



FLEXAGOLD Tablets ; A SYNERGISTIC BLEND OF NATURAL INGREDIENTS SUPPORTING JOINT HEALTH

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ABSTRACT

Nutraceuticals are dietary compounds which have a role in the balance of anabolic and catabolic signals in joints. Their regulatory function on homeostasis of cartilage metabolism nutraceuticals is increasingly considered for the management and, above all, the prevention of osteoarthritis (OA). OA is a degenerative disease characterized by cartilage and synovium inflammation that can cause joint stiffness, swelling, pain, and loss of mobility. It is a multifactorial disease and, due to the great percentage of people suffering from it and the general increase in life expectancy, OA is considered as one of the most significant causes of disability in the world. OA impairs the structural integrity of articular cartilage that greatly depends on a balance between the anabolic and catabolic processes which occur in chondrocytes and synovial fluid of the joints, therefore the integration with nutraceutical compounds in diet increases the treatment options for patients with established OA beyond traditional rehabilitation, medications, and surgical strategies. This review summarises the current available scientific literature regarding the effect of FLEXAGOLD Tablets, A Synergistic blend of natural ingredients in supporting joint health.

Key words: FLEXAGOLD Tablets, Natural Ingredients, Supporting Joint Health.

INTRODUCTION

Osteoarthritis (OA) is a degenerative disease characterized by cartilage and synovium inflammation that can cause joint stiffness, swelling, pain, and loss of mobility [1–3]. OA is a very complex and multifactorial disease. Due to the high percentage of people suffering from this disease, with a greater percentage in women after menopause (18%) than in men (9.6%), and the increase in life expectancy, OA is considered one of the most significant causes of disability in the world [4–7]. Although OA mainly affects the joints of knees, hands, and hips [8], it also results in alterations in other joint tissues such as ligaments, synovium and subchondral bone [9]. OA impairs the structural integrity of articular cartilage that greatly depends on a balance between anabolic and catabolic processes, which occur in chondrocytes and synovial fluid of the joints [10,11]. Nutraceuticals are dietary compounds plays a role in these processes within articular cartilage [12].

Micro and Macroscopic Features in Early and Severe Osteoarthritis (OA)

OA is characterized by impairments in the

structure and functionality of joint cartilage in consequence of an imbalance between anabolic and catabolic processes in the cartilage tissue that could cause its degradation; if cartilage degradation exceeds reparative processes, the OA goes on and advances [14,15] (Figure 1). This degenerative disease is characterized by several changes (narrowed joint space, thickening, formation of osteophytes, and cysts in the subchondral bone) that are radiographically visible, even if radiographs do not indicate the degree of cartilage degeneration [16]. It is possible to detect osteophytes also through magnetic resonance imaging (MRI), that allow us also to detect geodes or subchondral cysts in advanced stages of OA [17]. Microscopic alterations in joint cartilage are evaluated by the Mankin [18] score or a modified version by Sakakibara et al. [19], that consider several factors such as cell morphology, extracellular matrix staining, and appearance of the tidemark. The highest scores highlighting the most severe damage of joint tissues are 14 for the Mankin score and 32 for the modified Mankin score. Alterations to healthy joint cartilage usually do not exceed grades of 1–3 [20]. Histological grading

criteria of Kraus0 modified Mankin score [18,21] and histopathology OARSI system [22,23] are used as semi-quantitative methods to healthy cartilage [30]. Chondrocytes are very active cells but they normally do not divide, so only small defects associated with minimal loss of matrix components can be repaired by regeneration; if more wide defects exceed the repair capacity, the damage can become permanent [14]. Because OA involves progressive loss of the structure and functionality of articular cartilage due to an imbalance between anabolic and catabolic processes in the cartilage tissue, preventive and therapeutic interventions are necessary to prevent OA and/or improve the regeneration capacities of joint cartilage [30].

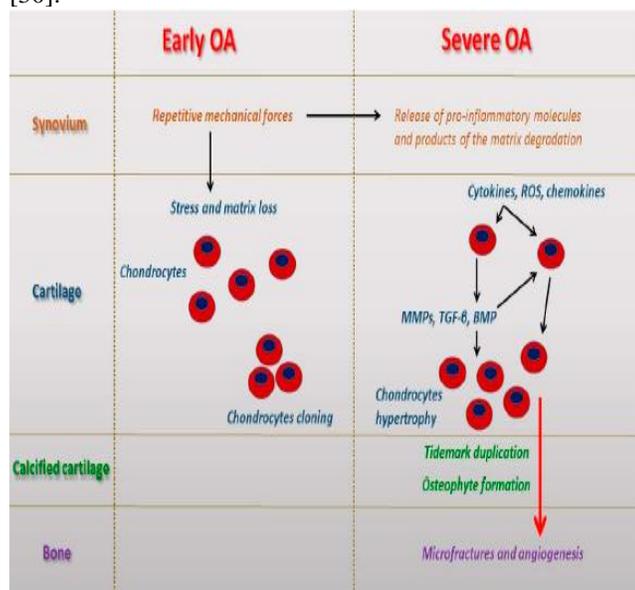


Figure 1. Early and severe osteoarthritis (OA) causes and molecular events in the different tissues involved in the joints. BMP: Bone morphogenetic proteins; MMPs: Matrix metalloproteinases; ROS: Reactive oxygen species; TGF-Transforming growth factor

Cartilage is mainly composed of collagen type II and the proteoglycan aggrecan and it is characterized by viscoelastic and compressive properties thanks to the extracellular matrix [24–27]. Healthy joint cartilage has a smooth surface and it is white, shiny, and elastic. In OA, cartilage instead shows a dull and irregular surface with discoloration and softening and more synovial fluid may be produced, with newly invaded blood vessels [28]. In particular, at the early stage of degeneration, minimal changes are detected in the cartilage surface in which glycosaminoglycans remain homogeneously distributed; as the disease progresses, there is a loss of proteoglycans, and in severe OA the cartilage surface is rough and broken by fissures and cracks [16].

In healthy joint cartilage, four layers are recognizable: superficial zone, middle zone, deep zone, and calcified zone. In the superficial zone, cells are flat and spindle-shaped, parallel to the joint surface [14,26]. The

superficial zone contains the majority of collagen fibers, parallel to the surface, which results in high tensile modulus to resist shear stress at the joint surface [14]. In early OA, mild fibrillations are found in the superficial zone [16] and cartilage presents thickening, a consequence of hypertrophy. As the disease advances, cells of the intermediate and radial zone show mild to moderate hypercellularity; necrotic chondrocytes with pyknotic nuclei in the intermediate and radial zone are found; the synovial membrane includes hyperplasia of synovial lining cells, thickening of the synovial membrane, infiltration of inflammatory cells, and fibrosis [14,29]. In severe OA, the cartilage shows extensive degeneration: hypertrophic villi and full-thickness defect areas can be seen where the cartilage is missing completely and the subchondral bone is exposed; the subchondral plate itself is thicker and more dense; cells are arranged in clusters especially around fissures or disappear completely as the disease progresses; the cartilage is replaced by fibrocartilaginous, scar-like tissue with fibroblast-like cells [16,28]. In other cases, full-thickness defects develop, where the bone lacks the cartilage completely; the loss of proteoglycan content reaches the deep zones; the tidemark becomes unclear and finally is invaded by blood vessels from the subchondral bone, which penetrate into the calcified zone [28]. Osteophytes are found in early stages of the diseases, but become more pronounced in advanced stages of OA. The rate of OA progression depends on species and joint localization, and the extent of damage could be dependent on the joint area, which can be explained by different loading conditions in distinct regions [28]. Articular cartilage is not vascularized nor innervated, so nutrients and cellular repair molecules are transported to the chondrocytes by diffusion from the synovial fluid. Thus, articular cartilage has limited capacities for self-regeneration and, in OA, shows reduced mechanical capacities compared to healthy cartilage [30]. Chondrocytes are very active cells but they normally do not divide, so only small defects associated with minimal loss of matrix components can be repaired by regeneration; if more wide defects exceed the repair capacity, the damage can become permanent [14]. Because OA involves progressive loss of the structure and functionality of articular cartilage due to an imbalance between anabolic and catabolic processes in the cartilage tissue, preventive and therapeutic interventions are necessary to prevent OA and/or improve the regeneration capacities of joint cartilage [30].

Composition

Supplement Facts	
Serving Size : 1 Tablet	Servings per container : 120
Each coated tablet contains :	
Boswellia Serrata Extract 25%	100mg
Glucosamine Hydrochloride	750mg
Curcuminoids 95%	50mg
Bromelain Extract	50mg
Rose Hip Extract	75mg

Pharmacological Action of each ingredients

***Boswellia serrata* Extract**

The resin of *Boswellia* species has been used in medicines since time immemorial. *Boswellia serrata* (*Salai/Salai guggul*), is a moderate to large sized branching tree of family Burseraceae (Genus *Boswellia*), grows in dry mountainous regions of India, Northern Africa and Middle East. Oleo gum-resin is tapped from the incision made on the trunk of the tree and is then stored in specially made bamboo basket for removal of oil content and getting the resin solidified. After processing, the gum-resin is then graded according to its flavour, colour, shape and size. The oleo gum-resins contain 30-60% resin, 5-10% essential oils, which are soluble in the organic solvents, and the rest is made up of polysaccharides. Gum-resin extracts of *Boswellia serrata* have been traditionally used in folk medicine for centuries to treat various chronic inflammatory diseases. The resinous part of *Boswellia serrata* possesses monoterpenes, diterpenes, triterpenes, tetracyclic triterpenic acids and four major pentacyclic triterpenic acids i.e. β -boswellic acid, acetyl- β -boswellic acid, 11-keto- β -boswellic acid and acetyl-11-keto- β -boswellic acid, responsible for inhibition of pro-inflammatory enzymes. Out of these four boswellic acids, acetyl-11-keto- β -boswellic acid is the most potent inhibitor of 5-lipoxygenase, an enzyme responsible for inflammation.

Glucosamine hydrochloride

Glucosamine is a naturally occurring substance found in the synovial fluid around our joints. It is naturally present in animal bones, bone marrow, shellfish and fungi. Glucosamine plays a vital role in building cartilage and is commonly consumed as a supplement by people with arthritis, especially osteoarthritis. Glucosamine is vital for building cartilage because it is a precursor for glycosaminoglycans which is a major component of joint cartilage. With aging, glucosamine levels go down, which can lead to eventual joint deterioration.

Several scientific studies have shown that glucosamine supplements may help patients with osteoarthritis (OA), especially of the hip or knee.

The effects of glucosamine are manifested by:

- Reduction in osteoarthritis-related pain
- Improved function in patients with knee or hip osteoarthritis
- Reduced stiffness and swelling in the joints
- Continued to provide relief of symptoms up to 3 months after patients stopped treatment.

Curcuminoids

Curcuminoids in Curcumin has been demonstrated as antiapoptotic activity in Chondrocytes. Curcumin have been reported as beneficial effect on cartilage matrix. This study was performed using immortalized human OA chondrocytes, which can explain

the discordance with previous studies. However, one study tested the clinical efficacy of a herbomineral formulation containing a component rich in curcumin in people with OA in a randomized, double-blind, placebo-controlled, crossover study. Positive results in pain management and mobility were obtained in the treated group.

Bromelain extract

Bromelain is a mixture of different thiol endopeptidases and other components like phosphatase, glucosidase, peroxidase, cellulase, escharase, and several protease inhibitors. *In vitro* and *in vivo* studies demonstrate that bromelain exhibits various fibrinolytic, antiedematous, antithrombotic, and anti-inflammatory activities. Bromelain is considerably absorbable in the body without losing its proteolytic activity and without producing any major side effects. Bromelain accounts for many therapeutic benefits like the treatment of angina pectoris, bronchitis, sinusitis, surgical trauma, and thrombophlebitis, debridement of wounds, and enhanced absorption of drugs, particularly antibiotics. It also relieves osteoarthritis, diarrhea, and various cardiovascular disorders. Bromelain also possesses some anticancerous activities and promotes apoptotic cell death.

The studies investigating bromelain were a series of case reports on 28 patients, with moderate or severe rheumatoid or osteoarthritis. Bromelain, was compared to diclofenac in 103 patients with osteoarthritis of the knee. After six weeks, both treatments resulted in significant and similar reduction in the pain and inflammation. Bromelain is a food supplement that may provide an alternative treatment to nonsteroidal anti-inflammatory drug (NSAIDs). It plays an important role in the pathogenesis of arthritis. Bromelain has analgesic properties which are thought to be the result of its direct influence on pain mediators such as bradykinin.

Rose hip extract

Several human studies with Rose hip powder were carried out over the last couple of years. The powder showed pain reducing properties and could also reduce symptoms such as e.g. stiffness, or even the need for additional medication. However, the daily amount of approx. 5 g over a period of 12 weeks showed moderate beneficial effects, but also a low compliance and demonstrated the limits of a treatment with Rose hip powder. Herbal drug powders are usually not as stable and uniform as extracts.

Supplement Facts

Presentation: Tablets

Usage:

- **Helps to promote joint Health & function.**
- **Provides Nutritive support for cartilage Regeneration.**

Helps to Reduce symptoms of Pain & Stiffness in Joints.

Contra-indications: Product is contra-indicated in persons with Known hypersensitivity to any component of the product hypersensitivity to any component of the product.

Recommended usage : *Adults:* .1-2 Tablets twice a day with water or liquid of choice twice daily
 “Do not exceed the recommended daily dose”

Administration: Taken by oral route at anytime with food.
Precautions: Do not exceed the recommended daily dose.
Warnings: If you are taking any prescribed medication or has any medical conditions always consults doctor or healthcare practitioner before taking this supplement.
Side Effects: Very Mild side effects like nausea, headache and vomiting in some individuals may be observed.
Storage: Store in a cool, dry and dark place.

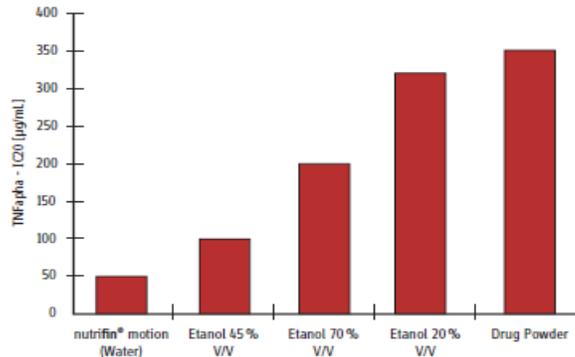


Fig. 1: Anti-Inflammatory potential of Rose hip preparations (in-vitro) - Inhibition of the mediator Tumor Necrose Faktor-alpha (TNFalpha)

CONCLUSION

At present, the current modalities for treating OA are symptomatic and have not been shown to block or reverse the cartilage degradation and joint destruction. This has resulted in heightened interest in the use of nutraceuticals like flexagold tablets for OA management. Many studies have been carried out to highlight the potency of several nutraceuticals and dietary supplements for the treatment of OA. Nutraceuticals like flexagold tablets offers a wide range of effects. They open new and large

horizons for the treatment of degenerative joint diseases.

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CONFLICTS OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

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