Hrana u zdravlju i bolesti, znanstveno-stručni časopis za nutricionizam i dijetetiku (2022) 11 (1) 21-28
Food in Health and Disease, scientific-professional journal of nutrition and dietetics (2022) 11 (1) 21-28

DIETARY SUPPLEMENTS AND HERBAL PREPARATIONS AS A SUPPORT FOR PATIENTS WITH SOME TYPE OF ARTHRITIS

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review paper

Summary

Introduction: It is estimated that today 54 million people in the world live with some type of arthritis. The three most common forms of arthritis are infectious, rheumatoid and osteoarthritis. Although disease occurs most commonly in the old age, rheumatoid arthritis can affect people in the most productive period of life, between ages of 20 and 40. First line of medical treatment for this disease are anti-inflammatory drugs, but corticosteroids and antibiotics are also used very commonly, along with various measures of physical medicine. Dietary supplements and herbal preparations are used only sporadically, despite accumulated evidence of their beneficial effect on arthritis symptoms.
The aim of paper: The aim of the paper was to collect and analyse literature data on dietary supplements and herbal preparations in support of arthritis treatment.
Results: Herbal preparations based on willow, red pepper and most recently, turmeric show potential in the treatment of arthritis. Dietary supplements as antioxidants (vitamins C and E, minerals zinc and selenium), chondroitin, glucosamine, collagen and hyaluronic acid also show positive effects. In addition, numerous food ingredients poses anti-inflammatory effects, such as acetylsalicylic acid, omega-3 fatty acids, polyphenols and flavonoids. These research findings suggest that a proper food selection and menu planning, combined with some of the aforementioned could affect the symptoms and progression of the disease.
Conclusion: Although medical treatment is still the first choice for people with arthritis, accumulating evidence supports the use of various dietary supplements and herbal preparations to alleviate symptoms of arthritis. Additionally, given that many foods contain ingredients with potent anti-inflammatory characteristics, proper food selection could add the additive effect and improve quality of life of people with arthritis.

Keywords: arthritis, herbal preparations, dietary supplements

Introduction

The word arthritis comes from the Greek word „arthros“, which means joint and from the word „itis“ which means inflammation. Arthritis is often used as a term for any disorder that causes joint damage or inflammation. Symptoms most commonly include join pain and stiffness (NIAMS, 2014). Other symptoms may include redness, heat and swelling and the decreased range of motion of arthritic joints (CDC, 2016). In some types of arthritis can be affected and other organs. There are over 100 types of arthritis described in the literature, and the most common forms that occur are osteoarthritis and rheumatoid arthritis (NIAMS, 2014).
Osteoarthritis is a degenerative joint disease and usually occurs with age, affecting the fingers, knees and hips, while rheumatoid arthritis is an autoimmune disease and most commonly affects hands and feet (NIAMS, 2014). Except these two most common types, it often occurs as septic arthritis, which is also known as infectious arthritis, and is usually caused by bacteria. It can also be caused by a virus or fungus. This type of arthritis is an inflammation of the joints caused by a microorganism. Other common type of arthritis include gout, systemic lupus, fibromyalgia and others (CDC, 2015). Today with the increase in life expectancy, the prevalence of osteoarthritis, which is also the most common type of arthritis, has increased (Pradeep, 2019). Although osteoarthritis is not necessarily a consequence of aging, there is a strong relationship between age and the increasing incidence of this disease. The connection could be correlated with the aging of cartilage *in vivo* chondrocytes, which in turn causes an age-related decline in the ability of cells to maintain articular cartilage. That means, increasing age increases the risk of osteoarthritis because chondrocytes lose the ability to replace their extracellular matrix (Martin et al., 2002). The body cartilage located on the joints erodes during osteoarthritis which in turn causes pain and can lead to the loss of joint function in affected individuals. The pathophysiology of osteoarthritis is still insufficiently studied and there are currently no treatments that modify the disease. Today, joint replacement remains as the only final treatment. Basic and clinical research are now focused on

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understanding the aging process of cartilage and its role in osteoarthritis (Pradeep, 2019).

Rheumatoid arthritis is an autoimmune disease whose outcome is difficult to predict (Combe, 2009). Early diagnosis is crucial for optimal therapeutic effect, especially the patients with well-characterized risk factors for poor outcomes, such as: high disease activity, the presence of antibodies and early joint damage (Josef et al., 2016). Although it most commonly occurs in the elderly, rheumatoid arthritis affects people in the most reproductive period of life, between the ages of 20 and 40. In most patients, disease progression occurs with bone erosion and cartilage fracture resulting in joint destruction, functional impairment and increased mortality. The goal of treating patients should be to achieve clinical remission to prevent structural damage and long-term disability. The early use of effective anti-rheumatic drugs that modify the disease is a key point in patients at risk of developing persistent and erosive arthritis. Intensive treatment such as combined DMARDs (disease modifying anti-rheumatic drugs) with steroids or biological therapies can induce high remission rates and control radiological progression. In most cases, it provides better outcomes than the DMARD monotherapy in the early detection of rheumatoid arthritis, so it is desirable to consider this therapy very early in high-risk patients. Careful monitoring of disease activity and radiographic progression is mandatory to adjust DMARD therapy and strategy (Combe, 2009).

Infectious arthritis is a disabling and potentially life-threatening condition that requires fast diagnosis and treatment (Learch, 2003). It can be caused by bacteria, viruses, fungi or parasites. It can occur in the context of another systemic infectious disease when microorganisms spread through the bloodstream from the primary focus to the joint, and less often, it is caused by direct injury to the joint during trauma, surgery or puncture of the joint. The main pathogen in adults is *Staphylococcus aureus* and therefore the initial treatment therapy is focused on this microorganism. Early recognition and detection of infectious arthritis can prevent a poor outcome, especially in elderly patients or those with underlying joint disease (Smith, 1990). Detection of emerging arthrogenic viruses has altered the ethology of infection-related arthritis. The role of viruses in the pathogenesis of chronic inflammatory diseases such as rheumatoid arthritis is increasingly recognized (Ashish etal., 2014).

Herbal preparations and dietary supplements to support arthritis treatment

Chronic inflammatory joint disorders such as osteoarthritis and rheumatoid arthritis lead to an increase in inflammation and oxidative stress resulting in progressive histological changes and disabling symptoms. Conventional drugs are powerful, but at the same time, they are often associated with serious and sometimes life-threatening side effects. Although medical treatment with conventional drugs is still the first choice of arthritis sufferers, various herbal preparations and dietary supplements can help primary medical therapy. They can reduce the number of the symptoms and affect disease progression. This can improve and control further course of the disease, but it is important to include them with the right choice of foods.

Herbal preparations

Willlow (Salix alba)

Willow extract has been used for thousands of years as an anti-inflammatory, analgesic and antipyretic drug. However, a small number of clinical studies have supported the use of willow bark extract in chronic lower back pain, joint pain and osteoarthritis pain (Mohd et al., 2015). However, the effectiveness of willow bark extract in treating painful movement disorders, such as back pain and arthritis pain, has been attributed to the content of salicin and its salicylate prodrug derivatives (Nahrstedt et al., 2007). It is already known that osteoarthritis is a disorder associated with aging, and that it can be caused by the accumulation of advanced glycation products (AGE). Excessive degradation of collagen and aggregate type II by matrix metalloproteinase (MMPs) disintegrants, and AGE-induced thrombosporin-type metalloproteinase (ADAMTS) is a key event in the pathogenesis of arthritis (Gao et al., 2019). Activation of the nuclear kappa B factor pathway (NF-kB) induces the expression of a cascade of pro-inflammatory cytokines such as interleukin (IL)-1β and tumour necrosis factor α (TNF-α). The study examined the effects of salicin on AGE induced by articular extracellular matrix degradation in human chondrocytes (SW1353). The study found a new beneficial role of salicin in saving the breakdown of collagen and type II aggregates, reducing oxidative stress, reducing pro-inflammatory cytokine expression and inhibiting NF-kB pro-inflammatory signalling pathway activation in AGE-stimulated chondrocytes. Therefore, salicin may have great potential as safe and effective therapy against development and progression of osteoarthritis (Gao et al., 2019). In recent years, various *in vitro* studies have shown that the anti-inflammatory action of willow bark extract is associated with a decrease in

the regulation of inflammatory mediators TRF-α and NF-kB. Although willow extracts are mostly standardized to salicin, other salicylates are also contained as well as polyphenols and flavonoids that may also play an important role in therapeutic terms. Side effects are minimal compared to nonsteroidal anti-inflammatory drugs including aspirin. The reason to concern due to use may relate to allergic actions in persons sensitive to salicylate (Mohd et al., 2015).

Red pepper (Capsicum annuum)

Capsaicin is a hot alkaloid of red pepper and has been extensively studied for its biological effects, which are of great pharmacological importance. It has many effects but its potential clinical value for pain relief, cancer prevention and weigh loss is of great importance. Capsaicinoids have been shown to be potential capsaicin receptor agonists (TRPV1). Therefore, they could act in a receptor-dependent way, but also in a receptor-independent way. The involvement of neuropeptides, substance P, serotonin and somatostatin in the pharmacological activities of capsaicin was intensively investigated during the study of their action. It has been proven that topical application of capsaicin relieves pain in arthritis, postoperative neuralgia, diabetic neuropathy, etc. The anti-inflammatory and antioxidant properties of capsaicin have been established by numerous studies (Srinivasan, 2016). Long-term use of capsaicin reversibly depletes stores of substance P and possibly other neurotransmitters from sensitive nerve endings. This reduces or eliminates the transmission of painful stimulation from peripheral nerve fibres to higher centres. In clinical studies of patients with post-hepatic neuralgia, diabetic neuropathy or osteoarthritis, adjuvant topical capsaicin therapy achieved greater relief in most studies. Topical capsicin is not associated with serious systemic side effects, but many patients report burning and stinging, especially during the first week of use. Therefore, because of its effects, local capsaicin deserves consideration as adjunctive therapy in chronic pain conditions, including osteoarthritis, which is difficult to treat (Rains et al., 1995). There is also interest in the use of capsaicin in injections to treat conditions such as focal pain, arthritis and other musculoskeletal disorders. Recently, capsaicin injection has shown therapeutic efficacy in a patient with Morton's neuroma, a painful condition of the foot associated with compression of one of the digital nerves. Pain relief is associated with changes in tactile sensitivity. Although injection causes short-term pain, short systemic exposure and the potential to establish long-term analgesia without other sensory changes create an attractive clinical profile. Short-term and long-term effect result from functional and structural changes in nociceptive regions (Chung et al., 2016).

Turmeric (Curcuma longa)

Curcumin is a polyphenolic compound derived from turmeric. It has various pharmacological effects including anti-inflammatory, antioxidant, antiproliferative and antiangiogenic activity. Numerous studies have examined its effects. In a first phase clinical trial, curcumin was shown to be safe even at high doses of 12g/day in humans, with poor bioavailability. The main reason contributing to low plasma and tissue concentrations of curcumin are the consequences of poor absorption, rapid metabolism and rapid systemic elimination. To improve the bioavailability of curcumin, a number of approaches have been taken, from the use of piperine that interferes with glucuronidation, the use of liposomal curcumin, the production of curcumin nanoparticles, and the use of curcumin phospholipid complexes and the use of structural curcumin analogues (Anand et al., 2007). A study was conducted in which curcumin was derived from ordinary spicy turmeric and formulated into biodegradable nanoparticles with the aim of improving oral bioavailability. *In vivo* pharmacokinetics found that nanoparticles show at least a 9-fold increase in oral bioavailability compared to curcumin given with piperine as an adsorption enhancer indicating the potential of this method (Shaikh et al., 2009). However, despite low bioavailability the therapeutic efficacy of curcumin in various diseases including cancer, cardiovascular disease, diabetes, arthritis, neurological disease and Crohn's disease has been documented (Anand et al., 2007). Numerous clinical studies of curcumin supplementation on a variety of disease including osteoarthritis have been conducted in recent decades. The mechanism of acting of curcumin including modulation of the eicosanoid pathway toward the anti-inflammatory pathway and modulation of serum lipid levels was investigated, and minimal or no side effects were observed (Yung et al., 2019). In one study, the highly available form of curcumin in the all-natural matrix of turmeric was evaluated for its ability to improve the clinical symptoms of rheumatoid arthritis. A randomized, double-blind, placebo-controlled parallel study was conducted to evaluate comparative efficacy of two different doses of curcumin with that of placebo in patients with active rheumatoid arthritis. Twelve patients in each group received placebo, 250 or 500 mg of curcumin

product twice daily for 90 days. Patient responses were assessed using the American College of Rheumatology (ACR) responses, visual analogue scale (VAS), C-reactive protein (CRP), disease activity assessment (DAS28), erythrocyte sedimentation rate (ESR) and rheumatoid value factor (RF). Patients with rheumatoid arthritis who received low and high doses of curcumin reported statistically significant changes in clinical symptoms at the end of the study. These results were confirmed by significant changes in ESR, CRP and RF values in patients receiving the study product compared to initial values and placebo. The results suggest that curcumin in the turmeric matrix acts as an analgesic and anti-inflammatory agent for the treatment of rheumatoid arthritis (Amalraj et al., 2017).

Vitamin and mineral based dietary supplements

A functional immune system is essential for a healthy life. This is achieved by coordinated activation and interaction of different immune cells. Yet, activating the immune response is just as important as deactivating it when pathogens are out of the organism, otherwise host tissue damage can occur, where damage can reach life-threatening levels. Autoimmune diseases (AD) affect five to eight percent of the world's population and are the result of attacks by one's own immune cells on other tissues and organs. In recent years, the incidence has been steadily rising, reaching alarmingly high numbers especially for: type 1 diabetes mellitus, Crohn's disease, rheumatoid arthritis, Sjogren's syndrome and multiple sclerosis. It is important to concentrate on the importance of diet for balancing immune function (Wassels et al., 2020).

Rheumatoid arthritis as an autoimmune and inflammatory disease can cause joint damage. Among the risk factors, diet plays an important role as it can make it worse or reduce inflammation. Selenium is considered an essential trace element that is structural component of antioxidant enzymes, but its concentration can be affected by diet, medication and genetic polymorphism. Studies have shown that patients with rheumatoid arthritis have a deficit of nutrients from some groups, which is related to the parameters of disease activity. There has been shown to be a change in serum selenium levels in this population. Experimental studies examining the effects of new selenium nanoparticles in rheumatoid arthritis-induced models have shown promising results in restoring antioxidant enzyme levels. Glutathione peroxidase (GPx), which is an important protein for selenium and may have a modulating effects on inflammatory processes in rheumatoid arthritis, plays a special role (Turrubiates-Hernandez et al., 2020).

Zinc is a nutritionally essential mineral and plays a role in arthritis as an effector of the immune system, inflammation and metabolism. Patients with rheumatoid arthritis have decreased levels of zinc in their blood. It is unknown if this change is just manifestation of the acute phase of the inflammatory response or relates to altered zinc availability in tissues, and therefore requires zinc-related dietary changes. Zinc is a cofactor in over 3.000 human proteins and as a signal ion affects many pathways relevant to arthritis as a disease. How will the zinc affect the disease depends not only on zinc status, but also on many proteins that maintain cellular zinc homeostasis. The conclusion is that this metal ion in arthritis should be routinely monitored and that it has untapped potential for treatment (Frangos et al., 2020).

Vitamin D affects physiological systems that extend far beyond its established functions in calcium and bone homeostasis. Among them were the strong immunomodulatory effects of the active form of vitamin D, 1,25-dihydroxyvitamin D3 (1,25 (OH) 2D3) highlighted. The nuclear vitamin D receptor (VDR) for 1,25-(OH) 2D 3 is expressed by many cells within the immune system. Vitamin D deficiency has been associated with a variety of autoimmune disorders including rheumatoid arthritis (Harrison et al., 2020). The positive effects of vitamin D on the immune system include an increase in the microbicide capacity of monocytes/ macrophages and a decrease in inflammatory cytokines produced by lymphocytes. Despite some controversy, most research supports the idea that lower vitamin D levels correlate with more severe clinical manifestations in rheumatoid arthritis and other rheumatic diseases. Therefore, vitamin D supplementation is important to establish normal serum vitamin D levels. The effect of vitamin D is associated with proteoglycan (PG) which is a specific cartilage antigen (Ishikawa et al., 2017).

Chondroitin and glucosamine

Chondroitin sulphate is a sulphated glucosaminoglycan composed of alternating saccharide chains, more precisely from N-acetilgalactosamine and glucuronic acid. It is usually attached to proteins as part of proteoglycans. It is an important structural component of cartilage and allows it to withstand greater pressure (Baeurle et al., 2009). For the production of chondroitin sulphate (CS) the industry uses sources that originate from animal tissue, both terrestrial and aquatic animal

species. Chondroitin sulphate possesses a heterogeneous structure, and the physicochemical profile in different species and tissues is responsible for the different and specialized functions of these macromolecules (Volpi, 2019).

Glucosamine is an amino sugar in which the hydroxyl group of glucose is replaced by an amino group. It is an important part of the polysaccharides chitin and chitosan and is very hydrophilic. It represents an important compound required for the formation of cartilage cells and represents one of the elementary units of the cartilaginous matrix (Ma et al., 2019).

Chondroitin sulphate an glucosamine sulphate have beneficial effects on the metabolism of *in vitro* cell models derived from synovial joints: chondrocytes, synoviocytes and subchondral bone cells involved in osteoarthritis. They increase the synthesis of collagen and proteoglycans type I in human joint chondrocytes and are able to reduce the production of some anti-inflammatory mediators and proteases, reduce the process of cell death and improve the anabolic/catabolic balance of the extracellular cartilage matrix (ECM). The structure-altering effects of these compounds have been reported and analysed in recent meta-analysis. Results from the osteoarthritis of the knee show a small but significant narrowing of the joint space (Henrotin et al., 2014). Therefore, glucosamine sulfate and chondroitin sulfate are often used to prevent further joint degeneration in osteoarthritis.

Methylsulfonylmethane (MSM) is a compound that contains organic sulphur and has also been shown to slow the anatomical progression of joints in knee osteoarthritis. MSM is often combined with glucosamine and chondroitin sulphate. A study was conducted to compare the clinical outcome of glucosamine-chondroitin sulphate (GC), glucosamine-chondroitin sulphate-methylsulfonylmethane (GCM) and placebo among patients with knee osteoarthritis. 147 patients participated in this double-blind randomized controlled clinical study (Lubis et al., 2017). They were rated by the WOMAC score, which represents the arthritis index of the University of Western Ontario and MaMaster and is widely used in the evaluation of osteoarthritis of the hip and knee. It is formulated in the form of a questionnaire that is conducted independently and consists of 24 items that are divided into three subscales: pain, stiffness and physical function (ACOR, 2013). Patients were divided into three groups: GC (n=49), GCM (n=50) and placebo (n=48). The GC group received 1500 mg of glucosamine + 12000 mg of chondroitin sulphate + 500 mg of saccharumlactis. The GCM group received 1500 mg glucosamine sulphate + 1200 mg chondroitin sulphate + 500 mg MSM, while the third group received placebo. The drugs were given once a day for three consecutive months. After twelve weeks, significant differences were found between the three treated groups according to the WOMAC score (p=0.03) and according to the VAS score (p=0,004). The results showed that the combination of glucosamine-chondroitin sulfate-methylsulfonylmethane showed clinical benefit for patients with osteoarthritis of the knee compared with GC and placebo (Lubis et al., 2017).

Collagen

Articular cartilage is a connective tissue consisting of a specialized extracellular matrix (ECM) that predominantly dominates. Collagen and type II aggregate are the major ECM proteins in cartilage. The group of minor collagens includes collagen types IV, VI, IX, X, XI, XII and XIII. Although they make up only a small part of the mature matrix, smaller collagens play important structural roles in the mechanical properties, organization and shape of articular cartilage and fulfil certain biological functions. Progressive destruction of the cartilage includes the breakdown of matrix components including small collagen (Luo et al., 2017). Undenatured collagen type II (UC-II) is used as a dietary supplement and is obtained from chicken thoracic cartilage. A study was conducted to evaluate the effectiveness and tolerability of UC-II on knee arthritis pain and associated symptoms compared with placebo and glucosamine hydrochloride plus chondroitin sulphate. A randomizes study conducted with volunteers divided in three groups for 180 days. The results showed that in the group of volunteers who used UC-II there was a significant decrease in the total WOMAC score compared to placebo (p=0,002) and GC (p=0,04). Supplementation with UC-II also resulted in significant changes for all three WOMAC subscales: pain (p=0.0003 versus placebo, p=0,016 versus GC), stiffness (p=0,004 versus placebo, p=0,044 in relation to GC) and physical function (p=0,007 in relation to placebo). The study concluded that UC-II improved knee joint symptoms in subjects with osteoarthritis of the knee and was well-tolerated (Lugo et al., 2016).

Hyaluronic acid

Hyaluronic acid is polyanionic natural polymer that occurs as a linear polysaccharide composed of glucuronic acid and N-acetyl glucosamine that is repeated via a β-1,4 bond. It has a wide range of

applications due to its excellent physiochemical properties such as biodegradability, biocompatibility, non-toxicity and no immunogenicity. It serves as an excellent tool in the following biomedical applications: osteoarthritis surgery, ophthalmic surgery, plastic surgery, tissue engineering and drug delivery. It is a powerful antioxidant and one of the most famous properties is that it binds water to tissue (Sudha et al., 2014). It is synthesized by the bioactivity of hyaluronan synthase (HAS) which is said to have three isoforms (HAS 1, HAS 2 and HAS 3) in humans (Itano et al., 1999). Hyaluronic acid is widespread but is mainly localized in the extracellular matrix and body fluid, where it contributes to the high elasticity of fluid and the elasticity of connective tissue absorbing mechanical stress, for example between cartilage and cartilage surface (Neustadt et al., 2007). Regarding pain suppression, hyaluronic acid alleviates prostaglandin or bradykinin-induced pain in animal experiments (Gotoh et al., 1993). Hyaluronic acid binds to CD44 signalling receptor and mediated mobility receptor (RHAMM) molecules. Since CD44 is the primary receptor for hyaluronic acid and has been found to bind to other matrix components including collagen, chondroitin sulphate and osteopontin (Taylor et al., 2006). In the treatment of arthritis it can be administered in the form of injections where it is administered intraarticularly and in tablets form where it is administered orally. Intraarticular application of hyaluronic acid is widespread in the treatment of osteoarthritis (Simon et al., 2007). Hyaluronic acid injection provides transient pain relief but its mechanism of action has not yet been fully elucidated. According to a recent recommendation by the International Society for Osteoarthritis Research (OARSI) (Zhang et al., 2008) in the treatment of osteoarthritis of the hip and knee, the strength of the recommendation (SOR) for intraarticular hyaluronic acid is relatively low (64%), whereas in nonsteroidal anti-inflammatory drug (NSAID) for oral administration as an analgesic it is 92-93 %. The effect of hyaluronic acid in osteoarthritis is often attributed to its potential use in viscosity supplementation (Neustadt et al., 2007). A direct effect of hyaluronic acid against inflammation and cartilage degradation in osteoarthritis has been proposed. In addition to osteoarthritis, intraarticular injection of hyaluronic acid has also been used in patients with inflammatory arthritis such as rheumatoid arthritis (Matsuno et al., 1999).

Omega 3-fatty acids

Osteoarthritis and rheumatoid arthritis are characterized by abnormal lipid metabolism that manifests as an altered fatty acid profile of synovial fluid and tissue. The way in which dietary supplements can affect the symptoms of rheumatoid arthritis in particular is being investigated. In addition to classical eicosanoids, the potential role of polyunsaturated fatty acids has become the focus of more intensive research (Mustonen et al., 2021). Eicosaoentaenoic acid (EPA) and decosahexaenoic acid (DHA) are omega 3 (n-3) fatty acids found in fatty fish and various oils. These fatty acids can partially inhibit many aspects of inflammation, including leukocyte chemotaxis, adhesion molecule expression and leukocyte-endothelial interactions, production of eicosanoids such as prostaglandins and leukotrienes from n-6 fatty acid, arachidonic acid, production of inflammatory cytokines and reactivity of helper T lymphocytes 1. EPA induces eicosanoids, which often have lower biological potency than those produced from arachidonic acid, and EPA and DHA cause anti-inflammatory mediators that address inflammation, called resolvins, protecins and marexins. Animal experiments show the benefit of marine n-3 fatty acids in rheumatoid arthritis models (Calder, 2015). The Western diet is deficient in omega-3 fatty acids, but in contrast, it has excessive amounts of omega-6 fatty acids compared to the diet on which human beings evolved and on which their genetic patterns were determined. Excessive amounts of omega-6 polyunsaturated fatty acids (PUFAs) and the very high omega-6/omega-3 ratio found in today's Western diet promote the pathogenesis of many diseases including: cardiovascular diseases, cancer, inflammatory and autoimmune diseases, whereas increased omega-3 levels PUFA (lower omega-6/omega-3 ratio) has suppressive effects. A ratio of 2-3/1suppresses inflammation in patients with rheumatoid arthritis. A lower ratio of omega-6 and omega-3 fatty acids is more desirable to reduce the risk of many chronic diseases of high prevalence in Western societies as well as in developing countries (Simopoulos, 2008). Because n-3 PUFA and γ-linolenic acid (GLA) are well-known anti-inflammatory agents that can help treat inflammatory disorders, a study was performed in patients with rheumatoid arthritis. The method used was randomized, prospective study lasting 12 weeks. Sixty patients with active rheumatoid arthritis participated in the study. They are supplemented with fish oil (group I), fish oil with night primrose oil (group II) and without additives (group III). The results showed a score of disease activity 28, the number of painful joints and the result on a visually analogous scale were significantly reduced after supplementation in groups I and II (Veselinovic et al., 2017).

Polyphenols and flavonids

Polyphenols are compounds that have been extensively tested for their anti-inflammatory,

antioxidant and immunomodulatory properties in many chronic inflammatory conditions. Among the polyphenols: epigallocatechin gallate, carnosol, hydroxytyrosol, curcumin, resveratrol, kaempferol and genistein are the most studied in arthritis. The most important results of the study show that polyphenolic compounds are able to inhibit the expression and release numerous anti-inflammatory mediators and proteolytic enzymes, the activity of various transcription factors and the production of reactive oxygen species *in vitro*. Studies in animal models of rheumatoid arthritis, osteoarthritis and gout show results in terms of tissue damage reduction, restored cartilage homeostasis and reduced uric acid levels (Oliviero et al., 2018). Fruits such as pomegranate and berries represent a rich selection of various bioactive compounds in the diet, especially polyphenolic flavonoids that are associated with antioxidant, anti-inflammatory and analgesic effects. Recent research shows the protective role of fruits and their polyphenols in preclinical, clinical and epidemiological studies of osteoarthritis and rheumatoid arthritis. Fruits such as blueberries, raspberries, strawberries and pomegranate have shown promising results in reducing pain and inflammation in experimental models and clinical studies of arthritis in humans. There are also some evidence of a role for specific fruit polyphenols such as quertcetin and citrus flavonoids in alleviating the symptoms of rheumatoid arthritis (Basu et al., 2018). There is growing evidence that food polyphenols can show therapeutic efficacy in rheumatoid arthritis through their: antioxidant, anti-inflammatory, apopoptic and immunosuppressive effects and modulation tumour necrosis factor-α (TNF-α), interleukin (IL)-6, mitogen-activated protein kinase (MAPK). IL-1β and others (Behl et al., 2021).

Conclusion

Although medical treatment is still the first choice for people with arthritis, various herbal preparations and dietary supplements with the right choice of food could help primary medical therapy and reduce the number of symptoms and affect the progression of arthritis.

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