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The Role of VARVIMAX™ In the Treatment of Chronic Inflammation and Pain in Arthritis and Fibromyalgia

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

Background: Arthritis and fibromyalgia are chronic inflammatory conditions that cause significant pain and discomfort in affected individuals. Current treatments, such as nonsteroidal anti-inflammatory drugs (NSAIDs), are associated with adverse effects and do not always provide adequate relief. Therefore, there is a need for safe and effective treatments for chronic inflammation and pain in arthritis and fibromyalgia.
Review of the Literature: This review aims to evaluate the safety and efficacy of VARVIMAX™, a dietary supplement derived from a plant extract, for managing chronic pain in arthritis and fibromyalgia. According to the literature, the prevalence of fibromyalgia and arthritis is still high and even these two conditions occur together. VARVIMAX™ is a dietary supplement derived from a plant extract. VARVIMAX™ contains high levels of anthocyanins, such as Astaxanthins have been shown to possess anti-inflammatory and antioxidant properties. The formulation includes amino acids and flavonoids such as choline L-bitartrate, GABA, L-arginine, black pepper (piperine), docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), trans-resveratrol 98% (polygonum cuspidatum extract), which all have anti-inflammatory effects and play a significant role in pain management. Studies have shown that these ingredients have been effective in reducing pain, and

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inflammation, and improving joint function in patients with arthritis, fibromyalgia, and other inflammatory conditions. The most common side effects reported were gastrointestinal symptoms, such as nausea and diarrhea.

Conclusion: VARVIMAX™, a dietary supplement derived from a plant extract Ephedra, shows promise as a safe and effective treatment for chronic pain in arthritis and fibromyalgia. It is composed of several anthocyanins, amino acids, and flavonoids that impart it its characteristic anti-inflammatory and antioxidant properties. This results in reducing pain and inflammation, and improving joint function. Further research is needed to establish its long-term safety and efficacy in a wider range of inflammatory conditions.

Keywords: VARVIMAX™; medical food; chronic pain; anti-inflammatory; safety; efficacy.

1. INTRODUCTION

Chronic suffering is not just a crucial manifestation of rheumatic maladies but instead has been identified as "an illness in itself" with wide-ranging biopsychosocial implications [1]. Arthritis-related discomfort involves a variety of mechanisms, including inflammation of the articular and periarticular structures, with both peripheral and central mechanisms being implicated [2]. As the disease progresses, pain may stem from structural alterations within the joint [3].

The most widespread type of arthritis is osteoarthritis which is non-inflammatory arthritis [4]. Inflammatory arthritis may also occur in several contexts, with autoimmune processes such as “ankylosing spondylitis”, “psoriatic arthritis”, and rheumatoid arthritis. and so, on causing inflammation. Inflammation can also be induced by crystal deposition, as in pseudo gout, gout, and basic calcium phosphate disease, or by infections such as “lyme’s arthritis” and “septic arthritis” [4].

Likewise arthritis, Fibromyalgia is a complex disorder that induces an array of diverse symptoms, though the most common manifestations include muscle aches, tenderness, and fatigue [5]. Studies have consistently shown a higher prevalence of fibromyalgia in individuals afflicted with inflammatory conditions like ankylosing spondylitis, psoriatic arthritis, and rheumatoid arthritisin comparison with the general population [6,7]. This is perhaps due to the theory that protracted chronic pain can sensitize the neurons of the human body, resulting in the likelihood of them overreacting to external stimuli [8]. While traditional treatments such as nonsteroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs (DMARDs) are often used, they may come with unwanted side effects or may not be effective for all patients [9]. As a result, there's an increased interest in alternative therapies for managing chronic inflammation and pain.

One such medical product is VARVIMAX™, a natural supplement containing a combination of herbs and natural ingredients believed to have anti-inflammatory and analgesic properties. The natural ingredients in VARVIMAX™, such as Astaxanthin, Curcumin, Panasang Ginyang, and Matcha green tea powder have been traditionally used in different parts of the world for their medicinal properties, and scientific studies have demonstrated their anti-inflammatory and analgesic effects. Earlier research has shown that Ast can decrease the expression of MMP induced by IL-1β in chondrocytes and improve cartilage loss in osteoarthritis experiments [10].

Similarly, curcumin has been shown to be very effective in decreasing pain associated with osteoarthritis and fibromyalgia. A study proposed that at a concentration of 50 μM, curcumin was found to prevent the activation and movement of NF-κB triggered by IL-1β, which led to the expression of pro-inflammatory genes COX-2 and VEGF that are induced by NF-κB [11]. Additionally, research has shown that EGCG, found in green tea, may have protective effects on bones and cartilage by reducing the production of molecules in the immune system that can cause inflammation and joint pain [12].

Drinking green tea has also been found beneficial for managing fibromyalgia pain, as it positively impacts serotonin and GABA levels in the body. A randomized controlled trial showed that P. ginseng was found to decrease the number of tender points and enhance the quality of life of patients, as measured by the Fibromyalgia Impact Questionnaire after administration for 12 weeks [13]. On the basis of these studies, it can be assumed that

VARVIMAX™ may be a promising natural alternative for managing chronic inflammation and pain in individuals with arthritis and fibromyalgia.

The purpose of this review article is to investigate the efficacy of VARVIMAX™ as a treatment option for chronic inflammation and pain in individuals with arthritis and fibromyalgia. The review will examine the current scientific literature related to VARVIMAX™ and its potential benefits as a natural alternative to traditional treatments.

2. LITERATURE REVIEW

2.1 Prevalence of Arthritis and Fibromyalgia

Fibromyalgia is more prevalent in women than in men, with a prevalence rate of 6.4% in the United States (7.7% in women and 4.9% in men) [14]. Studies conducted in Europe and South America have reported prevalence rates ranging from 3.3% to 8.3% [15]. The prevalence of fibromyalgia tends to increase with age, and between the ages of 20 to 55 years, fibromyalgia is the leading cause of generalized musculoskeletal pain in women [15]. Adolescents also experience a similar prevalence rate to adults in many studies. In tertiary care pain clinics, more than 40% of referred patients meet the criteria for fibromyalgia [7]. The risk of developing fibromyalgia is higher in individuals with existing rheumatic diseases.

Regarding arthritis, more than one-third of the American population has arthritis detected through imaging, and this number is expected to rise as the average population age increases [16]. Osteoarthritis is the most prevalent type of arthritis, with knee osteoarthritis affecting 19% to 30% of adults over the age of 45, while hand and hip osteoarthritis affects 27% each [17]. It is estimated that 40% of men and 47% of women will develop osteoarthritis in their lifetime, with the risk increasing to 60% for those with a body mass index over 30 [18].

Gout is the most common inflammatory arthritis in the United States, impacting over 8 million individuals with a prevalence of 3.9% [19]. Among individuals aged 60 and above, the prevalence of gout exceeds 9% [20]. The incidence of gout is over 45 cases per 100,000 population, and both the incidence and prevalence of gout have significantly increased over the past few decades [21]. Pseudogout, another form of arthritis, affects approximately 4% to 7% of the adult population, with more than half of the patients experiencing knee arthritis [22].

2.2 Current Treatment Approaches for Arthritis and Fibromyalgia

The management of osteoarthritic joints focuses on reducing pain and improving function. Optimal care usually involves a combination of non-pharmacological and pharmacological treatments. According to the research, non-pharmacological approaches include targeted exercises, physical therapy, bracing, acupuncture, and weight reduction. Pharmacological management involves the use of topical and oral medications [23].

Frequently utilized medications for osteoarthritis include oral and topical non-steroidal anti-inflammatory drugs (NSAIDs), topical capsaicin, and duloxetine [23]. In most cases, first-line therapy consists of topical NSAIDs, capsaicin, and other ointments. If these measures do not provide relief or if the disease is more widespread, oral NSAIDs may be initiated [23].

In research, Duloxetine has shown benefits, particularly in knee osteoarthritis, especially for patients who cannot use NSAIDs due to medical contraindications. In cases where non-pharmacological and pharmacological treatments prove ineffective, intra-articular corticosteroid injections may offer symptom relief. It is important to avoid the use of opioids [24].

For fibromyalgia, medications are often prescribed to alleviate symptoms. Antidepressants, particularly selective serotonin reuptake inhibitors, help manage pain and improve sleep quality. Anticonvulsant medications like pregabalin can also reduce nerve-related pain. Muscle relaxants, such as cyclobenzaprine, are used to address muscle spasms [25]. Besides pharma-logical interventions, non-pharma logical treatment options such as CBT and physical therapy have also been found to be effective in treating fibromyalgia symptoms [25].

2.3 Introduction to VARVIMAX™ as a Potential Treatment

Varvimax™ offers a unique composition of compounds, including essential amino acids and

flavonoids, which are not typically obtained through a regular diet. These components provide distinct benefits for individuals seeking to address chronic pain, fatigue, or inflammatory conditions. Flavonoids, found naturally in various sources such as fruits, vegetables, cocoa, red wine, and green tea, possess remarkable anti-inflammatory properties. These organic molecules have the capacity to reduce inflammation within the body, contributing to improved overall well-being [26]. Meanwhile, essential amino acids like arginine and tryptophan play a significant role in neurotransmission, facilitating the transmission of information between cells [27]. As essential building blocks for neurotransmitters, these amino acids have a vital function in regulating pain and inflammation in the body. Individuals experiencing chronic pain, fatigue, or inflammatory conditions may be deficient in these essential amino acids. By addressing these deficiencies through supplementation with varvimax™, individuals have the potential to restore balance and support their body's natural mechanisms for pain regulation, inflammation control, and overall health. Varvimax™ stands as an exceptional dietary supplement, harnessing the power of essential amino acids and flavonoids to offer a promising solution for those seeking relief from chronic pain, fatigue, or inflammatory conditions.

2.4 Review of Different Ingredients Found in VARVIMAX™

2.4.1 Choline L- Bitartrate

Choline L- Bitartrate is the amino acid that synthesizes acetylcholine and acts as Anti Nociceptive. There are no direct studies that have examined the role of Choline L- Bitartrate in reducing the symptoms of fibromyalgia and arthritis. However, different research has shown that they are effective in reducing pain and inflammation in different inflammatory conditions. For example, research has shown that choline selectively acts as an agonist of “alpha 7-type nicotinic acetylcholine receptors” expressed in “neuronal” and “non-neuronal cells” responsible for transporting pain signals. Choline bitartrate leads to a cascade of reactions causing anti-inflammatory effects. A study showed that when these are used in postoperative patients, choline decreases the symptoms of inflammatory hyperalgesia [19]. Another study demonstrated that administering choline can significantly reduce the intensity of mechanical hyperalgesia. Moreover, choline has anti-inflammatory properties that can also alleviate hyperalgesia even when treatment is initiated 1-2 days after Complete Freund's adjuvant induction [28]. This is particularly relevant from a clinical perspective as it indicates that choline may be a viable treatment option for patients who present with hyperalgesia after the onset of inflammation. Recent research has also explored the role of choline in reducing hyperalgesia in other contexts. For instance, studies have shown that activating α7nAChRs with choline can reduce hyperalgesia in osteoarthritis induced by monoiodoacetic acid injection in the rat knee joints [29]. This suggests that choline may have wider applications in treating hyperalgesia in other inflammatory conditions. In addition, α7nAChR-selective agonists have also been found to potentially reverse CFA-induced reductions in paw withdrawal thresholds through a central mechanism [30]. This highlights the importance of the α7nAChR pathway in reducing hyperalgesia. Interestingly, research has also demonstrated that mice lacking α7nAChRs are more susceptible to hyperalgesia and CFA-induced allodynia.

2.4.2 GABA

GABA, an inhibitory neurotransmitter in the central nervous system, plays a crucial role in reducing the hyperactivity of nerve cells. Although it cannot provide a cure for arthritis or fibromyalgia, it has the potential to alleviate the symptoms associated with these conditions, leading to improvements in overall well-being. By helping to regulate nerve cell activity, GABA offers the possibility of symptom relief and enhanced management of arthritis and fibromyalgia.Studies indicated thatin arthritis, GABA reduces the transmission of the pain signals received by the brain [31]. It helps to reduce the severity of the pain signals and reduces pain and inflammation by modulating the activity of nerve fibers. In fibromyalgia, GABA may play a role in reducing the sensitivity of the nervous system to pain, thereby reducing the severity of pain experienced by individuals with this condition. One study found that GABA levels were significantly reduced in the spinal fluid of patients with fibromyalgia, suggesting a potential role for GABA in the development of this condition. Other studies have suggested that GABA may be involved in the regulation of immune responses, which could also be relevant to the pathophysiology of arthritis. However, it is important to note that GABA supplementation or

modulation should only be done under the guidance of a healthcare professional, as it can have potential side effects and interact with other medications.

2.4.3 L-Arginine

L-Argininеis an amino acid that plays a substantial role in the production of Nitric oxide, which is used to regulate the immune system and dilation. Several studies have shown that L-Arginine resulted in significant improvements in disease activities and reduced the inflammatory markers in the blood. A study aimed to investigate the effects of L-arginine supplementation in murine arthritis models and its metabolic action during osteoclast differentiation in the presence of inflammation [32]. Three arthritis models were used and analyzed with microCT and histomorphometry analyses to measure bone erosion and osteoclast numbers. In vitro osteoclastogenesis was performed with L-arginine and TNFa, and TRAP staining, pit formation assay, and Polymerase chain reaction analysis were conducted. Results show that L-arginine supplementation reduced arthritis severity, bone erosion, and osteoclast numbers. L-arginine inhibited osteoclastogenesis by altering the RANKL/RANK/Traf6 pathway and promoting mitochondria-driven oxidative phosphorylation. These findings suggest that L-arginine could potentially ameliorate bone erosion in RA and reduce joint inflammation and destruction through its immunometabolism action.

Regarding fibromyalgia, in 2015, a study suggested that L-Arginine could potentially decrease pain and depression in individuals with fibromyalgia. During the study, some participants were administered 1500 mg of ALCAR (L-Arginine) daily for a period of 12 weeks, while others were given an antidepressant, duloxetine (Cymbalta) [32]. The results showed that both groups experienced an improvement in their symptoms; however, the researchers stated that further studies are necessary to confirm these findings.

2.4.4 Black Pepper (Piperine)

The role of black pepper in relieving pain and inflammation associated with fibromyalgia and arthritis has also been investigated in a few studies. For example, the researchevaluated the impact of piperine on human OA chondrocytes that had been pre-treated with piperine and analyzed its activity on different inflammatory biomarkers. The researchers especially measured the production of prostaglandins (PGE2)and NO nitric oxide, as well as the gene expression and protein production of MMP-3, MMP-13, iNOS, and COX-2 [33]. The results of the study showed that piperine had a significant impact on reducing the production of NO and PGE2 induced by IL-1β. Piperine was also found to inhibit the expression of genes and proteins related to COX-2,iNOS, MMP-13, and MMP-3. Moreover, piperine was observed to prevent the activation of “NF-κB” induced by “IL-1β” by suppressing the degradation of its inhibitory protein IκBα in the cytoplasm. These findings suggest that piperine could potentially be used as a treatment for osteoarthritis due to its anti-inflammatory properties in human chondrocytes affected by osteoarthritis.

There is currently no research available on the effectiveness of Bioperine alone for the treatment of fibromyalgia. However, the findings of one research suggested that short-term supplementation of a combination of curcuminoids and piperine can significantly improve the inflammatory and oxidative status of patients with MS [34].

2.4.5 Docosahexaenoic Acid (DHA)

Docosahexaenoic Acid (DHA) is an “omega-3 fatty acid” that can reduce the severity of Arthritis symptoms in rats with “collagen-induced arthritis”. That’s becauseit has anti-inflammatory effects that help to reduce joint damage and inflammation [9]. Researchdetermined whether docosahexaenoic acid (DHA), which is an omega-3 fatty acid commonly found in the central nervous system, could prevent neuroinflammation and reduce pain in the spinal cord of mice following the injection of carrageenan [35]. The researchers discovered that when DHA was injected before carrageenan, it decreased hypersensitivity to pain for over six hours, and when it was injected after carrageenan, it reversed the symptoms of mechanical allodynia and heat hyperalgesia. Treatment via DHA also decreased the microglia activation, the “phosphorylation of p38 mitogen-activated protein kinase” (MAPK), and the formation of “pro-inflammatory cytokines” in the spinal cord. Additionally, when cultured microglial cells were exposed to DHA, it reduced the phosphorylation of p38 and the production of proinflammatory cytokines and chemokines induced by lipopolysaccharide (LPS) in a “dose-

dependent manner". These findings suggest that DHA has an "antinociceptive effect" on "inflammatory pain" by inhibiting p38 MAPK activation and suppressing microglia-mediated inflammatory responses. Currently, there is no research on its efficacy in fibromyalgia patients.

2.4.6 Eicosapentaenoic Acid (EPA)

"Eicosapentaenoic acid" is an "omega-3 fatty acid" found in oily fish, for example, salmon and mackerel. EPA has been shown to have anti-inflammatory effects, which may be beneficial for managing arthritis. Several studies have investigated the potential benefits of EPA for arthritis, including RA and OA. One study found that supplementing with EPA reduced disease activity and improved joint tenderness and swelling in patients with RA. The study also found that EPA improved symptoms of depression in these patients. Another study published in the Annals of Rheumatic Diseases found that supplementation with docosahexaenoic acid, omega three fatty acid EPA omega-3 fatty acid, reduced pain and stiffness in patients with OA [9] However, there is no research on the direct use of this ingredient in fibromyalgia.

2.4.7 Trans-Resveratrol98% (polygonum cuspidatum extract)

Trans-resveratrol is a naturally occurring substance that can be found in a variety of plants, including the roots of the knotweed Polygonum cuspidatum. Trans-resveratrol may be useful in treating the symptoms of arthritis, according to some research. In a 2017 study that appeared in the journal Nutrients, trans-resveratrol supplementation decreased inflammation and enhanced joint function in arthritic rats. Another 2018 study indicated that trans-resveratrol supplementation decreased pain and stiffness in human volunteers with knee osteoarthritis. This study was also published in the Journal of Medicinal Food. The possible anti-inflammatory and antioxidant properties of trans-resveratrol in the setting of arthritis were covered in a review paper that appeared in the year 2020 issue of the journal Molecules. Trans-resveratrol may lessen inflammation by preventing the synthesis of inflammatory cytokines and enzymes, and it may also shield joint tissues from oxidative damage, according to the authors. It's crucial to note that although some studies indicate that trans-resveratrol may have potential advantages in the treatment of arthritis, more researchers are needed to determine the complete scope of these advantages and the most effective ways to take advantage of them. The source and processing of the Polygonum cuspidatum extract utilized may also have an impact on the supplement's quality and efficacy [13]. However, there is no research on the direct use of this ingredient in fibromyalgia.

2.4.8 Matcha-Green Powder

Matcha-Green Powderis rich in Antioxidants and reduces pain and stiffness. It has a high content of Polyphenols which reduce joint damage and inflammation in a mouse model of RA [10]. In a recent study, researchers investigated the impact of Matcha green powder and supervised exercise on bone metabolism and disease activity markers in patients with rheumatoid arthritis. The results showed that patients who received treatment with Matcha green tea powder alone or in combination with "infliximab" or exercise experienced a significant improvement in disease activity indicators such as tender joint, erythrocyte sedimentation rate, and C-reactive protein. Additionally, patients who received green powder treatment exhibited an increase in serum levels of bone resorption markers. When compared to infliximab or exercise alone, the combination of exercise and green powder resulted in greater clinical improvement in disease activity, potentially due to the higher antioxidant activity of green tea. Overall, the study suggests that green tea and exercise may offer promising treatment options for patients with rheumatoid arthritis. The study concluded that both exercise and green tea interventions could be useful as non-drug modulators for rheumatoid arthritis disorders. No direct study exists about the role of Matcha green powder in fibromyalgia.

2.4.9 L-Glutamine

L-glutamine is an amino acid that is naturally found in the body and is considered a not essential amino acid. It plays a vital role in the body's metabolism. In some cases, L-glutamine may be used as a medical food supplement to help reduce pain. Apart from being a pain reliever, it also helps in building a stronger immune system and aiding the tissue renewal processes along with the enhanced absorption of nutrients. It is also involved in the production of neurotransmitters, which can affect the pathways of pain perception [36]. Studies have suggested that L-glutamine supplementation may help to

reduce pain associated with conditions such as inflammatory bowel disease, chemotherapy-induced neuropathy, and irritable bowel syndrome [37]. This may be due to its ability to support tissue repair and reduce inflammation, as well as its potential role in modulating neurotransmitter levels. L-glutamine may also help to reduce muscle soreness and fatigue after exercise. This is because L-glutamine is involved in the production of energy in muscle cells, and may help to prevent the breakdown of muscle tissue during intense exercise. While L-glutamine may have potential therapeutic effects in reducing pain, it should only be used under the strict supervision of a pharmacist or doctor to avoid any toxic effects. Additionally, no direct study of its efficacy in arthritis and fibromyalgia exists.

2.4.10 L-Serine

A study published in the Journal of Rheumatology in 2014 investigated the effects of L-Serine on joint pain and inflammation which proved that it is beneficial to reduce chronic pain and inflammation [38]. Another research investigated the L-serine-O-sulfate in reducing nociceptive levels in rat arthritic pain. N-methyl-D-aspartic acid receptor (NMDAr) activation requires the presence of D-serine, which is synthesized from L-serine by a pyridoxal 5′-phosphate-dependent serine racemase (SR). The study found that LSOS decreased wind-up activity in normal and monoarthritis rats, indicating that inhibiting SR reduces D-serine levels and subsequently decreases NMDAr activity, this could potentially aid in decreasing the occurrence and persistence of chronic pain. This is the first evidence presented for the potential of SR inhibitors to lower D-serine levels and reduce chronic pain *In-vivo*.

Serotonin, a neurotransmitter that regulates mood, sleep, and memory, depends on tryptophan, an essential amino acid, for its production. However, the body can also produce tryptophan from L-serine, an amino acid found in some foods. By increasing L-serine consumption, it is possible to boost tryptophan synthesis, which may lead to increased serotonin production, potentially improving mood, sleep, and memory. Recent studies suggest that this may also help manage symptoms of fibromyalgia [39].

2.4.11 Curcumin

Curcumin is a compound that is found in turmeric. It has been famous for its use as an antioxidant and anti-inflammatory agent. Curcumin reduces arthritis symptoms in multiple ways. Firstly, curcumin has antioxidant properties that neutralize free radicals in the body, which can cause inflammation and lead to pain [40]. It is believed that curcuminoids, found in turmeric, can be included in a diet to reduce the risk of disease and its effects. Secondly, Curcumin has the potential to inhibit the immune system's production of “tumor necrosis factor”, a chemical that causes inflammation associated with different forms of arthritis [41]. Thirdly, curcumin has been found to have the chemical properties of a COX inhibitor, which can provide modest pain relief [42]. However, while curcumin's COX-inhibiting properties have been identified, experts have not yet found a reliable way to harness them for the significant relief of moderate to severe arthritis pain and oxidative stress and for improving joint function in patients with osteoarthritis.

Curcumin has been found to inhibit various mediators involved in the inflammatory response, including cytokines, chemokines, adhesion molecules, growth factors, and other mediators such as cyclooxygenase-2, inducible nitric oxide, tissue factor, and epigenetic alterations [43]. This inhibition occurs through the “NFkB pathway” and other pro-inflammatory signaling pathways such as “COX-2”, “AP-1”, “Egr-1”, MAP kinases, and STAT [44]. Curcumin also has antinociceptive effects and has been shown to provide analgesic effects in mice with neuropathic pain. By inhibiting the cyclooxygenase pathway, curcumin regulates pain by affecting the activity of the enzyme that converts arachidonic acid to prostaglandins, which are key mediators in pain sensation [45]. Recent studies have demonstrated that curcumin can also inhibit transient receptor potential cation channels, including TRPA1 and TRPV1, which play a role in generating painful stimuli. A purified curcumin extract called Flexofytol has been developed as a food supplement to improve musculoskeletal flexibility and has been suggested as an alternative treatment for fibromyalgia [46].

2.4.12 5-HTP

There is some evidence to suggest that 5-HTP may help reduce inflammation and alleviate symptoms of fibromyalgia. However, further research is required to verify these effects. Fibromyalgia is a chronic pain condition that is characterized by widespread pain, fatigue, and

other symptoms. It is thought to be related to abnormalities in the way that the brain processes pain signals, as well as abnormalities in neurotransmitter levels.

5-HTP is believed to help reduce pain and inflammation by increasing serotonin levels in the brain. Serotonin has been shown to have anti-inflammatory effects, and increasing serotonin levels may help reduce the production of inflammatory cytokines in the body. In a small clinical trial, researchers found that taking 5-HTP supplements for eight weeks led to significant improvements in pain, fatigue, and sleep quality in people with fibromyalgia. However, more research is needed to confirm these effects and determine the optimal dose and duration of 5-HTP supplementation for fibromyalgia. It's important to note that while 5-HTP may be helpful for some people with fibromyalgia, it is not a cure for the condition and should be used as part of a comprehensive treatment plan that includes lifestyle modifications, physical therapy, and other treatments recommended by a healthcare provider [47]. There is no evidence of the use of 5-HTP efficacy in arthritis.

2.4.13 Vitamin B6

Vitamin B6 helps to reduce pain by strengthening the nervous system of people who face chronic pain.Studies have found that vitamin B6 can partially reduce thalamic-evoked nociceptive burst discharge and relieve mechanical allodynia in diabetic rats [48]. Furthermore, it has been demonstrated that vitamin B6 possesses antioxidant properties and anti-inflammatory when used to treat inflammatory conditions. Patients with rheumatoid arthritis who were supplemented with vitamin B6 experienced lower levels of IL-6 and TNF-α in their serum, and vitamin B6 has been shown to suppress IL-1β production [49]. A “randomized controlled trial” evaluating the efficacy of fibromyalgia provided opposite results [50]. According to this study, there was no notable distinction observed in the treatment of fibromyalgia between placebo and vitamin B6. However, given the potential benefits of vitamin B6 in improving pain and psychological symptoms and its relative safety, larger future studies are needed to further investigate its potential as an adjuvant treatment for fibromyalgia.

2.4.14 Astaxanthin

For its potential to lessen pain and inflammation in the body, astaxanthin has been researched. There are various hypotheses on the precise mechanism by which astaxanthin lessens pain [51]. According to one idea, astaxanthin lessens inflammation and oxidative stress in the body. Chronic pain problems including arthritis and neuropathic pain are known to develop and worsen as a result of oxidative stress and inflammation [52]. The antioxidant and anti-inflammatory qualities of astaxanthin may assist to reduce oxidative stress and inflammation, which in turn may aid to lessen pain. According to a hypothesis, astaxanthin lessens pain by controlling the activity of specific pain receptors in the body. Pain is frequently brought on by the body's pain receptors, such as the TRPV1 receptor [53]. In animal experiments, astaxanthin was found to regulate the activation of TRPV1 receptors, which may aid in pain relief [54].

Furthermore, astaxanthin has been demonstrated to boost the synthesis of endogenous opioids like beta-endorphins, which are known to relieve pain.Overall, astaxanthin appears to have a number of potential pain-relieving mechanisms, including lowering oxidative stress and inflammation, modifying pain receptor function, and upregulating endogenous opioid synthesis. To completely comprehend the mechanisms by which astaxanthin lessens pain, more research is necessary [55].

2.4.15 Panax Ginseng Powder

For its medical effects, which may include helping to manage arthritis, Panax ginseng root powder has been used for centuries. Although more studies are required to completely understand the scope of these advantages, some research suggests that Panax ginseng may have anti-inflammatory and pain-relieving properties that may be advantageous for arthritis sufferers.

In a study that was published in the Journal of Ginseng Research, it was discovered that a Panax ginseng extract decreased joint damage and inflammation in rheumatoid arthritis-affected rats. Another study in the Journal of Ethnopharmacology discovered that Panax ginseng and green tea together improved osteoarthritis patients' joint pain and stiffness [56].

Panax ginseng was mentioned in a review paper in the Journal of Ginseng Research as having anti-inflammatory properties and immune system-modulating properties that may help

manage arthritis [57]. It's important to note that although these studies point to potential advantages, additional research is necessary to fully comprehend the scope of these advantages and the best ways to make use of them. Additionally, it's crucial to see a doctor before beginning any new supplements because Panax ginseng may mix with some drugs and have undesirable side effects when taken in large dosages [58]. However, no research exists about the use of Panax ginseng in fibromyalgia. But based on these anti-inflammatory properties in osteoarthritis, it can be assumed that it can be an effective option in the treatment of fibromyalgia.

3. CONCLUSION

Medical food supplements that are rich in amino acids and flavonoids may have the potential to aid in treating chronic pain, depending on the specific cause of the pain. Amino acids are the building blocks of proteins, which are necessary for the growth, repair, and maintenance of tissues in the body. Flavonoids are plant compounds that have been shown to have anti-inflammatory and antioxidant properties. Chronic pain is often associated with inflammation and oxidative stress, which can lead to tissue damage and the activation of pain receptors. Amino acids and flavonoids may help to reduce inflammation and oxidative stress, thereby reducing pain. For example, amino acids such as L-arginine and L-carnitine have been shown to have anti-inflammatory properties and may be beneficial in treating conditions such as osteoarthritis and neuropathic pain. Flavonoids such as quercetin and resveratrol have also been shown to have anti-inflammatory and antioxidant properties and may help reduce pain associated with conditions such as fibromyalgia and rheumatoid arthritis. However, it is important to note that medical food supplements should not be used as a substitute for medical treatment, and it is always important to consult with a healthcare provider before taking any supplements or making changes to your treatment plan.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that he or she has no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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