

Comparative Efficacy of Bromelain versus Diclofenac Sodium in Temporomandibular Joint Osteoarthritis: A Randomized, Double-Blind Clinical Trial

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ABSTRACT

Background: This study aimed to evaluate the effect of oral Anaheal (bromelain 500 mg) compared to diclofenac sodium (50 mg) on reducing pain and symptoms in patients with temporomandibular joint osteoarthritis (TMJ OA).

Methods: This randomized, double-blind, parallel-group clinical trial conducted from 2024 to 2025 at Mashhad dental school and Velayat Hospital, Mashhad, Iran. Forty patients with radiographically confirmed TMJ OA were randomly assigned to receive either Anaheal 500 mg (intervention group, n=20) or diclofenac sodium 50 mg (control group, n=20) orally twice daily for 7 d. Pain intensity was assessed using a visual analog scale (VAS, 0-10), and maximum mouth opening (MMO) was measured at baseline (T0), day 1 (T1), day 7 (T2), and day 14 (T3). Joint clicking was also evaluated at all-time points.

Results: Both groups demonstrated significant within-group improvements in pain and MMO over time ($P < 0.001$). At T2, a decrease in pain and an increase in MMO were observed in both groups without significant between-group differences. At T3, Anaheal maintained a lower mean pain (7.5 ± 1.3) compared to diclofenac (7.9 ± 1.5), though this was not statistically significant ($P = 0.398$). Notably, between-group comparison of pain change from T0 to T3 showed significant superiority for Anaheal ($+0.5 \pm 0.9$ vs. -0.5 ± 0.9 ; $P = 0.004$). Similar sustained functional benefit was observed in MMO change from T0 to T3 favoring Anaheal, but without statistical significance ($P = 0.308$). Joint clicking persisted unchanged in all patients at all-time points.

Conclusion: Anaheal (bromelain 500 mg) and diclofenac sodium 50 mg provide comparable acute pain relief and functional improvement in TMJ osteoarthritis. However, Anaheal offers more stable pain control after treatment cessation. These findings support Anaheal as a safe and effective conservative therapy for TMJ osteoarthritis, though larger and longer-term studies are needed.

KEYWORDS

Arthritis; Degenerative; Bromelain; Clinical trial randomized; Diclofenac; Maximum mouth opening; Pain management; Temporomandibular joint disorders

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INTRODUCTION

Temporomandibular joint osteoarthritis (TMJ OA) is a significant type of temporomandibular joint pathology, distinguished by progressive degenerative changes affecting all articular structures¹. Epidemiological evidence concerning TMJ OA indicates a prevalence ranging from 8% to 16% within the general population, exhibiting considerable variation based on diagnostic criteria and demographic characteristics². TMJ OA is notably higher among female patients, aligning with the observed pattern of sex distribution in temporomandibular disorder (TMD)^{2,3}.

The etiology of TMJ OA is multifactorial, involving both local and systemic factors. Local factors contributing to trauma, internal derangement disorders, unstable occlusion, inadequate muscular function, various mechanical stresses, and parafunctional habits. Systemic factors include age, female gender, genetic predisposition, hormonal influences, and concomitant systemic arthritic diseases³.

The management of temporomandibular disorders (TMD) follows to a stepwise hierarchical protocol emphasizing conservative, reversible interventions before advancing to invasive therapeutic methods⁴. Conservative treatment, including physiotherapy, occlusal splint therapy, and pharmacotherapy; less invasive surgical methods, comprising intra-articular injections and arthrocentesis; and ultimately, invasive surgical techniques (arthroscopy and open joint surgery)⁴. There are three main goals for treating TMJ OA: 1) relief of symptoms including pain control, 2) disabling the disease, and 3) ultimately restoring normal joint function⁵.

Pharmacological interventions have been demonstrated to play a crucial role in the management of TMD, particularly with regard to pain control and inflammation reduction. Nonsteroidal anti-inflammatory drugs (NSAIDs) constitute first-line pharmacotherapy, possessing both analgesic and anti-inflammatory properties that address multiple aspects of TMD pathophysiology^{6,7}. Diclofenac sodium, a phenylacetic acid-derived NSAID, shows notable therapeutic efficacy in TMJ pathology through selective cyclooxygenase inhibition and consequent attenuation of prostaglandin synthesis. Clinical evidence demonstrates the therapeutic

utility of diclofenac administered as monotherapy or as an adjunctive agent in combination with complementary therapeutic approaches, resulting in significant pain reduction, functional improvement, and decreased inflammatory biomarkers⁸⁻¹⁰. Bromelain, commercially available as Anaheal in Iran, is a complex mixture of proteolytic enzymes primarily extracted from the stems of pineapple (*Ananas comosus*). In recent years, it has garnered considerable attention due to its diverse therapeutic properties and potential applications in inflammatory conditions, including musculoskeletal disorders^{11,12}. The application of bromelain in TMD represents an emerging area of clinical research with promising preliminary results. The unique pathophysiology of TMJ conditions, which encompasses both inflammatory and mechanical components, aligns well with the multifaceted mechanism of action of bromelain^{10,13}.

Nevertheless, few studies are available regarding the efficacy of bromelain in temporomandibular disorders, particularly TMJ OA, and this research gap prompted the present study to investigate the therapeutic effectiveness of Anaheal (bromelain) in the treatment of patients with TMJ OA in an Iranian population.

MATERIAL AND METHODS

Study Design and Ethical Considerations

This investigation was conducted as a randomized, double-blind clinical trial with a parallel-group design, in accordance with CONSORT 2025 guidelines¹⁴. The trial employed a two-arm, controlled design comparing Anaheal (bromelain 500 mg) with diclofenac sodium (50 mg) as the comparator in patients diagnosed with TMJ OA.

The current study adhered to the principles of the Declaration of Helsinki, and all participants provided written informed consent prior to enrollment. Ethical approval was obtained from the Regional Institutional Ethics Committee at the Mashhad University of Medical Sciences (approval code: IR.MUMS.DENTISTRY.REC.1403.153). Additionally, the trial was registered and approved in the Iranian Registry of Clinical Trials (IRCT) under the registration code IRCT20241021063454N1.

Participants

This trial was conducted from 2024 to 2025 at the Department of Oral and Maxillofacial Surgery, Mashhad University of Medical Sciences, and Velayat Hospital, Mashhad, Iran. Eligibility criteria for participants were as follows:

Inclusion Criteria:

- Clinical diagnosis of temporomandibular joint osteoarthritis (TMJ-OA) based on Okeson JP criteria¹⁵, including pain at rest or during mandibular movement and restricted mouth opening.
- Radiographic confirmation of osteoarthritic changes in the TMJ demonstrated by appropriate imaging and evidence of bony alterations consistent with osteoarthritis.
- Provision of informed consent and willingness to comply with study protocol requirements and follow-up assessments.

Exclusion Criteria:

Patients were excluded from the study if any of the following were present:

- Myogenic masticatory muscle pain as the primary cause of symptoms.
- TMJ ankylosis or severe structural deformity of the joint.
- Recent history (within 6 months) of trauma, joint lavage, or surgical intervention on the temporomandibular joint.
- Known allergic reactions or contraindications to the study medications.
- Severe systemic diseases (including significant cardiovascular, renal, or hepatic conditions).
- Active psychiatric or psychological disorders that could interfere with study participation.
- Pregnancy or breastfeeding.
- Current use of medications that may interfere with study outcomes or pose safety concerns.

Intervention

Control Group: Participants received 50 mg diclofenac sodium tablets orally twice daily for 7 d.

Intervention Group: Participants received 500 mg Anaheal (bromelain) tablets orally twice daily for 7 days.

Outcomes

Primary outcome measures

Pain assessment: Pain intensity was measured using

a visual analogue scale (VAS) ranging from 0 to 10, where 0 represents “no pain” and 10 represents “worst pain imaginable”.

Secondary outcome measures

Maximum mouth opening (MMO): Maximum mouth opening capacity measured as the distance between the upper and lower incisors, providing an objective measure of mandibular function.

Articulation sounds

Assessed through history and clinical examination and recorded as present or absent.

Follow-up time

Outcome measurements were performed on day 0 (T0), day 1 (T1), day 7 (T2), and day 14 (T3) to provide a comprehensive temporal analysis of treatment effects.

Sample size

With a confidence level of 95% and a power of 80%, using the study by Gupta et al.¹⁶ and according to the sample size calculation formula for comparing two independent means, the sample size was calculated to be 18 patients for each group, and ultimately 20 patients were included in the study in each group (N=20).

Randomization

Randomization was performed using simple random sampling to ensure equal probability of allocation to each treatment group. Allocation concealment was implemented using sequentially numbered, opaque, sealed envelopes (SNOSE) to prevent selection bias and maintain the integrity of the randomization process.

Blinding

This trial employed a double-blind design in which both participants and outcome assessors remained blinded to treatment allocation throughout the study period. Study medication for both groups was supplied in identical, unbranded packaging by an independent third-party investigator, who acted as

the study coordinator and was the only individual aware of the allocation protocol.

Statistical Analysis

Data analysis was performed using SPSS software version 25 (IBM Corporation, USA). The normality of data distribution was assessed using the Shapiro–Wilk test. Quantitative data were presented as mean $\pm$ standard deviation, while qualitative data were reported as frequency percentages. Between-group comparisons at each time point were analyzed using the independent samples t-test or Mann–Whitney U test. Within-group temporal changes were evaluated using repeated measures ANOVA or Friedman test. Pairwise comparisons between time points were conducted using the Bonferroni adjustment method and Dunn's Test to identify specific time intervals demonstrating significant changes. The significance level for all statistical tests was set at $P < 0.05$.

RESULTS

Forty subjects, including 28 females (70%) and 12 males (30%), with a mean age of 37.10 ± 14.34 yr and an age range of 16 to 63 yr, participated. Table 1 shows the detailed demographic information of the patients.

Pain assessment

In the between-group assessment, there was no significant difference in pain intensity between the groups at any of the assessment times ($P > 0.05$) (Table 2).

Both treatment groups demonstrated significant within-group reductions in pain intensity throughout the study period ($P < 0.001$).

In the within-group analysis, the control group (diclofenac) demonstrated a reduction in pain scores (VAS) from a baseline mean of 7.4 ± 1.7 at T0 to 6.7 ± 1.3 at T2 (day 7). However, pain scores increased at T3 (day 14) to 7.9 ± 1.5 , exceeding baseline values ($\chi^2 = 25.64$, $P < 0.001$). Pairwise comparisons of time points using Dunn's test revealed a statistically significant increase in mean pain scores at T3 compared to T2 ($P < 0.001$), whereas all other pairwise time point comparisons showed no statistically significant differences in pain scores. In the intervention group (Anaheal), pain scores decreased from a baseline mean of 8.0 ± 1.5 at T0 to 6.7 ± 1.4 at T2 and similarly increased at T3 to 7.5 ± 1.3 . Unlike the control group, the T3 pain scores did not exceed the baseline values ($\chi^2 = 32.19$, $P < 0.001$). Pairwise comparisons of time points using Dunn's test demonstrated that mean pain scores at T2 were significantly lower compared to T0, T1, and T3

Table 1. Demographic information of the patients

Variable	Groups		P-value*
	Control	Intervention	
Age, mean $\pm$ SD	38.05 $\pm$ 15.90	36.15 $\pm$ 12.95	0.799 ¹
Gender, n (%)	Male	6 (30%)	1.00 ²
	Female	14 (70%)	

*The significance level was considered to be $P < 0.05$.

1- Mann-Whitney U test

2- Chi-square test

Table 2. Comparative evaluation of pain score (VAS) between groups

Time	Groups		Independent t-test/ Mann–Whitney U test	P-value*
	Control	Intervention		
T0	7.4 $\pm$ 1.7	8.0 $\pm$ 1.5	1.28	0.210 ¹
T1	7.2 $\pm$ 1.5	7.6 $\pm$ 1.1	0.87	0.414 ²
T2	6.7 $\pm$ 1.3	6.7 $\pm$ 1.4	0.12	0.908 ¹
T3	7.9 $\pm$ 1.5	7.5 $\pm$ 1.3	0.89	0.398 ²
Friedman test	25.64	32.19		
P-value	<0.001	<0.001		

*The significance level was considered $P < 0.05$.

1. Independent t-test

2. Mann–Whitney U test

($P<0.001$, $P=0.011$, and $P=0.016$, respectively), while all other pairwise time point comparisons revealed no statistically significant differences in pain scores ($P>0.05$) (Figure 1).

In comparative analysis of pain changes between groups, the Anaheal group demonstrated a significantly greater pain reduction (0.5 ± 0.9) compared to the diclofenac group (-0.5 ± 0.9) in terms of overall pain changes from T0 to T3 ($Z = 3.03$, $P=0.004$). Similarly, pain changes from T1 to T3 also showed a statistically significant difference, with the Anaheal group exhibiting substantial pain reduction (0.1 ± 0.8) compared to the diclofenac group (-0.7 ± 1.0) ($Z = 2.5$, $P=0.020$). Bromelain treatment provides more sustained pain control compared to the control group following treatment cessation. No statistically significant differences

were observed in other intergroup pain change comparisons. Detailed results of intergroup pain change comparisons are presented in Table 3.

Maximum mouth opening (MMO) assessment

Regarding MMO, functional improvement between groups was comparable throughout the study period, with no statistically significant intergroup differences at baseline (T0), T1, T2, and T3 ($P>0.05$). Between-group comparisons of MMO across follow-up intervals are detailed in Table 4.

According to Table 4, in both groups, the highest level of MMO was evident in the T2 time interval, which decreased at T3, indicating the recurrence of MMO.

Within-group analysis demonstrated that in both

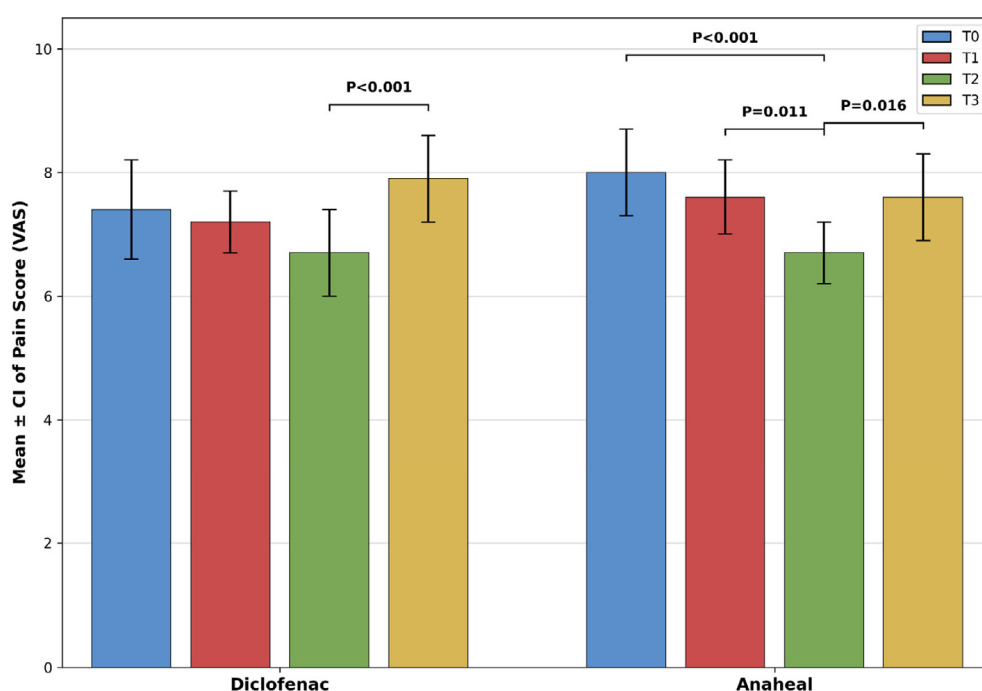


Figure 1. Mean and 95% confidence interval of pain score (VAS) by groups and study times

Table 3. Comparison of pain changes (Δ VAS) between study groups

Times	Δ VAS (mean $\pm$ SD)		Mann-Whitney U test	P-value*
	Control	Intervention		
T0-T1	0.2 $\pm$ 0.6	0.4 $\pm$ 0.7	0.97	0.461
T0-T2	0.7 $\pm$ 0.9	1.3 $\pm$ 0.9	2.03	0.052
T0-T3	-0.5 $\pm$ 0.9	0.5 $\pm$ 0.9	3.03	0.004
T1-T2	0.5 $\pm$ 0.6	0.9 $\pm$ 0.8	1.65	0.134
T1-T3	-0.7 $\pm$ 1.0	0.1 $\pm$ 0.8	2.50	0.020
T2-T3	-1.2 $\pm$ 1.0	-0.8 $\pm$ 0.6	1.27	0.242

* The significance level was considered $P<0.05$.

control and intervention groups, baseline MMO values exhibited an increasing trend through T2, followed by a decline at T3, reflecting a statistically significant temporal change (control: $F=26.40$, $P<0.001$ vs. intervention: $F=27.11$, $P<0.001$). Bonferroni pairwise comparisons in the control group revealed that mean MMO at T2 was significantly greater compared to all other time points (T0, T1, and T3) ($P<0.001$), with no statistically significant differences observed among the remaining time point comparisons ($P>0.05$).

Similarly, in the intervention group, mean MMO at T2 was significantly greater compared to T0, T1, and T3 ($P<0.001$), and notably, mean MMO at T3 was significantly greater than at baseline (T0) ($P=0.008$),

whereas all other pairwise time point comparisons showed no statistically significant differences ($P>0.05$) (Figure 2).

Between-group comparison of MMO changes revealed that changes in MMO from T0 to T3 in the intervention group (-2.5 ± 2.9) were greater than in the control group (-1.4 ± 2.6); however, this difference was not statistically significant ($P=0.165$). In all other temporal comparisons, no statistically significant intergroup differences in MMO changes were observed across time points (Table 5).

Articulatory sound assessment

Regarding joint clicking, there was a clicking sound in all patients and at all times studied.

Table 4. Comparative evaluation of maximum mouth opening (mm) between groups

Time	Groups		Independent t-test	P-value*
	Control	Intervention		
T0	23.1±5.8	23.8±6.5	0.39	0.702
T1	23.8±5.5	25.2±6.5	0.74	0.466
T2	28.3±6.0	29.6±6.1	0.71	0.482
T3	24.5±5.2	26.3±5.8	1.03	0.308
repeated measures ANOVA	26.40	27.11		
P-value	<0.001	<0.001		

*The significance level was considered $P<0.05$.

1. Independent t-test

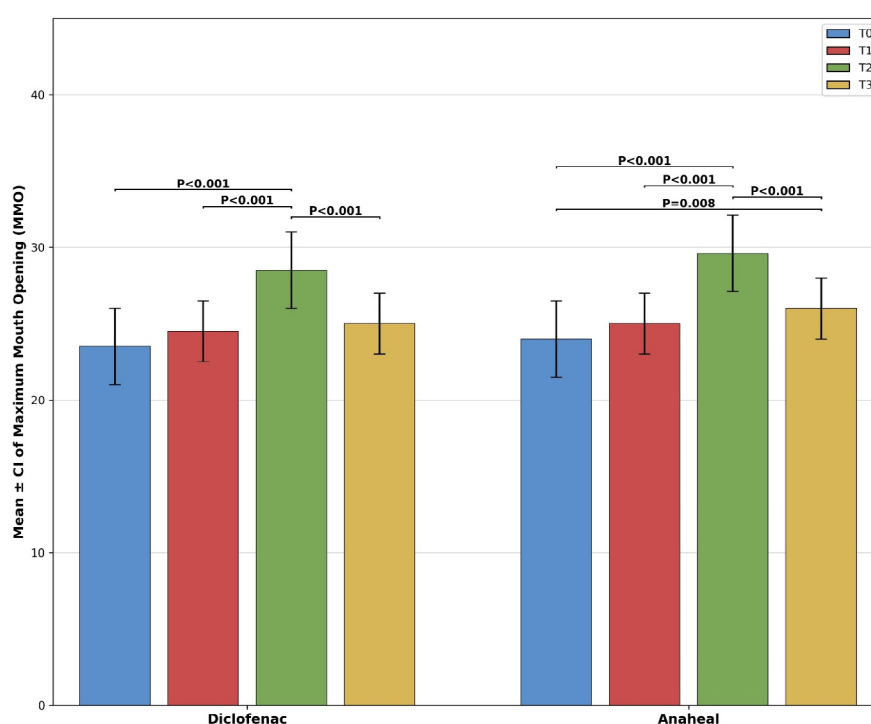


Figure 2. Mean and 95% confidence interval of MMO (mm) by groups and study times

Table 5. Comparison of MMO changes (Δ MMO) between study groups

Times	Δ MMO (mean $\pm$ SD)		Mann-Whitney U test	P-value*
	Control	Intervention		
T0-T1	-0.8 $\pm$ 1.3	-1.4 $\pm$ 2.3	0.81	0.478
T0-T2	-5.2 $\pm$ 4.1	-5.8 $\pm$ 3.8	0.71	0.495
T0-T3	-1.4 $\pm$ 2.6	-2.5 $\pm$ 2.9	1.45	0.165
T1-T2	-4.5 $\pm$ 3.7	-4.4 $\pm$ 3.4	0.08	0.947
T1-T3	-0.7 $\pm$ 2.2	-1.1 $\pm$ 2.7	0.66	0.529
T2-T3	3.8 $\pm$ 2.3	3.4 $\pm$ 2.7	0.81	0.429

* The significance level was considered $P < 0.05$.

DISCUSSION

Patterns of pain and MMO over time showed that the diclofenac group showed marked initial improvement followed by significant rebound effects, while the Anahil group maintained more sustained treatment benefits throughout the observation period, although these changes were not significantly different at most time points.

TMJ OA is a low-grade arthritic disorder that involves the entire joint structure, including articular cartilage, subchondral bone, joint capsule, synovial membrane, ligaments, and even adjacent muscles⁵. The variable prevalence of TMJ OA has made this degenerative joint disease (DJD) more prevalent than other systemic rheumatic diseases¹⁷, emphasizing the importance of addressing its various clinical aspects.

Demographic characteristics of patients with TMJ OA show consistent patterns in several studies, a female predominance (2:1 ratio in the present study) and an increase in this ratio, especially after menopause, indicating hormonal influences on disease development^{18,19}.

Conservative, nonsurgical management remains the cornerstone of treatment for TMJ OA, with multiple treatment modalities available with varying degrees of evidence support. Pharmacological interventions for TMJ OA include NSAIDs remaining the most commonly prescribed medications, with diclofenac sodium receiving the most research attention. However, the evidence for the effectiveness of NSAIDs specifically in TMJ OA remains limited, with most studies demonstrating high heterogeneity and insufficient sample sizes to draw definitive conclusions⁹.

Mejersjö et al⁸ conducted a randomized, single-blind study investigating the efficacy of occlusal splint therapy (15 patients) versus diclofenac

sodium treatment (14 patients) in the management of TMJ OA. Diclofenac sodium was administered three times daily at a dose of 50 mg until TMD symptoms resolved. Both groups received treatment for 3 months (90 d). Although diclofenac sodium resulted in more rapid symptom improvement in TMD, the findings demonstrated no statistically significant differences between the two groups. However, diclofenac administration at a daily dose of 150 mg for at least 90 d is associated with increased risk of myocardial infarction or cardiovascular death. Adverse effects that enzymatic therapy such as bromelain may not produce. Nevertheless, no difference exists between oral and topical application of diclofenac sodium in the management of TMD²⁰. Topical application eliminates the potential risk of systemic adverse effects that may occur with oral diclofenac sodium administration. However, the target population in the Businco et al²⁰ study was TMD and not specifically TMJ OA. In a similar study, treatment with occlusal stabilizing splints combined with diclofenac sodium therapy (specific drug dosage was not reported) for 42.15 $\pm$ 61.91 d significantly improved TMJ OA¹⁹. Patients received combined treatment (splint therapy plus diclofenac sodium), determining the precise individual effect of NSAIDs versus splint therapy on TMJ OA management may not be feasible. Nevertheless, the authors recommended combining both therapeutic modalities to reduce mechanical loading on the TMJ and simultaneously eliminate chemical inflammatory mediators from the joint.

A conservative treatment approach remains advocated, yet the current findings remain inconclusive and equivocal. Macías-Hernández et al²¹ demonstrated thermotherapy, manual therapy, and therapeutic exercise to be effective in TMJ OA management, and a systematic review²² of 1,417 articles recommended manual therapy and splint

therapy. Nevertheless, the evidence supports a non-invasive, patient-centered approach emphasizing patient education and symptom management prior to considering more invasive modalities such as intra-articular injections and arthrocentesis.

Other NSAIDs investigated in studies include celecoxib and naproxen in a study by Ta et al.²³. They evaluated the efficacy of celecoxib, naproxen, and placebo in patients with TMJ pain secondary to disc displacement (with reduction). Their intervention consisted of celecoxib 100 mg twice daily, naproxen 500 mg twice daily, or placebo for six weeks. Naproxen appeared to be most effective in reducing TMJ pain, while celecoxib was slightly better than placebo. Naproxen significantly reduced TMJ pain intensity within three weeks of treatment. To achieve the highest efficacy in reducing TMJ pain, both COX isoforms COX-1 and COX-2 must be inhibited.

Among other pharmacological interventions, glucosamine supplementation deserves attention. Glycosaminoglycans are attached to a protein core and form proteoglycans, which are part of the extracellular matrix of articular cartilage²⁴. Derwich et al.²⁴ conducted a systematic review evaluating the efficacy of oral glucosamine in TMJ OA management. Insufficient scientific evidence exists to definitively confirm the clinical efficacy of glucosamine supplements in TMJ OA treatment based on available literature. The most significant factor influencing the clinical efficacy of oral glucosamine in TMJ OA management was the total duration of administration. Prolonged oral glucosamine uses for extended periods (specifically 3 months) resulted in substantial reduction in TMJ pain and significant improvement in MMO.

Novel therapeutic approaches include mRNA-based anti-inflammatory interventions targeting interleukin-1 receptor antagonist pathways, which demonstrated promising results in animal models of TMJ OA in the study by Deng et al.²⁵.

Our results are in close agreement with those of Gupta et al.¹⁶ who evaluated a combination of trypsin, rutoside, bromelain, and diclofenac (intervention group) versus diclofenac alone in internal derangement (ID) of TMJ. Their study of 30 patients showed a highly significant improvement ($P<0.001$) in pain reduction, chewing ability, mouth opening, and articulation sounds with the intervention group. Although within-group analysis

in the current study did not demonstrate statistically significant differences in pain and MMO, pain changes from T1 to T3 and T0 to T3 were statistically significant in the Anaheal group, indicating superior pain sustainability and control with Anaheal therapy. Differences between the two studies regarding intervention design and sample size may account for the observed statistical variations. Similarly, a randomized clinical trial¹⁰ involving 30 patients with temporomandibular joint osteoarthritis showed that the combination of bromelain-trypsin-rutoside with diclofenac produced significantly better outcomes than diclofenac monotherapy in all parameters measured. While previous studies used combined enzyme formulations, our investigation specifically examined bromelain monotherapy and provided clearer insights into the individual therapeutic effects of this proteolytic enzyme.

Recent mechanistic studies provide an explanation for our observed clinical results. Henrotin et al.²⁶ showed in a randomized crossover trial of 43 patients with knee osteoarthritis that combined bromelain-trypsin-rutoside treatment significantly increased interleukin-10 levels ($P<0.0001$) while decreasing urinary carboxyl-terminal telopeptide of type II collagen (urinary CTXII) ($P=0.038$). This anti-inflammatory cytokine modulation may explain the sustained pain relief observed in our intervention group at T3. The molecular mechanisms of bromelain's efficacy have been further elucidated by Pothacharoen et al.²⁷, who showed that bromelain extract suppressed TNF- α -induced NF- κ B and MAPK signaling pathways in synovial fibroblasts and exerted chondroprotective effects in IL-1 β -stimulated cartilage. The therapeutic effects of bromelain go beyond simple anti-inflammatory activity and include chondroprotective mechanisms, a process that may also be effective in alleviating osteoarthritis pain.

However, pain and MMO recurrence may be due to various reasons, such as drug tolerance because repeated use of NSAIDs leads to a decrease in receptor responsiveness. Moreover, NSAIDs only treat symptoms and not the cause of the disease. Another reason for pain recurrence may be because the sudden cessation of cyclooxygenase inhibition leads to increased prostaglandin synthesis²⁸.

The comparable acute efficacy of bromelain and diclofenac during active treatment, combined with superior post-treatment stability of bromelain and

an established safety profile, make this natural proteolytic enzyme an attractive first-line or adjunctive therapy in the conservative management of TMJ osteoarthritis. Furthermore, the preserved functional improvement in MMO observed with bromelain treatment demonstrates its potential to simultaneously address both pain and functional limitations, rendering it particularly valuable in comprehensive TMJ disorder management protocols where patient quality of life and long-term outcomes represent primary therapeutic objectives. However, due to pain recurrence and symptom relapse in patients, this therapy may not represent the definitive treatment, and more invasive interventions such as joint lavage may constitute the final therapeutic option for such patients.

Although the monotherapy approach allowed for the independent evaluation of bromelain effects in this study and was a strength of that, the study also had some limitations. The relatively small sample size, the short follow-up period of 14 d, which may not be sufficient to fully assess long-term effects, and the lack of assessment of inflammatory biomarkers such as cytokines and MMPs, which could provide a better understanding of the mechanisms of action, are limitations of this study.

CONCLUSION

The both bromelain (Anaheal 500 mg) and diclofenac sodium (50 mg) provided comparable and mostly equivalent pain relief and improvement in MMO in patients with TMJ OA. Although acute analgesic and functional benefits during the active treatment phase were similar, bromelain demonstrated more sustained symptom control over time. Bromelain, as an enzyme complex with favorable immunogenic properties, could be used as a treatment for TMJ OA, or at least as an adjunct therapy. However, more future studies are needed to confirm these results. While conservative oral therapeutic approaches remain first-line management, clinicians should be prepared for recurrence of symptoms. In these cases, more invasive interventions such as temporomandibular joint lavage may ultimately be required to achieve definitive symptom control.

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CONSENT FOR PUBLICATION

All study participants were informed of the purpose of the study and their written informed consent was obtained before entering the study.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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