

Helps to relieve joint pain associated with osteoarthritis. Protects against the deterioration of cartilage. A factor in the building of healthy cartilage.

RxBalance™ Joint-Plex targets multiple levels in inflammation control by providing anti-inflammatory, detoxification and structural support to help ease the pain of osteoarthritis. Taking glucosamine sulfate orally improves symptoms of joint pain and decreased functionality while diminishing joint degeneration. Boswellic acids inhibit the synthesis of 5-lipoxygenase and leukotrienes, and decrease human leukocyte elastase (HLE) activity, the mechanisms for its anti-inflammatory properties. They also help to reduce glycosaminoglycan degradation and cartilage damage. Ginger extract is added for pain relief, and sulforaphane glucosinolate for its anti-inflammatory and detoxification properties.

Ingredients: Medicinal

Each tablet contains:

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| Glucosamine sulfate (glucosamine sulfate 2KCl from shellfish exoskeleton) | 500 mg |
| Boswellia (<i>Boswellia serrata</i> gum) extract (std. to 25% boswellic acid) | 300 mg |
| Ginger (<i>Zingiber officinale</i> rhizome) extract (std. to 16.5% gingerols) | 100 mg |
| Broccoli (<i>Brassica oleracea</i> seed) (std. to 10% sulforaphane glucosinolate) | 95 mg |

Ingredients: Non-medicinal

Cellulose, croscarmellose sodium, stearic acid, hypromellose, magnesium stearate, silicon dioxide, hypromellose, glycerin.

This product does not contain dairy, egg, gluten, soy, sulfites, or artificial flavours, colours or preservatives.

Recommended Use

Helps to relieve joint pain associated with osteoarthritis. Protects against the deterioration of cartilage and is a factor in maintaining joint health.

Recommended Dose

Adults take 1 tablet with a meal three times daily. Use for a minimum of four weeks to see beneficial effects.

Risk Information

Do not use if you are pregnant or breastfeeding. For prolonged use or if symptoms worsen, consult a health care practitioner.

Interactions with Drugs/Supplements

None known.

Dosage Form Description

Pale yellow oblong tablet with brown speckles.

Packaging

Available in bottles of 90 tablets.

Stability

Shelf-life of 3 years when stored in a cool, dry place.

Ingredient Description

Glucosamine is an amino sugar, which is a constituent of cartilage proteoglycans and is required for the synthesis of glycoproteins, glycolipids and glycosaminoglycans (also known as mucopolysaccharides). These carbohydrate-containing compounds are found in tendons, ligaments, cartilage, synovial fluid, mucous membranes, and structures in the eye, blood vessels and heart valves. In osteoarthritis, glucosamine stimulates the metabolism of chondrocytes in the articular cartilage and synovial tissues. There is evidence suggesting that glucosamine might have a disease-modifying effect, stopping or slowing the progression of osteoarthritis. Preliminary research suggests that glucosamine inhibits protein N-glycosylation and cytokine-stimulated production of inflammation mediators and cartilage degradation. Glucosamine seems to inhibit interleukin 1-beta (IL-1beta), which stimulates the gene expression and protein synthesis of cyclooxygenase-2 (COX-2).¹

The principle constituents of *Boswellia serrata* gum extract are boswellic acid and alpha- and beta-boswellic acid. In preliminary research, extracts of *Boswellia*, or Indian frankincense, have shown both anti-inflammatory and antiarthritic effects. Boswellic acid inhibits 5-lipoxygenase and leukotriene synthesis, and decreases human leukocyte elastase activity, which are the likely mechanisms for its anti-inflammatory properties. Boswellic acids may also have disease modifying effects, decreasing glycosaminoglycan degradation and cartilage damage.¹

Ginger (*Zingiber officinale*) extract is sometimes indicated for inflammatory conditions such as rheumatoid arthritis. Researchers speculate that certain constituents of ginger might inhibit cyclooxygenase and lipoxygenase pathways. It may also inhibit tumor necrosis factor alpha (TNF- α). It also seems to inhibit the synthesis of prostaglandin-E2 (PGE2) and thromboxane B2 (TXB2), which mediate inflammation.

In 1992, researchers targeting the potential chemoprotective effects of certain vegetable varieties isolated and identified **sulforaphane glucosinolate**, a natural compound found in broccoli, cauliflower and cabbage. They theorized that chemoprotective compounds take advantage of the body's Phase 2 detoxification enzymes that help neutralize cancer-causing chemicals, as well as free radicals, before they can damage DNA and initiate the development of cancer. Sulforaphane glucosinolate functions as an indirect antioxidant; as such, it does not directly neutralize free radicals, but rather induces (or boosts) the activity of the Phase 2 detoxification enzymes. The effects of these indirect antioxidants remain even after they have left the body - unlike direct antioxidants, which neutralize only one molecule of a radical at a time, and are destroyed in the process. The indirect antioxidant effects are long-lasting, triggering an ongoing process that continues to be effective and may last for days.

Reason for Combination

The combination in RxBalance™ Joint-Plex is based on well-established evidence of glucosamine sulfate and its effects on the relief of joint pain associated with osteoarthritis, its protection against the deterioration of cartilage and its contribution in the building of healthy cartilage. This ingredient, dosed at the proper therapeutic level, fully supports the efficacy of the product. *Boswellia serrata* extract (BSE) was included because of research done by Kimmatkar and colleagues, who conducted a randomized, double-blind, placebo controlled, crossover trial in 30 patients with osteoarthritis of the knee with resultant statistically significant mean improvements in the BSE group compared to placebo in terms of pain, flexion, and walking distance.² The oleoresin constituents in *Zingiber officinale*, as well as the phenolic substances paradol and shogaol, were shown to possess an inhibitory action on cyclooxygenase-2 enzymatic activity and to have inhibitory effects on leukotriene and prostaglandin biosynthesis, both of which are important in the inflammatory process.^{3,4,5} Sulforaphane glucosinolate has shown anti-inflammatory, detoxification and anticarcinogenic effects postulated to be mediated not only by modulation of biotransformation enzymes but also by regulation of genes involved in the inflammation pathway.⁶

Research Synopsis

1. An open study was carried out by 252 doctors throughout Portugal to assess the effectiveness and tolerability of oral glucosamine sulfate in the treatment of arthrosis. The patients received 500 mg of glucosamine sulfate three times daily over a mean period of 50 +/- 14 days. The results from 1,208 patients were analyzed and showed that the symptoms of pain at rest, on standing, and on exercise and limited active and passive movements improved steadily through the treatment period. The improvement lasted for a period of 6 to 12 weeks after the end of treatment. Objective therapeutic efficacy was rated by the doctors as "good" in 59% of patients, and "sufficient" in a further 36%; therefore, 95% of patients achieved benefit. Oral glucosamine was fully tolerated by 86% of patients, and the onset of possible side-effects was significantly related to pre-existing gastrointestinal disorders and related treatments.⁹
2. Osteoarthritis is a common, chronic, progressive, degenerative skeletal disorder, which commonly affects the knee joint. The *Boswellia serrata* tree is commonly found in India. The therapeutic value of its gum (guggul) has been known to possess good anti-inflammatory, anti-arthritis and analgesic activities. A randomized, double-blind, placebo-controlled crossover study was conducted to assess the efficacy, safety and tolerability of *Boswellia serrata* extract (BSE) in 30 patients with osteoarthritis of the knee, 15 each receiving active drug or placebo for eight weeks. After the first intervention and washout, the groups were crossed over to receive the opposite intervention for eight weeks. All patients receiving the BSE treatment reported decreased knee pain, increased knee flexion, and increased walking distance. The frequency of swelling in the knee joint was decreased. Radiologically, there was no change. The observed differences between BSE-treated and placebo, being statistically significant, are clinically relevant. BSE was well tolerated by the subjects except for minor gastrointestinal adverse reactions. BSE is recommended in the patients of osteoarthritis of the knee with possible therapeutic use for arthritis.²
3. Ginger (*Zingiber officinale*) extract supplementation has been shown to improve the severity of symptoms and decrease the nonsteroidal anti-inflammatory drug (NSAID) requirements in patients with osteoarthritis (OA). A study was conducted to assess the effects of ginger extract as an alternative to NSAIDs and as a supplement drug in the symptomatic treatment of OA. Between April and October 2002, 120 outpatients with OA of moderate to severe pain, requiring the use of NSAIDs, were enrolled into a double-blind, randomized, placebo controlled clinical trial. These patients were randomized into three groups of 40, including the placebo (PL), ginger extract (GE), and ibuprofen (IBP) groups. After a washout period of one week,

patients received either 30 mg ginger extract in two 500 mg capsules, a placebo, or three 400 mg ibuprofen tablets daily for one month. Acetaminophen was prescribed as a rescue analgesic during the study. The clinical assessments included a visual analog scale (VAS) for pain, gelling or regressive pain after rising, joint swelling measurement, and joint motion slope measurement. The improvement of symptoms (defined as reduction in the mean change) was superior in the ginger extract and ibuprofen groups than the placebo group. VAS scores and gelling or regressive pain after rising scores were significantly higher in the PL group than both the GE and IBP groups, a month after the treatment ($P < 0.0001$). However, there was no significant difference in VAS and gelling pain scores between the ginger extract and the ibuprofen groups. Ginger extract and ibuprofen were significantly more effective than the placebo in the symptomatic treatment of OA.⁷

4. Sulforaphane is a natural, biologically active compound extracted from cruciferous vegetables such as broccoli or cabbage. It possesses potent anti-inflammation and anti-cancer properties. The mechanism by which sulforaphane suppresses COX-2 expression remains poorly understood. In the present report, the effect of sulforaphane on the expression of COX-2 in lipopolysaccharide (LPS)-activated Raw 264.7 cells was investigated. Sulforaphane significantly suppressed the LPS-induced COX-2 protein and mRNA expression in a dose-dependent manner. The ability of sulforaphane to suppress the expression of COX-2 was investigated using luciferase reporters controlled by various cis-elements in the COX-2 promoter region. Electrophoretic mobility shift assay (EMSA) verified that NF-kappaB, C/EBP, CREB and AP-1 were identified as responsible for the sulforaphane-mediated COX-2 down-regulation. In addition, EMSA also demonstrated the signal transduction pathway of mitogen-activated protein kinase (MAP kinase) in LPS-induced COX-2 expression. Taken together, these results demonstrate that sulforaphane effectively suppresses the LPS-induced COX-2 protein via modulation of multiple core promoter elements (NF-kappaB, C/EBP, CREB and AP-1) in the COX-2 transcriptional regulation. These results will provide new insights into the anti-inflammatory and anti-carcinogenic properties of sulforaphane.⁸

References

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