Nutritional Factors and Osteoarthritis: A review article

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(Received 18 April 2008 and accepted 22 June 2008)

ABSTRACT: Osteoarthritis (OA) is the most common disease according to TNS Arogya survey 2007. Although OA was previously thought to be a progressive degenerative disorder, it is now known that spontaneous arrest or reversal of disease can occur. Conventional medications are often effective for symptomatic relief but they can also cause significant side effects and do not slow the progression of disease. Though the role of nutritional factors in OA has been suggested as early as 700 BC, it was first established in the 1960s. Several nutritional factors are helpful in relieving the symptoms of OA and they might positively affect the progression of the disease without any side effects. Preliminary evidences suggest several of these may have a role in influencing the course of OA. Studies have proven the role of these factors and experiment based results have established their therapeutic role. Research is ongoing on the beneficial properties of plant derived extracts for OA and nutraceuticals industries are accordingly making firm contribution to this sector. This article focuses the role of nutrients to slow down the progression of OA and their future aspects.

KEY WORDS: Osteoarthritis; Dietary factors; Nutrition; Review

INTRODUCTION

Osteoarthritis (OA) is one of the most prevalent and disabling chronic disease affecting the elderly. The current concept holds that osteoarthritis involves the entire joint organ, including the subchondral bone, menisci, ligaments, periarticular muscle, capsule, and synovium[1]. Its most prominent feature is the progressive destruction of articular cartilage which results in impaired joint motion, severe pain, structural and functional failure of synovial joints[2]. Broadly OA can be subdivided in to two types: Primary OA and Secondary OA. Idiopathic (Primary) OA is most common form of disease and no predisposing factor is apparent. Secondary OA is pathologically indistinguishable from idiopathic OA but attributable to an underlying cause like accidental injury to joints, inflammatory disease, healed infections of the joints, sports injuries, obesity, avascular necrosis of head of femur, congenital disorder, etc. Onset and progression of disease depends on various factors like obesity, joint injury, metabolic diseases, bone and joint malformation, genetic factors and nutritional factors[3-6]. Management of OA includes conventional pharmacological treatment of OA consisting primarily of non steroidal anti inflammatory drugs (NSAID's) and physiotherapy. While these medications often relieve symptoms, they are not ideal therapeutic agents. NSAIDs in particular, can cause serious side effects including peptic ulcer and hepatic or renal failure. Neither of these classes of medications prevents or delays the progression of OA[7,8].

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The role of nutrition and nutritional supplements in the development and progression of osteoarthritis is now a topic of considerable public, industrial, and academic interest. A number of substances that occur naturally in the body may have value for the prevention and treatment of OA. Some of these compounds have been shown to provide symptomatic relief and preliminary evidence suggests that some of them positively affect the progression of disease and can be used to prevent the degradation, or enhance the repair of the joint cartilage. This review focuses a role of nutritional factors or nutritional supplements in the management of osteoarthritis.

HISTORICAL BACKGROUND

Correlation of OA and diet is as old as 700 BC, when use of millets was restricted for patients of joint pain when the cause was not known.

Year	Conclusions
1960's	Association of dietary factors or other consequences of obesity with OA and role of niacinamide is identified in OA
1970's	Role of vitamin C, E and Zn is identified but not proven.
1980's	Role of Obesity, Folic acid, Vitamin C, D, E, β-carotene, Zn, Se, Role of ROS known.
1990's	Role of n-3 fatty acid, ROS, Leutin and Zeaxanthin and weight reduction in OA.
2000's	Nutraceutical application of Conjugated linoleic acid (CLA), Poly unsaturated fatty acid (PUFA), Flavanoid
2005	Dietary supplementation programs and nutraceuticals used in conjunction with nonsteroidal, anti- inflammatory drugs may offer significant benefits to patients with OA. Significantly positive correlation was found between synovial fluid *Se-Cu* values in patients with RA but not with OA
2006	Weight loss has improved the physical function of the OA patients.
2007-2008	Recent studies assessed oxidative stress and antioxidant status in OA. They suggest higher oxygen free radical provides support to oxidative stress in OA. Micronutrient might mediate the OA process by blocking oxidative damage. Role of plant extracts and Nutraceutical was found against OA.

BIOLOGICAL EVIDENCE OF ROLE OF NUTRITIONAL FACTORS IN BONE PHYSIOLOGY

The bone is a living tissue from which substances are constantly being removed and replaced. Bone is made up of a protein matrix, on which hydroxyapatite (a crystalline structure made up of calcium and phosphorus) is deposited. Magnesium, zinc and fluoride are also deposited in the protein matrix, although calcium is the most abundant mineral in bone. Bone formation is laid down in two phases: *special organic matrix is laid down by Osteoblasts* and *then mineralization or calcification takes place*. Bone is continuously being remodeled, that is old bone tissue is replaced by new. Bone formation and bone resorption (replacement of old bone tissue) take place throughout life. Bone formation and bone resorption are influenced by a variety of factors including diet and physical activity. Bone formation is greater than bone resorption until the age of 30-35 years, when peak bone mass is reached, the net effect being an increase in bone mass. After this bone resorption occurs at a faster rate than bone formation. The consequence of this is a gradual fall in bone mass with aging; bone minerals and proteins are lost slightly more quickly as from the age of about 35 years than they are replaced. The amount of calcium in bone gradually decreases. In women, bone loss is accelerated following the menopause, particularly during the first 5 years. This is because the hormone estrogen (production of which ceases after the menopause) protects bone, and bone formation and loss is negatively influenced by such hormones.

PATHOPHYSIOLOGY OF OSTEOARTHRITIS

Pathology of OA starts from fibrillation and ends at sclerosis as shown in **Figure 1**.

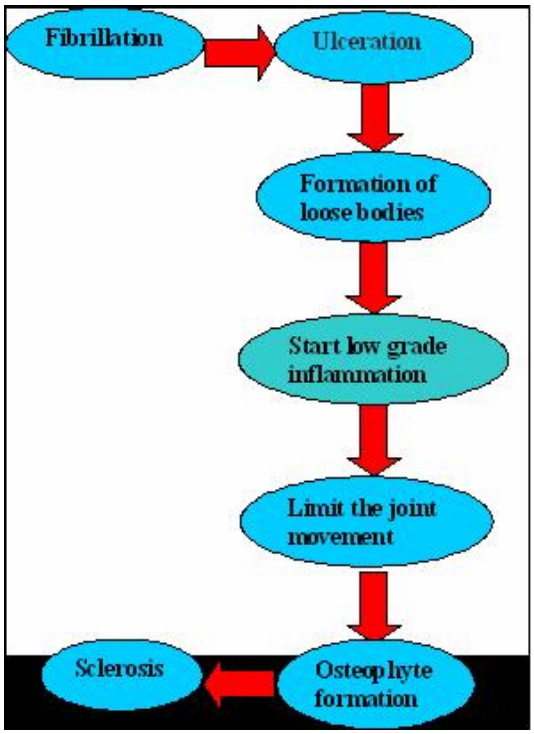

Figure 1: Pathophysiology of osteoarthritis

OBESITY

Overweight people are at considerably increased risk for the development of OA in their knees. They may also be more susceptible to both hip and hand joints involvement irrespective of the mechanisms. Weight reduction in a person through dietary or other means may reduce a risk for the development or progression of the OA[9]. Obese osteoarthritis patients were benefited from the weight loss and foods that supply the nutrients such as vitamin D, folacin, vitamin B6, zinc, and pantothenic acid in which they are deficient[10]. An intensive weight loss intervention incorporating deficit diet and exercise training improves physical function in older obese OA knee adults, greater improvements in function being directly proportional to the greater weight loss[11]. **Miller et al**[12] performed longitudinal, controlled clinical trial of weight loss and exercise interventions in older adults with knee osteoarthritis to determine the effect of weight loss and exercise interventions on serum leptin and to investigate the relationship of physical function and osteoarthritis (OA) severity with serum leptin in older overweight and obese adults with knee OA. There was a significant effect of weight loss on serum leptin. Decrease in serum leptin may be one mechanism by which weight loss improves physical function and symptoms in OA patients[12].

Recent research results indicate that an intensive weight-loss intervention in older obese adults with knee pain can help in improving inflammatory biomarkers- interleukin 6 (IL-6), tumor necrosis factor alpha (TNFÎ±), C-reactive protein, and soluble receptors for TNF1± (sTNFR1 and sTNFR2)) and that changes in these concentrations showed associations with physical function[13].

REACTIVE OXYGEN SPECIES (ROS)

ROS is implicated in the pathophysiology of a number of common age related conditions[14]. OA similarly can be regarded as a prototypical age related degenerative disease. There is evidence that cells within the joint produces ROS, and that oxidative damage is physiologically important[15]. **Surapaneni et al**[16] assessed oxidative stress and antioxidant status in patients with osteoarthritis. Levels of erythrocyte lipid peroxidation products, GSH, ascorbic acid, plasma vitamin E; and activities of antioxidant enzymes were measured in patients with osteoarthritis. The study suggests higher oxygen-free radical production evidenced by increased MDA and decreased GSH, ascorbic acid, vitamin E and catalase activity, support to the oxidative stress in osteoarthritis. The increased activities of antioxidant enzymes may be a compensatory regulation in response to increased oxidative stress[16]. Micronutrients might mediate the osteoarthritis process by blocking oxidative damage. Nitric oxide and reactive oxygen species inhibit collagen and proteoglycan synthesis, activate matrix metalloproteinases, increase the susceptibility of cartilage to injury by other oxidants, and induce apoptosis.

ASCORBIC ACID

Ascorbic acid (Asc) is required for the synthesis of the most abundant protein in cartilage, type II collagen. Asc exists in 2 forms: the reduced form (AA) and the oxidized form, dehydroascorbate (DHA). Both AA and DHA are available through the diet from fruits and vegetables and are absorbed throughout the entire length of the small intestine[17]. Diet constitutes the sole source of Asc for humans as they lack the enzyme gulonolactone oxidase which is necessary for the

synthesis of Asc from glucose[18]. Two distinct pathways of Asc transport across cellular membranes have been discovered to date, the sodium-dependent vitamin C transporters (SVCTs)[19] and the glucose transporters (GLUTs)[20,21]. The majority of vitamin C in plasma exists as AA, which is transported by the SVCTs[22]. It was recently shown that human chondrocytes express SVCT-2, but not SVCT-1, In contrast, the GLUTs are numerous and are ubiquitous in their expression. Of the GLUTs currently known to transport DHA, only GLUT-1 and GLUT-3 are expressed by human articular chondrocytes[23,24]. However, the fact that has not taken into consideration is that articular cartilage is avascular and functions at a lower oxygen tension than most tissues. This may alter the tissue redox state and, thus, the local concentration of DHA, and/or it may regulate the transport pathways for DHA[25-27]. In vitro, ascorbate and ascorbic acid increased protein and proteoglycan synthesis by articular chondrocytes[28-30] and increased the mRNA levels of type I and II collagen[29,31] and aggrecan and α-prolyl 4-hydroxylase[27]. It decreased the lipopolysaccharide (LPS)-induced GAG release[32]. It also affected the activities of lysosomal enzymes, decreasing the activities of arylsulfatase A and arylsulfatase B, an *N*-acetylgalactosaminidase-4-sulfatase, but increasing the activity of acid phosphatase in normal and OA chondrocytes[33]. Ascorbic acid can cross-link collagen and other proteins by non-enzymatic glycation, leading to the formation of advanced glycation endproducts (AGEs). Threose, a metabolite of ascorbic acid, increases the AGE content of articular cartilage in vitro[34]. These cross-links increase the stiffness of the collagen network, which is hypothesised to increase cartilage susceptibility to OA. High in vitro levels of ascorbic acid (756μM) also increased protein carbonylation, one type of oxidative damage. However, when guinea pigs were fed with diets containing different levels of ascorbic acid, no changes in the AGE content of articular cartilage were detected[35].

Schwartz and **Adamy** reported a decreased level of active proteinase in the presence of ascorbic acid and found further that sulphated proteoglycan biosynthesis, a presumed measure of repair was significantly increased in the cartilage in the presence of ascorbic acid[29]. **Manson et al**[34] suggested ascorbic acid stimulates collagen synthesis and modestly stimulates synthesis of aggrecan (a proteoglycan present in articular cartilage). Framingham epidemiological study found a threefold reduction in risk of OA progression for both the middle and highest tertiles of vit C intake and an inverse association between vit C intake and cartilage loss[35]. Guinea pigs do not possess gulonolactone enzyme which make them unable to synthesize ascorbic acid. Schwartz and Leveille in two studies showed that high vitamin C (which would correspond to vitamin C in humans of at least 500 mg/ day) is helpful in preventing cartilage fibrillation, structural changes in the joint and eburnation in guinea pigs[36]. **Meacock** and colleagues on third guinea pig trial reported, an increase of extra ascorbic acid appeared to have some chondroprotective effect on the development of spontaneous lesions but gave no significant protection against surgically induced OA[37]. The long term safety of such high doses of vitamin C in OA patients need to be evaluated and confirmed by long RCTs.

VITAMIN E

Natural vitamin E (vit E) comprises eight different forms, α-, β-, γ-, and δ-tocopherol and α-, β-, γ-, and δ-tocotrienol, produced solely by plants. **Tiku et al**[38] showed that when chondrocytes were submitted to an oxidative burst, vit E reduced the catabolism of collagen by preventing the protein oxidation mediated by aldehydic down products of lipid peroxidation. Vit E strongly increased glucosaminoglycan sulfatation or increased glucosaminoglycan synthesis while reducing glycoproteins or glycolipids synthesis. Like vit C, vit E affected the activities of lysosomal enzymes: it decreased the activities of arylsulfatase A and of acid phosphatase in cultures of human articular chondrocytes[38,39]. There is some evidence suggesting that isoform concentrations relative to each other may be important in preventing specific types of oxidative damage[40-43] with γ-tocopherol possibly being more important than α-tocopherol in removing nitrogen oxides and other electrophilic mutagens. Epidemiological studies examining the role of antioxidants, specifically tocopherols, in human osteoarthritis are few. Several methodologically limited clinical trials have suggested that vitamin E supplementation might be superior to placebo and equal in effectiveness to anti inflammatory medication in relieving osteoarthritis symptoms, but other studies have failed to show an effect[43-47]. To date, no studies have examined biomarkers of individual tocopherols in relation to radiographic knee osteoarthritis.

Black et al[48] demonstrated that incubation of rabbit articular cartilage with α-tocopherol preserved cartilage load-carrying capacity and viability. **Machtey et al**[43] in a six week double blind placebo controlled trial of 400 mg - a tocoferol (vitamin E) in 56 OA patients showed vitamin E treated patient's experienced greater improvement in every efficacy. **Mc Alindon et al**[35] showed vitamin E were associated with a reduced risk of progression of radiographic knee osteoarthritis but were not protective against incident disease. A randomized, double blind, placebo- controlled trial of 500 IU vitamin E daily to 77 patients for six months revealed neither vitamin E nor placebo showed a significant improvement in pain, stiffness, or physical function[45]. One trial suggested that vit E was no less efficient than diclofenac in decreasing pain. In a 3-week double-blind RCT on OA, no significant difference was found between 544 mg of α-tocopherylacetate three times a day and 50 mg diclofenac three times a day on VAS of pain[49]. On the other hand, a two-year randomized, double-blind, placebo-controlled trial examining the effect of vitamin E supplementation (5001U) on knee cartilage volume in 136 patients with OA of the knee showed no significant effect of supplemental vitamin E or the major dietary antioxidants (vitamin C, beta-carotene, or retinol activity equivalents) on the rate of loss of tibial knee cartilage[44]. More recently, **Kurz et al**[50] reported that a diet containing vitamins E, C, A, B_6, and B_2 and selenium increased the expression of antioxidative enzymes and decreased the incidence of osteoarthritis in STR/1N mice. In the light of these results the role of vitamin E remains controversial and needs further longitudinal RCTs.

VITAMIN D

Vitamin D3, or cholecalciferol, is synthesized in the skin. Its precursor, 7-dehydrocholesterol, is converted by the UV light of the sun (UVB 290–315 nm) into previtamin D3, which is slowly isomerized to vitamin D3. The action of 1,25-$(OH)_2$D on bone is not well understood. It stimulates the osteoblasts to produce osteocalcin and alkaline phosphatase and decreases the production of type I collagen by fetal rat calvaria[51]. On the other hand, 1,25-(OH)2D stimulates bone resorption *in vitro*[52,53]. The effects of 1,25-(OH)2D on bone mineralization appear to be indirect by stimulating the calcium and phosphate supply, mainly by absorption from the gut.

Two longitudinal studies showed that vitamin D status is unrelated to the risk of joint space or cartilage loss in OA patients[54]. A prospective study showed that low intake and low serum levels of vitamin D appears to be associated with an increased risk for the progression of OA Knee[35]. **Lane NE**, in an eight years prospective study of 237 individuals (aged 65 years or older) showed that low serum levels of *25*- hydroxyl vitamin D were associated with an increased risk of developing OA of the hip, as defined by joint-space narrowing[55]. These findings suggests that adequate intake of vitamin D (adequate light exposure) may slow the progression of disease.

VITAMIN B

Researchers at the University of Southern California, School of Medicine in Los Angeles discovered that B_{12} also stimulates osteoblasts, another type of bone cell that generates not red blood cells but bone. That is important to people with osteoarthritis, because below degenerating cartilage, bone also deteriorates, causing additional pain and further cartilage erosion. Researchers at the University of Missouri in Columbia found that people who took 20 micrograms of B_{12} (3.3 times the daily value of 6 micrograms) and 6,400 micrograms of folic acid, for two months had fewer tender joints and better hand strength and took less medicine for pain than people not getting this B vitamin combo. The vitamin is thought to somehow improve the metabolism of joint cartilage.

Rosenberg et al[56] in a dietary survey of patients with OA found this population to have folate intakes lower than RDA. **William Kaufman** reported that high dose niacinamide a form of vitamin B3 of 900-4000mg/day was beneficial in OA and as well as rheumatoid arthritis. He documented improvements in joint function, range of motion, increased muscle strength and endurance and reduction in erythrocyte sedimentation rate (ESR)) over long findings in these patients[57]. **Flynn et al**[58] diagnosed 26 subjects for an average 57 years with idiopathic OA of the joints in the hand and the number of tender hand joint was greater in those using NSAIDs when compared to cobalamin folate supplementation.

VITAMIN A (B- CAROTENE)

Machlin et al[59] and **Anderson et al**[60] indicated that antioxidants ascorbic acid, α-tocoferol and β-carotene are free radical scavenging nutrients that protect the cells from damage by pro-oxidants. **Martin et al**[61] in a cross sectional study

showed lutein and zeaxanthin intake was associated with a decreased risk of cartilage defects and the β-cryptoxanthin intake was inversely associated with the tibial plateau bone area after adjusting for vitamin E intake. Other carotenoids were not significantly associated with cartilage or bone measures. Except for beta-carotene, none of the compounds examined in this study had been previously evaluated for involvement in the OA disease process. Participants with serum levels of lutein or beta-cryptoxanthin in the highest tertile were approximately 70% less likely to have knee OA than controls. Those are the highest tertile of trans- beta- carotene and zeaxanthin were more likely to have OA[62].

VITAMIN K

Prospective observational cohort of Framingham Offspring Study on plasma phylloquinone (the primary form of vitamin K) showed that prevelance for osteophytes and the adjusted mean number of knee joints with osteophytes decreased significantly with increasing plasma phylloquinone level so it shows significantly an association between low plasma levels of vitamin K and increased prevalence of OA manifestations in the hand and knee[63].

MINERALS

In a case control study of synovial fluid and plasma concentrations of selenium (Se), zinc (Zn), copper (Cu) and iron (Fe) in patients with RA and OA, plasma albumin levels were measured as an index of nutritional status. Plasma Se, Cu and Zn concentrations were determined by atomic absorption spectrophotometry. There was a significantly positive correlation between synovial fluid Se and Cu values in patients with RA but not with OA[64]. **Walker et al**[65] gave opinion that Zn plays a beneficial role in progression of OA due to anti-inflammatory and antioxidant property. A histological study of bone and articular cartilage was conducted on specimens from rats fed on low selenium (Se) diet. Electron microscopy disclosed chondrocytes in the deep layer showing degeneration of nuclei and endoplasmic reticular ballooning. A decrease in bone mineral density was noted, as well as a decrease in sulfotransferase activity, which is involved in synthesis of glycosaminoglycan[66].

Femoral OA bone contains less boron, a nonmetallic trivalent chemical element which suggests that the boron might have a beneficial effect in OA[67]. A small 8-week double-blind placebo-controlled RCT suggested that intake of 6mg/day sodium tetraborate decahydrate was more efficient than placebo in reducing a patient's assessment scale of symptoms[68]. This RCT, however, was of low quality hence, longer and higher-quality RCTs were required to evaluate thoroughly the benefits of boron for OA.

A small pilot study evaluated the impact of treatment with a natural multi-mineral supplement from seaweed on walking distance, pain and joint mobility in subjects with moderate to severe osteoarthritis of the knee. This small preliminary study suggested that a multi mineral supplement may reduce the pain and stiffness of osteoarthritis of the knee over 12 weeks of treatment and warrants further study[69].

POLYUNSATURATED FATTY ACIDS

Polyunsaturated fatty acids (PUFA) fall into 3 major classes the n-3, n-6, and n-9 groups. Specific long-chain polyunsaturated fatty acids (PUFA) belonging to omega-3 and omega-6 families are substrates for prostanoids that influence the differentiation and activity of cells in bone and cartilage tissues. These PUFA appear to alter prostanoid formation, cell-to-cell signaling processes, and impact transcription factors in vivo. **Watkins et al**[70] reported that dietary fatty acids and their derivatives (eicosanoids) represent a recent focus of investigation on bone and cartilage metabolism. Epidemiological, clinical and experimental evidence suggests that fatty acids may have an effect (due to their chemical structure) on calcium metabolism in animals and man. Fatty acid deficiency in animals can lead to a loss of bone calcium and matrix, resulting in, marked bone demineralization, and treatment with a mixture of omega-3 and omega-6 po1yunsaturated fatty acids can induce significant reduction in some biochemical markers of bone reabsorption[71]. **Colker et al**[72] in their six week double blind placebo control study showed that daily consumption of the nutritional beverage containing milk based micro nutrients vitamins and minerals was beneficial in alleviating the symptoms and dysfunction in subjects with osteoarthritis. **Pritchett** [73] showed that taking fish oils reduced the amount of lipid in bone marrow by 20%. Lipid profiles of disturbed marrow and joint fluid from patients who took statins or dietary fish oil showed an increase in the proportion of unsaturated fatty acids and longer-chain fatty acids relative to pretreatment profiles. The ability to change the

amount and character of bone and joint lipids may have major importance for strengthening bone, reducing the severity or preventing osteonecrosis, and enhancing joint lubrication[73]. **Sperling**[74] said the increase consumption of n-3 fatty acid ameliorates the symptoms of OA. In vitro, effects of 10 to 100µg/ml of n-3 (linolenic, eicosapentaenoic, and docosahexaenoic acids) on chondrocytes have been investigated. n-3 did not affect the spontaneous or the IL1-induced decrease in glycosaminoglycan (GAG) synthesis, but dose-dependently inhibited the IL1-induced GAG degradation. n-3 dose-dependently decreased the IL1-induced aggrecanase activity and basal aggrecanase and collagenase activity, whereas, in contrast, n-6 stimulated the basal aggrecanase and collagenase activity[74-77]. n-3 also decreased the IL1-induced mRNA expression of ADAMTS-4 (aggrecanase), COX-2, 5-LOX, FLAP (5-LOX-activating protein), IL1α, and tumour necrosis factor (TNF) α and the basal mRNA levels of these genes. Finally, n-3 decreased the basal and IL1β-induced mRNA and protein levels of MMP-3 and MMP-13. All these parameters were unaffected by n-6 PUFAs. Taken together, these results indicate that n-3 PUFAs have anticatabolic and anti-inflammatory properties. Nevertheless, too low of an n-6/n-3 ratio can be detrimental. A diet with very low levels of n-6 PUFAs induced occasional surface irregularities and localised proteoglycan depletion in cartilages in rats[78].

Watkins et al[79] in recent investigations with growing rats given butter fat and supplements of CLA demonstrated an increased rate of bone formation and reduced ex vivo bone PGE2 production, respectively. The effects of CLA on bone biology in rats (IGF action and cytokines) appear to be dependent on the level of n6 and n-3 fatty acids in the diet, Anti-inflammatory diets, including nutraceutical applications of CLA, may be beneficial in moderating cyclooxygenase -2 (COX-2) activity or expression (influencing PGE2 biosynthesis) and might help to reduce rheumatoid arthritis (secondary osteoporosis). This experiment indicates that CLA isomers possess anti-inflammatory activity in bone by moderating prostanoid formation.

PHYTOCHEMICALS AND PLANT EXTRACTS

Flavonoids, a group of polyphenolic compounds widely distributed throughout the plant kingdom, are thought to contribute to the health benefits of diets rich in fruits and vegetables. In vivo effects of several flavonoids (tea-containing catechins, soy isoflavones) have been reported in the literature**. Perdey et al**[80] reported that plants derived phenolic compounds such as flavonoids have antioxidant properties capable of reducing risk of developing these joint diseases. **Bromelain** (aqueous extract obtained from both the stems and immature fruits of pineapple plant) contain a number of proteolytic enzymes. Bromelain is suggested to have anti-inflammatory, analgesic, antioedematous, antithrombic, and fibrinolytic effects, Three different preparations containing bromelain mixed with diverse enzymes have been tested in nine trials on knee OA[81,82]. ***Rosa canina*** a standardised rose-hip powder made from the seeds and husks of the fruits from a subtype of *R. canina* (Hyben Vital™ produced by Hyben Vital International, Langeland, Denmark), and the common wild-briar rose of English hedgerows, were evaluated in three RCTs[83,84]**.** ***Harpagophytum procumbens*** also called devil's claw, is a South African plant that grows in regions bordering the Kalahari, is used for exacerbations of chronic musculoskeletal pain. Secondary tuberous roots are used to prepare powders or extracts, which were tested in several RCTs[85]. ***Uncaria tomentosa*** **and** ***Uncaria guianensis*** **(cat's claw)** is a vine from the basin of the Amazon River. There are two species, *U. tomentosa* and U. guianensis, which are traditionally used in South America for their anti-inflammatory properties[86]. The anti-inflammatory, antipyretic, and analgesic effects of ***Salix sp.*** **(willow bark)** have been known since antiquity[87].

GINGER AND TURMERIC

Ginger and turmeric are used in traditional Japanese Kampo, Ayurvedic, and Chinese medicine as anti-inflammatory agents for musculoskeletal diseases. Three RCTs evaluated ginger extracts prepared from the rhizomes of ***Zingiber officinale*** and ***Alpinia galanga***. An extract prepared from the Indian and Japanese turmerics ***Curcuma domestica*** and ***Curcuma xanthorriza***, was tested on hip and elbow OA in an 8-week double-blind randomised trial in dogs[88]. No significant difference on the kinetic gait analysis was found between extract and placebo. The gummy oleoresin from the bark of ***Boswellia serrata***, a tree from northwest India, is used for inflammatory diseases in Ayurvedic medicine[89]. The pilot clinical trial conducted by Douglas S showed that daily supplementation with oral hyaluronic acid from a natural extract of chicken combs was useful to enhance several

markers of quality of life in adults with osteoarthritis of the knee. The results warrant further study in larger sample sizes[90].

DISCUSSION AND CONCLUSION

The nutritional factors tested in above mentioned studies such as vitamins C, D, E, A, B, minerals (Zinc, Selenium, Boron), lipids (polyunsaturated fatty acids), and Plant extracts like flavonoid, bromelain, *Rosa canina*, *Harpagophytum procumbens* (devil's claw), *Uncaria tomentosa*, *Uncaria guianensis* (cat's claw), *Salix sp.* (willow bark) suggest correlation in the progression of OA. Evidences suggest weight reduction in a person through dietary or other means reduces the risk for development and/or progression of the OA. Vitamin C has been found to have chondroprotective effect especially in high doses. Low intake and low serum levels of vitamin D appear to be associated with an increase risk for the progression of OA knee. Role of vitamin E remains controversial and needs further longitudinal studies. The evidence of efficacy and the safety records of plant extracts should be considered to be product specific given that the composition of the extracts from a same plant can vary widely between manufacturers. The vitamins and some of the lipids reviewed here are sold as nutraceuticals but can also be incorporated in functional foods.

Nutrition can improve the symptoms of declared OA. However, the role of nutrition in slowing down progression of disease remains to be seen. Only a few nutrients have been tested, and research remains mainly on a pharmacological type of approach (one molecule/one target) rather than on a nutritional, more holistic type of approach (multiple ingredients/ multiple targets). The full potency of nutrition for patients with declared OA thus remains to be evaluated. No study has evaluated the value of nutrition in the prevention of OA. Based on the above review, we can conclude that nutritional factors have proven role in improvement of the disease condition in OA. While planning the prescription for any patient, we should not forget that Vitamin C, D, Boron, plant extracts such as flavanoids, bromelain, etc should be adequately supplemented or enriched in the diet so that the pathology of the disease is well taken care of. These factors have established role in the management of OA. Besides them, other factors have also shown beneficial effect in the cartilage-regeneration. Their supplementation can decrease the rate of disease progression.

LIST OF ABBREVIATION

CLA: Conjugated Linoleic Acid; PUFA: Ploy Unsaturated Fatty Acid; GSH: Gastro Stimulating Hormones; OA: Osteoarthritis; GAG: Glycosaminoglycan; PGE: Prostaglandin E; AGE's: Advanced Glycation Endproducts; COX-2: Cyclooxygenase-2; DHA: Dehydroascorbate

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