



# Nutraceuticals for Arthritis Management: Beyond Nutrition, Targeting Inflammation, and Immunity

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Article Info: Received: 23-01-2024 / Revised: 20-02-2024 / Accepted: 14-03-2024

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DOI: <https://doi.org/10.32553/jbpr.v13i1.1066>

Conflict of interest statement: No conflict of interest

## Abstract:

Nutraceuticals, bridging the gap between "food" and "pharmaceuticals," are gaining significant traction in modern healthcare due to their potential to address chronic diseases like arthritis. This shift towards preventative and holistic approaches emphasizes the power of nutrition in managing health. Nutraceuticals encompass a diverse range of bioactive compounds derived from natural sources – vitamins, minerals, plant extracts, proteins, and dietary supplements. Their appeal lies in their purported ability to offer health benefits beyond basic nutrition, including antioxidant, anti-inflammatory, and immunomodulatory properties. Rheumatoid arthritis (RA) presents a significant health concern in India, affecting an estimated 0.75% of adults – exceeding the global average of 0.46%. This prevalence might be linked to genetic similarities between North Indians and Caucasians. Notably, RA affects women more disproportionately. This review explores the potential of nutraceuticals in managing arthritis in India, focusing on their ability to combat inflammation and modulate the immune system, offering benefits beyond simple dietary intervention.

**Keywords:** *nutraceuticals, arthritis management, nutrition, targeting inflammation, immunity.*

## 1. INTRODUCTION

**1. A. Arthritis**, derived from the Greek word for "joint" and "inflammation," encompasses a spectrum of musculoskeletal disorders characterized by joint pain and dysfunction. These disorders can be acute or chronic, and their manifestations typically include pain, stiffness, limited mobility, and potential joint deformity. Due to the heterogeneity of arthritis, management strategies are individualized based on the specific type. Diagnosis relies primarily

on a thorough medical history and physical examination, often supplemented by laboratory investigations and imaging modalities when necessary [1-3].

### 1. B. Rheumatoid Arthritis

Rheumatoid Arthritis (RA) stands out as the predominant autoimmune disorder and the second most prevalent form of joint inflammation, succeeding osteoarthritis.

Characterized by an immune system response leading to persistent inflammation and degeneration within the synovial joints, RA involves a complex interplay of immune cells and molecules, resulting in chronic joint inflammation, cartilage erosion, and bone damage. This often leads to substantial disability and diminished quality of life for affected individuals (O'Dell JR. R et al; 2011). Research indicates that RA may result in disability, complications, and premature mortality (Ramos M, Tak P Lebre M, 2014). Uncontrolled active rheumatoid arthritis can lead to joint deterioration; disability, compromised quality of life, and cardiovascular comorbidities (Scott DL, Frederick WF, Huizinga TWJ 2010). Clinically distinguishing RA from osteoarthritis (OA), the affected sites in rheumatoid arthritis encompass the fundamental interphalangeal and metacarpophalangeal bones, while osteoarthritis predominantly affects the distal interphalangeal joint. Unlike RA, which impacts both sides of the body, OA typically affects only one side. Rheumatoid arthritis sufferers often experience prolonged morning stiffness lasting at least an hour, whereas patients with OA may endure morning stiffness that typically resolves within 20-30 minutes (McGonagle D et al; 2015). RA, a systemic connective tissue condition affecting joint cartilage, manifests in genetically susceptible individuals as an immunological allergic reaction triggered by environmental stimuli. Among these environmental factors, diet plays a significant role and may either exacerbate or alleviate RA symptoms. Despite evidence supporting the benefits of certain foods, such as omega-3 polyunsaturated fatty acid-rich seafood, and highlighting adverse health consequences of high-fat and high-sugar diets on RA occurrence, movement, and treatment response, adherence to a nutritious eating plan is limited among RA patients. Current understanding of nutrition in RA explores how dietary factors can either prevent or promote the development of rheumatoid arthritis and influence disease activity (Marta Skoczyńska, Jerzy Świerkot et al; 2018). Rehabilitation objectives for RA

primarily focus on reducing joint inflammation and discomfort, improving joint function, and preventing joint degeneration and deformity. Treatment modalities such as medications, weight-bearing physical activity, patient education, and rest are tailored to each patient's specific needs, considering factors such as disease progression, affected connective tissue, age, overall health, occupation, treatment adherence, and comprehension of the condition (Staheli LT et al; 1998).

## **2. Dietary elements of protein can cause rheumatoid arthritis:**

*Porphyromonas gingivalis* bacteria can create an enzyme that citrullinates amino acids, leading in the formation regarding antibodies against citrullinated proteins (ACPA) (Tsauda et al., 2015). ACPA from rheumatoid arthritis (RA) patients' the bloodstream and citrullinated proteins have been shown to cross-react with infectious agents (EBNA-1), microorganisms (*M.luteus*, *Mycobacterium gastri*, *Nocardia brasiliensis*), fungi (*Aspergillus fumigatus*, *Candida albicans*, *Cryptococcus neoformans*), and herbs (*Oryza sativa*, *Solanum lycopersicum*, *Glycine max*). Consumption of goods comprising these antigens in patients infected with *P. gingivalis* may cause ACPA synthesis, probably contributing to the appearance of rheumatoid arthritis through interactions with connective tissue antigens.

## **2. A.N-3 PUFAs can improve rheumatoid arthritis**

Arachidonic acid, omega-6 polyunsaturated fatty acids (PUFA), particularly the chemicals called prostaglandins it produces have been linked to discomfort during inflammation. While omega-6 PUFAs are known to cause inflammation, omega-3 polyunsaturated fatty acids have been demonstrated to have anti-inflammatory properties. Supplementing with n-3 polyunsaturated fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) can improve the omega-6 to omega-3 fatty acid ratio, reducing discomfort, inflammation, and progression of

the disease in people with rheumatoid arthritis (RA). In the research reviewed, discomfort levels were assessed by patients, physicians, or both. Out of the eighteen studies evaluated, ten

found a reduction in pain among patients who drank omega-3 PUFAs. The majority supported an everyday intake of n-3 PUFAs ranging from 3 to 6 grams (Abdulrazaq M et al; 2017).

**Table 1: A dietary factor affects the occurrence of rheumatoid arthritis (RA). Ref [28-41].**

Strategies that prevent rheumatoid arthritis	Factors encouraging rheumatoid arthritis
The AHEI (2010) assesses dietary habits aligned with healthy eating guidelines.	Obesity
N-3 PUFAs (in positive for serology individuals)	Drinks that contain fructose, such as sweetened beverages, carbonated beverages, fruit juice, and apple juice.
Mushrooms	Seeds extracted from plants contain lectins.
Citrus fruits, such as freshly squeezed orange juice.	Porphyromonas gingivitis infects pathogenic organisms (EBNA-1), bacteria (M. luteus, Mycobacterium gastri, Nocardia among other brasiliensis), parasites (fungi such as fumigatus being, a species of Candida albicans, the microorganism neoformans), and herbs (the plant Oryza sativa varieties Solanum lycopersicum, Glycine max).

### 3. Osteoarthritis

Osteoarthritis (OA) is a deterioration induced by inflammation illness damaging cartilage in joint surfaces, which now affects around fifty-eight million youngsters that is estimated to expand to 78.4 million by 2040(Hoot man J.M., et al; 2015). Globally, it stands as the primary cause of joint pain and functional impairment (Szychlinska M.A. et al; 2016). This ailment manifests with symptoms like pain, stiffness, and limited joint mobility. Over time, these symptoms can heighten the risk of obesity, diabetes, falls, and fractures (Aiello F.C., et al; 2017). Factors contributing to OA encompass both local biochemical elements, such as joint damage and physical activity levels, and general factors like gender, age, comorbidities such as obesity, and nutritional considerations (Fajardo M et al; 2008).Current treatment guidelines for

OA advocate for a multi-faceted approach involving three main strategies, which may be combined as needed. The first method comprises pharmaceutical therapies, such as moderate anti-inflammatory effects medicines (NSAIDs), opioids, and COX-2-specific medications. On the other hand traditional pharmaceutical treatments for OA serve primarily as palliative measures, alleviating symptoms without addressing the underlying cartilage degeneration. Additionally, these medications may pose potential side effects, particularly with long-term use, which can reduce patient compliance due to concerns about gastrointestinal issues, cardiovascular complications, and other adverse reactions (Sengupta et al; 2008). Considering the chronic nature of OA-related pain, which often leads to disability, the use of nutraceuticals presents an intriguing alternative for pain management.

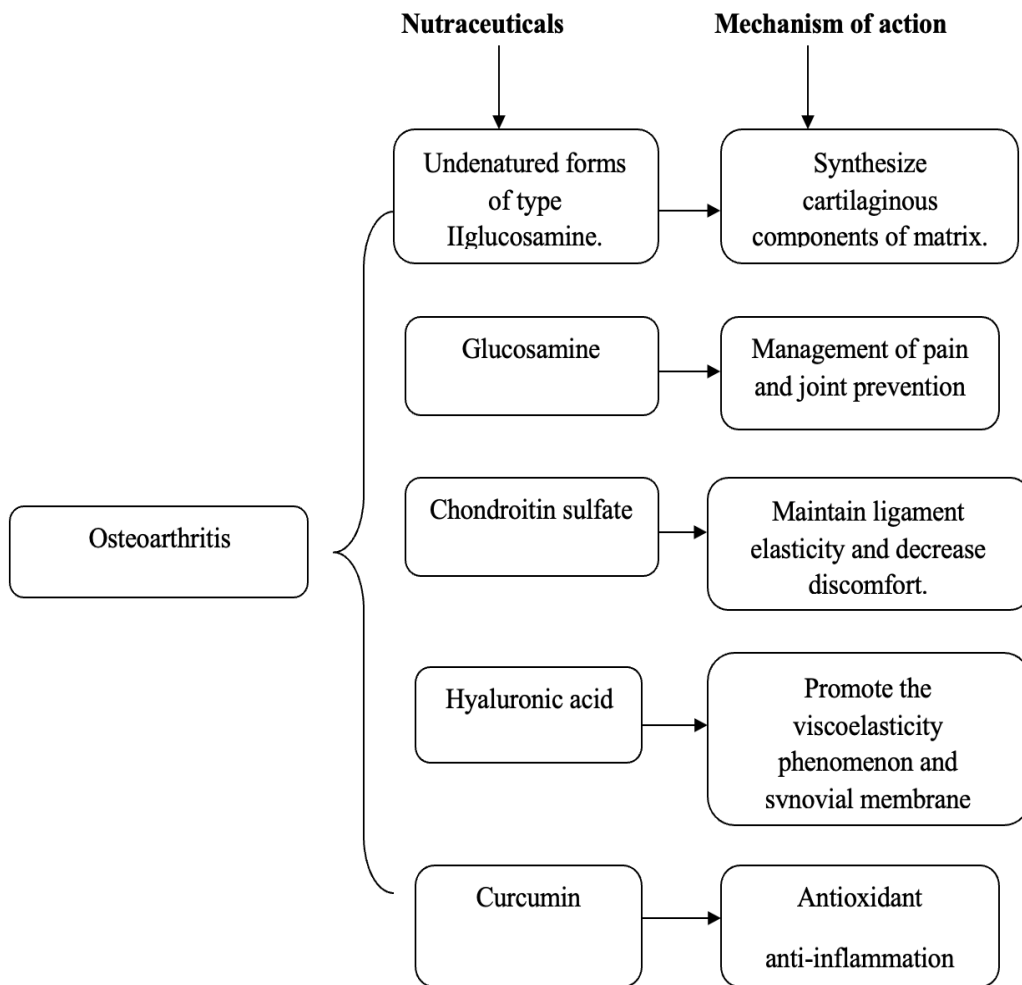
Common measures for determining the severity of OA pain revolve around the visual analogue scale (VAS) or mathematical scale of ratings (NRS), the discomfort component associated with the Western Ontario as well as McMaster University Higher education institutions Arthritis the index (WOMAC), and the knee-related component of the Knee Injury and Osteoarthritis Outcome Score (KOOS)(Neogi T et al; 2013).

**3. A. Physiological modification in osteoarthritis**

The key pathophysiological feature of osteoarthritis (OA) involves the deterioration of cartilage in the synovial joint, leading to

noticeable reductions in joint mobility detectable on plain radiographs. Attempts to cure this damage frequently result in more cartilage loss and joint disturbance, which causes the production of new bone and the manifestation of subchondral systemic sclerosis and osteophytes. With the emergence of increasingly powerful imaging tools, particularly magnetic resonance imaging (MRI), OA has grown increasingly universally believed to be a disorder that affects the entire cartilage structure, encompassing tendons and ligaments, the cartilage, synovial fluid (leading in synovitis), and the capsule that surrounds the joint (Loeser RF et al; 2012).

**3. B. Role of nutraceuticals in arthritis**



**Fig.1: Role of nutraceuticals in arthritis**

#### 4. Septic arthritis

Septic arthritis (SA) is a synovial fluid inflammation disease primarily affects young children. Infection can occur by way of hematogenous dissemination, direct injection, or osteomyelitis spread in the surrounding area. The assessment and classification of SA may be complex. It usually has an immediate onset, with the affected child becoming irritable, feverish, and unable for carrying weight on the involved extremity. Nevertheless, it might manifest in inconspicuous manners, which includes a newborn's difficulty to feed. From the beginning in the disease's course, screening laboratory tests may appear normal, and fluid from the synovial sac cultivating may be not successful regardless of there being evidence of an advanced infection. Treatment, including antibiotic duration and surgical method, varies and is supported by inadequate evidence. In affluent nations, the prevalence of SA among young people ranges from one to five per 100,000. Septic arthritis frequently occurs monoarticular, especially the cartilage in the knees and hips being the most commonly afflicted, but it can affect any joint. Bacteria induce joint inflammation. Bacteria account for more than 95% of infections. This infection is sporadic and may be caused by fungi or parasites. Septic arthritis presents a serious clinical condition characterized by rapid joint degeneration and significant morbidity and mortality rates. While relatively uncommon, it affects approximately 2-5 individuals per 100,000 in the general population annually. On the other hand, the incidence tends to be greater in certain categories, including children and adolescents (5.5-12 occurrences per 100,000 per year), patients with rheumatoid arthritis (28-38 instances per 100,000 per year), and those having prosthetic knee replacements (40-68

cases per 100,000 per year)(Kherani R, et al; 2007).

#### 5. Psoriatic arthritis

Psoriatic arthritis (pa) encompasses a multifaceted autoimmune condition that comprises autoimmune diseases such as nail autoimmune diseases such as peripheral joint disease, axial joint disease, enthesitis, and dactylitis(Ritchlin CT et al; 2017). Clinical presentations vary significantly among individuals. PsA can show as either oligoarticular joint involvement, often asymmetrically, or it may represent polyarticular disease affecting a minimum of five joints, generally overall a distribution that is symmetrical similar to rheumatoid arthritis (RA)(Gladman DD.et al; 2015). Arthritis mutilans, a severe form characterized by extensive joint damage and deformation, such as telescoping digits, affects approximately 5% of PsA cases (Haddad A, et al, 2015).

##### 5. A. Early identification of psoriatic arthritis

Inappropriate PsA identification may have been associated to decreased physical function(Tillet W et al; 2013). Haroon et al. discovered that simply having and a six-month patiently wait between the start of symptoms and the initial visit to the rheumatologist (consultation delay) contributed to a worse prognosis for individuals with PsA.

This patient group has a higher risk of coronary artery disease, insulin resistance, a disorder called metabolic syndrome, and depressive disorders, which is frequently related to the prolonged inflammatory condition caused by untreated Psoriatic Arthritis (PsA) (Kaine J et al; 2019). Furthermore, they may have more peripheral joint erosions, sacroiliitis, and worse scores on the Health Assessment Questionnaire (HAQ)(Haroon et al; 2015).

5. B. ROLE OF NUTRACEUTICALS IN MUSCLE CRAMPS

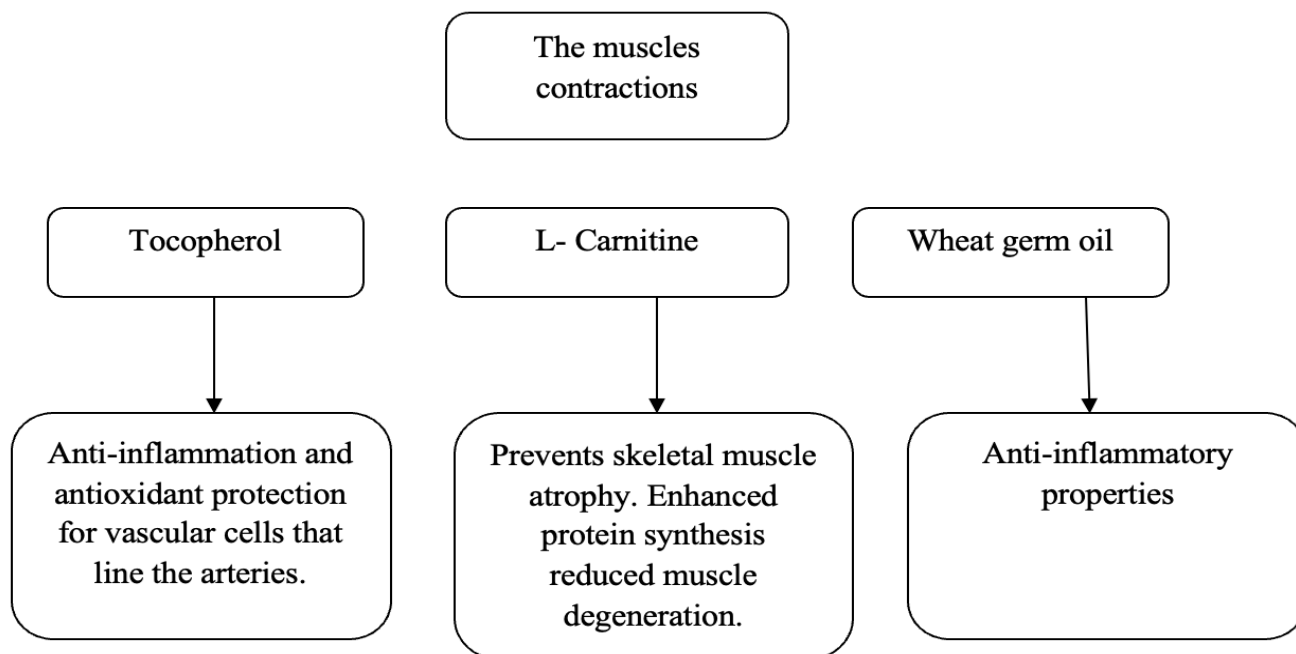
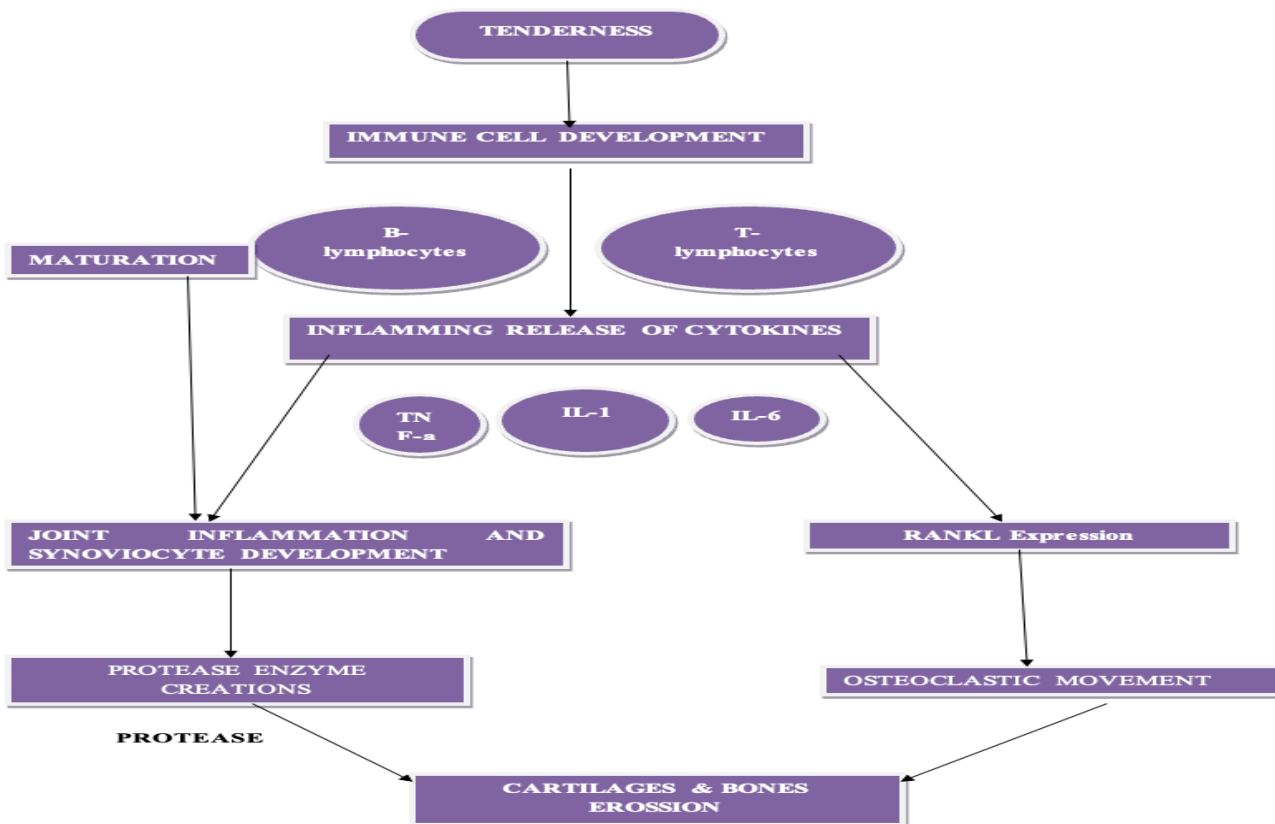


Fig.2: Role of nutraceuticals in muscle cramps

6. Etiology of arthritis

The causes of arthritis differ depending on the particular kind of arthritis. Key indicators of risk for osteoarthritis include advanced age, female gender, musculoskeletal traumas, and obesity. Mutations in chromosomes encoding collagen categories second, fourth, fifth, and sixth has been used as well identified. In contrast, rheumatoid arthritis (RA) is characterized by inflammatory systemic inflammation. It is caused by a mix of hereditary and environmental factors, such as smoking, which leads to immune system malfunction and consequent inflammation. In gout, joint inflammation occurs due to the accumulation of uric acid in the joints, resulting from hyperuricemia. While several genetic

variations may contribute to hyperuricemia, they account for less than 10% of gout cases. Most gout patients are considered under-excretory, indicating their inability to eliminate all the uric acid produced through either endogenous or exogenous purine metabolism. Septic arthritis, characterized by acute joint inflammation, is relatively uncommon in the population as a whole. People who are having additional risk factors such as immunodeficiency, aging, diabetes, transformation ligaments, inflammation of the joints, and intravenous (IV) medication misuse, stand an increased risk of developing this illness(Reginato AM et al; 2002).



**Fig.3: Etiology of arthritis**

**7. General treatment of arthritis**

The major goal of pharmacological treatment for autoimmune diseases such as rheumatoid arthritis and negative for serology spondyloarthropathies is to bring about early disease remission while avoiding radiological progression. Early treatment with disease-modifying antirheumatic medications (DMARDs) combining biological materials is far more successful than using steroid hormones and non-steroidal anti-inflammatory medications individually (NSAIDs) (Singh JA et al; 2014). Anti-inflammatory medications can be utilized to reduce inflammation during active disease periods. Regular monitoring of symptoms is essential, and adjustments to medication dosage are made as needed, even after symptoms have improved. Corticosteroids may be necessary to manage severe disease flare-ups (Kirwan JR et al; 2007). The primary goal in managing osteoarthritis is to alleviate pain and enhance joint function. Effective care

often combines alternatives to medication (conservative) and medication-based treatments. Nonpharmacological therapies include focused physical activity, physical treatment, assistive equipment, acupuncture, and weight control. Osteoarthritis can be treated with both mechanical and oral medicines. No steroidal anti-inflammatory drugs (NSAIDs), cutaneous a compound called caps or duloxetine as are all regularly used pharmaceuticals. Corticosteroids may be administered directly into the afflicted joint. Initially, topical NSAIDs, capsaicin, and other topical treatments are often recommended. However, if symptoms persist or if the condition is more systemic, oral NSAIDs may be prescribed. Duloxetine can be advantageous for people who have medical contraindications to using NSAIDs, particularly those with arthritis of the knee. When non-medicinal and medication-based therapies fail, intra-articular

injections of corticosteroid may offer comfort (McAlindon TE, et al; 2014). Acute arthritis caused by gout can be excruciatingly painful. Anti-inflammatory drugs are essential for alleviating symptoms and deserve to be used as soon as possible, ideally throughout the first 24 hours of gout over time flare. These prescription medications include ingestion of corticosteroids, NSAIDs such indomethacin or high-dose naproxen, and colchicine. Steroids administered intraarticular may be beneficial for people with only a few damaged joints. When oral medication is not an option, corticosteroids can be delivered intramuscularly or intravenously. Uric acid-lowering medicines should not be used to treat acute flares, however they are indicated for those who have repeated fireworks, chronic illnesses renal illness, kidney stones, or tophi (Neogi T. 2011).

**8. Nutraceuticals**

The term "nutraceuticals" was coined in 1989 by combining both the terms "nutrition," which refers to the science of food and its impact on the body, and "pharmaceutical," which refers to chemicals used for medicinal purposes. Nutraceuticals are defined by Health Canada as food-derived products that have been separated or refined, sold in medical forms, and

demonstrated to have a preventive impact against chronic diseases (Health Canada, 2002). However, this definition excludes the use of these substances as potential treatments for illnesses. Despite ongoing debates regarding the quality of scientific evidence, often misinterpreted by the media and exaggerated by corporations marketing these products, there is undoubtedly a role for "biologically active molecules with demonstrated physiological benefits" (as defined by Health Canada) in disease therapeutics. Medical research and legislation must keep pace with consumer demand for these compounds. Recent surveys have indicated that nutraceuticals are primarily used for "improving" or "maintaining" health (Bailey R et al; 2013). These compounds are popular, with 70-75% of the population consuming them, driven by factors such as concerns about the declining quality of processed foods, increasing health consciousness among consumers, the thriving global supplement industry, or a combination of these factors. Additionally, a significant issue arises from the fact that up to 69% of prescription drug users fail to disclose their use of dietary supplements to their healthcare providers (Gardiner P et al; 2006).

**TABLE 2. THE BELOW PROVIDES A SUMMARY OF THE NUTRACEUTICALS DISCUSSED AND THEIR PROPOSED MECHANISM OF ACTION**

Nutraceuticals	Tested everyday dosages	Impact of OA and related behaviors	References
Collagen	4000-10000 mg	Pain levels on the Visual Analogue Scale (VAS) were reduced, while WOMAC scores for discomfort, restricted functioning, and condition as a whole improved.	Garcia-Cornado J.M et al; 2019
Glucosamine	500-1500 mg	Reduced VAS pain, WOMAC reduced Analgesic and NSAIDs usage	Waly N.E. et al; 2017
Hyaluronic acid	80-200 mg	Reduced VAS pain, WOMAC Therigidity of the function and total	Altman RD et al; 2015
Vitamin C	500-2000 mg	Reduced VAS pain	Carr A.C. et al; 2017



Anthocyanin produced the juice of pomegranates	300-600 mg	Reduced pain levels as evaluated by the Visual Analogue Scale (VAS) and WOMAC pain scores.	Ghoochani N et al;2016
Capsaicin, derived with chili peppers	10 mg	Decreased VAS discomfort WOMAC Inflammation	Rondanelli M.et al;2016
Avocado /Soybean	300 mg	Reduced VAS pain WOMAC pain reduced	Appelboom T et al;2001
Acetyl-keto-β-boswellic acid (AKBA)	150-250 mg	Reduced VAS pain, WOMAC pain	Belcaro G et al; 2014
Omega -3 (EPA and DHA)	500-4500 mg (EPA+DHA)	Reduced WOMAC ratings for pain, stiffness, and function, decreased usage of analgesics and NSAIDs, and decreased symptoms of osteoarthritis, such as morning stiffness and hip and knee discomfort.	Jacquet A et al;2009
Gingerols (from ginger)	250-400 mg ginger (5%gingerols)	Reduced VAS pain WOMAC pain	Altman R.D et al;2001

**Conclusion**

Nutraceuticals, rich in natural bioactive compounds, are emerging as a potential treatment for arthritic symptoms. These compounds have anti-inflammatory, antioxidant, and cartilage-protective properties, which could deter arthritis progression and promote joint health. Nutraceuticals offer a more comprehensive approach, addressing the underlying causes of arthritis and promoting long-term joint well-being. Research shows the efficacy and safety of various nutraceuticals in mitigating arthritis, making them attractive for those seeking natural and sustainable approaches. Nutraceuticals offer a diverse range of options, including glucosamine, chondroitin sulfate, omega-3 fatty acids, and herbal extracts. Further research should focus on elucidating molecular mechanisms, exploring synergistic effects, identifying patient-specific factors, modifying disease course, and conducting long-

term clinical trials to evaluate the long-term safety and efficacy of nutraceuticals in arthritis management.

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