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ORIGINAL ARTICLE

Nutritional Supplements in Osteo-Arthritis

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ABSTRACT

Authors in this research paper enumerated the works of different researchers upon nutrient supplements for osteo-arthritis replacing traditional allopathic medicines with various side effects. Authors explained significant, proven and medically certified neutraciticals worked in suppressing multiple ill effects related to cartilage degeneration. They have taken 7 supplements Glucosamine, Chondriotin Sulphate, Hyaluronic acid, MSM, Boswellia Serrata, Curcumin and Ginger essential in diminishing and eliminating different arthritis. Authors discussed pharmacology, mode of action and benefits of studied supplements. To large extent they succeeded letting other new researchers know the value of such nutrients in removing such dread full wide spreads disease across the globe.

Key Words: *neutraciticals, Glucosamine, Boswellia Serrata, pharmacology*

INTRODUCTION

A wide population of world is suffering from very painful and life disturbing disease known as osteosteoarthritis. Around 26 million U.S.A. population being effected from such ailment. Among all arthritis is knee arthritis is severe and highly symptomatic since it blocks essential activities of life especially when people are to be commuters to run families.

Osteoarthritis (OA) is often a progressive and deactivating disease resulting from a several risk factors, like age, heredity, trauma, and knee alignment and unevenness of physiological processes resulting in inflammatory cascades on a molecular level [1].

What actually Osteosteoarthritis does as in this situation the cartilage at the joints turns into stiff and gives up its elasticity, making it much prone to graded damage. As time goes on, the cartilage goes wear away in some places, decreasing its ability of shock absorbing to large extent. As the cartilage wears off, tendons and ligaments go stretchable, causing pain on rest or movement. If the condition getting worse, the bones at joints start rubbing against each other.

Cartilage is comprised of four substances viz collagen, proteoglycans, water, and chondrocytes.

Collagen: Collagen provides cartilage strength and durability and forms a framework that keeps the other components of cartilage. Apart from being a key component of cartilage, the protein collagen is also present in the tendons and skin.

Proteoglycans: This substance is amalgamation of protein and carbohydrate. Proteoglycans are woven around and through collagen, letting cartilage to adjustment shape while compressing. Proteoglycans trap water in cartilage, which is redistributed while movement happens.

Water: Healthy cartilage has over 70% of water. Besides functioning as the shock absorber in cartilage, water lubricates and nourishes the cartilage.

Chondrocytes: These cartilaginous cells produce proteoglycans and new collagen in cartilage existence. Chondrocytes release enzymes too helping break down and dispose of aged collagen and proteoglycans.

Treatment of indicative osteosteoarthritis of the articular joints specially knee is concentrated on regulation and relieving the pain, preserving patients' practical individuality, and improving their quality of day to day life activities, with next aim in preventing deterioration of joints with the hope of get rid of knee replacement. In light of the medical management of symptomatic osteosteoarthritis of the knee and waist looks forward a multidisciplinary approach that includes drugless measures (patient awareness, physio-occupational therapy, aerobic and muscular

strengthable exercises, weight control, and procedure of assistive devices) and medicinal support i.e. general treatment line prescribed by orthopedic physician/surgeon (oral and topical analgesic drugs like aciclofenac, acetaminophen, serratiopeptidases etc, nonsteroidal anti inflammatory drugs [NSAIDs] including cyclooxygenase-2–selective inhibitors and intra articular therapies such as corticosteroids and hyaluronan injections, PRP procedure and finally joint replacement) as per need [2, 3, 4, 5, 6].

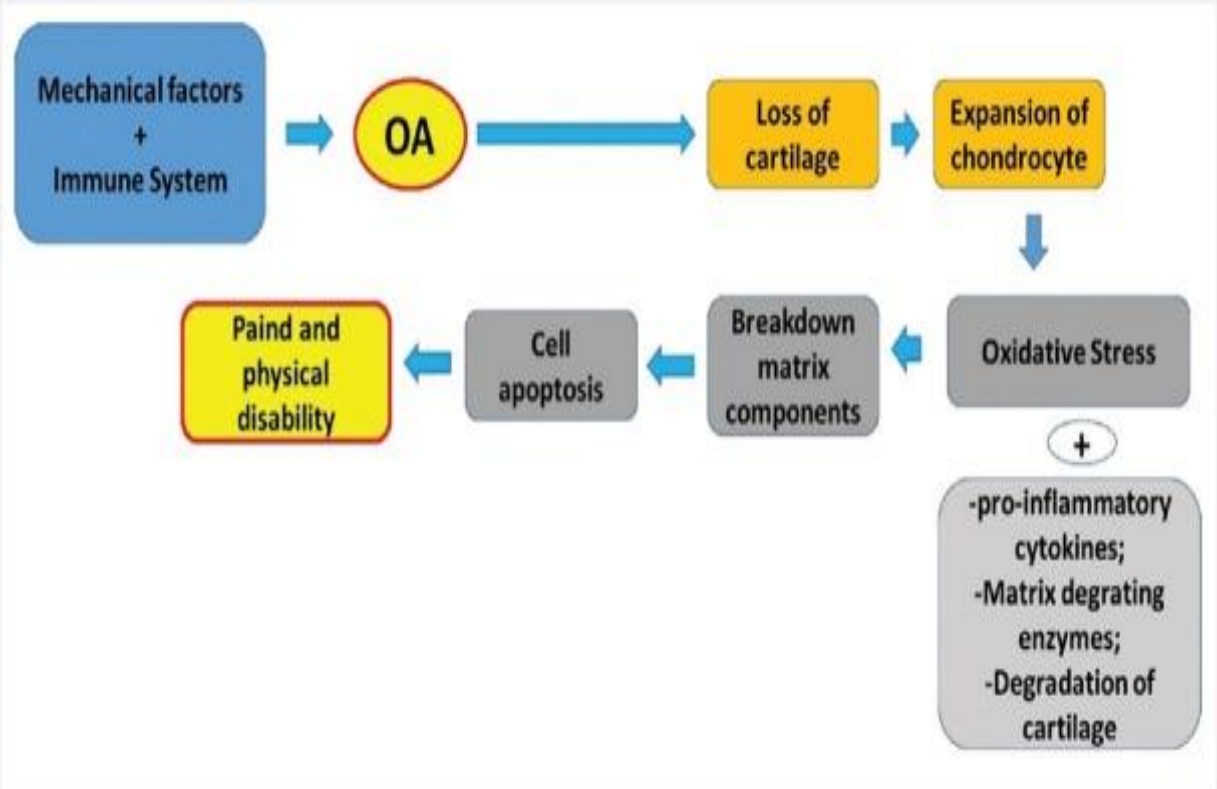

Fig. 1: In the Osteo-arthritis researcher can observe a interruption in the homeostasis of matrix and succeeding damage of cartilage, expansion of chondrocytes gives rise to acceleration in releasing pro-inflammatory cytokines and surge in the production of different reactive oxygen species. This episode is related to the breakdown of matrix components leading to cell apoptosis manifested as pain, cramp and physical disability Modified from Lee *et al*. 2010

In current world and situation Dietary and nutritional supplements are replacing conventional ones, including glucosamine and chondroitin sulfate, are used frequently by patients and are increasingly recommended by medical practitioners [7, 8].

Following this many researchers became successful in term of using nutritional supplements in the form of tablets and capsules available in markets instead of conventional drugs in treating osteoarthritis. Sufferers must take such supplements but strictly on advice of physician or surgeon, must not take by own will.

GLUCOSAMINE

Glucosamine compound can be take out from chitin which is mostly found in the exoskeleton of crustaceans (crabs, prawns, and lobsters), in the cell membranes of mushrooms as well. Within cartilage, it is most needed for the formation of chondroitin sulfate, hyaluronic acid and keratin sulfate, which are along with the collagen fibers, the most essential components of the extracellular matrix of the articular cartilages and the synovial fluid within.

Glucosamine is found in two forms like Glucosamine sulfate and glucosamine hydrochloride is compounds which are nutritional supplements. Many findings showed glucosamine delays the

tearing and repair impaired cartilage. There are some evidences available proving significance of glucosamine hydrochloride is convincing.

Glucosamine is present naturally in human body. It provokes in making glycosaminoglycans and glycoproteins, which are essential building material of many parts of our joints, tendons, ligaments, synovial fluid and cartilages. Osteoarthritis is pathological manifested as joint rigidity, pain, local inflammation, more or less deformity, and dysfunction in various degrees. The clinical morphology of osteoarthritis is progressive destructive and degenerative of articular cartilage, graded chondral osteosclerosis, hyperplasia of synovium, osteophyte extrusion at the joint edge, hypertrophy of the joint capsule, and contraction or relaxation of ligament [9].

Glucosamine sulfate, natural amino acid plus monosaccharide, supplement to the cartilage matrix, postponement the cartilage ruining and raise the synthesis of proteoglycan in chondrocytes, which is a basic food for cartilage [10]. Glucosamine sulfate alleviates dread joint pain, delay and modify the pathological process of osteoarthritis, and specially supply the cartilage matrix in articular cartilages, and bring back the normal functions.

It was shown that glucosamine enriches the production of cartilage matrix components in chondrocytic culture, like aggrecan and collagen type II [11, 12]. Glucosamine increases hyaluronic acid construction in synovium explants [13]. Followig experiments have revealed that glucosamine prevents degeneration of collagen in chondrocytes by inhibiting protein oxidation and lipoxidation reactions [14].

Recently a drug, etoricoxib is a specific inhibitor of cyclooxygenase-2 (COX-2) and a NSAID type has analgesic, anti-inflammatory, and antipyretic effects [15], which is being widely used to relieve pain, reduce wake up stiffness, and mend the joint functioning in osteo arthritis and rheumatoid arthritis.

Glucosamine is a basic substance in human articular cartilages required for synthesis of aminoglycans. Oral glucosamine sulfate directly nourishes the cartilage matrix, delays cartilage filth, assists the synthesis of cartilage protein and chondrocyte matrix secretion recovery finally improves the articular cartilage structure [16]. Etoricoxib selectively inhibits the synthesis of cyclooxygenase and prostaglandin playing an anti-inflammatory work, so effectively lessen swollen joint and pain [17].

CHONDRIOTIN SULPHATE

Chondroitin sulfate (CS) is a natural glycosaminoglycan comprised of the alternating sugars D-glucuronic acid and N-acetyl-D-galactosamine. It is vital component of the extracellular matrix ECM. Chondroitin sulfate is the most common GAG into the cartilage aggrecan molecule. Chondroitin is synonym for chondroitin sulfate and chondroitin sulfuric acid. Chondroitin sulfate is a combined state of chondroitin and mineral salt [18]. Owing to the negative charge of C.S., it is accountable for the water retention capacity of the cartilage, which is imperative for pressure resistance. It can be extracted from the cartilaginous tissue of fish, birds, cows, pigs and is ingested in the diet. or it can be prepared in laboratories. Many clinical trials by different researchers demonstrated ability of CS to decelerate the progress of osteoarthritis [19, 20, 21]. Chondroitin sulfate upsurges the hyaluronan (*hyaluronic acid)* production through man›s synovial cells, that leaves beneficial effect and improvement on upholding viscosity and synovial fluid levels [22].

It has been demonstrated that C.S. elicits the chondrocyte metabolic cycle, leading to the anabolism of collagen and proteoglycan, the basic components of fresh cartilage. Moreover, C.S. inhibits the activities of enzymes leukocyte elastase and hyaluronidase, which are present in high concentration in the synovial fluid of osteoarthritis patients. As a whole, C.S. inhibits cartilage obliteration processes and stimulates the productive phases involved in new-fangled cartilage construction [23, 24]. The positive effect of and retrogression by C.S. on osteoarthritis had also been clinically approved and confirmed by meta-analyses, which all revealed a significant favorable influence of C.S. above placebo [25, 26, 27].

METHYL SULFONYL METHANE (MSM)

MSM is used for a number of health solutions. The most important one is an anti-inflammatory agent. [28] A pilot study upon 100 people above the age of 50 has been conducted; the participants

felt decrease in pain having taken 1,200 mg MSM for 12 weeks in comparison with a placebo [29]. In another study, patients with osteoarthritis of knee who took MSM for 12 weeks showed an improvement in physical mechanic function and got helped in pain reduction. Although an improvement was found, even now more studies need to be assessed to conclude a clinical significance [30].

MSM possess anti-inflammatory properties, chemo preventive properties, inhibition of prostacyclin (PGI_2) synthesis, anti-atherosclerotic pharma effect, helpful impact on eicosanoid metabolic pathways and free radical hunting activity.

In a 12-week trial (n = 118), patients affected from osteoarthritis of knee was dosed either 1.5 g MSM or 1.5 g glucosamine sulfate, 1.5 g MSM and glucosamine sulfate, or on placebo. Significant fall in the Lequesne Index was noted with MSM, glucosamine sulfate, and their combination ($P < 0.05$). The authors recorded 33% less pain in MSM group; joint movement and mobility, swelling and inflammation, global appraisal, and walking time also got improved. Having the global acceptance of MSM and claimed improvements in osteoarthritis pain in researcher" s mind , surplus efficacy and safety trials of MSM will probably be valuable in recommending practitioners and patients in the proper usage, if found for arthritis management. On the other hand a murine model has been testified in decreasing and joint degeneration and graded loss. However due to the initial proposal and little mediation period, treatment reactions were observed to a limit in osteoarthritis symptoms, and not included radiographic alterations of the joints resulting intervention.

HYALURONIC ACID

Hyaluronic acid is naturally found in the human body. It is a gel-like substance which be responsible for lubrication, growth and development of bones and cartilages and lessens inflammation. Hyaluronic acid (HA, Hyaluronan) and Collagen Hydrolysate, have been used and using in recent times by practioners in osteoarthritis patients.

Studies have publicized that taking oral supplements of hyaluronic acid can help osteoarthritis patients managing mild knee pain [31]. Moreover other study stated that hyaluronic acid injections can reduce inflammation in the ankle and foot joints present in rheumatoid arthritis [32]. In context to collagen hydrolysate, on the basis of present in vitro and in vivo studies as well as clinical trials [33, 34], fact can be established as collagen hydrolysate is absorbed by the G.I. tract and finally incorporated into the joint cartilage. It might lead to increased mobility and physical functional temperament with moderate pain relief.

In accordance with basic pharmacological researches done earlier it can be spoken that oral administration of high-molecular-weight *Hyaluronic acid* which reached in the joints [35], which assures validation for the oral supplementation of *Hyaluronic acid*. Researchers of a clinical pilot study [36] concluded that *Hyaluronic acid* improves multidimensional quality of life in human with knee osteoarthritis. However a larger sample size shall be inevitable to confirm these results.

When sysadosteoarthritis treatment was examined in a recent research using the grade system [37] experts arrived on the conclusion that additionally to chondroitin sulfate or glucosamine sulfate, hyaluronic acid pain reduction property and physical mobility improvement with very little toxicity, in light of moderate to high qualitative evidences [37].

TURMERIC AND CURCUMIN

Turmeric is an inevitable spice from our kitchen which is modified root of *Curcuma longa*. It has been consuming in India for thousands of years in the form of spice and medicinal herb. Turmeric has a warm, bitter taste and is frequently used to flavor or color different food stuffs. Recently, researchers science claiming that turmeric contains bio active compounds with medicinal properties It contains a chemicals called curcuminoids, Curcumin is chief one and the most active component in turmeric, is a organically dynamic phytochemical [38, 39], which help in reducing swelling (inflammation) in any part of human torso especially healing of internal injuries.

Turmeric is a root modified as rhizome belongs to the family Zingiberaceae. Curcumin, main type of curcuminoid main ingredient in turmeric that helps to stop inflammation and acts as blood-thinner and blood purifier. Many studies in recent times suggested that turmeric's anti-inflammatory, anti ageing and antioxidant properties, anti-oxidative stress and anti-catabolic activities render in

helping prevent degenerative diseases like osteoarthritis. It is also used for hay fever, depression, dyslipidemia, healing in different wounds. It may also shows hypocholesterolemic, anti-apoptotic, neuroprotective, chondroprotective and anti-proliferative effect. Haroyan *et al.* [40] did a randomized, double-blind, placebo-controlled assessment on the effects of curcumin from turmeric rhizome on osteoarthritis. They also evaluated its in combined effect with boswellic acid (Boswellia serrate) extract. They found that these compounds helped to reduce inflammation in osteoarthritis. Cao *et al*. [41] planned the effects of curcumin on cartilage formation i.e., chondrogenesis in stem cells of mesenchyme. Mesenchymal stem cells got utilized as germ cells in cartilage tissue production. They testified that curcumin operated in maintaining cartilage equilibrium.

Li *et al*. [42] stated that curcumin subdues inflammatory lanes by its actions on a specific signaling enzyme in the large joints. These researchers strongly recommend that curcumin should be investigated as a preventative dealing of osteoarthritis in humans and desired animals. Murugan *et al*. [43] reported that turmeric upregulates the type II collagen gene. This could be another mechanism on how turmeric helps reduce inflammation.

Evidence from many recent in vitro demos suggests that curcumin shows to alleviate the inflammatory process by subsiding synthesis of inflammatory mediators like interleukin (IL)-1β, IL-6, IL-8, tumor necrosis factor (TNF)-α, cyclooxygenase-2 (COX-2) and prostaglandin E2 (PGE_2) [44, 45, 46] altogether inhibit IL-1β-induced extracellular matrix degradation [47] and chondrocyte apoptosis [48, 49].

As well as they all mitigate the over-production of reactive oxygen and nitrogen species [50, 51]. Additionally, curcumin, doing inhibition of the activator protein 1 (AP-1) pathway [52] and doing nuclear factor kappa B (NF-kB) activation [52, 53, 54], suppresses the gene expression of several matrix metalloproteinases (MMPs), which have critical contributions in t breakdown of the cartilage extracellular matrix [52-55].

GINGER

Ginger is a flowering plant. Its root is regularly used in various cooking including tea ingredient. Its sharp, distinct flavor and taste is unique, and liked by most of people. Moreover its cooking uses, ginger has been serving as a folk medicine for many years. Ginger has anti-inflammatory, antioxidant, and anticancer properties thus boost our overall immunity. Ginger has been using in recent times may combating symptoms of osteoarthritis. The phytosterols found in ginger have anti-inflammatory properties that help in relieving inflammation and pain in the larger joints [56]. A study have shown so far reveal that ginger drops the pro-inflammatory gene expression and also rises the capability to increase anti-inflammatory genes [57]. Ginger is available in many forms as raw roots in vegetable market, Powder, Tea, Oil and Capsules. The suggested normal amount is 2 gm in three times a day or 3-4 cups of tea daily. The mild side effects of ginger come as heartburning, nausea, and gas. If some one taking blood thinners or have gallstones, consultation is must.

Ginger comprised of a combination of bio active compounds, of which ingredients like gingerols, shogosteoarthritisls and paradols are reported having anti-inflammatory properties [58]. Many clinical trials done have shown that ginger inhibits action of cyclooxygenase (COX), mainly the inducible form of COX- 2, instead of the constitutive form (COX-1). Ginger also acts as inhibitor of lipo-oxygenase, leading to suppression in the synthesis of the inflammatory leukotriene [59]. Moreover Ginger extracts inhibit the expression of tumor necrosis factor (TNF)-a in synoviocytes triggered by either interleukin (IL)-1b or TNF-a [60]. Surprisingly in one study [61] it was investigated that ginger extract was found as effective an anti-inflammatory agent as betamethasone or prednisolone.

BOSWELLIA SERRATA

Boswellia serrata is a tree with modest height, has been growing in hilly regions of India. The beneficial value of dried resinous gum called guggulu, derived from pitter-patter the Boswellia tree was known since bay back. Boswellia resinous gum is mentioned in the ancient Ayurvedic book "Sushrita Samhita" and "Charaka Samhita". The resinous gum of the Boswellia serrata has been utilizing for the treatment of the inflammatory ailments in the traditional Indian ayurvedic

medicine since ancient times. Resinous gum extracted from Boswellia has good anti-inflammatory, analgesic, antispasmodic and anti-arthritic activity, significantly reduces the total leucocytes in the joint fluid, restoring the integrity of blood capillaries demolished by spasm or internal injury [62, 63]. However there is considerable supporting studies regarding the effect of Boswellia in the treatment of knee osteoarthritis are available.

Boswellia extract in different forms available in market has already promised in the treatment of asthma [64], bronchitis, rheumatoid arthritis [65], Crohn's disease [66], osteoarthritis of the knee and other articular joints [67, 68, 69] immunobooster and collagenous colitis [70]. The biological active compound in Boswellia serrata is boswellic acids, of which AKBA, 3-O-acetyl-11-keto-boswellic acid is the most reactive and abundant [71-74]. AKBA in fact was found to have as inhibitor of the lipoxygenase pathway in arachidonate metabolism and keeps significant anti-inflammatory, antioxidative stress and anticancer properties. Glycosaminoglycan synthesis is obligatory for cartilage repair and regeneration. Boswellia serrata prevents to be lessening in glycosaminoglycan levels, whereas NSAI Drugs might interrupt glycosaminoglycan synthesis, which, in turn, may hasten cartilage destruction. Moreover non-acid section of the gum has too analgesic properties [75]. Boswellia serrata has been found and confirmed in reverting osteoarthritis of knee investigated in recent researches, thus many medical professionals are advising to take Boswellia in complete eradicating of osteoarthritis.

Clinical studies performed by many scientists have shown that Boswellia serrata extract not only devours anti-inflammatory and anti-arthritic features, but also mends pain management and physical work [76, 77, 78, 79]. Through in vitro experiments it was established that Boswellia serrata excerpt must inhibit the expression of inflammatory dynamics like adhesion molecules [80, 81, 82, 83, 84].

Pertaining to the safety of Boswellia serrata, latest studies showed that Boswellia serrata extract like 5-Loxin and Aflapin don't have toxic side effects even at higher doses [84, 85, 86]. These indicate that the active compound of Boswellia extract i.e., AKBA is most safe phytochemical observed based on current substantiation [84, 86].

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