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Glucosamine, Chondroitin and MSM: A Complementary Approach to Managing OA and RA

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Abstract

Joint disorders, including osteoarthritis (OA) and rheumatoid arthritis (RA), are increasingly prevalent and pose a significant public health burden, particularly among older adults and populations in regions with higher socio-demographic indices. Lifestyle factors such as sedentary behaviour, smoking, and environmental exposures further contribute to disease onset and progression, underscoring the need for multimodal therapeutic strategies. This phase I pilot study assessed the safety and preliminary efficacy of a nutraceutical combination of glucosamine sulphate (GS), chondroitin sulphate (CS), and Methyl Sulfonyl Methane (MSM) in individuals with OA, RA, and related musculoskeletal pain syndromes. The formulation is hypothesized to support joint health by modulating inflammation, reducing oxidative stress, and maintaining cartilage and extracellular matrix integrity. Participants showed improvements in waist pain, backache, and sciatic pain, with 60% reporting significant relief. Older adults (56–70 years) exhibited slightly stronger response trends. The combination was well tolerated, with minimal adverse effects, suggesting its potential as a complementary intervention for joint health.

Keywords: Glucosamine; Chondroitin; MSM; Osteoarthritis; Musculoskeletal pain syndromes; Nutraceuticals; Joint Health

1. Introduction

Osteoarthritis (OA) is a progressive degenerative joint disorder characterized by the gradual deterioration of cartilage between the joints, progressive joint remodelling and joint inflammation (Poole, 2012; Yue & Berman, 2022). It typically develops progressively as a result of aging, mechanical stress, obesity, previous joint injuries, or an underlying genetic predisposition. OA is especially prevalent in individuals over the age of 40 and is one of the leading causes of joint pain and functional limitation in older adults (Griffin & Guilak, 2008; Valdes & Spector, 2011; Castañeda et al., 2014; Magnusson et al., 2024; Li et al., 2025). The condition predominantly affects weight-bearing joints such as the knees, hips, spine, as well as the hands and feet (Allen et al., 2022; Tang et al., 2025). As of 2021, osteoarthritis (OA) affected approximately 7.7% of the world's population. The condition showed regional variability, with age-standardized prevalence rates corresponding to a rate of 5.68% in Southeast Asia, rising to over 8.6% in high-income Asia Pacific areas. The knee was identified as the most commonly impacted joint. Globally, the age-standardized prevalence rate in

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2021 was approximately 6.97% of the population, with an incidence rate of 0.535% and a Years Lived with Disability (YLD) rate of 0.2445% (Xie et al., 2025). The figure 1 presents the age-standardized prevalence of osteoarthritis across selected regions (Figure a) and the global prevalence, incidence, and YLD rates for 2021 (Figure b). Trends from 1990 to 2021 indicate a consistent rise in the prevalence, incidence, and disability burden of OA, with notable differences across countries (Ren et al., 2025). Forecasts suggest that by 2035, the age-standardized prevalence of osteoarthritis (OA) is expected to increase slightly among older age groups (55–59 years), while a small decline is projected among younger age groups (30–34 years). According to the Global Burden of Disease (GBD) framework, high body mass index (BMI) and metabolic risks remain the only two recognized attributable risk factors for OA. Countries with higher socio-demographic index (SDI) scores tend to bear a disproportionately greater OA burden, and SDI-related disparities have widened over time (Sun et al., 2025).

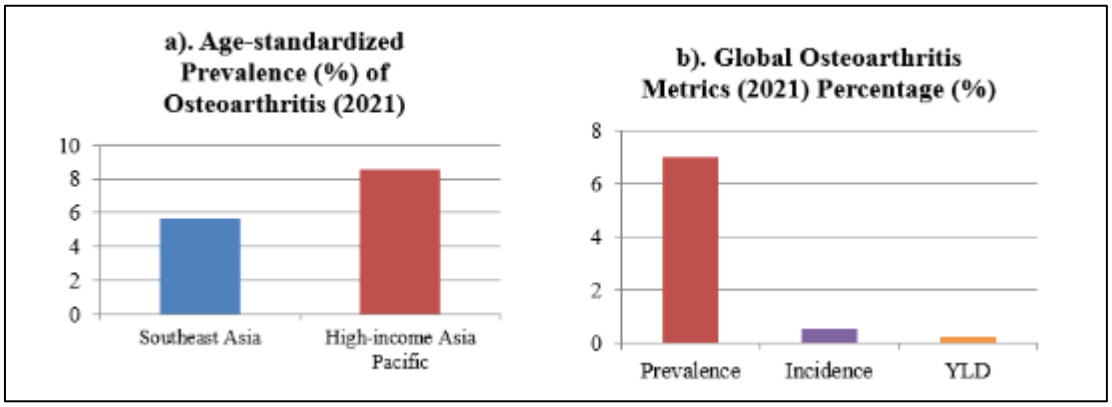

Figure 1 Global Osteoarthritis Metrics and Regional Prevalence (2021)

Given the growing and unequal burden of OA globally, effective management strategies are essential to reduce disability and improve quality of life among affected individuals. According to Sinusas (2012), treatment approaches for osteoarthritis were classified based on the severity of the condition mild, moderate, and severe with therapeutic regimens tailored to accommodate the patient's clinical status. The study further noted that for patients with moderate to severe osteoarthritis, the combined use of glucosamine sulphate and chondroitin sulphate was recommended as part of the management strategy (Sinusas, 2012). Glucosamine and chondroitin are commonly co-formulated in dietary supplements aimed at alleviating the symptoms of arthritis (Clegg et al., 2006; Sinusas, 2012; Vasiliadis & Tsikopoulos, 2017). Building on this established combination, the nutraceutical capsule formulated in this study incorporates Methyl Sulphonyl Methane (MSM), glucosamine sulphate (GS), and chondroitin sulphate (CS) as active ingredients. These components are hypothesized to act synergistically to enhance therapeutic efficacy in supporting joint health and mitigating arthritic symptoms.

To provide a mechanistic basis for this formulation, glucosamine sulphate is known to play a crucial role in joint health by promoting the synthesis of hyaluronic acid within the synovium (Uitterlinden et al., 2008). By stimulating synoviocytes, it enhances the secretion of hyaluronic acid into the synovial fluid, thereby supporting cartilage function (Meulyzer et al., 2008; Igarashi et al., 2011). GS also inhibits catabolic enzymes like matrix metalloproteinases (MMPs) and A Disintegrin And Metalloproteinase with Thrombospondin Motifs (ADAMTS) that contribute to cartilage degradation (Orth et al., 2008; Tang et al., 2025). Additionally, it prevents apoptosis of chondrocytes the cells responsible for maintaining the cartilage matrix thereby reducing matrix breakdown (James & Uhl, 2001). Some studies have further reported that GS can increase the anabolic molecules like Collagen II and Aggrecans (Chan et al., 2007), and sulphate ions absorption, supporting glycosaminoglycans (GAGs) and proteoglycans synthesis (Hua et al., 2007). Oxidative stress also plays a role in cartilage degeneration, with nitric oxide (NO) and reactive oxygen species (ROS) mediating mitochondrial dysfunction and chondrocyte apoptosis in osteoarthritis (Kang et al., 2015). GS exerts antioxidant effects by upregulating molecules such as glutathione (GSH) and reducing prostaglandin E2 (PGE2) production, thereby protecting cartilage tissue (Mendis et al., 2008; Kapoor et al., 2012; Van Vulpen et al., 2015). Clinical studies using bovine cartilage explants have suggested that GS, particularly in combination with chondroitin sulphate, can suppress cumulative NO release, indicating a protective effect on cartilage (Chan et al., 2007). In a population study conducted in Pakistan, GS was evaluated in a dose-dependent manner versus placebo in patients with rheumatoid arthritis (RA). The study reported that GS reduced erythrocyte sedimentation rate (ESR), indicating decreased inflammation, and suggested improvements in joint pain, stiffness, and physical activity (Noor et al., 2021). Collectively, these findings indicate that glucosamine sulphate may reduce inflammation, protect cartilage, and improve joint function through multiple mechanistic pathways (Hua et al., 2007; Al-Saadi et al., 2019). Chondroitin sulphate (CS)

contributes to the management of arthritis through its immunomodulatory and analgesic properties (Du Souich et al., 2009; Olaseinde & Owoyele, 2021). It helps maintain the articular cartilage structure, as cartilage proteoglycans contain multiple CS chains, and it stimulates hyaluronan synthesis in the synovial joints (Hardingham, 1998; Bishnoi et al., 2016; Schwartz & Domowicz, 2022). At the cellular level, chondrocytes exposed to IL-1β activate inflammatory and apoptotic pathways. CS mitigates these harmful responses by inhibiting key signaling molecules such as p38MAPK, Erk1/2, and NF-κB (Jomphe et al., 2008). Experimental studies in animals have further demonstrated CS's anti-inflammatory potential, including reductions in γ-glutamyl transferase (GGT) activity, suppression of IgE and Th2 responses, and significant decreases in C-reactive protein (CRP) levels (Iovu et al., 2008; Bauerová et al., 2011; Olaseinde & Owoyele, 2021). Notably, Olaseinde and Owoyele (2021) reported that CS alleviated sciatic pain in mice by promoting functional nerve recovery and reducing inflammation-mediated nerve damage. Although glucosamine sulphate and chondroitin sulphate have been primarily studied in osteoarthritis, similar pathophysiological processes such as cartilage degradation, synovial inflammation, and matrix metalloproteinase activation are also observed in autoimmune arthritis, namely rheumatoid arthritis (RA) (Harris, 1990; Derksen et al., 2017). Animal studies suggest that both glucosamine sulphate (GS) and chondroitin sulphate (CS) may reduce joint swelling in RA models (Bauerová et al., 2011; Wang et al., 2023).

Similarly, Methyl Sulphonyl Methane (MSM) a naturally occurring water-soluble sulphur-containing organic compound, has demonstrated protective effects in arthritis. MSM taken orally significantly reduced joint deformation and swelling in DBA/1J mice with type II collagen-induced arthritis compared with untreated controls, indicating a protective effect on arthritis progression (Hasegawa et al., 2004). MSM's therapeutic benefits are primarily attributed to its anti-inflammatory and antioxidant properties (Ezaki et al., 2013). It alleviates joint pain and stiffness, enhancing joint mobility and functional capacity (Debbi et al., 2011; Butawan et al., 2019), likely through inhibition of pro-inflammatory cytokines (such as IL-1β and TNF-α), reducing oxidative stress, and supporting the synthesis of collagen and other connective tissue components, collectively improving joint structure and function (Ezaki et al., 2013; Butawan et al., 2019). These shared mechanisms suggest that this nutraceutical interventions may offer adjunctive benefits beyond supporting Joint Health, in both osteoarthritic and rheumatoid arthritic conditions. However, real-time clinical study to validate the nutraceutical capsules efficacy is essential. This manuscript reports findings from a phase I clinical pilot study conducted in participants diagnosed with arthritis, evaluating the efficacy of the nutraceutical formulation containing glucosamine sulphate, chondroitin sulphate, and MSM.

2. Materials and Methods

2.1. Clinical Validation of a Nutraceutical Capsule

2.1.1. Study Design and Ethical Approval

This study was a prospective, Phase I, open-label, single-centre, community-based Human pilot clinical study designed to evaluate the efficacy of a nutraceutical capsule composed of Glucosamine sulphate, Chondroitin Sulphate and Methyl Sulphonyl Methane (MSM). The trial was conducted under the supervision of the Contract Research Organization (CRO), Ashram Siddha Research Institute. The study protocol (Protocol Number: AB-114-04-24) was reviewed and approved by the Institutional Ethics Committee for Clinical Research of the CRO, as constituted under Rule 7 and registered under Rule 8 of the Central Drugs Standard Control Organization (CDSCO), operating under the Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. The study complied with the ethical guidelines for biomedical research on human participants as per the 2006 AYUSH-ICMR guidelines. In accordance with the Declaration of Helsinki, written informed consent was obtained from all participants prior to enrolment, and they were thoroughly briefed on the study's purpose, procedures, potential risks, and benefits.

2.1.2. Study Population

The trial was conducted in the city Salem, Tamil Nadu, India, where the estimated prevalence rates of Sandhisoola (Joint diseases), Vatavyadhi (Pain all over body), Katisoola (Waist pain), Gridrasi (Sciatic pain) and Parinaamasoola (Backache) etc., exceeds 40% of the local population. The study was conducted over a 30-day period, from April 8, 2024, to May 7, 2024. Participants were recruited through an open-label, non-randomized, community-based process. Inclusion and exclusion criteria were determined based on comprehensive clinical examinations and reviews of medical histories. A total of ten participants, aged 41 to 70 years and presenting with the specified clinical symptoms, were enrolled in the trial. Individuals above 70 years of age or those with a history of osteoarthritis, drug or alcohol abuse, night or shift work, diabetic complications, psoriatic arthritis, or endocrine disorders were excluded from the study. Additionally, participants were withdrawn from the trial if their symptoms worsened or if they developed any serious condition requiring urgent medical attention.

2.1.3. Intervention

The investigational product administered in this study was a nutraceutical tablet containing a standardized blend of turmeric and black pepper extracts along with coconut oil. Each capsule was formulated with Glucosamine sulphate, Chondroitin Sulphate from Bovine (terrestrial) and Methyl Sulphonyl Methane (MSM). Participants were instructed to take one to two capsules orally, twice daily in the morning and evening, with lukewarm water, for the duration of the study. In addition to the daily capsule supplement, all participants received lifestyle counselling that included personalized dietary recommendations, physical activity guidance, and general health education to support therapeutic outcomes and encourage self-management of their condition. Compliance monitoring was conducted on patients to ensure adherence, participants were instructed to complete weekly adherence diaries to record daily intake.

2.2. Clinical Assessment and Evaluation

Comprehensive clinical evaluations were conducted on Day 1 (baseline) and Day 30 (end of study) by qualified Siddha and Ayurveda practitioners. Detailed case records were maintained for each participant throughout the study. Diagnostic assessments were carried out in accordance with traditional Siddha diagnostic protocols which involves the eightfold diagnostic method Envagai Thaervu, Tridosha Naadi a pulse diagnosis to assess the balance of Vata, Pitta, and Kapha. These assessments provided a holistic understanding of the participants' health status and were used to monitor progress during the study. The primary outcome measure was defined as a minimum 10% reduction in presenting symptoms, as reported by the participants and confirmed by the clinical judgment of the attending physicians. This reduction was considered a clinically significant indicator of therapeutic success. Participants received detailed information about the study, including potential side effects, expected benefits, the right to withdraw at any time, and procedures for follow-up and referral, all communicated in their native language to ensure complete understanding. As depicted in figure 2, the study cohort consisted of 6 participants aged 40-55 years and 4 participants aged 56–70 years. The efficacy of the nutraceutical supplement was evaluated over a one-month period by monitoring improvements in the listed clinical symptoms.

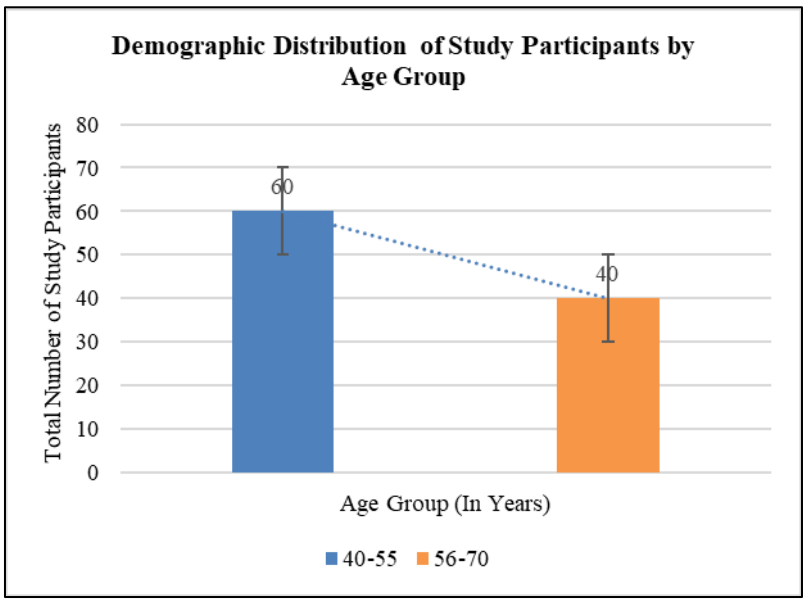

Figure 2 Age Distribution of Participants Enrolled in the Joint-Health Nutraceutical Study

3. Results

A total of 10 patients with joint-related disorders were enrolled in the study, with 60% belonging to the 40–55-year age group and the remaining 40% aged 56–70 years. All participants completed the 30-day intervention period, and no dropouts or discontinuations were recorded, indicating full adherence and tolerability of the intervention throughout the study duration. Across the cohort, clinically meaningful reductions in pain intensity, functional limitations, and musculoskeletal discomfort were documented. Improvements were observed in all assessed symptom categories, though the magnitude and distribution varied slightly between age groups and symptom types.

In Sandhivata (Bones and Joint Pain), patients with acute onset symptoms of at least 3 months showed notable rates of improvement, with 40% of individuals aged 40–55 years and 60% of those aged 56–70 years demonstrating measurable

clinical benefit. Among patients experiencing chronic symptoms lasting more than 3 months, the pattern differed, with 60% improvement in the younger cohort and 40% in the older group. These findings indicate that both acute and chronic symptom presentations responded favourably to the intervention, with improvement occurring across age categories. The figure 3 provided below summarizes improvements in generalized pain in the bones and joints (Sandhivata) categorized by acute and chronic onset across two age groups.

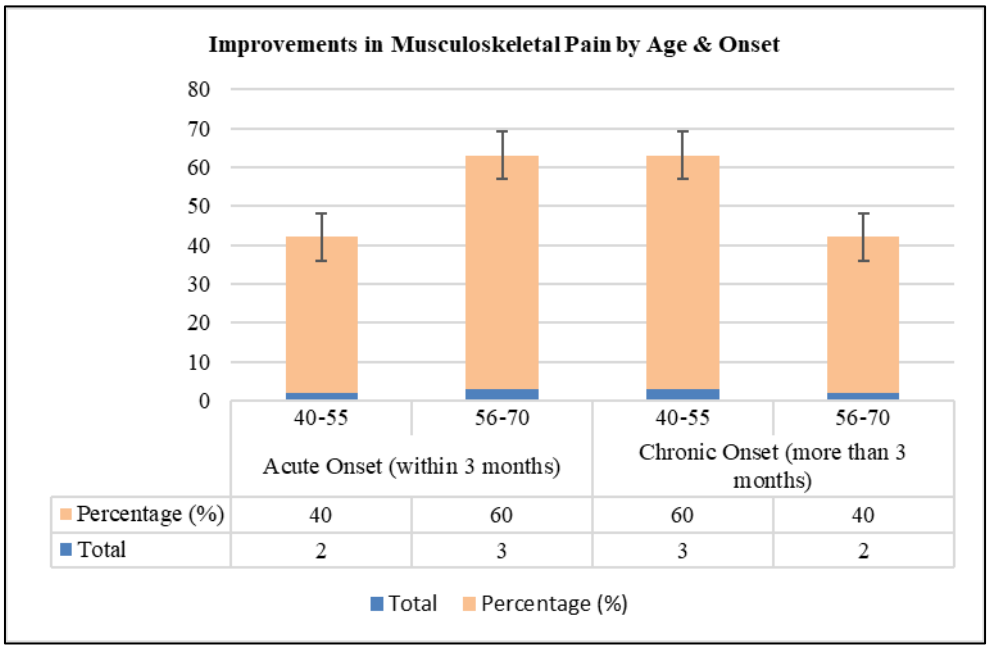

Figure 3 Improvement in Sandhivata (Bones and Joint Pain) After One Month of Intervention

Substantial alleviation of Katisoola (waist pain) was also documented. All patients within the 40–55-year group achieved complete symptom improvement by day 30, representing a 100% response rate in this subgroup. Among patients aged 56–70 years, 75% reported improvement within the same timeframe. This consistently high level of response suggests robust symptomatic relief in both age strata, with the intervention demonstrating particularly strong effects in younger participants. Parinaamasoola (backache) exhibited similarly favourable outcomes. Improvement rates reached 75% in the 40–55-year group and 83% in the 56–70-year group by day 30. Both cohorts demonstrated progressive reductions in backache and discomfort between day 15 and day 30, indicating a steady trajectory of improvement rather than an early plateau. A comparable trend was observed for Gridrasi (sciatic pain), with 75% improvement in patients aged 40–55 years and 84% in those aged 56–70 years, reflecting consistent benefit across age groups. The figure 4 reports the degree of symptomatic improvement in Katisoola (waist pain), Parinaamasoola (backache), and Gridrasi (sciatic pain) at 15 and 30 days across different age groups. While the table 1 presents the percentage of symptomatic improvement in the clinical symptoms of Katisoola, Parinaamasoola, and Gridrasi after 30 days of intervention with the nutraceutical capsule.

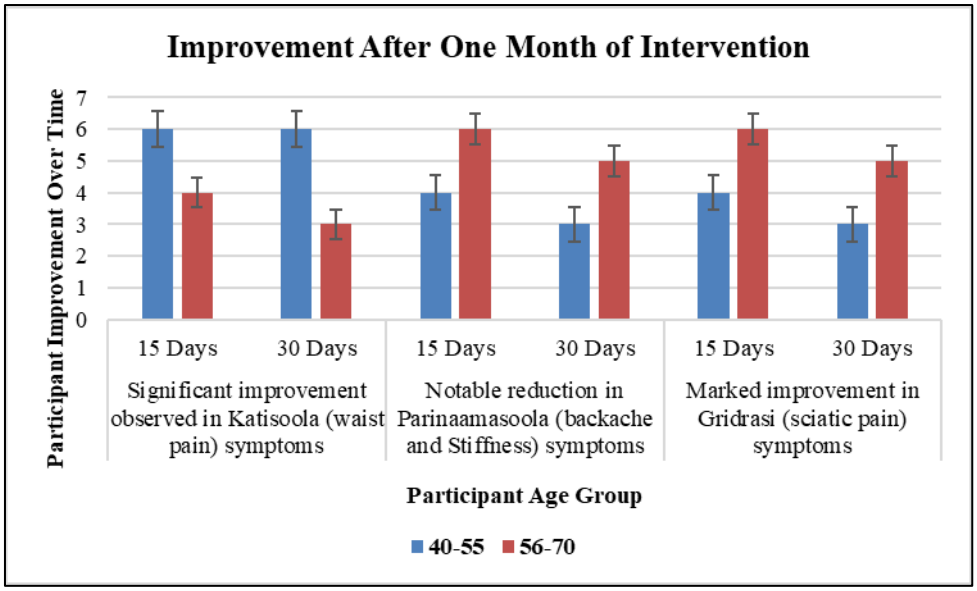

Figure 4 Degree of Symptomatic Improvement in Katisoola, Parinaamasoola, and Gridrasi at 15 and 30 Days Across Different Age Groups

Table 1 Percentage of Symptomatic Improvement in Katisoola, Parinaamasoola, and Gridrasi after 30 Days of Intervention

Age Group (In Years)	Percentage (%) of improvement observed in Katisoola (waist pain) symptoms	Percentage (%) of improvement observed in Parinaamasoola (backache) symptoms	Percentage (%) of improvement observed in Gridrasi (sciatic pain) symptoms
40-55	100	75	75
56-70	75	83	84

When all symptom categories were analysed collectively, 60% of patients experienced very good improvement across multiple domains, 20% demonstrated moderate improvement, 10% showed mild benefit, and 10% reported no significant relief. The figure 5 presents the aggregate clinical response, categorizing patients into levels of improvement (very good, moderate, mild, none). The absence of dropouts, coupled with high rates of improvement across diverse symptom types, indicates that the intervention was well-accepted and produced measurable therapeutic benefits across a broad range of musculoskeletal conditions within the study population.

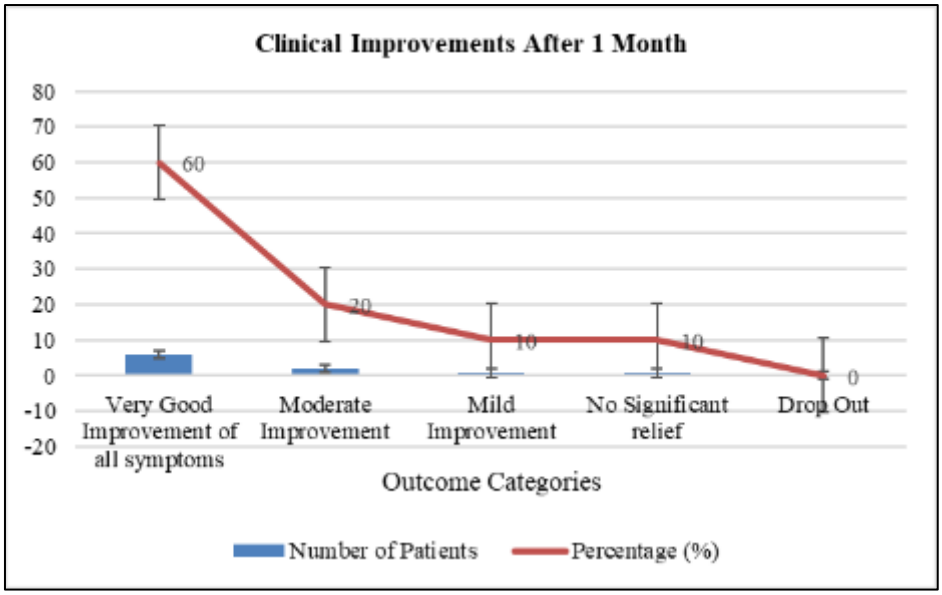

Figure 5 Overall Clinical Outcomes Following One Month of Intervention

4. Discussion

The present study highlights the growing prevalence of joint disorders, particularly osteoarthritis (OA) and rheumatoid arthritis (RA), which continue to impose a significant burden on public health worldwide (Xie et al., 2025; Sun et al., 2025). Epidemiological data indicate that older adults and populations in regions with higher socio-demographic indices are disproportionately affected, emphasizing the need for interventions that not only alleviate symptoms but also potentially slow disease progression. Lifestyle factors, including sedentary behaviour, smoking, and environmental influences, further contribute to disease onset and progression, accentuating the need for multimodal therapeutic strategies. Our findings demonstrate that the nutraceutical formulation combining glucosamine sulphate (GS), chondroitin sulphate (CS), and Methyl Sulfonyl Methane (MSM) may offer meaningful clinical benefits for individuals with joint-related conditions, including OA, RA, and associated musculoskeletal pain syndromes (Hasegawa et al., 2004; Debbi et al., 2011; Butawan et al., 2019). This combination is hypothesized to provide multi-targeted support for joint health by modulating inflammation, reducing oxidative stress, supporting cartilage integrity, and maintaining extracellular matrix homeostasis (James & Uhl, 2001; Chan et al., 2007; Jomphe et al., 2008; Kapoor et al., 2012). The rationale for combining these compounds lies in their complementary mechanisms: GS and CS primarily support cartilage structure and synthesis, whereas MSM may exert anti-inflammatory and antioxidant effects, collectively offering a holistic approach to joint health management.

The improvements observed across multiple symptom domains including Katisoola (waist pain), Parinaamasoola (backache), and Gridrasi (sciatic pain) suggest that this nutraceutical combination exerts broad therapeutic effects. Notably, a substantial proportion of participants (60%) reported significant symptomatic relief, indicating that the formulation may serve as an effective adjunct to conventional therapies. The consistent improvement in both acute and chronic presentations of Vatavyadhi suggests adaptability across different stages and severities of joint disease, which is clinically relevant given the chronic, progressive nature of OA and RA. Interestingly, participants in the older age group (56–70 years) exhibited slightly stronger response trends in back and sciatic pain despite often presenting with more advanced degenerative changes. This observation may indicate that the formulation retains efficacy even in long-standing musculoskeletal conditions and could be particularly valuable in older adults, who are at higher risk for functional decline. The tolerability profile was favourable, with no dropouts reported and only one participant failing to achieve significant improvement, underscoring the safety of the nutraceutical combination in this population. These results are consistent with previous literature on the individual and synergistic effects of GS, CS, and MSM, which have been associated with reduced joint pain, improved mobility, and modulation of inflammatory markers in preclinical, in vitro, and observational human studies (Hasegawa et al., 2004; Debbi et al., 2011; Butawan et al., 2019). However, the majority of evidence prior to this study has been limited by small sample sizes, heterogeneous populations, and lack of standardized outcome measures, highlighting the importance of controlled clinical trials to establish real-world efficacy and safety. Our phase I pilot study addresses this gap by providing foundational data on tolerability, preliminary efficacy, and symptom improvement trends, thereby laying the groundwork for larger randomized controlled trials.

The observed multimodal benefits of the nutraceutical formulation likely reflect its influence on several pathophysiological pathways involved in OA and RA, including chronic inflammation, oxidative stress, cartilage degradation, and neuromuscular aches. By targeting these mechanisms simultaneously, the combination may provide holistic symptom relief while supporting long-term joint health. Given the increasing prevalence of OA and RA and the limitations of current pharmacological interventions, which often focus primarily on symptom management and carry potential adverse effects, nutraceuticals such as GS, CS, and MSM represent a promising adjunctive therapeutic option. In conclusion, this pilot study demonstrates that a combination of GS, CS, and MSM is well tolerated and associated with meaningful improvements in musculoskeletal symptoms across multiple age groups and stages of joint disease. These findings support the potential role of this nutraceutical formulation as a complementary strategy for joint health.

5. Conclusion

In summary, this phase I pilot study demonstrates that the combined nutraceutical formulation of glucosamine sulphate, chondroitin sulphate, and methyl sulfonyl methane is safe, well tolerated, and associated with clinically meaningful improvements in pain and functional symptoms across a spectrum of joint-related disorders, including osteoarthritis, rheumatoid arthritis, and associated musculoskeletal pain conditions. The observed benefits across age groups and disease stages highlight its potential as an effective adjunct to conventional management strategies by targeting multiple pathophysiological mechanisms underlying joint degeneration and inflammation. Overall, these findings reinforce the value of evidence-based nutraceutical strategies in enhancing quality of life, reducing the burden of chronic joint diseases on individuals and healthcare systems, and provide a scientific foundation for continued clinical integration and refinement of holistic joint health interventions for societal benefit.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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