

AyuFlex™ for Joint Health

Introduction

Osteoarthritis (OA) is one of the most common forms of arthritis and is the leading cause of disability in American adults. It is a chronic condition that is known to affect weight-bearing and other moveable joints. In the United States, an estimated 27 million people older than 25 years have clinical OA. Risk factors for OA include age greater than 50 years, obesity, occupational habits (e.g., heavy lifting), physical stress to the hip, and major injuries. Several factors lead to damage of the bone and synovium, including genetic, metabolic, biochemical, and biomechanical influences on the joint. There is no single factor that is the direct cause of abnormalities with chondrocytes. Damage from physical forces within the joint leads to release of degradative enzymes which eventually results in degeneration of cartilage. Loss of cartilage causes friction between the bones, leading to pain and limitation of joint mobility. Commonly affected joints include the finger, knee, hip, spine and metatarsophalangeal joints of the foot. Osteoarthritis can be classified into primary (idiopathic) or secondary (e.g., joint trauma from obesity). The goals of treatment in osteoarthritis include resolution of symptoms, prevention or reduction in disease progression, and improvement of functional ability. These goals can be accomplished with non-pharmacologic and pharmacologic therapies.

There are several different pharmacologic therapies, including acetaminophen and oral NSAIDs which are most commonly used. Acetaminophen is a first line agent and is used effectively for patients with mild to moderate pain; however, it may not fully relieve the pain of severe OA. Acetaminophen is commonly used due to its relative safety profile; however, reports of acetaminophen-induced hepatotoxicity have increased in recent years. Oral NSAIDs, such as ibuprofen and naproxen, are recommended as initial therapy in more moderate to severe cases of OA. Patient-related factors should be considered prior to initiating oral NSAIDs due to the adverse risks associated with these medications, including gastrointestinal toxicity, kidney impairment, and cardiovascular risks.

Glucosamine and chondroitin, both of which are found naturally in healthy joints, have been marketed as dietary supplements for improving joint health. However, evidence is conflicting regarding the efficacy of glucosamine and chondroitin for OA. The current American College of Rheumatology (ACR) guidelines do not recommend the use of these supplements. According to the GAIT (Glucosamine/Chondroitin Arthritis Intervention Trial) study, glucosamine, chondroitin, and their combination were no more effective than placebo. In addition to the lack of clinical support, these supplements have a delayed onset of 2-3 months, can cause GI adverse effects, are derived from shellfish and shark/bovine cartilage (therefore not vegetarian), and they can potentially increase blood glucose levels.

AyuFlex™ is a clinically proven, water-soluble, vegetarian, organic, non-GMO product for joint health. It is derived from edible fruits of *Terminalia chebula*, an ancient Ayurvedic plant, and standardized to high levels of bioactives. It has been used in India for thousands of years for its anti-inflammatory and analgesic effects without the adverse effects that are associated with acetaminophen and NSAIDs.

AyuFlex™ Clinically Proven For Osteoarthritis

In one randomized, double-blind, placebo-controlled trial, patients with osteoarthritis for at least 6 months duration and meeting the ARA functional class I to III with radiological evidence were randomized to receive AyuFlex™ 250mg twice daily, AyuFlex™ 500mg twice daily, or placebo. This was a 12 week trial which assessed mWOMAC scores, knee swelling index, and VAS (visual analog scale) for pain, stiffness, and disability. Patients were allowed to use acetaminophen as a rescue medication. Results from this study showed that patients with osteoarthritis taking AyuFlex™ had a significant reduction in WOMAC scores, knee swelling index, and VAS-pain, VAS-stiffness, and VAS-disability (Figs. 1-3)

Fig 1. Mean % Reduction of mWOMAC Scores

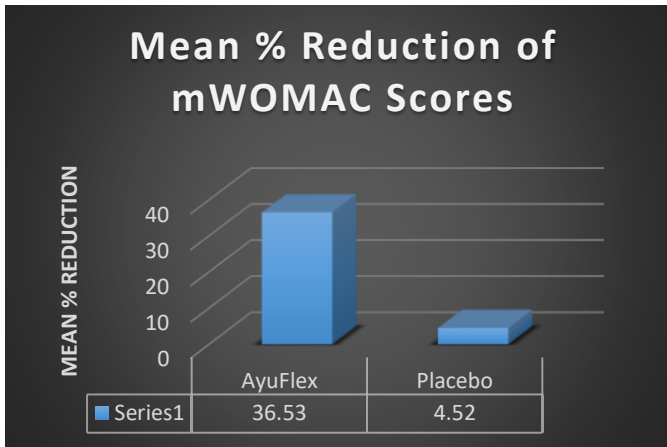


Fig 2. Mean % Reduction in Knee Swelling Index

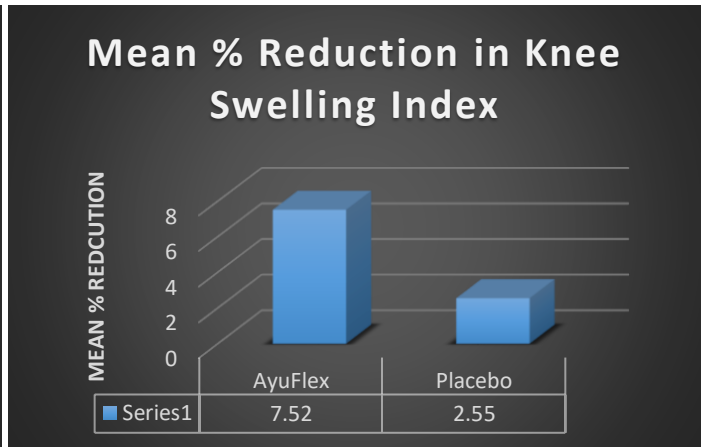
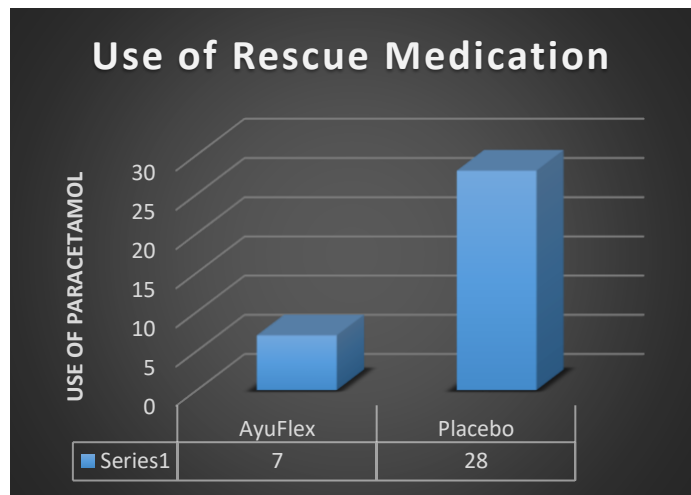
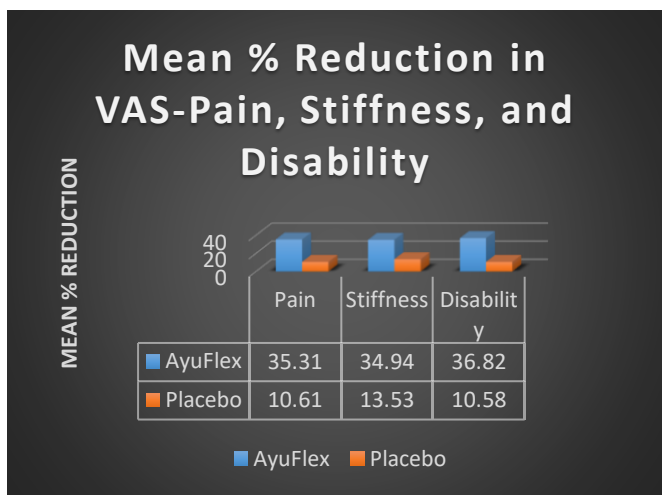


Fig 3. Mean % Reduction in VAS-Pain/Stiffness/Disability Fig 4. Use of Rescue Medication



Of note, patients taking AyuFlex™ used significantly less rescue medication (paracetamol) compared to the placebo group (Fig.4). In regards to safety, all renal, hematologic, and hepatic parameters were within normal limits in the treatment group. GI adverse effects, such as dyspepsia and diarrhea were the most commonly reported in the treatment group (n = 3). AyuFlex™ was well tolerated and no serious adverse events were observed during this study.

In addition to the study in moderately osteoarthritic patients, there are two randomized, double-blind placebo controlled crossover studies that were completed to examine the analgesic activity of AyuFlex™ in healthy human volunteers. In these studies, subjects were given a single 1000mg dose of AyuFlex™ and subjected to a hot air pain model or a mechanical pain model. Both force and time for pain threshold and pain tolerance from both these studies were statistically significant at $p < 0.001$ compared to placebo (Figs. 5-10).

Mechanical Pain Model

Fig 5. Mean % Change in Threshold Force

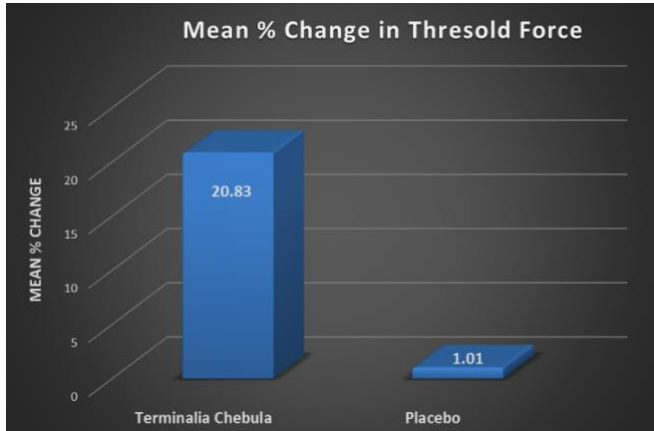


Fig 6. Mean % Change in Threshold Time

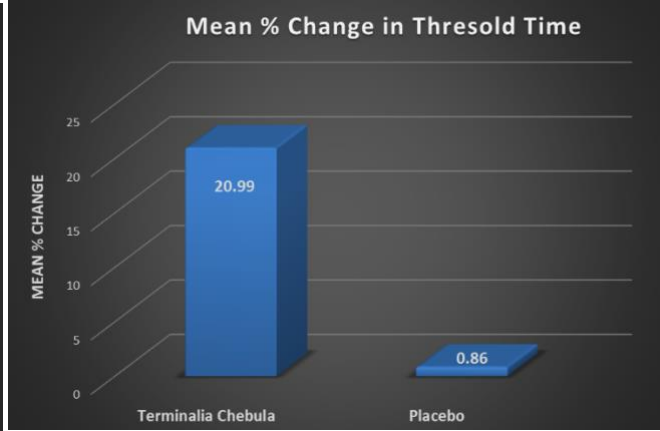


Fig 7. Mean % Change in Pain Tolerance Force

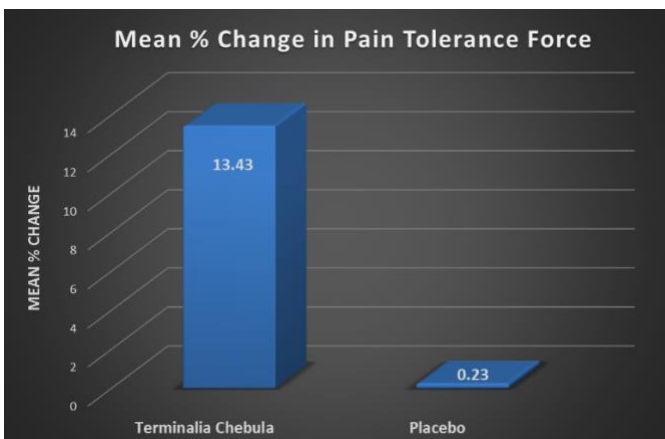
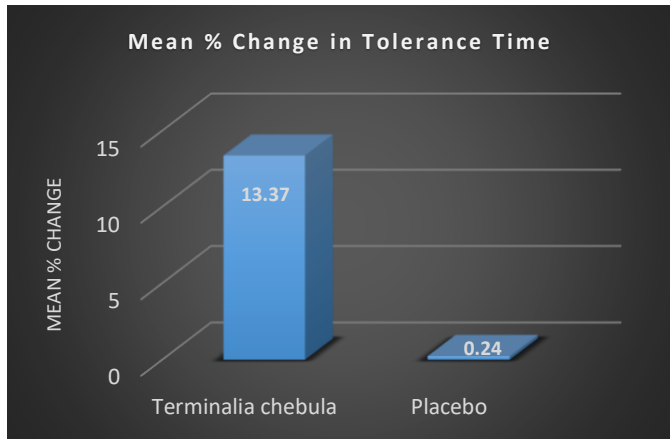


Fig 8. Mean % Change in Tolerance Time



Hot Air Pain Model

Fig 9. Mean % Change in Pain Threshold

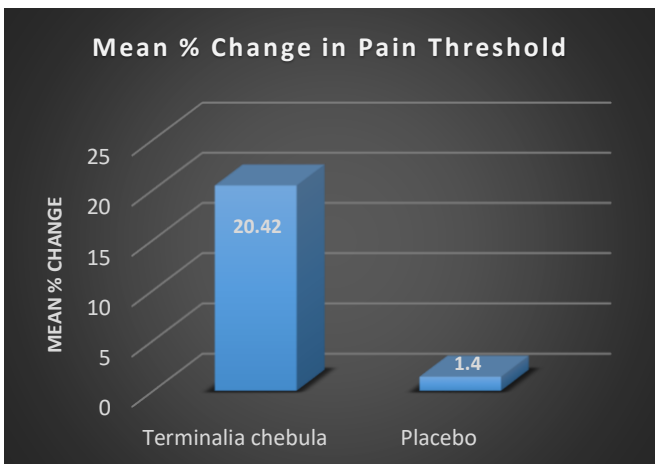
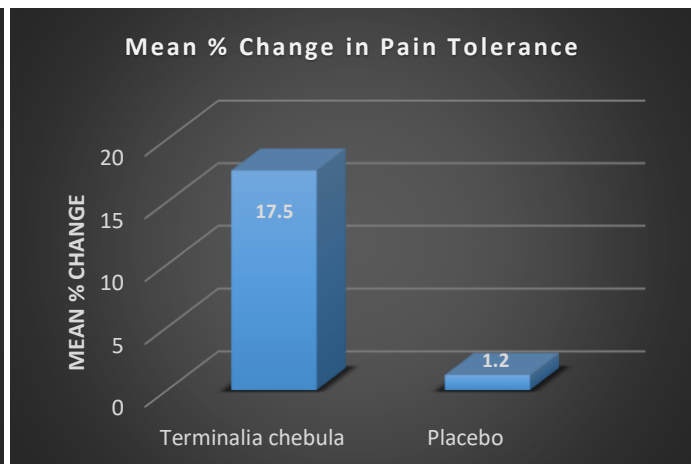


Fig 10. Mean % Change in Pain Tolerance



Conclusion:

Osteoarthritis is one of the leading causes of disability in the United States. Due to adverse effects associated with traditional treatments of OA, such as oral NSAIDs and acetaminophen, patients are turning to dietary/herbal supplements. Glucosamine and chondroitin have been marketed for years in the United States; however, recent evidence is suggesting a lack of efficacy with these agents. AyuFlex™, which is derived from the ancient Ayurvedic plant *Terminalia chebula*, is an optimal choice for joint health. AyuFlex™ is standardized to pharmaceutical quality and recent studies have shown significant reductions in mWOMAC scores, knee swelling index, and VAS-pain, stiffness, and disability scales. In addition, only 3 patients experienced mild adverse effects (diarrhea and dyspepsia) during treatment with AyuFlex™ and no subjects discontinued the study due to adverse events. Thus, AyuFlex™, a vegetarian, organic, non-GMO and water-soluble product, should be considered a superior choice amongst dietary supplements for improving joint health.