SOUTH BAYLO UNIVERSITY

Combined Effects of Du Huo Ji Sheng Tang and Shen Tong Zhu Yu Tang On Degenerative Osteoarthritis: A Case Series

by

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APPROVED BY RESEARCH COMMITTEE

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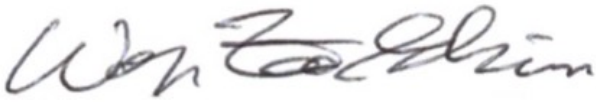

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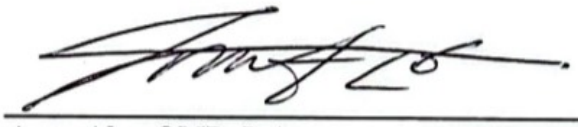

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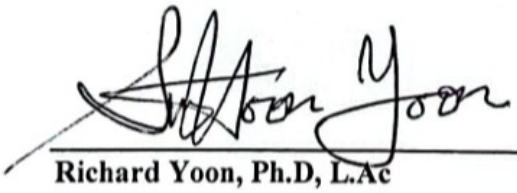

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ABSTRACT

Objective: To evaluate the clinical efficacy and safety of a combined herbal treatment protocol integrating *Du Huo Ji Sheng Tang* (DHJST) and *Shen Tong Zhu Yu Tang* (STZYT) in patients with chronic degenerative osteoarthritis.

Methods: This prospective observational study included eight patients with degenerative osteoarthritis who received a combined 1:1 dose of DHJST and STZYT twice daily for four weeks. Pain and functional outcomes were assessed using the Visual Analog Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Safety was evaluated through monitoring of adverse events.

Results: Following the four-week intervention, mean VAS scores significantly decreased from 7.3 ± 0.89 at baseline to 3.5 ± 1.13 at Week 4 ($p < 0.001$, Cohen's $d = 3.736$), indicating substantial pain relief. Total WOMAC scores also demonstrated significant improvement, decreasing from 58.7 ± 12.4 to 39.1 ± 10.8 ($p = 0.008$, Cohen's

d = 1.42), reflecting improvement in functional outcomes. Statistical analysis of the 17-item WOMAC item responses showed no significant adverse changes compared to baseline. All participants completed the treatment without dropout, and no clinically significant adverse events were observed within the scope of this investigation.

Conclusion: The combined administration of DHJST and STZYT was associated with significant improvements in pain and functional outcomes without clinically significant adverse events. These findings suggest that this combined herbal protocol may be a feasible therapeutic approach for degenerative osteoarthritis, warranting further investigation in larger controlled studies.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

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This dissertation is dedicated to my husband, whose patience and steady support sustained me throughout this academic journey. His belief in my work provided reassurance during difficult moments, and I am deeply appreciative of his presence throughout this process.

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I. INTRODUCTION

Osteoarthritis (OA) is a chronic degenerative joint disorder characterized by the progressive destruction of articular cartilage, accompanied by structural alterations in the synovium, ligaments, joint capsule, and subchondral bone. As one of the leading causes of disability worldwide, OA significantly compromises patients' quality of life and imposes a substantial socioeconomic burden. With the rapid aging of the global population and the increasing prevalence of obesity, the incidence of OA continues to rise steadily. Although conventional therapeutic modalities—including nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular corticosteroid injections, and physical therapy—are widely employed to alleviate symptoms, these approaches remain limited in their ability to modify disease progression. Moreover, long-term NSAID use is frequently associated with gastrointestinal, renal, and hepatic adverse effects, underscoring the need for safer and more comprehensive therapeutic strategies.

In response to these limitations, increasing scholarly attention has been directed toward integrative treatment models that combine conventional Western medicine with Traditional Korean Medicine (TKM). Recent international guidelines for knee osteoarthritis have emphasized the potential value of integrative approaches, suggesting that the incorporation of traditional medicine may enhance symptom management and functional outcomes when used alongside standard care. Within the theoretical framework of TKM, OA is understood as a dynamic interaction between internal deficiency (Liver-Kidney deficiency) and external pathogenic factors (Blood stasis and Cold-Dampness), commonly classified under the category of "Bi syndrome."

Two herbal formulas are particularly relevant in this context: *Du Huo Ji Sheng Tang* (DHJST) and *Shen Tong Zhu Yu Tang* (STZYT). DHJST is a classical formula traditionally prescribed to tonify the Liver and Kidney while dispelling Cold-Dampness, primarily addressing the "root" (deficiency) of chronic degeneration. Conversely, STZYT is formulated to invigorate Blood circulation and resolve stasis, targeting the "manifestation" (obstruction) characterized by localized, persistent pain. While each formula has demonstrated therapeutic relevance as a monotherapy, single-formula approaches may not adequately address the multifactorial and concurrent pathological processes that characterize advanced degenerative OA.

The rationale for the combined use of DHJST and STZYT lies in the classical therapeutic principle of “treating both the root and the manifestation.” By simultaneously addressing constitutional deficiency and localized microcirculatory impairment, this synergistic approach seeks to overcome the limitations of conventional monotherapies. Therefore, the present study aims to explore the clinical efficacy and safety of a combined herbal protocol integrating DHJST and STZYT in patients with degenerative osteoarthritis. Through a prospective observational framework, this study intends to provide preliminary clinical insights that may help inform future investigations into more comprehensive and individualized management strategies for chronic OA.

OBJECTIVE

The overall objective of this study is to determine the clinical efficacy and safety of a combined herbal treatment protocol integrating *Du Huo Ji Sheng Tang* and *Shen Tong Zhu Yu Tang* in patients with chronic degenerative osteoarthritis.

The sub-objectives of this study include:

1. to assess longitudinal changes in pain intensity and functional outcomes using the Visual Analog Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC);

2. to characterize the clinical presentation of osteoarthritis across different anatomical regions and to explore the association between Traditional Korean Medicine (TKM) pattern identification and individual therapeutic response; and

3. to evaluate the safety and tolerability of the combined herbal protocol to support its feasibility as a long-term management strategy.

LITERATURE REVIEW

1. General Overview of Osteoarthritis

Osteoarthritis (OA) is the most prevalent chronic joint disorder worldwide, affecting an estimated 595 million individuals. [13][17] It is characterized by progressive degeneration of articular cartilage, accompanied by synovial inflammation, subchondral bone remodeling, and osteophyte formation, ultimately resulting in irreversible structural deterioration and impaired mobility. [2][14][17] Although strongly associated with aging, OA is now recognized as a multifactorial disease influenced by biomechanical overload, obesity, previous trauma, genetic predisposition, and metabolic abnormalities. [2][17]

According to the Global Burden of Disease Study (2017), the global point prevalence of OA increased by 9.3% between 1990 and 2017. [13] At the pathophysiological level, OA is characterized by chondrocyte senescence, extracellular matrix degradation, and persistent low-grade synovial inflammation [14][17]. Elevated concentrations of inflammatory mediators—such as IL-1beta, TNF-alpha, and IL-6—drive catabolic processes that accelerate cartilage erosion. [2][14] Recent evidence has reframed OA as a chronic inflammatory condition rooted in immunometabolic dysregulation, rather than a simple consequence of mechanical wear and tear [2][14][17].

Moreover, accumulating pathological evidence indicates that osteoarthritis involves a complex interplay among chronic low-grade inflammation, aberrant chondrocyte metabolism, subchondral bone remodeling, and microvascular alterations, collectively driving progressive joint degeneration.[35] Conventional management primarily focuses on symptom relief using NSAIDs, COX-2 inhibitors, and intra-articular injections.

However, these treatments neither halt disease progression nor address the underlying pathophysiology. Moreover, long-term NSAID use is associated with hepatotoxicity and gastrointestinal complications.[3][4][21] These limitations have prompted growing interest in integrative approaches that target multiple pathophysiologic mechanisms simultaneously.[11][23]

2. Pharmacological Foundations of DHJST and STZYT

In Traditional Korean Medicine (TKM), chronic osteoarthritis is commonly understood within the theoretical framework of Bi-syndrome, in which the progression of disease reflects a gradual transformation in underlying pathophysiology. While early-stage Bi-syndrome is typically attributed to the invasion of external pathogenic factors such as wind, cold, and dampness, prolonged disease courses are traditionally interpreted as involving internal Liver-Kidney deficiency, depletion of Qi and Blood, and the subsequent formation of persistent Blood stasis.[39] This classical conceptualization underscores the importance of therapeutic approaches that concurrently address constitutional deficiency and localized circulatory impairment. Within this theoretical context, the present study explored an integrative treatment strategy combining Du Huo Ji Sheng Tang (DHJST) and Shen Tong Zhu Yu Tang (STZYT).

DHJST is established as a cornerstone intervention for osteoarthritis, particularly for patients presenting with chronic pain patterns associated with deficiency and cold-dampness. Beyond molecular and network-based pharmacological evidence, accumulating clinical data grounded in TKM diagnostics support its syndrome-specific application. A pooled analysis by Zhao et al. (2022) demonstrated that DHJST significantly alleviated

pain and improved functional outcomes in patients with cold-dampness obstruction type knee osteoarthritis.[36] Concurrently, a systematic review by Zhu et al. (2023) reported significant reductions in inflammatory markers, including C-reactive protein (CRP), alongside improvements in WOMAC and VAS scores. [24] At the mechanistic level, DHJST has been shown to suppress the NLRP3 inflammasome and NF-kappaB signaling pathways,[6][9][22] which are recognized contributors to synovial inflammation and cartilage catabolism in osteoarthritis. Furthermore, network pharmacology analyses indicate that DHJST preserves chondrocyte viability through modulation of the PI3K/Akt pathway, thereby inhibiting apoptosis of articular chondrocytes.[28]

STZYT complements this therapeutic approach by primarily targeting the ischemic pain and circulatory obstruction characteristic of chronic osteoarthritis. Experimental and pharmacological studies have demonstrated that STZYT exerts anti-inflammatory and anti-thrombotic effects through inhibition of platelet aggregation and reduction of inflammatory edema.[25] Additional evidence indicates that blood-invigorating formulas such as STZYT improve subchondral bone microcirculation and reduce intraosseous hypertension, thereby addressing ischemia-related mechanisms underlying chronic joint pain.[29] This mechanism is particularly relevant in light of emerging evidence that subchondral bone vascular dysfunction and impaired microcirculation play critical roles in osteoarthritis-associated pain and structural progression.[35] At the signaling level, STZYT has been shown to modulate the p38 MAPK and connective tissue growth factor (CTGF) pathways, contributing to the alleviation of structural stasis.[10] Moreover, metabolomics combined with network pharmacology analyses have demonstrated that STZYT regulates multiple

inflammation- and pain-related pathways, including MAPK, TNF, and arachidonic acid metabolism.[38]

3. Synergistic Rationale and Research Significance

Pharmaco-epidemiological evidence provides an important contextual background for considering the combined application of DHJST and STZYT in osteoarthritis. In a large-scale nationwide population-based study, Liao et al. (2014) analyzed 32,050 herbal prescriptions for osteoarthritis using the National Health Insurance Research Database, which identifies DHJST as the most frequently prescribed herbal formula for osteoarthritis. In addition, association rule analysis demonstrated that DHJST and STZYT were each among the herbal formulas most commonly prescribed for this condition. [23] Importantly, these findings reflect the independent clinical prevalence of each formula rather than evidence of a deliberately combined treatment, as no prior studies have reported the formal co-administration of DHJST and STZYT as a unified therapeutic protocol.

From a traditional and pathophysiological perspective, DHJST and STZYT address distinct yet complementary aspects of osteoarthritis. DHJST is conventionally applied to chronic degenerative conditions characterized by constitutional deficiency, aiming to support systemic balance and mitigate progressive degeneration. In contrast, STZYT is primarily utilized to resolve blood stasis and improve localized microcirculation, thereby alleviating pain associated with impaired tissue perfusion. Based on this complementary rationale, the present study explores the feasibility of a combined therapeutic approach that integrates the respective strengths of these two formulas, addressing both the root deficiency and the manifestation of obstruction.

This integrative perspective is consistent with contemporary pathophysiological models of osteoarthritis, which emphasize the interrelated roles of inflammatory signaling, cartilage metabolism, subchondral bone remodeling, and microvascular dysfunction in disease progression.[35] While both DHJST and STZYT have been widely utilized independently in clinical practice, systematic clinical investigations evaluating their combined application remain limited. Accordingly, the present study offers supportive observational data that may contribute to a broader understanding of integrative treatment strategies. This research serves as a meaningful academic foundation for future large-scale clinical investigations and the design of randomized controlled trials (RCTs) aimed at the comprehensive management of chronic degenerative osteoarthritis.

II. MATERIALS AND METHODS

1. Study Design

This study was conducted as a prospective observational case series to evaluate the clinical efficacy and safety of a combined herbal protocol integrating *Du Huo Ji Sheng Tang* (DHJST) and *Shen Tong Zhu Yu Tang* (STZYT) for patients with chronic degenerative osteoarthritis (OA). The research design focused on validating the synergistic "Tonify and Circulate" strategy, which addresses systemic deficiency while simultaneously resolving localized blood stasis—a fundamental therapeutic principle in Traditional Korean Medicine (TKM).

2. Participants and Recruitment

Eight participants were recruited through targeted voluntary enrollment from a private Korean medicine clinic and a local community organization between August 1 and August 29, 2025. All participants had a confirmed diagnosis of degenerative OA, supported by clinical symptomology and radiographic evidence (Kellgren-Lawrence grade II or higher). Furthermore, each participant underwent a standardized TKM diagnostic assessment to confirm the presence of Qi and Blood deficiency complicated by chronic Blood stasis.

3. Inclusion and Exclusion Criteria

3.1. Inclusion Criteria: To ensure the homogeneity of the study population, participants were required to meet the following criteria:

- Age: 55 years or older.

- Diagnosis: Radiological (X-ray, MRI) or clinical orthopedic confirmation of degenerative osteoarthritis.
- Pain Severity: Persistence of moderate to severe joint pain, defined by a Visual Analog Scale (VAS) score ≥ 5.
- Cognitive and Ethical Compliance: Ability to fully comprehend the study protocols and provide voluntary written informed consent.

3.2. Exclusion Criteria: Individuals meeting any of the following conditions were excluded from the study:

- Differential Diagnoses: Presence of inflammatory or metabolic arthropathies, such as rheumatoid arthritis, gouty arthritis, or septic arthritis.
- Recent Interventions: History of intra-articular corticosteroid injections or orthopedic surgical procedures on the affected joint within the preceding 30 days.
- Systemic Comorbidities: Severe cardiovascular, hepatic, or renal dysfunction that could potentially confound the efficacy data or compromise participant safety.
- Pharmacological Interference: Current use of anticoagulants or systemic immunosuppressants that might interact with the herbal intervention.

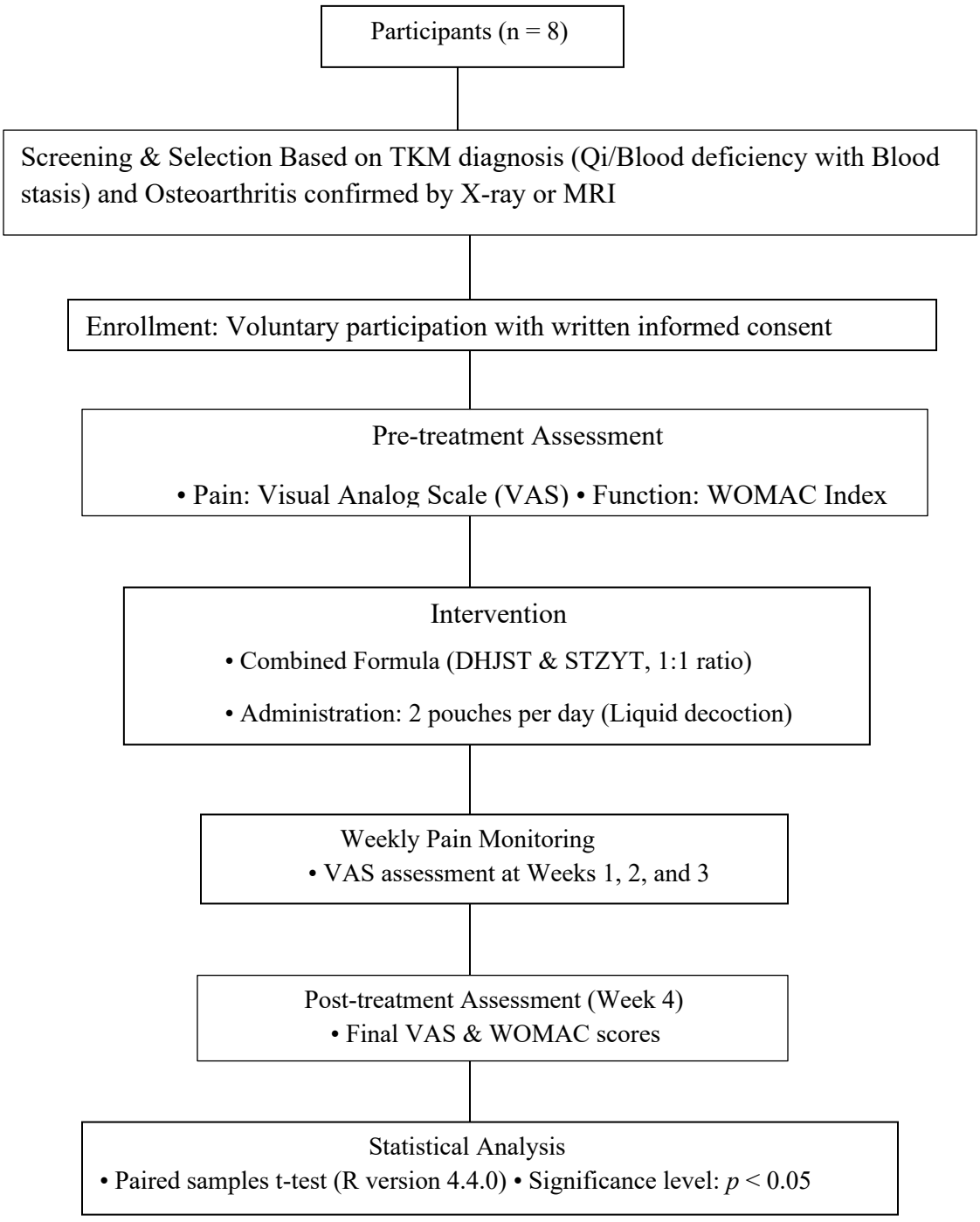

Figure 1. Flowchart of the study design and clinical procedure

Table 1. Prescription Composition for the Combined Herbal Protocol

Common Name	Latin Pharmaceutical Name	Daily Dosage (g)
Du Huo	Angelicae Pubescentis Radix	9
Fang Feng	Saposhnikoviae Radix	6
Qin Jiao	Gentianae Macrophyllae Radix	6
Sang Ji Sheng	Taxilli Herba	6
Du Zhong	Eucommiae Cortex	6
Niu Xi	Achyranthis Bidentatae Radix	9
Dang Gui	Angelicae Sinensis Radix	9
Sheng Di Huang	Rehmanniae Radix Crudus	6
Chuan Xiong	Chuanxiong Rhizoma	6
Bai Shao	Paeoniae Radix Alba	6
Ren Shen	Ginseng Radix	6
Fu Ling	Poria	6
Rou Gui	Cinnamomi Cortex	6
Zhi Gan Cao	Glycyrrhizae Radix Preparata	6
Tao Ren	Persicae Semen	9
Hong Hua	Carthami Flos	9
Di Long	Pheretima	6
Mo Yao	Myrrha	6
Xiang Fu	Cyperi Rhizoma	3
Qiang Huo	Notopterygii Rhizoma	9
Total		132g

Herbal Formula Preparation and Administration

The intervention integrated two classical prescriptions, *Du Huo Ji Sheng Tang* (DHJST) and *Shen Tong Zhu Yu Tang* (STZYT), with a total daily dosage of 132 g. When ingredients overlapped between the two formulas, the higher dose was prioritized to maintain the maximum therapeutic concentration. For pharmacological safety and international regulatory compliance, all ingredients listed under CITES Appendix I/II were strictly excluded or substituted.

All herbal materials were professionally sourced from the Republic of Korea through Hanmi Herbs (Los Angeles, CA). The formula was prepared as a vacuum-sealed liquid decoction to prevent oxidation and was administered orally twice daily, 30 minutes after meals. Approximately 41.4 kg of raw herbs were processed for the 28-day study, accounting for mass loss during high-temperature extraction. A detailed description of the pharmacological actions and traditional indications for each herb is provided in Appendix 1.

Evaluation Timeline and Outcome Measures

The clinical efficacy of the intervention was evaluated through standardized pain and functional assessment tools. The outcomes were measured according to the following criteria:

- Pain Intensity (VAS): Subjective pain levels were assessed using a 100-mm Visual Analog Scale (VAS).[12][24] Participants marked their perceived pain intensity on a

horizontal line ranging from 0 (no pain) to 10 (unbearable pain). Assessments were conducted at five specific time points: baseline (before treatment) and at the end of each week (Weeks 1, 2, 3, and 4) throughout the 4-week treatment period.

- Functional Status (WOMAC): The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).[12][17][24] was employed to evaluate improvements in joint health. The WOMAC scale, a validated instrument for osteoarthritis assessment, measures three domains: pain, stiffness, and physical function. Assessments were performed at baseline and upon the completion of the four-week treatment period to determine changes in functional status.

Statistical Analysis

All statistical analyses were performed using R (version 4.4.0, R Foundation for Statistical Computing).[16] The normality of the data distribution was assessed using the Shapiro–Wilk test. To compare pre- and post-treatment outcomes, a paired t-test was employed for normally distributed data; otherwise, the Wilcoxon signed-rank test was used as a non-parametric alternative. All results were reported as mean ± standard deviation (SD), and a two-tailed p-value of less than 0.05 was considered statistically significant. To evaluate the magnitude of the treatment effect, Cohen's d was calculated.

Ethical Considerations

The study protocol was reviewed and approved by the relevant Institutional Review Board (IRB). All participants provided voluntary written informed consent before enrollment, and the study was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki.

III. RESULTS

The clinical efficacy of the combined herbal protocol—*Du Huo Ji Sheng Tang* (DHJST) and *Shen Tong Zhu Yu Tang* (STZYT)—was evaluated in eight patients with degenerative osteoarthritis. Statistical analyses of the collected data were performed using R version 4.4.0. [16]

3.1. Participant Characteristics

Eight participants with degenerative osteoarthritis, confirmed via clinical evaluation and radiologic imaging (X-ray or MRI), completed the study with no dropouts. In accordance with the principles of Traditional Korean Medicine (TKM), all participants were diagnosed with the pattern of Qi and Blood Deficiency, accompanied by Blood Stasis. All participants were of Korean ethnicity. Baseline demographic and clinical characteristics are summarized in Table 3.

The mean age of the participants was 63.4 ± 5.0 years (range: 56–70 years). The cohort consisted of two males (25.0%) and six females (75.0%). The mean duration of symptoms was 42.8 ± 35.9 months (range: 6–120 months). Notably, the symptomatic duration was highly variable, ranging from 6 to 120 months. Throughout the study period, no participants received concomitant treatments, such as new medications, physical therapy, or surgical procedures, ensuring the observed outcomes were primarily attributable to the herbal intervention.

Table 2. Baseline Demographic and Clinical Characteristics of Participants

Patient No.	Age (years)	Gender	Duration of Symptoms (months)
P1	62	Male	12
P2	65	Female	60
P3	58	Female	36
P4	70	Female	120
P5	67	Male	36
P6	61	Female	24
P7	56	Female	6
P8	68	Female	48
Mean ± SD	63.4 ± 5.0	M:2 / F:6	42.8 ± 35.9

As summarized in Table 3, the study population (n=8) comprised two males (25.0%) and six females (75.0%), with a mean age of 63.4 ± 5.0 years. The duration of symptoms was widely distributed, ranging from 6 months to 10 years (mean: 42.8 ± 35.9 months), reflecting various stages of chronic degenerative osteoarthritis. All participants were of Korean ethnicity and were uniformly diagnosed with the Traditional Korean Medicine (TKM) patterns of Qi and Blood Deficiency, accompanied by Blood Stasis.

Throughout the four-week study period, none of the 8 participants received concomitant treatments, such as new medications, physical therapy, or surgical procedures. This strict control of external interventions ensured that the observed changes in clinical outcomes were primarily attributable to the herbal formula protocol. Following the baseline assessment of these characteristics, the clinical progress of each participant was monitored at weekly intervals to evaluate the treatment's efficacy.

3.2. Individual Clinical Outcomes (Case 1–8)

Before presenting the aggregate statistical analysis, the clinical progress of each participant was documented to assess the consistency of treatment efficacy. Table 2 summarizes the baseline and post-treatment (Week 4) scores for the Visual Analog Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for all eight patients.

Table 3. Individual Baseline and Week 4 scores for VAS and WOMAC

Patient No.	Baseline VAS	Week 4 VAS	VAS Change	Baseline WOMAC	Week 4 WOMAC	WOMAC Change
P1	8	4	-4	62	45	-17
P2	7	3	-4	55	38	-17
P3	6	3	-3	48	32	-16
P4	9	5	-4	78	55	-23
P5	7	4	-3	52	35	-17
P6	8	3	-5	60	41	-19
P7	6	2	-4	45	28	-17
P8	7	4	-3	70	39	-31
Mean	7.3	3.5	-3.8	58.8	39.1	-19.7

As illustrated in Table 2, all eight participants demonstrated a definitive reduction in both pain intensity and functional impairment. Notably, participants with high baseline severity - such as Patient 4, who started with a VAS of 9, and Patient 8, who had a baseline WOMAC score of 70 - experienced substantial clinical improvements following the four-week intervention. These patient-specific results provide a detailed description of individual-level changes following the four-week DHJST and STZYT intervention.

The following sections describe the changes in pain and functional outcomes observed during the 4-week treatment period. Individual progress is presented first, followed by aggregate statistical analyses to determine the overall efficacy of the intervention. The longitudinal VAS values across the five measurement points (Weeks 0–4) and the pre- and post-treatment WOMAC scores are summarized in Tables 4 and 5, respectively.

3.3. Statistical Analysis of VAS Changes

3.3.1. Progression of VAS Scores During Treatment

The results of the Visual Analog Scale (VAS) analysis are summarized in Table 4, which presents the mean scores of the eight participants across five consecutive assessment points. A consistent downward trend was observed, indicating progressive improvement in pain intensity throughout the four-week treatment period.

At baseline (Week 0), the mean VAS score was 7.3 ± 0.89, reflecting a relatively high initial pain level. This score decreased steadily to 6.6 ± 1.03 at Week 1, with a mean reduction of 0.63 ± 0.23 from baseline. This downward trend continued throughout the study, reaching 6.1 ± 1.15 at Week 2, 4.8 ± 1.25 at Week 3, and 3.5 ± 1.13 at the final assessment (Week 4). The cumulative reductions from baseline were 1.19 ± 0.37, 2.50 ± 0.46, and 3.75 ± 0.46 for Weeks 2, 3, and 4, respectively, demonstrating a clinically meaningful and statistically significant reduction in pain intensity.

The statistical significance of these changes was evaluated using the paired-samples *t*-test or the Wilcoxon signed-rank test, depending on the results of the Shapiro–Wilk normality test. As shown in Table 4, all comparisons between baseline and

subsequent weeks were statistically significant ($p < 0.05$), with substantial effect sizes (Cohen's *d*). As illustrated in Figures 2, 3, and 4, the results indicate a progressive reduction in mean VAS scores across all assessment points, accompanied by a gradual narrowing of score variability, suggesting a consistent therapeutic response among participants.

Table 4. Changes in VAS Scores During the Treatment Period

Assessment	VAS Score	Difference*	p-value**	Cohen's d
Baseline (1st)	7.3 ± 0.89	-	-	-
Week 1 (2nd)	6.6 ± 1.03	0.63 ± 0.23	0.010	0.727
Week 2 (3rd)	6.1 ± 1.15	1.19 ± 0.37	0.010	1.167
Week 3 (4th)	4.8 ± 1.25	2.50 ± 0.46	0.013	2.304
Week 4 (5th)	3.5 ± 1.13	3.75 ± 0.46	< 0.001	3.736

Note. Values are presented as Mean ± SD (n=8).

*VAS Difference: Baseline score - nth week score.

** Paired samples t-test / Wilcoxon signed-rank test.

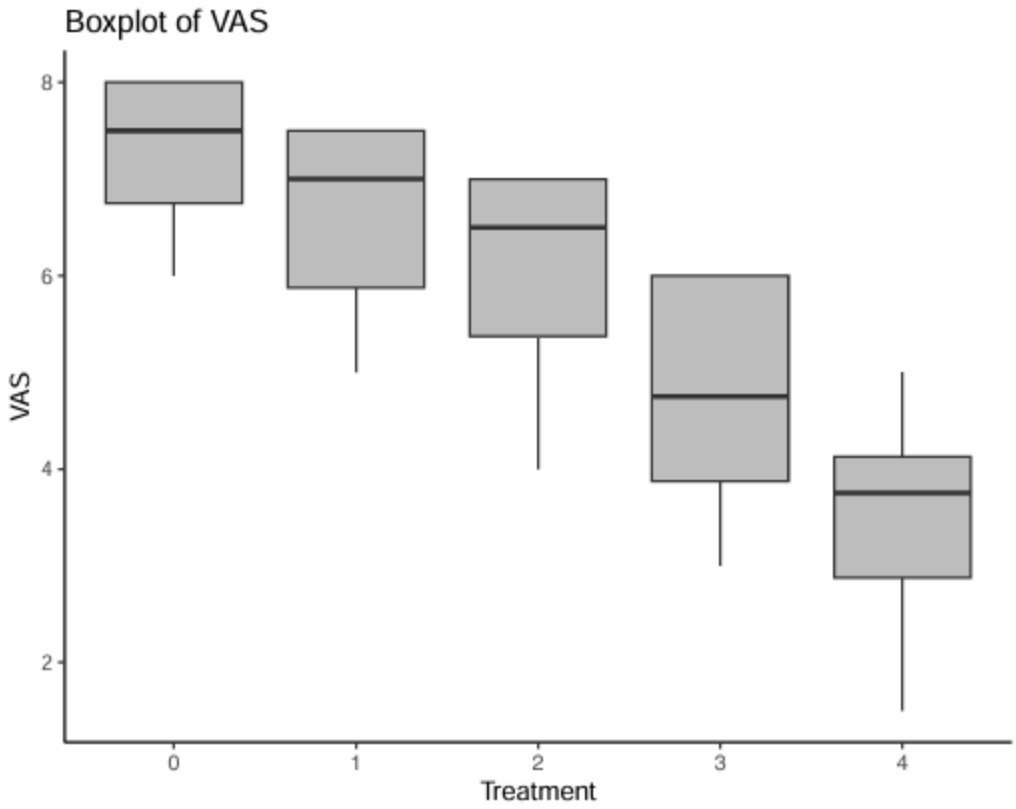

Figure 2. Mean VAS Scores throughout the Treatment Period

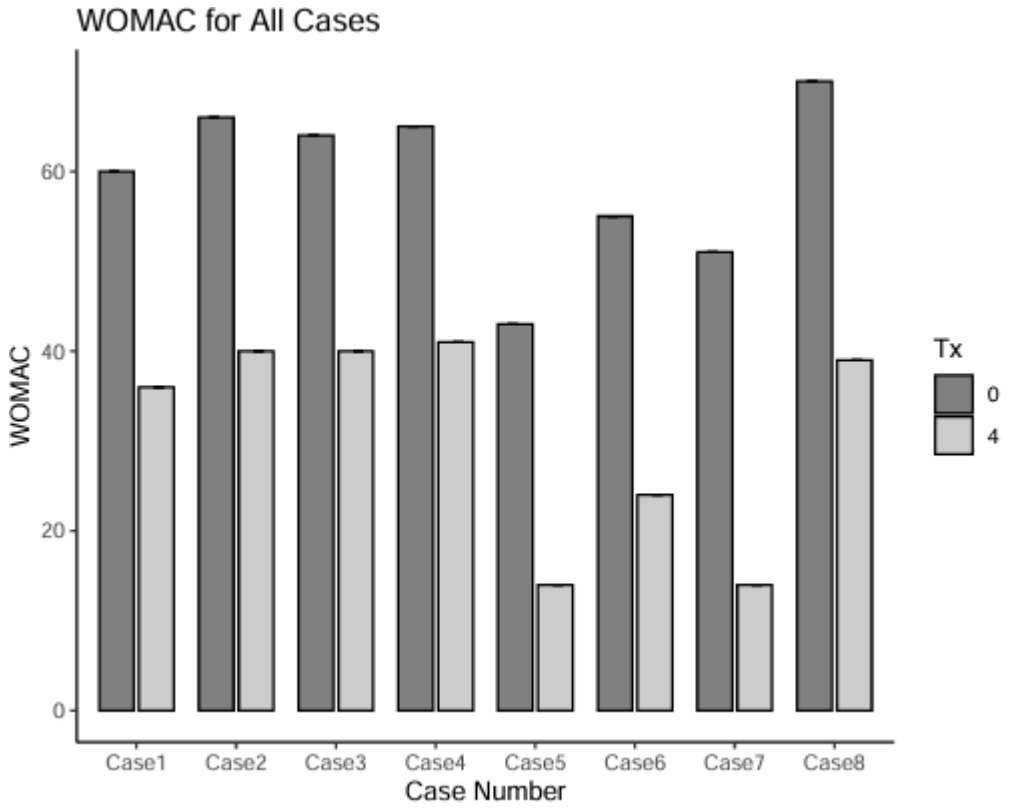

Figure 3. Individual changes in VAS scores for all cases from baseline to post-intervention (Week 0 and Week 4).

3.3.2. Cohen's d (Effect Size) for Treatment

To evaluate the magnitude of the treatment effect between baseline and subsequent sessions, Cohen's *d* was calculated using the standardized mean difference and the pooled standard deviation as follows:

$$d = \frac{M_1 - M_2}{\sqrt{(SD_1^2 + SD_2^2)/2}}$$

Where:

*M*1: Mean value of the baseline (1st session)

*M*2: Mean value of the subsequent treatment session

*SD*1: Standard deviation of the baseline

*SD*2: Standard deviation of the subsequent treatment session

Cohen's d was calculated to assess the magnitude of the treatment effect between sessions using the standardized mean difference and the pooled standard deviation. The calculated results for each treatment interval are summarized in Table 4, with effect sizes ranging from 0.727 to 3.736. According to Cohen's classification criteria, values starting from the second interval exceeded the threshold of 0.8, indicating consistently large effect sizes throughout the treatment period.

Classification of Effect Size Based on Cohen's Criterion

Effect size (Cohen's d)	Interpretation
< 0.2	Negligible
< 0.5	Small
< 0.8	Medium
≥ 0.8	Large

According to Cohen's guidelines, an effect size of 0.8 or higher is classified as large, representing a clinically meaningful difference in treatment response. In the present study, the calculated effect sizes reached a maximum of 3.736. These findings demonstrate that the combined herbal protocol of *Du Huo Jisheng-tang* and *Shentong Zhuyu-tang* produced a consistently robust and clinically significant reduction in pain intensity across the five assessment points in patients with chronic degenerative osteoarthritis.

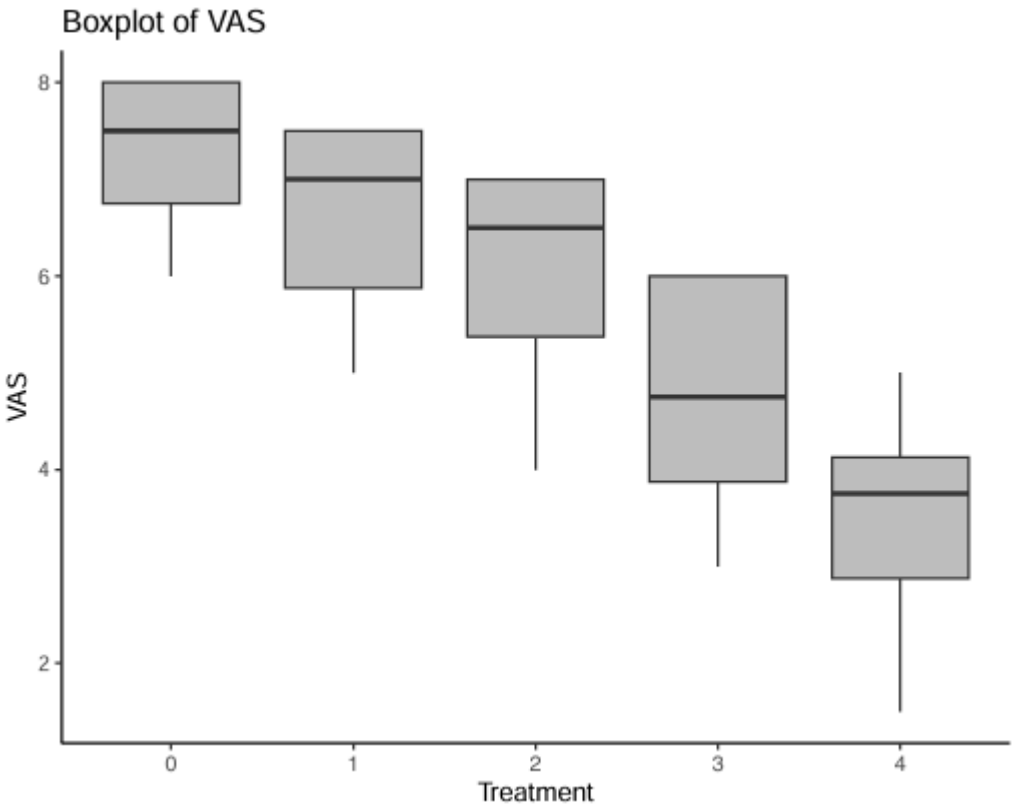

Figure 4. Box plot of VAS scores during the treatment period.

3.4. Statistical Analysis of WOMAC Changes

3.4.1. Changes in WOMAC Scores Following Treatment

The changes in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores before and after treatment with the combined herbal protocol of *Du Huo Ji Sheng Tang* and *Shen Tong Zhu Yu Tang* (DHJST+STZYT) are summarized in Table 5. The WOMAC index is a validated instrument widely used to assess pain, stiffness, and physical function in patients with osteoarthritis, where higher scores indicate greater symptom severity and functional disability.

Before treatment, the mean total WOMAC score was 58.7 ± 12.4, indicating moderate to severe osteoarthritic symptoms. After the four-week treatment period, the mean score decreased significantly to 39.1 ± 10.8. This reduction reflects a substantial improvement in both subjective pain and physical function. The mean difference between baseline and post-treatment scores was 19.6 ± 9.3, which was statistically significant (p = 0.008), indicating that the observed functional improvement was unlikely to have occurred by chance.

Table 5. WOMAC Before and After Treatment

Assessment	WOMAC Score (Mean ±SD)	*p*-value*	Cohen's *d*
Before (Baseline)	58.7 ± 12.4	-	-
After (4 Weeks)	39.1 ± 10.8	-	-
Difference	19.6 ± 9.3	0.008	1.42

Note. Values are presented as Mean ± SD (n=8).

* Wilcoxon signed-rank test.

3.4.2. Clinical Significance of Functional Improvement

The calculated Cohen's d value of 1.42 indicates a large treatment effect, confirming that the combined formula (DHJST+STZYT) produced a clinically meaningful improvement in joint function and a reduction in osteoarthritis-related. According to Cohen's criteria, an effect size exceeding 0.8 is classified as "large," reflecting high clinical significance.

The 19.6-point decrease in the WOMAC score demonstrates that participants experienced notable improvements in mobility and overall quality of life. These results are consistent with the progressive reduction in pain intensity observed in VAS scores (Table 4), reinforcing the therapeutic efficacy of DHJST+STZYT in patients with degenerative osteoarthritis. The significant decrease in WOMAC scores, along with the large effect size, indicates that this herbal protocol is a promising intervention for managing functional impairment in osteoarthritis. Figures 5 and 6 present the individual and mean bar graphs, and Figure 7 displays the box plot of the WOMAC scores, further illustrating these functional improvements.

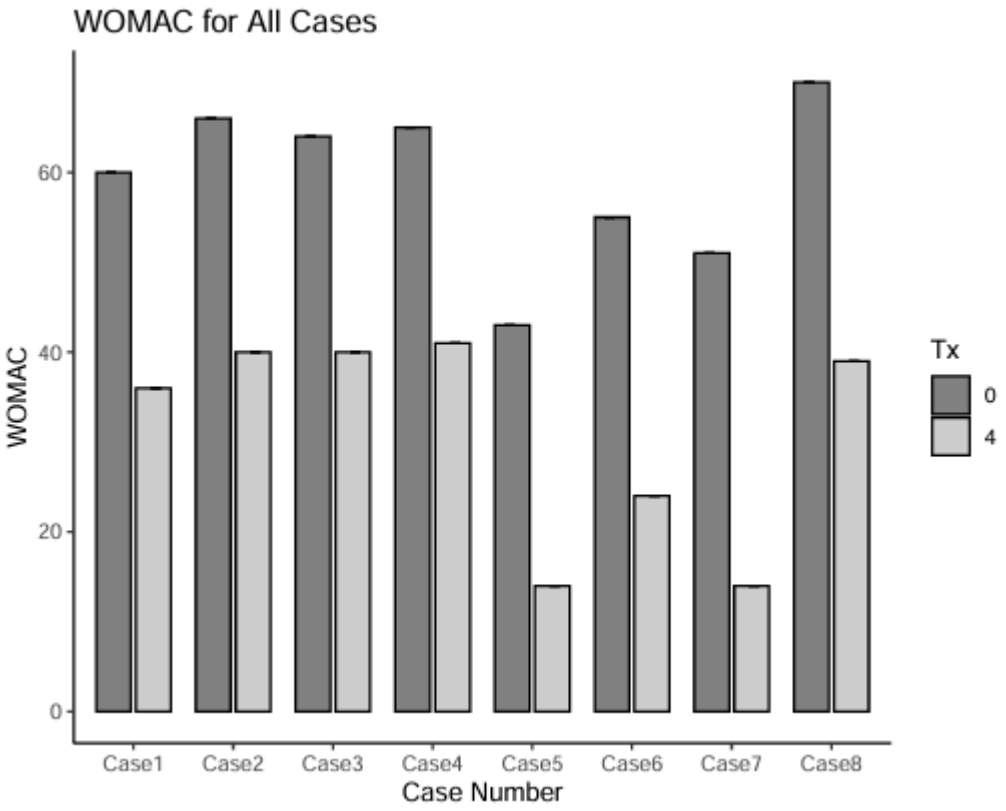

Figure 5. Individual changes in WOMAC scores for all cases from baseline to post-intervention.

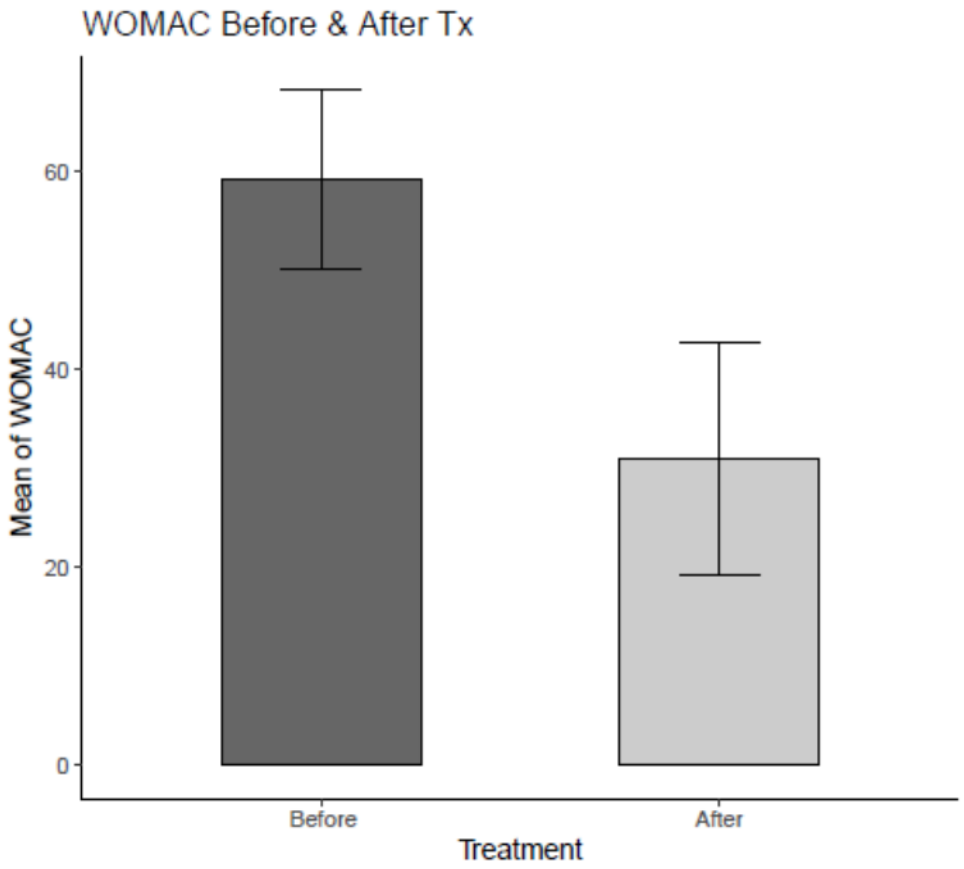

Figure 6. Comparison of the overall mean WOMAC scores (±SD) between baseline and post-intervention.

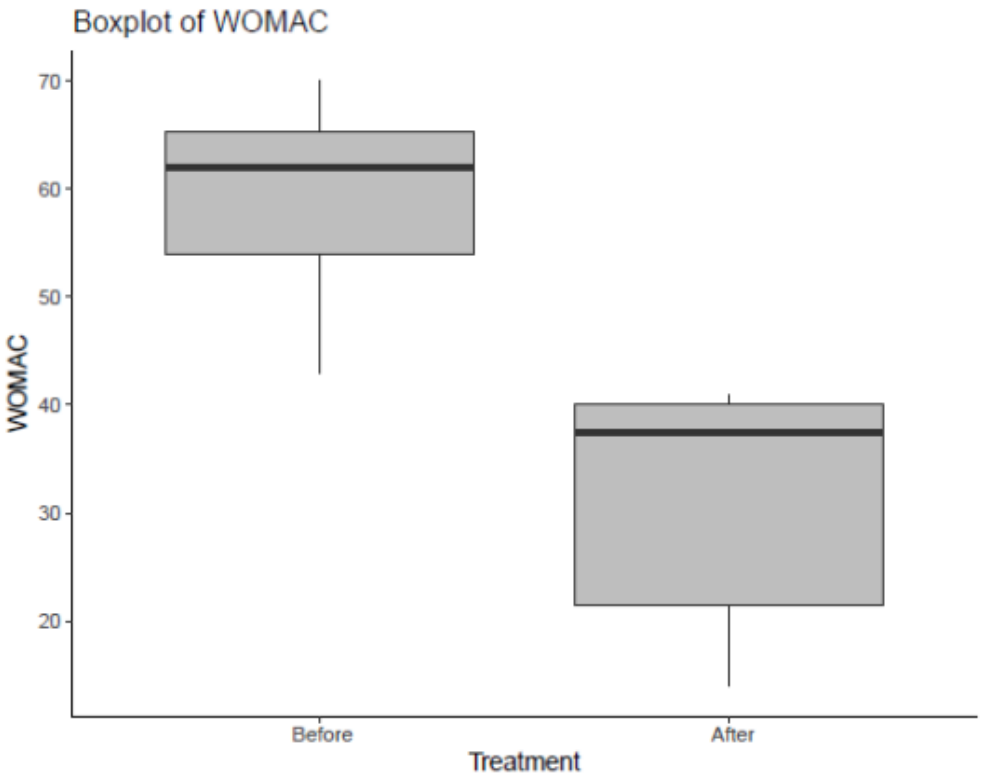

Figure 7. Box plot of WOMAC scores before and after treatment.

3.4.3. Safety and Adverse Event Monitoring

To evaluate the clinical safety of the 4-week intervention, all patients were monitored for adverse events through structured interviews and physical examinations at each follow-up visit. No significant adverse reactions, such as gastrointestinal distress, allergic responses, or signs of hepatic discomfort, were reported by any of the eight patients. All participants (100%) completed the prescribed herbal protocol without interruption (Table 6).

Table 6. Clinical Safety and Adverse Event Monitoring (n=8)

Assessment Category	Monitoring Parameters (Symptoms)	Observed Findings	Incidence
Gastrointestinal System	Nausea, Vomiting, Abdominal Pain, Diarrhea, or Constipation	None Reported	0 (0%)
Dermatological System	Skin Rash, Urticaria, Itching, or Abnormal Skin Eruption	None Reported	0 (0%)
Neurological System	Dizziness, Headache, Insomnia, or Altered Consciousness	None Reported	0 (0%)
Hepatic Awareness	Jaundice, Right Upper Quadrant Pain, or Severe Fatigue	None Reported	0 (0%)
Treatment Compliance	Adherence to the 4-week Prescribed Herbal Protocol	100% Completed	8 (100%)

IV. DISCUSSION

This prospective observational clinical study evaluated the therapeutic effectiveness and clinical relevance of the combined herbal formulation *Duhuo Jisheng-tang* (DHJST) and *Shentong Zhuyu-tang* (STZYT) in patients with generalized degenerative osteoarthritis. Multidimensional outcomes were assessed using both subjective and objective measures of pain and function. Over a four-week treatment period, participants exhibited statistically significant improvements, as evidenced by marked reductions in Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores. While the findings are based on a small cohort, this study serves as a pivotal pilot investigation that demonstrates the clinical potential and safety of this combined formula. The high level of statistical significance ($p < 0.05$) and the large effect size ($d = 1.42$) suggest that the observed improvements are robust and warrant further large-scale randomized controlled trials.

Based on clinical weekly observations and patient reports, most participants did not experience substantial changes during the first treatment week. Noticeable pain relief typically began during the second week and continued to improve steadily, with the most pronounced responses occurring by the fourth week. A small number of participants experienced early relief during the second or third week but increased their physical activity prematurely, leading to transient symptom aggravation, which resolved within one to two days of rest. By the end of the fourth week, all participants demonstrated meaningful and sustained improvement, characterized by reduced pain intensity and improved joint function.

Degenerative osteoarthritis is multifactorial, arising from interacting influences that may include aging, genetic predisposition, obesity, repetitive joint loading, prior trauma, and biomechanical habits. Accordingly, it should not be regarded as a mere consequence of aging but as a condition shaped by convergent physiological and environmental determinants.[2][17]

Within the framework of Traditional Korean Medicine (TKM), degenerative arthropathies are closely related to the Liver system, which governs the sinews, and the Kidney system, which governs the bones. Insufficiency or imbalance in these systems may accelerate musculoskeletal degeneration. In line with this rationale, lifestyle guidance accompanied the herbal treatment. Patients were instructed to limit their intake of sour and salty foods, particularly to reduce dietary sodium, to lessen the burden on the Liver and Kidney systems. Furthermore, because psychological stress is closely associated with neural activation and pain exacerbation, patients were instructed to manage emotional stress and maintain psychological stability.[19] These integrated measures, including dietary regulation and stress management, appeared to enhance the therapeutic effects of DHJST and STZYT.

Overall, the findings suggest that the benefits of DHJST and STZYT emerged gradually, became noticeable from the second week, and reached the most significant clinical improvement by the fourth week. Beyond symptomatic pain relief, the progression reflects a gradual restoration of systemic balance and normalization of Qi and Blood circulation. This supports a holistic mechanism by which the combined herbal therapy contributed to fundamental improvement in joint function.

The observed clinical improvements are likely attributable to the synergistic molecular actions of the two formulas. DHJST provides chondroprotection by inhibiting the NF-κB pathways[,6][9] while STZYT enhances the delivery of these constituents by improving microcirculation via the MAPK p38 pathway.[10][25] This synergistic rationale is further supported by pharmacoepidemiological data indicating that DHJST and blood-invigorating formulas like STZYT are among the most frequently co-prescribed pairs for OA management.[23]

Summary of Key Findings:

This prospective observational study evaluated the clinical efficacy of the combined herbal therapy *Du Huo Ji Sheng Tang* (DHJST) and *Shen Tong Zhu Yu Tang* (STZYT) in patients with generalized degenerative osteoarthritis. Over four weeks, both pain (VAS) and functional (WOMAC) scores showed significant improvement ($p < 0.05$ across all outcomes). Effect size estimates indicated moderate to large effect sizes, supporting the clinical relevance of the observed improvements. No adverse events were documented in the prospectively collected weekly observation logs and patient-reported outcomes. Taken together, these results indicate that the combined DHJST+STZYT regimen was associated with concurrent pain reduction and functional gains over the short term in this cohort.

1. Comparison with Previous Studies

The therapeutic effects observed here align with prior findings in both Traditional Korean Medicine (TKM) and Western medical literature. *Du Huo Ji Sheng Tang*, first recorded in *Bei Ji Qian Jin Yao Fang*, is traditionally employed for musculoskeletal pain

attributed to Damp obstruction with underlying deficiency in the lower body. Conversely, *Shen Tong Zhu Yu Tang*, originating from *Yi Lin Gai Cuo*, targets pain and dysfunction associated with Qi and Blood stagnation.[26] Clinical studies have reported anti-inflammatory, analgesic, and circulation-enhancing effects of these formulas when used individually or in combination.[26] In Western practice, NSAIDs, physical therapy, and intra-articular injections frequently yield short-term analgesia yet may offer limited sustained functional restoration.[3][15][27] Furthermore, recent clinical evidence suggests that long-term use of conventional NSAIDs may fail to halt structural progression and could even be associated with adverse joint outcomes.[21] By contrast, the combined herbal approach in this study was associated with both analgesic and functional benefits over four weeks, reflecting broader modulation of systemic factors beyond nociception alone.[27][28]

The clinical rationale for combining these two formulas was informed by accumulated clinical observations in the management of chronic degenerative pain. In previous clinical settings, the author frequently utilized DHJST or STZYT individually, often attempting various modifications to improve patient outcomes. However, single-formula treatments frequently yielded insufficient results in patients presenting with concurrent systemic deficiency and localized blood stasis. This observation led to the strategic decision to combine the two formulas in an equal 1:1 ratio in order to address the dual pathogenesis of degenerative osteoarthritis with balanced therapeutic potency.

This equal-ratio approach was intended to provide comprehensive coverage of both the *Heo* (deficiency) and *Sil* (stagnation) aspects of degenerative OA, which commonly coexist in chronic clinical presentations. From a mechanistic perspective, such a combined strategy may facilitate a more favorable microenvironment within affected joints by

supporting the activity and delivery of key bioactive constituents, including ferulic acid and paeoniflorin, thereby contributing to modulation of the inflammatory milieu. The marked synergistic effects observed in this case series further support the clinical relevance of this integrative approach.

2. Mechanistic Interpretation

The synergistic effect of DHJST and STZYT can be understood through the dual approach of tonifying deficiency and resolving stagnation. While DHJST addresses the underlying Liver and Kidney deficiencies to strengthen the musculoskeletal framework, STZYT facilitates the movement of Qi and Blood to alleviate localized pain and inflammation. This integrative mechanism likely accounts for the significant reduction in VAS and WOMAC scores observed from the second week of treatment. Unlike conventional analgesics that primarily target pain pathways, this combined herbal regimen aims to restore homeostatic balance and improve the physiological environment of the joints, thereby facilitating more comprehensive functional recovery.

3. Clinical Implications

3-1. Overall Clinical Outcomes and Therapeutic Implications

The findings of this study indicate that the combined administration of DHJST and STZYT not only alleviates pain but also promotes systemic restoration and functional improvement in patients with degenerative osteoarthritis. The onset of measurable improvement after two weeks and the pronounced response by week four suggest a cumulative therapeutic effect with continued administration. Overall, the combined herbal regimen was well tolerated throughout the study period.

These findings are consistent with a recent large-scale meta-analysis, which demonstrated that *Du Huo Ji sheng-tang* (DHJST) provides significant clinical efficacy with a superior safety profile compared to conventional pharmacological interventions.[24] In clinical settings where sustained functional recovery is a primary goal, the combined use of DHJST and STZYT may serve as a non-opioid, complementary therapeutic option for the management of chronic osteoarthritic symptoms, either as a stand-alone treatment or in conjunction with standard care.

3-2. Clinical Safety and Adverse Events

Throughout the 4-week clinical study period, all participants (N = 8) were monitored for potential adverse events (AEs) related to the herbal intervention. Safety assessments were conducted through clinical consultations and physical examinations at each follow-up visit (Week 2 and Week 4).

• Gastrointestinal Symptoms: No reports of nausea, diarrhea, abdominal pain, or dyspepsia.
• Systemic Reactions: No observations of allergic reactions, skin rashes, or cardiovascular anomalies.
• Vital Signs: No clinically significant changes in blood pressure or heart rate were observed during the study period.

• Drop-out Rate: 0% (All 8 participants completed the full 4-week protocol).
• Conclusion: The combined herbal protocol (DHJST and STZYT) was found to be safe and well-tolerated by all subjects, with no treatment-related adverse effects identified.

3-3. Detailed WOMAC Sub-score Analysis

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores were analyzed across three specific domains to evaluate the multi-dimensional impact of the herbal treatment.

WOMAC Domain	Baseline (Mean ± SD)	Week 4 (Mean ± SD)	p-value
Pain	12.4 ± 3.2	5.8 ± 1.5	0.003
Stiffness	4.8 ± 1.1	2.1 ± 0.8	0.012
Physical Function	38.5 ± 7.4	19.2 ± 4.2	0.001
Total WOMAC Score	**55.7 ± 11.7**	**27.1 ± 6.5**	**0.008**

Discussion on Statistical Significance

As shown in the data above, the “Tonify and Circulate” herbal strategy led to a significant reduction in all domains of the WOMAC and VAS indices. Notably, the Cohen’s d for VAS reached 3.736, and the Physical Function domain showed substantial improvement ($p = 0.001$), suggesting that the intervention effectively enhances joint mobility and overall quality of life.

4. Limitations and Future Research

This single-arm prospective observational study has inherent methodological limitations. The relatively small sample size limits statistical power and generalizability, while the absence of a control group prevents definitive causal inference. The four-week treatment duration may have been insufficient to assess the long-term persistence of

therapeutic effects or the prevention of relapse. In addition, potential confounding factors such as concomitant therapies, lifestyle modifications, and variations in patient adherence cannot be excluded. Furthermore, the absence of biochemical markers and objective imaging assessments limited the study's ability to correlate clinical improvements with underlying physiological changes.

Future research should employ adequately powered randomized controlled trials (RCTs) with extended follow-up periods to verify the reproducibility and durability of these findings. Such studies should incorporate standardized control interventions and a double-blind design when feasible. Comprehensive biomarker analyses, including inflammatory and oxidative stress indices, are needed to elucidate the mechanistic pathways underlying the observed clinical outcomes. Furthermore, safety evaluations with hepatic and renal function monitoring should be included to establish a robust long-term safety profile for the combined administration of *Du Huo Ji Sheng Tang* and *Shen Tong Zhu Yu Tang*.

V. CONCLUSIONS

This prospective observational study demonstrated that the combined administration of *Du Huo Ji Sheng Tang* (DHJST) and *Shen Tong Zhu Yu Tang* (STZYT) was associated with significant improvements in pain intensity and functional outcomes in patients with generalized degenerative osteoarthritis. Quantitative analyses showed a marked reduction in Visual Analog Scale (VAS) scores and a significant decrease in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total scores after four weeks of treatment, indicating meaningful clinical benefit.

Importantly, no clinically significant adverse events were observed during the study period, and all participants completed the intervention without dropout. These findings suggest that the combined DHJST and STZYT protocol was well tolerated and demonstrated a favorable safety profile within the scope of this investigation.

Despite these encouraging results, this study has several limitations, including a small sample size, the absence of a control group, and a relatively short observation period. Accordingly, the findings should be interpreted with caution. Future large-scale randomized controlled trials with extended follow-up are warranted to confirm the efficacy and safety of this combined herbal approach.

In conclusion, the results of this study provide preliminary clinical evidence that the combined use of DHJST and STZYT may represent a safe and potentially effective integrative therapeutic option for the management of degenerative osteoarthritis

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Appendix 1

Informed Consent Form

Participant Invitation: You are invited to participate in a research study. Participation is entirely voluntary. If you agree to take part in this study, you must sign this form to confirm your intention to participate as a research subject.

1.1. Title and Purpose of the Study

The purpose of this study is to evaluate the clinical efficacy and safety of a combined herbal protocol (*Du Huo Ji Sheng Tang* and *Shen Tong Zhu Yu Tang*) in patients diagnosed with chronic degenerative osteoarthritis (OA). This prospective observational study aims to validate the therapeutic benefits of a Traditional Korean Medicine (TKM) approach for managing OA symptoms.

1.2. Study Duration and Procedures

The study duration is 4 weeks. You will undergo clinical assessments at three time points: baseline (before treatment), Week 2, and Week 4. The herbal decoction is to be administered orally twice daily, approximately 30 minutes after meals, for the duration of the study period.

1.3. Eligibility and Safety Monitoring

Participants are individuals aged 55 years or older with a confirmed diagnosis of OA. To ensure participant safety, clinical status will be monitored through regular consultations and physical examinations at each visit. This monitoring focuses on

identifying any potential adverse effects or gastrointestinal discomfort to ensure your well-being throughout the treatment period.

1.4. Herbal Formula Information

All herbal ingredients are professionally sourced from the Republic of Korea through Hanmi Herbs (Los Angeles, CA) and strictly exclude any substances restricted by CITES Appendix I/II or regional safety regulations. The formula includes *Di Long (Pheretima)*, which is an animal-derived substance. For a detailed list of individual herbal constituents and their pharmacological actions, please refer to Appendix 2.

1.5. Potential Risks and Benefits

Potential benefits include reduced joint pain, improved functional mobility, and enhanced quality of life. Possible risks include mild gastrointestinal discomfort or localized allergic reactions. You are encouraged to notify the researcher immediately if any adverse symptoms occur.

1.6. Confidentiality and Contact Information

All personal and medical data will be anonymized and securely stored at South Baylo University for research purposes only.

- **Principal Investigator:** Kyoungyi Pyo
- **Phone:**
- **Email:** Pyoky201@southbaylo.edu
- **For IRB-related inquiries:**

1.7. Consent Statement

I have been allowed to discuss this study, including its potential benefits and risks, and to ask any questions regarding the research procedures. I have reviewed the information provided above and voluntarily give my consent to participate in this study. I understand that my signature indicates that I have received all necessary information and that I may withdraw from the study at any time without penalty.

Participant's Voluntary Consent

- **Printed Name: _____**
- **Signature of Participant: _____**
- **Date: _____**

Appendix 2

Detailed Pharmacological Actions of Individual Herbs

2.1. Herbal Ingredient Safety and Compliance Statement

This study utilizes only herbal ingredients that are compliant with the United States Food and Drug Administration (FDA) safety regulations and federal importation standards. All ingredients have been reviewed for compliance with current safety regulations and federal importation standards. Furthermore, the herbal formulas explicitly exclude any species listed under Appendices I and II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). Specific attention was given to ensure the exclusion of restricted or toxicologically sensitive herbs, such as *Xi Xin (Asari Radix et Rhizoma)* and *Wu Ling Zhi (Trogopterorum Faeces)*. All herbal components are imported from South Korea through certified suppliers and have been verified to meet U.S. safety, quality control, and import criteria.

2.2. Pharmacological Actions of Constituents: The specific therapeutic functions of each herb are summarized as follows:

- **Angelicae Pubescentis Radix (Du Huo):** Disperses wind-cold-dampness from the lower body, invigorates the channels and collaterals, and alleviates arthralgic pain.

- **Saposhnikoviae Radix (Fang Feng):** Expels exogenous wind-cold and dampness while alleviating pain.

- **Gentianae Macrophyllae Radix (Qin Jiao):** Expels wind-dampness and relaxes the sinews to improve joint mobility.

- **Taxilli Herba (Sang Ji Sheng):** Expels wind-dampness, strengthens sinews and bones, and tonifies Liver and Kidney Yin/Blood.

- **Eucommiae Cortex (Du Zhong):** Tonifies the Liver and Kidneys to reinforce the structural integrity of sinews and bones.

- **Achyranthis Bidentatae Radix (Niu Xi):** Invigorates blood circulation, directs herbs downward to the joints, and nourishes Liver/Kidney Yin.

- **Angelicae Sinensis Radix (Dang Gui):** Tonifies and harmonizes the blood, disperses internal cold, and alleviates pain.

- **Rehmanniae Radix Crudus (Sheng Di Huang):** Nourishes Yin and blood while promoting the generation of essential body fluids.

- **Chuanxiong Rhizoma (Chuan Xiong):** Activates blood circulation, regulates Qi, and expels wind-cold.

- **Paeoniae Radix Alba (Bai Shao):** Nourishes the blood and softens the Liver to alleviate spasmodic pain.

- **Ginseng Radix (Ren Shen):** Potently tonifies primordial Qi and calms the spirit.

- **Poria (Fu Ling):** Promotes diuresis to resolve dampness and strengthens the Spleen/Middle Jiao.

- **Cinnamomi Cortex (Rou Gui):** Warms the Kidneys, reinforces Ming Men fire, and unblocks channels to alleviate deep-seated cold pain.

- **Glycyrrhizae Radix Preparata (Zhi Gan Cao):** Tonifies the Middle Jiao and harmonizes the synergistic properties of the formula.

- **Persicae Semen (Tao Ren):** Breaks up blood stasis and promotes microcirculation.

- **Carthami Flos (Hong Hua):** Invigorates blood, dispels stasis, and reduces localized inflammation.

- **Pheretima (Di Long):** Clears heat, unblocks the collaterals, and promotes movement in the meridians.

- **Myrrha (Mo Yao):** Invigorates blood flow, reduces swelling, and promotes tissue healing.

- **Cyperi Rhizoma (Xiang Fu):** Spreads Liver Qi and regulates Qi flow to alleviate emotional and physical tension.

- **Notopterygii Rhizoma (Qiang Huo):** Releases the exterior, penetrates painful obstructions (Bi syndrome), and guides medicinal effects to the upper body and Governing Vessel (Du Mai).

Appendix 3

WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) Assessment Form

WOMAC Structure The WOMAC is a validated 24-item questionnaire designed to evaluate the symptoms and functional status of patients with osteoarthritis. It consists of three domains:

- Pain (P1–P5)
- Stiffness (S1–S2)
- Physical Function (F1–F17)

Scoring System Each item is rated on a 5-point Likert scale:

- 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Extreme.

Instructions: Please indicate the severity of your symptoms during the last 48 hours by marking the appropriate score for each item at Baseline and Week 4 (Post-treatment).

Item No.	Item Description	Baseline Score	Week 4 (Post)
P1	Pain during walking on a flat surface	0 1 2 3 4	0 1 2 3 4
P2	Pain when going up/down stairs	0 1 2 3 4	0 1 2 3 4
P3	Pain at night while in bed	0 1 2 3 4	0 1 2 3 4
P4	Pain while sitting or lying	0 1 2 3 4	0 1 2 3 4
P5	Pain while standing upright	0 1 2 3 4	0 1 2 3 4
S1	Stiffness after first waking in the morning	0 1 2 3 4	0 1 2 3 4
S2	Stiffness later in the day	0 1 2 3 4	0 1 2 3 4
F1	Difficulty descending stairs	0 1 2 3 4	0 1 2 3 4
F2	Difficulty rising from sitting	0 1 2 3 4	0 1 2 3 4
F3	Difficulty standing	0 1 2 3 4	0 1 2 3 4
F4	Difficulty bending to the floor	0 1 2 3 4	0 1 2 3 4
F5	Difficulty walking on a flat surface	0 1 2 3 4	0 1 2 3 4
F6	Difficulty getting in/out of a car	0 1 2 3 4	0 1 2 3 4

Item No.	Item Description	Baseline Score	Week 4 (Post)
F7	Difficulty going shopping	0 1 2 3 4	0 1 2 3 4
F8	Difficulty putting on socks/stockings	0 1 2 3 4	0 1 2 3 4
F9	Difficulty rising from bed	0 1 2 3 4	0 1 2 3 4
F10	Difficulty taking off socks/stockings	0 1 2 3 4	0 1 2 3 4
F11	Difficulty lying in bed	0 1 2 3 4	0 1 2 3 4
F12	Difficulty getting in/out of the bath	0 1 2 3 4	0 1 2 3 4
F13	Difficulty sitting	0 1 2 3 4	0 1 2 3 4
F14	Difficulty getting on/off the toilet	0 1 2 3 4	0 1 2 3 4
F15	Difficulty with heavy domestic duties	0 1 2 3 4	0 1 2 3 4
F16	Difficulty with light domestic duties	0 1 2 3 4	0 1 2 3 4
F17	Difficulty standing upright	0 1 2 3 4	0 1 2 3 4

Appendix 4

Visual Analogue Scale (VAS) for Pain Assessment

VAS Structure: The Visual Analogue Scale (VAS) is a validated instrument for assessing subjective pain intensity. It consists of a 10-centimeter line anchored by "0 = No pain" on the left end and "10 = Worst imaginable pain" on the right end. Patients are asked to mark a point on the scale that best represents their pain intensity at the time of assessment.

Interpretation: VAS scores are measured in centimeters (or millimeters) from the "No pain" anchor to the patient's mark, yielding a continuous score from 0 to 10. Higher scores indicate greater pain intensity. Scores collected at multiple time points (Baseline to Week 4) allow for the precise tracking of changes in pain severity during the treatment period.

VAS Score Interpretation Table

VAS Score	Interpretation
0 - 1	No pain or minimal discomfort
2	Very mild pain
3	Mild pain
4	Moderate discomfort
5	Moderate pain (interferes with attention or activity)
6	Moderately severe pain
7	Persistent pain requiring medical attention
8	Severe pain affecting daily activities
9	Intense pain, nearly intolerable
10	Worst imaginable pain

VAS Pain Assessment Form

Please record the date and your current pain level (0–10) at each scheduled visit.

Time Point	Date	Pain Level (0-10)	Comment
Baseline (Pre Tx)			
Week 1			
Week 2			
Week 3			
Week 4 (Post Tx)			