatoid arthritis-related pain remains limited, further studies in this area are essential.

Methods

The present study was a double-blind randomized clinical trial with a pretest-posttest-follow-up design and a control group. The statistical population included all patients with rheumatoid arthritis receiving treatment at Dr. Sedigheh Ravaneshad's clinic in 2025. In this study, 91 patients were selected using purposive sampling and randomly assigned to two groups. The experimental group consisted of 46 patients (cinnamon group), and the control group included 45 patients who received a placebo.

Inclusion criteria were: men and women aged 30 to 80 years, definitive diagnosis of rheumatoid arthritis by the treating physician according to the American College of Rheumatology criteria, disease duration of more than three months, written informed consent to participate in the study, no intra-articular corticosteroid injections in the past six months, no use of non-steroidal anti-inflammatory drugs (NSAIDs) in the past month, and a minimum score of 40 mm on the visual analogue scale (VAS).

Exclusion criteria included: liver failure or liver function tests exceeding 1.5 times the normal level, biliary disease, history of gastric ulcer, unwillingness to continue the study, high blood pressure, sensitivity to cinnamon, and history of using anti-inflammatory steroid medications.

The instrument used in this study was the Visual Analogue Scale (VAS) for pain, a subjective measure in which individuals indicate their pain level along a 10-cm (100-mm) line ranging from "no pain" to "worst imaginable pain" (63). The score interpretation for this scale is as follows: 0–10 mm (no pain), 10–20 mm (mild pain), 20–50 mm (moderate pain), 50–80 mm (severe pain), and 80–100 mm (very severe pain) (64, 65). All participants completed the VAS questionnaire before the start of the study.

The sample size was calculated based on the study by Shishehbor et al., which examined the effects of cinnamon on inflammatory markers in women with rheumatoid arthritis (58), resulting in 44 participants per group. Participants were selected using purposive sampling and randomly assigned to either the experimental or control group. Ultimately, as shown in Figure 1, 46 participants were assigned to the cinnamon group and 45 to the control group.

All participants discontinued their usual rheumatoid arthritis pain medications (ibuprofen and naproxen) one week before the study. For the intervention group, cinnamon capsules (15 capsules from Shari Company, code 685112) were prepared; the contents were transferred into identical capsules matching the control group in size and shape, with a dose of 500 mg. These capsules were administered four times daily for eight weeks (58). The control group received identical capsules containing starch.

This study was conducted as a double-blind, meaning that both participants and researchers were unaware of the capsule contents. The medications were coded by a nurse not involved in the study, and the code for each capsule was disclosed to the researchers only after the study concluded. During the study, another nurse instructed patients on the intervention and the method of capsule administration. After eight weeks, the VAS was administered to participants, and again one month later to assess the persistence of the treatment effects.

Data Analysis:

In this study, quantitative data were analyzed using mean, standard deviation, MANOVA, and the Mann–Whitney U test.

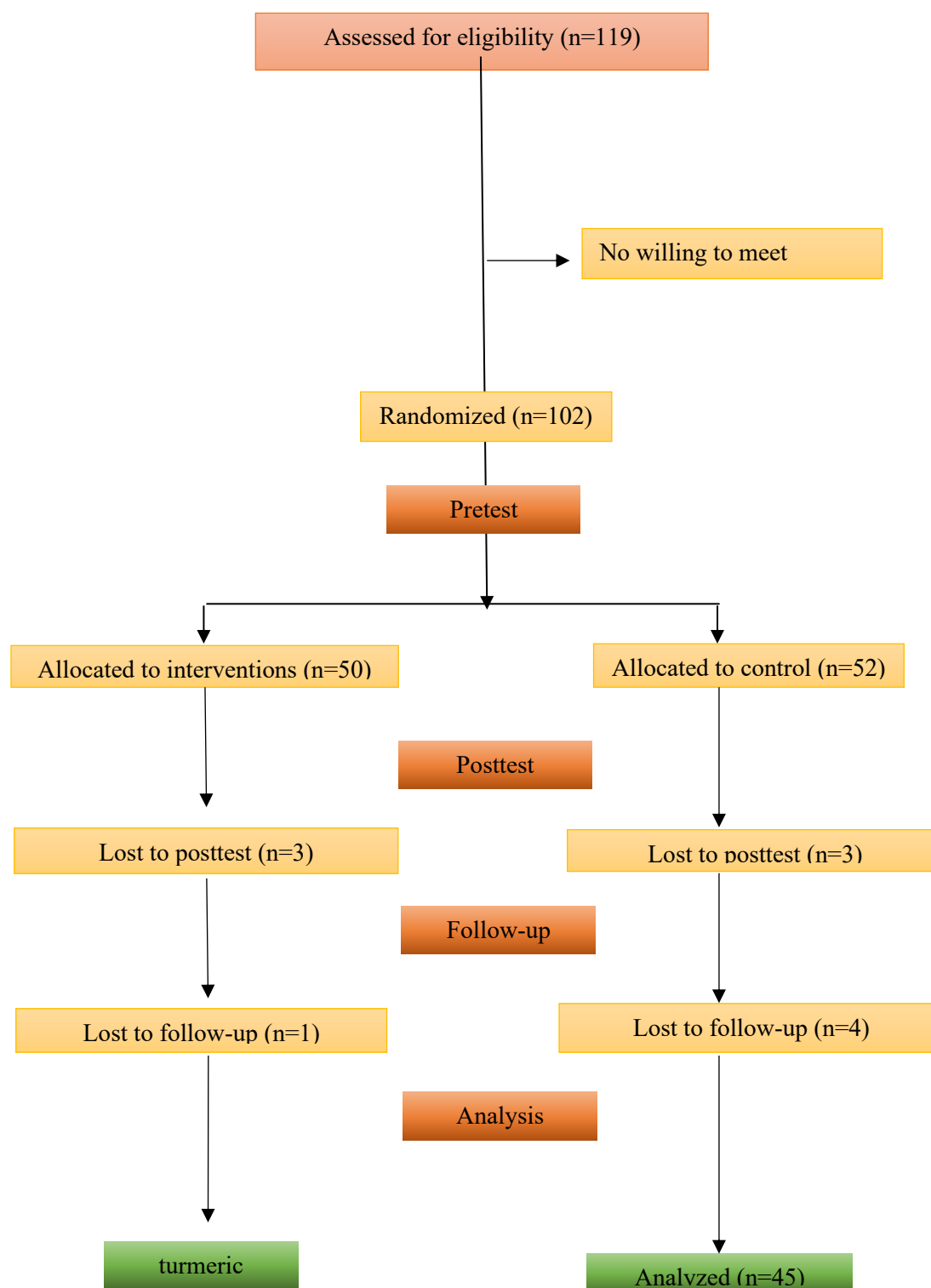


Figure 1: Random allocation of samples into the experimental and control groups

Results:

The findings of the study indicated that the experimental and placebo groups were comparable in terms of demographic variables, including gender, employment status, education level, and marital status. The detailed results are presented in Tables 1 and 2.

Table 1: Demographic and Clinical Characteristics of Participants (Chi-Square Tests)

variable	levels	group		Chi-Square	P
		placebo	experimental		
sex	Male	21	17	0.882	0.348
	Female	24	29		
Education	College education	16	19	0.318	0.573
	Non-university education	29	27		
Marital status	Single	15	17	0.131	0.717
	Married	30	29		
Job status	Employed	25	20	1.327	0.249
	Unemployed	20	26		

Table 2: Test Results (Mann–Whitney U)

Test Statistics	
	Age
Mann-Whitney U	1002.000
Wilcoxon W	2083.000
Z	-.262
Asymp. Sig. (2-tailed)	.793

The mean age and standard deviation in the placebo and treatment groups were 48.48 (13.49) and 48.02 (14.05), respectively. According to Table 2, the Mann–Whitney U test was not significant, indicating that the age distribution was similar between the two groups.

The mean and standard deviation of pain scores in the placebo group at pre-test, post-test, and follow-up were 67.38 (10.74), 66.68 (14.07), and 66.91 (14.27), respectively. In the experimental group, the corresponding values were 68.65 (13.48), 54.08 (16.55), and 56.52 (14.28). The detailed results are presented in Table 3.

Table3: Descriptive statics

	Group	Mean	Std. Deviation	N
Pre test	placebo	67.3778	10.74347	45
	cinnamon	68.6522	13.48945	46
	Total	68.0220	12.15820	91
Post test	placebo	66.6889	14.07419	45
	cinnamon	54.0870	16.55674	46
	Total	60.3187	16.55421	91
Follow up	placebo	66.9111	14.27302	45
	cinnamon	56.5217	14.28556	46
	Total	61.6593	15.12997	91

Results Analysis:

Before performing statistical tests, it is necessary to assess whether the data are normally distributed. The Kolmogorov–Smirnov test was used for this purpose. As shown in Table 4, all data at the pre-test, post-test, and follow-up stages were not significant at $P < 0.05$, indicating that the data were normally distributed.

Table 4: Kolmogorov–Smirnov Test

	Group	Kolmogorov-Smirnov		
		Statistic	df	Sig.
Pre test	placebo	.078	45	.200
	cinnamon	.058	46	.200
Post test	placebo	.060	45	.200
	cinnamon	.059	46	.200
Follow up	placebo	.052	45	.200
	cinnamon	.051	46	.200

In this section, the research questions were analyzed using inferential statistical methods. For the statistical analysis of the data, MANOVA was employed.

Assumption of Homogeneity of Covariance Matrices:

As shown in Table 5, the F value was not significant at $P < 0.05$, indicating that the correlations among the study variables were homogeneous. Therefore, the assumption of homogeneity of covariance matrices was satisfied.

Table 5: Results of M Box Test

Box's M	F	Df1	Df2	Sig
7.332	1.177	6	57312.328	0.315

Assumption of Homogeneity of Error Variance:

To examine the equality of error variances, Levene's test was used. As shown in Table 6, the error variances across the study groups were homogeneous, because the F values for all variables were not significant at $P < 0.05$. Therefore, the assumption of homogeneity of error variance was confirmed.

Table6: Levene's Test of Equality of Error Variances

		Levene Statistic	df1	df2	Sig.
Pre test	Based on Mean	3.094	1	89	.082
Post test	Based on Mean	.864	1	89	.355
Follow up	Based on Mean	.036	1	89	.850

Given that the assumptions of M Box and Levene's test—both prerequisites for MANOVA—were satisfied, Pillai's Trace was used to analyze the data and test the study hypothesis. The results, shown in Table 7, indicate that the null hypothesis is rejected, confirming that cinnamon has a significant effect on reducing pain scores associated with rheumatoid arthritis.

Table 8 shows that there was no significant difference between the cinnamon and placebo groups in pain scores at the pre-test stage ($P > 0.05$, $F = 0.248$). However, significant differences were observed at the post-test ($P < 0.05$, $F = 15.273$) and follow-up stages ($P < 0.05$, $F = 12.042$). These findings indicate that, compared to placebo, cinnamon effectively reduced pain scores in the post-test and follow-up periods. A summary of these results is illustrated in Figures 2–4.

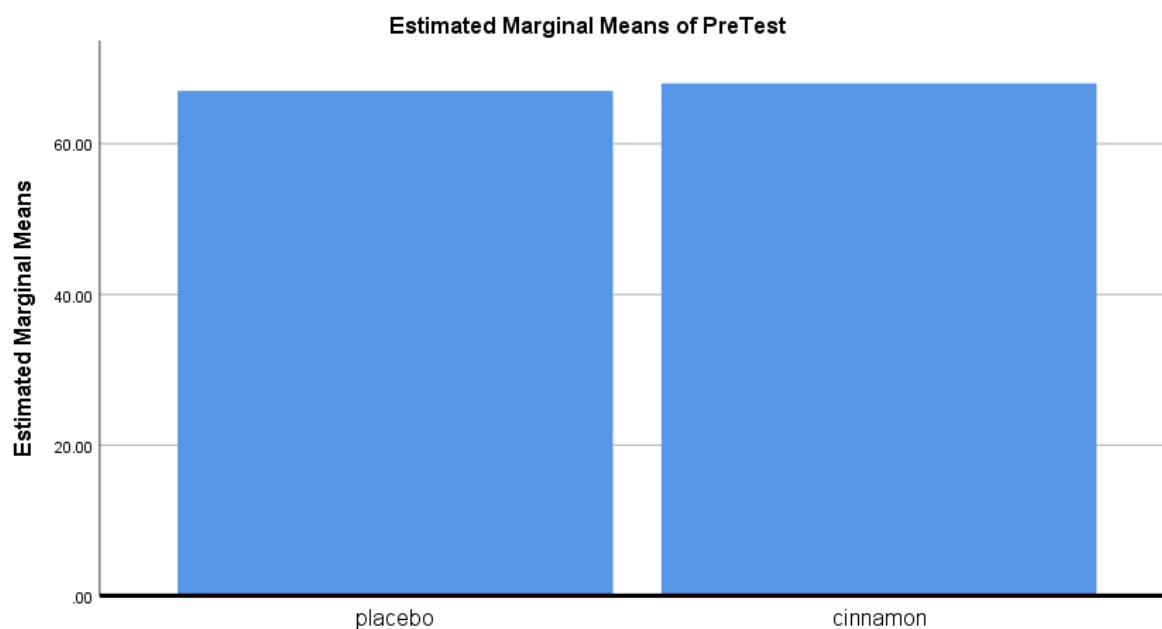
Table7: Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Intercept	Pillai's Trace	.980	1391.297	3.000	87.000	.000	.980
Group	Pillai's Trace	.234	8.844	3.000	87.000	.000	.234

Table8: Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	Pre test	36.943	1	36.943	.248	.620	.003
	Post test	3612.462	1	3612.462	15.273	.000	.146
	Follow up	2455.317	1	2455.317	12.042	.001	.119
Intercept	Pre test	420918.526	1	420918.526	2823.676	.000	.969
	Post test	331809.736	1	331809.736	1402.815	.000	.940
	Follow up	346569.603	1	346569.603	1699.702	.000	.950
Group	Pre test	36.943	1	36.943	.248	.620	.003
	Post test	3612.462	1	3612.462	15.273	.000	.146
	Follow up	2455.317	1	2455.317	12.042	.001	.119
Error	Pre test	13267.013	89	149.068			
	Post test	21051.297	89	236.531			
	Follow up	18147.123	89	203.900			
Total	Pre test	434360.000	91				
	Post test	355753.000	91				
	Follow up	366573.000	91				
Corrected Total	Pre test	13303.956	90				
	Post test	24663.758	90				
	Follow up	20602.440	90				

Figure 2: Changes in rheumatoid arthritis pain scores in the placebo and cinnamon groups at pre-test.



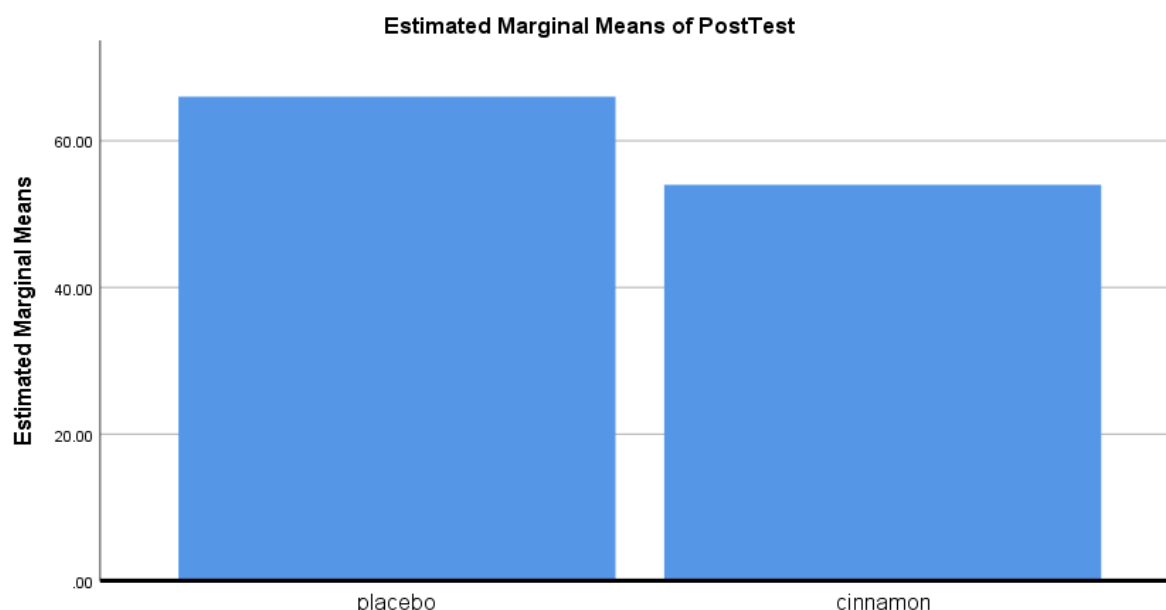


Figure 3: Changes in rheumatoid arthritis pain scores in the placebo and cinnamon groups at post-test.
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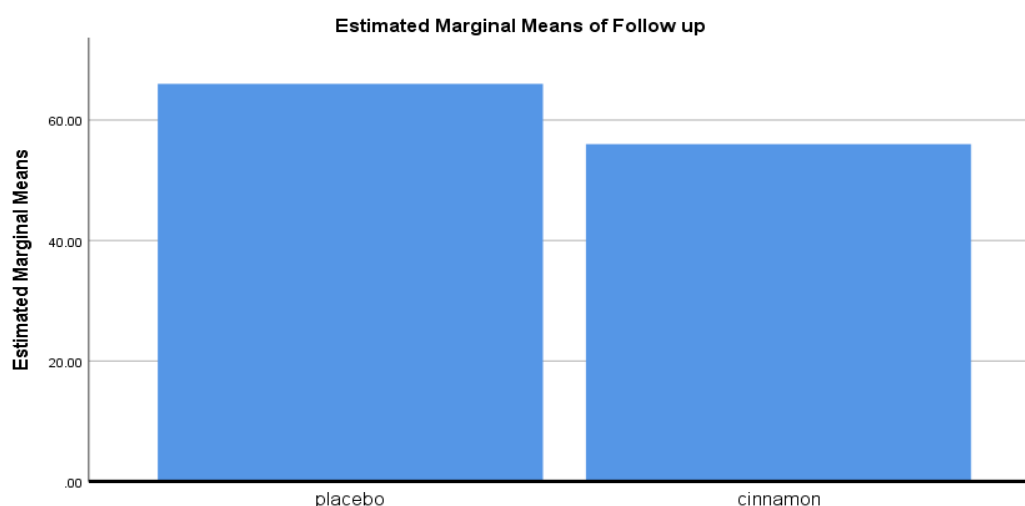


Figure 4: Changes in rheumatoid arthritis pain scores in the placebo and cinnamon groups at follow-up.

Discussion:

The results of this study indicate that taking 500 mg cinnamon capsules four times daily for eight weeks can effectively reduce pain associated with rheumatoid arthritis (RA). Participants in the cinnamon group showed a significant decrease in Visual Analogue Scale (VAS) pain scores at post-test and follow-up compared to the placebo group.

Previous studies support these findings. A review on non-pharmacological pain management for gout reported that herbal interventions—including cinnamon, ginger, lemon balm, Moringa leaf compresses, sour leaves, and CQBG granules—can reduce arthritis-related pain without causing side effects (66). Another review analyzing 47 studies on dietary polyphenols in RA suggested that polyphenols found in cinnamon, cranberry, saffron, curcumin, garlic, ginger, olive oil, pomegranate, and other plant sources can improve DAS28 scores, lower CRP and ESR levels, and reduce oxidative stress, thus contributing to RA management (67).

Animal studies further demonstrate cinnamon's potential. In male Wistar rats with adjuvant-induced RA, cinnamon aqueous extract reduced joint inflammation and normalized inflammatory markers (68). Research on eugenol and curcumin from *Syzygium aromaticum* and *Curcuma longa* showed that these antioxidant-rich compounds may prevent or reduce the severity of arthritis (69). Additionally, eugenol was effective in reducing cartilage damage and modulating inflammatory signaling pathways in a mouse osteoarthritis model, suggesting its therapeutic potential (70).

Mechanistic studies indicate that cinnamon can modulate inflammatory and immune pathways. A review of 208 studies concluded that cinnamon suppresses NF- κ B activity, inhibits TNF- α release from neutrophils, and decreases pro-inflammatory cytokine expression (57). Cinnamon has also been shown to alleviate symptoms of autoimmune diseases such as arthritis, diabetes, inflammatory bowel disease, and multiple sclerosis (59). In vitro and in vivo studies demonstrated that cinnamon can inhibit IL-1 β via the succinate/HIF-1 α axis and block NLRP3, suggesting its potential as a therapeutic agent in RA (71). A double-blind clinical trial on 36 women with RA confirmed that 500 mg cinnamon capsules taken four times daily can serve as a safe adjunct treatment to improve inflammation and clinical symptoms (58). Cinnamon water extract (CWE) was also found to reduce IFN- γ expression in activated T cells, modulating immune responses and lowering systemic inflammation (72).

The primary bioactive compounds in cinnamon responsible for these effects are cinnamaldehyde and eugenol (43, 47–50). Cinnamaldehyde, found in cinnamon bark (C₉H₈O), exhibits anti-inflammatory and antioxidant properties through central nervous system modulation (51–53). Eugenol (C₁₀H₁₂O₂) provides central analgesic effects by inhibiting calcium influx, reducing neurotransmitter release involved in pain signaling, and blocking voltage-gated sodium channels in the spinal dorsal horn (55, 56).

In summary, this study provides evidence that cinnamon can serve as a safe and effective complementary intervention for reducing pain and inflammation in patients with rheumatoid arthritis.

Conclusion:

The findings of this study indicate that administering 500 mg cinnamon capsules (Shari Company) four times daily for eight weeks can significantly reduce pain in patients with rheumatoid arthritis. These results suggest that cinnamon may serve as an effective complementary therapy for managing RA-related pain. However, further research is needed to establish the optimal dosage, evaluate potential interactions with conventional RA medications, and assess long-term safety, allowing clinicians to safely incorporate cinnamon into standard treatment protocols.

Limitations:

The main limitation of this study was the relatively small sample size, which could increase the risk of bias and affect the reliability of the results. Additionally, the research was conducted solely at Dr. Sedigheh Ravanshad Clinic in Isfahan, which limits the generalizability of the findings to other patient populations or clinical settings.

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