

Açaí, *Euterpe oleracea*: Rethinking Treatment for Inflammatory Conditions

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Abstract

Inflammatory conditions affect individuals of all ages, races, and genders and originate from a relatively unknown combination of biological and environmental factors. Despite their prevalence, research has fallen short in providing significant discoveries in regards to both their etiology and effective treatment. However, there may be a relatively simple, efficacious treatment strategy involving the drupe of the acai palm, *Euterpe oleracea*, more commonly known as açaí. Overwhelming evidence suggests that consumption of the açaí fruit in the appropriate form and concentration represents an avenue of or adjunct to treatment for inflammatory conditions not previously applied. This particular systematic review evaluated the potential efficacy of utilizing *E. oleracea* in the treatment of three representative and common inflammatory conditions with similar cellular pathophysiology – Fibromyalgia Syndrome, Chronic Fatigue Syndrome, and Rheumatoid Arthritis.

Keywords: Açaí; Anthocyanins; Antioxidant Activity; Chronic Fatigue Syndrome; Cytoprotection; *Euterpe Oleracea*; Fibromyalgia; Immunomodulation; Inflammatory Response; Rheumatoid Arthritis

Introduction

Each year, physicians across the country experience an influx of patients with complaints of chronic pain. These patients often present with symptoms including, diffuse myalgias and/or arthralgias, fatigue, stiffness, sleep disturbances, and high incidence of comorbidities [1, 2]. Often, these symptoms progress for months to years without successful diagnostic investigation, proper diagnosis, or relief via treatment. A simple solution may be emerging since research shows that there may be an efficacious treatment strategy involving the fruit of the açaí palm, *Euterpe oleracea*, commonly known as açaí. Based on these newly emerging data, a systematic review of the literature to evaluate the efficacy of utilizing *E. oleracea* in the treatment of select inflammatory conditions, including Fibromyalgia Syndrome, Chronic Fatigue Syndrome, and Rheumatoid Arthritis was performed. These particular conditions were chosen because they are representative of prevailing diagnoses in inflammatory conditions. We present the review data following.

Methods

Study design

A systematic review was used to conduct the research. In doing so, historical data and scientific information specific to substance properties and bioactivity were collected and reviewed for reliability, validity, and authenticity; this data was then grouped according to key points, and a conceptual hypothesis was formed. Historical research was also conducted in the examination of various inflammatory conditions; information gathered includes signs, symptoms, laboratory tests and values, involvement of multiple organ systems, and other pertinent information.

Data collection

Data and theoretical information regarding *E. oleracea* and its properties were obtained through comprehensive literature review. In addition, review and analysis of the integrity of numerical and statistical data was performed with regard to the substance's biological and chemical properties and its effects on multiple organ systems (i.e. polyphenolic concentration, free-radical scavenging activity, cell mortality). Defining characteristics (i.e. laboratory values and biochemical considerations), pathogenicity, and typical clinical presentation of several inflammatory conditions were also explored.

Information was obtained primarily from peer-reviewed journals and scholarly medical publications, including published case studies; a small amount of information was also gathered from commercial presentations relaying basic knowledge of the substance, such as origin and historical significance.

In systematic literature review, three levels were employed: initial, level one, and level two. In the initial review stage, all potential sources of information were evaluated for applicability to the research subject; those that focused on information irrelevant or inapplicable were excluded. Sources found to meet the initial criteria for review underwent a level one review, in which all information was evaluated for continuity across sources; the primary goal at this level was to identify inconsistencies in research and results. Finally, all remaining sources underwent the second level of systematic review – an evaluation of quality. It was at this level that qualitative/quantitative data soundness and the rigor with which they were collected and analyzed was examined. Sources that failed to utilize adequate sample sizes, randomization techniques, and bias-controlling measures were excluded, and those that remained were ranked in terms of relevance and quality. Based upon the remaining information, a hypothesis regarding the biological activity of açaí extract and its potential effectiveness in the treatment of select inflammatory conditions was made for theoretical consideration.

Trustworthiness & authenticity

Throughout the literature review, characteristics that remained the same trans-study were documented and examined in order to ensure data integrity and reliability. Scientific concepts and statistical data were included only from peer-reviewed, published, credible sources. The researcher considered scientific rigor when examining the processes with which the published researchers conducted their studies; likewise, rigor was employed during analysis of the resultant data and findings.

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Triangulation of one study against another was used often to examine the conceptual basis of the research question, and negative case analysis was performed on several occasions in order to compare and contrast various findings.

Fibromyalgia Syndrome

Fibromyalgia syndrome (FMS), perhaps one of the most commonly-diagnosed chronic musculoskeletal disorders, represents a group of signs and symptoms typically ranging in severity that include fatigue; chronic, widespread pain; prevalence of localized tender points; mild to moderate impairment of cognitive processes; disruption in sleep patterns; and, often, depression and/or anxiety [4-7]. According to Murphree, "Over 10 million Americans suffer from fibromyalgia; 90% of them are women between the age of 25 and 40" [4]. Researchers conclude that women are significantly more likely than men to develop FMS, though the reason for this difference is largely unknown. Contrary to popular belief, the development of the disease in both sexes has been only minimally correlated with stressful life situations [6]. Historically, FMS has commonly been misconstrued as a "catch-all" diagnosis for unexplained musculoskeletal symptoms. Science has proven, however, that FMS elicits very specific abnormal laboratory findings in several areas, including cellular characteristics, immunological activity, and certain components of the central nervous system [3, 5-16].

Etiology

To date, the cause of FMS is largely unknown; however, several key factors have been identified in its presentation and progression [11, 12]. For years, scientists suggested that severely traumatic events, both physical and emotional, played a significant role in the existence of FMS; this phenomenon was most commonly associated with war veterans and was subsequently termed *Gulf War Syndrome* [17]. Recently, however, researchers have begun to unearth perhaps some of the most significant etiological information regarding FMS thus far.

Sleep abnormalities and hormone dysregulation: According to researchers at the University of Maryland Medical Center, patients suffering from FMS commonly experience chronic sleep disturbances, which amplify existing symptoms, including pain and fatigue: "... patients with fibromyalgia have increased rates of cyclic alternating sleep pattern (CAP). Increased CAP produced serious sleep problems, which were strongly linked to symptom severity" [5]. Often linked to the disturbance or absence of deep sleep, hormonal dysregulation seems to play a part in FMS progression; in fact, recent studies have shown that FMS patients tend to also suffer from inadequate amounts of serotonin, cortisol, norepinephrine, dopamine, growth hormone (GH), and insulin-like growth factor (IGF-1) [3,5, 7, 13, 15]. Many of these deficiencies are thought to contribute to the hallmark symptoms of the disease; consider, for example, the fact that serotonin works closely with norepinephrine in the CNS to control the processing of pain signals [7]. Decreased serotonin levels, therefore, would alter the central nervous system's ability to process pain effectively. Additionally, the precise balance of serotonin and dopamine has proven vital for healthy sleep patterns, and cortisol and norepinephrine work closely to control the adrenals; thus, abnormalities in these areas would alter the body's ability to sustain energy and combat fatigue. Perhaps even more important is the relationship between low GH, low IGF-1, and the immune system's incapacity to repair damaged tissue and/or dispose of dead cellular matter [18]. Lastly, and perhaps most commonly noted by researchers and medical practitioners alike, a large percentage of FMS patients also suffer from a significant lack of Vitamin D. Studies indicate that this deficiency affects the body's ability to regulate calcium concentrations, particularly in the bones and muscles, contributing

significantly to muscle contractility and diffuse pain, dysregulation of the immune system, and inability to combat chronic inflammation [19-22] – all of which are hallmark characteristics of FMS.

CNS abnormalities: CNS abnormalities have been identified in a large percentage of FMS patients. Perhaps the most significant finding in this realm involves the discovery of elevated CSF concentrations of nerve growth factor (NGF) and substance P [3, 5-7, 16, 23]. Both substances significantly increase the body's sensitivity to pain, and many studies have found the concentrations of these chemicals in FMS patients to be up to four times higher than those of healthy individuals [3-5,7].

Research shows that CNS abnormalities in FMS hinge also on the chronic dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis serves primarily to maintain homeostasis within the body and does so largely via the stimulation, production, and circulation of hormones [3, 4]. Science has deemed the HPA axis one of the most influential factors in the existence and progression of FMS; in fact, theories suggest that its dysregulation may be one of the primary causative agents for the disease, resulting in many of the hormone abnormalities common in its progression [3, 4, 6, 7].

Molecular and cellular abnormalities: In terms of cellular structure, research indicates that individuals with FMS possess very specific abnormalities at the molecular level – fragmented DNA, absence of cell apoptosis, and low levels of cellular mitochondria – that, in combination, contribute to the fatigue, myalgia, and inflammatory-derived symptoms characteristic of the condition [9, 10].

DNA fragmentation equates to damaged cells and related components, which, in healthy individuals, results in apoptosis. However, FMS patients seem to lack the ability for apoptosis; subsequently, this continual cellular damage stimulates the release of inflammatory cytokines IL-1Ra, IL-8, IL-6, and TNF- α , initiating a wide-spread, uninterrupted inflammatory process that results in diffuse pain and increased nociception [8]. These particular cytokines also affect the hypothalamus [24]; coupled with decreased ATP production due to inadequate cellular mitochondria, the two tend to produce severe and prolonged fatigue.

Immunological Abnormalities: Researchers have long been divided on the subject of immunological involvement in FMS; some studies strongly suggest an immune component, while others negate it altogether. However, the discovery of elevated concentrations of inflammatory cytokines indicate that FMS patients do, in fact, possess some sort of immunological dysfunction [8, 14]. More recently, scientists have discovered the presence of anti-polymer antibodies (APAs) in FMS patients. These antibodies are thought to form in response to the disease itself. Though their mechanism of formation and physiological purpose are unknown to date, the APA assay has recently been proposed as the first concrete laboratory test for FMS [25], as these antibodies are not present in those suffering from similar conditions [3, 11, 12].

Free Radicals: Perhaps one of the most consistent concepts in FMS research is that of ROS involvement. Science suggests that FMS may develop, partially, as a result of high levels of oxidative stress in the body [9]. In several studies, FMS patients have been found to possess extremely high levels of particular free radicals and significantly low levels of SOD, the body's most powerful antioxidant [9]. In addition, those with the condition have been found to lack normal levels of CAT, indicating an insufficient antioxidant capacity to combat the large generation of ROS and the subsequent oxidative damage taking place [26]. Many researchers have postulated that this ROS damage

leads to tissue hypoxia, tender points, and diffuse myalgia, providing strong evidence that oxidative stress due to cellular damage, DNA fragmentation, and inflammation plays a key role in pathophysiology of the disease [9, 27-29].

Chronic Fatigue Syndrome

For years, chronic fatigue syndrome (CFS) has remained somewhat of a mystery to conventional medical practitioners. The disease often presents as an array of symptoms that can often be mistaken for or attributed to many temporary, less severe ailments; in addition to the presence of "...unexplained fatigue lasting 6 months or more," a recurrent ebb and flow of general, less-severe flu-like symptoms comprise the eight standard clinical indicators for suspected CFS [30, 31]. The disease affects millions annually, and research is ongoing in an attempt to discover a direct cause [32, 33].

Etiology

Sleep abnormalities and hormone dysregulation: The CFIDS Chronicle reports that, "Unrefreshing sleep is a major symptom of CFS, with 70-95% of people with the illness reporting this symptom..." [34]. Though researchers have been unable to clarify whether or not sleep disturbance functions at the pathogenic level, science has confirmed a significant imbalance of the hormones related to healthy sleep patterns. For example, reports show that CFS patients lack adequate levels of dopamine, melatonin, cortisol, norepinephrine, and possess high levels of serotonin – all of which contribute to altered sleep patterns and feed directly into impaired CNS functionality [31, 34, 35].

CNS Abnormalities: Research suggests that overstimulation of the sympathetic nervous system and dysfunction of the HPA axis operate as two of the most prevalent contributors to many of the hallmark signs and symptoms of the disease [30, 34, 37]. Chronic activation of the sympathetic nervous system puts the body in a continuous state of stress, requiring "...an exaggerated stress response" from the HPA axis [30]. This overstimulation of the HPA axis results in an eventual breakdown in its ability to assist in the maintenance of a homeostatic environment, and thus, plays a central role in the resulting in hormonal imbalance, fatigue, sleep disturbances, and the typical post-exertional malaise [30, 37].

Molecular and Cellular Abnormalities: At the forefront of CFS research is the existence of varying levels of mitochondrial damage, subsequent dysfunction, and disturbance in ATP production [34, 38]. Thought to arise from severe oxidative stress, mitochondrial membranes are compromised, thus decreasing the organelle's ability to produce and release ATP and NADH, two of the body's primary sources of energy. The damage typically extends beyond the membrane to the mitochondrial DNA, often permanently altering its capability to function at an optimal level (38). Such damage to the mtDNA severely impairs the body's capability for DNA repair; furthermore, mtDNA mutation has been linked to an array of serious diseases, such as a number of cancers, cyclic vomiting syndrome, and MELAS [39]. The extent of mitochondrial damage and DNA mutation, however, hits much closer to home for many, as science indicates that damage-induced ATP insufficiency is a significant contributor to CFS signs and symptoms: "Mental/emotional symptoms of poor attention, memory loss, lack of concentration, and depression may...be reflective of insufficient central nervous system ATP availability..." [40].

Immunological Abnormalities: A great deal of evidence exists implicating significant immunological involvement, primarily hyperactivity, in CFS patients [34, 41]. This results in the long-term, continual release of inflammatory cytokines and increased neutrophil

apoptosis [34, 36, 38]. Laboratory tests confirm these findings, as initial tests for the condition often reveal elevated levels of CRP (c-reactive protein) and WBCs [41, 42]. Further testing often identifies an increase in various inflammatory cytokines, evidence of oxidative damage (via the presence of certain molecules, such as methemoglobin), and a marked decrease in antioxidant enzymes – a combination that produces sort of a domino effect, spreading throughout the body until fatigued and more susceptible to illness [38, 41]. In fact, medical science has recently unearthed several defining immunological components important to understanding CFS pathology, including decreased number of NK cells, increased proteolysis, and increased levels of NO [31]. Research continues to confirm that this chronic overstimulation of the immune system is directly related to the characteristics of the disease: "[The presence of] an immune disturbance...is in line with one favored theory that many of the symptoms of chronic fatigue syndrome derive from excessive cytokine release" [41].

Free Radicals: Similar to the findings in FMS research, studies show that oxidative stress via ROS production is key to understanding the pathogenesis of many of the symptoms common to CFS [43]. Kennedy et al. found that CFS patients carried particularly high levels of plasma-bound isoprostanes, chemical markers that indicate severe oxidative stress [36]. Additionally, their study suggested that those with the condition lack sufficient levels of antioxidants, making these individuals more susceptible to oxidative stress and damage. As researchers continue to discover the underlying pathology for the disease, many have deemed ROS a significant factor: "It could be suggested that CFS is an inflammatory condition with many patients in a prooxidant state, and this could explain many of the pathological manifestations that underlie the illness" [36].

Rheumatoid Arthritis

Scientifically proven to be a disease of autoimmune nature, RA has been termed a "chronic inflammatory polyarthritis," meaning that the disease produces ongoing (often fluctuating in severity) inflammation and pain in multiple joints throughout the body [44-46]. Research shows that RA tends to be more prevalent in the female population, and the risk for the development of the disease increases with age (peaking, then decreasing, near age 70). Recently, researchers have associated RA with a decrease in life expectancy and an increase in comorbidities and mortality dependent upon the severity of the disease [47].

Etiology

Though a concrete cause has not yet been identified, researchers have discovered several risk factors for the development of the disease, including an array of environmental and biological factors such as diet, tobacco use, hormonal influence, and genetics. Research also suggests that RA may have a viral component [44, 45, 48, 49]. Science has recently uncovered a myriad of biological markers in patients suffering from the RA, providing us with key information and enhancing our understanding of the bioactivity and progression of the disease.

Sleep Abnormalities and Hormone Dysregulation: Much like its counterpart conditions, RA elicits significant signs and symptoms of sleep disturbance and hormone imbalance. In addition to chronic sleep abnormalities, patients suffering from the condition often lack normal levels of serotonin; this is especially important in understanding the intense pain experienced by many RA patients, as one of serotonin's many roles is the inhibition of substance P production [50, 51]. Additionally, laboratory tests have confirmed that RA sufferers also experience significantly decreased levels of cortisol, stress hormones, and IGF-1 – substances that, at normal levels, serve to derail chronic

inflammation and tissue damage [18, 51, 52]. Science has also pinpointed high dopamine levels and peaks and valleys in melatonin concentration as influential components in RA sleep disturbance [51, 53-55]. Perhaps one of the most significant discoveries in RA research, however, is that of consistently increased serum prolactin – a substance that, in high amounts, enhances chronic inflammatory response and increases one’s risk for “the development of autoimmunity” [51, 56].

CNS Abnormalities: Research continues to implicate the involvement of abnormal CNS activity in RA existence and progression. Dekkers, Geene, Godaert, Bijlsma, and Van Doornen observed – an abnormal elevation in sympathetic nervous system (SNS) functionality with no increase in parasympathetic activity [57]. Additionally, Mukai et al. discovered a blatant HPA axis disturbance – now considered characteristic of the condition – evidenced not only by chronic sleep abnormalities, but also by consistently altered levels of key substances, such as serum prolactin, norepinephrine, dopamine, serotonin, and IGF-1 [50, 54, 56]. Increased levels and abnormal activity of substance P also play a significant role in RA existence and progression [58-60].

Molecular and Cellular Abnormalities: Science indicates that somatic mitochondrial mutation and DNA fragmentation and damage are characteristic of RA. Both Hitchon and El-Gabalawy and Da Sylva et al. discovered that both nuclear and mitochondrial DNA are severely damaged, resulting in the body’s virtual inability to initiate and carry out DNA repair cycles, salvage its energy-building and releasing capabilities, protect itself from oxidative stress and further damage, and stave off chronic inflammation [45, 61]. In fact, researchers have indicated that this particular sort of damage to the mitochondria and DNA likely has the potential to produce very severe long-term effects: “If the mutations were in genes regulating cell survival, cells that would otherwise stop dividing and die (from DNA damage) may instead proliferate” [45].

Immunological Abnormalities: Research has long-since confirmed that, in those that suffer from RA, the immune system remains hyper-reactive and unable to recognize invader from self, attacking and eventually destroying healthy and functional tissue within the body [62-64]. Evidence also abounds for the involvement of inflammatory cytokines in the pathogenesis and progression of RA, particularly TNF- α , IL-1, and IL-6, often evidenced by high CRP levels [60, 64-68]. In addition, Da Sylva et al. and Cross et al. discovered a chronic pattern of abnormal cell apoptosis in RA patients, implicating and further proving the existence of chronic inflammation and tissue damage and altered immunoactivity [45, 68].

Free Radicals: ROS production occurs often in RA, producing significant and vast oxidative damage to important elements within the body, namely synovial tissue, lipids, proteins, and DNA [61]. In fact, research shows that those with the condition suffer high levels of lipid peroxidation and low levels of CAT and natural antioxidants – a recipe for chronic tissue damage, pain, and destruction of key functional structures [45, 59, 61, 70].

The Acai Fruit

Native to South America, acai, *E. oleracea*, is a palm tree belonging to the family Arecaceae [71]. The drupe of acai, deep red or purple in color and composed of a large seed, thin layer of edible fruit, and a thick, fibrous skin, is harvested twice per year from tall, multi-stemmed palm branches [72]. Though little research has been conducted by way of human trials, scientists confirm that the fruit’s pulp is rich in its applicability to medicine, health, and well-being. A staple of consumption in its indigenous environment, acai is high in powerful

antioxidants, valuable phytosterols, amino acids, and disease-fighting anthocyanins, and boasts an innate ability to combat inflammation, immunodeficiencies and abnormalities, chronic pain and disease, and, research suggests, even fight cancer [73-75]. It does so via: 1) antioxidant and enzyme-like activities, 2) immunomodulatory activity, 3) CNS regulation, 4) cellular repair, and 5) DNA repair mediation (Table 1).

Antioxidant Properties and Enzyme-Like Activity

FMS, CFS, and RA are similar in their ability and likelihood to produce high levels of ROS. Because ROS present a formidable threat to the healthy human body and potentiate the initiation and progression of chronic and debilitating disease, acai’s ability to derail them via antioxidant content provides the possibility for substantial medical advancement in the way of non-pharmacological treatment. In fact, acai boasts an Oxygen Radical Absorbance Capacity (ORAC) value of 1027, the highest value reported to date in comparison to other nutrient-dense fruits and vegetables. Researchers have discovered that the antioxidants present in acai enter the cellular environment with ease, providing the body with intense free radical-fighting power [76].

Laboratory experiments confirm that the free radical-scavenging capability of *E. oleracea* far exceeds that of other comparable fruit extracts [71, 76-78]. Specifically, acai prevents oxidative damage via its four distinct enzyme-like properties:

1. CAT – catalase, an enzyme that serves to protect cellular integrity via its ability to convert hydrogen peroxide to oxygen and water while avoiding the production of free radicals, is considered one of the most effective and efficient factors in the body’s ability to detoxify its tissues [79]. CAT levels are extremely low in CFS, FMS, and RA alike, which likely serves as a partial explanation for the continual oxidative damage characteristic of the conditions. In laboratory experiments, studies continue to confirm that acai possesses CAT-like detoxification properties [77].
2. SOD – superoxide dismutase, an enzyme present in oxygen-metabolizing cells, acts to protect the body from free radical damage and has been shown to play a role in the reversal of fibrotic conditions [80; 81]. Research shows that patients with CFS, FMS, and RA are extremely SOD-deficient, also playing a key role in effects of ongoing ROS damage. Studies confirm that acai possesses SOD-like capabilities, deeming it extremely effective in protecting the body from oxidative stress [77].

Table 1. Demonstrated benefits of açai (*E. oleracea*)

Antioxidant activity	free radical scavenging beneficial enzyme-like activity inhibits excessive ROS production
Immunomodulation	antimicrobial characteristics increased lymphocyte activity prevention of immunosuppression inhibits production of high levels of nitric oxide anti-inflammatory activity down-regulation of inflammatory cytokines
CNS regulation	promotes healthy production of serotonin promotes healthy production of dopamine pain regulation encourages homeostatic functionality of HPA axis promotes appropriate substance P levels
Cellular repair	encourages repair of damaged cell membranes promotes optimal ATP production in mitochondria
DNA repair mediation	promotes healthy function of DNA repair cycle

3. DPPH-scavenging – diphenylpicrylhydrazyl is a common free radical known to wreak oxidative havoc on the body and its tissues. Often, researchers measure an antioxidant's effectiveness based upon its ability to seek out and destroy the DPPH radical. Açai ranks quite satisfactorily in comparison to others in its DPPH-scavenging ability [77].
4. ROS inhibition – Reactive Oxygen Species are free radicals produced by the myriad of oxygen-metabolizing processes in the human body. While ROS can prove useful in certain immune processes in low concentrations, they can be extremely damaging to the body in large amounts; in fact, high concentrations of ROS can damage cell membranes, organelle structures, nucleic acids, and DNA strands [82]. In high doses, açai has been shown to inhibit the production of large amounts of ROS, thus providing the body with molecular and cellular protection [71].

Immunomodulatory Activity

Given the evidence for abnormal immune activity in CFS, FMS, and RA, logical speculation suggests açai's promise in being utilized in treating them. Research confirms the immunosupportive properties of açai, revealing not only its antimicrobial characteristics, but also its ability to protect the body's immune system via its ability to reduce oxidative stress [71, 78, 83]. Beta-sitosterol, one of açai's many components, has specifically been shown to prevent immune suppression and enhance lymphocyte activity [84]. Additionally, research confirms açai's ability to inhibit unhealthy levels of nitric oxide production, a compound that plays a key role in immunosuppression when present in excessive concentrations [85, 86].

Anthocyanins, another major component of açai, represent a strong group of antioxidants that also boast anti-inflammatory and analgesic properties [78, 87]. Cyanidin-3 glucoside, açai's primary anthocyanin, has been shown to regulate pain and inflammation quite effectively. Many studies indicate the anthocyanins in açai to be highly effective, "...capable of attenuating inflammation...[and down-regulating] expression of enzymes involved in inflammation..." [78]. Other researchers have likened the activity of these substances to prescription-strength treatments for painful, inflammatory conditions: "...anthocyanins offer powerful relief against inflammation and pain... [and have] provided effective reduction of painful inflammation comparable to that obtained with the non-steroidal anti-inflammatory drug, Indomethacin..." [88]. Studies have also shown açai to be effective in regulating the production of inflammatory cytokines, such as IL-1 α , IL-6, IL-8, and TNF- α common to all three conditions, thus controlling excessive inflammation to due cellular injury and/or damage [77, 78].

CNS Regulation

Research often speaks to açai's ability to improve CNS operation, a component altered in those suffering from CFS, FMS, and RA. Açai, given its high concentration of B vitamins, has a proven capability to aid in the healthy production of serotonin and dopamine, two of the most vital neurotransmitters to CNS functionality, pain relief, and homeostasis [89]. Not only does this regulation stabilize mental and emotional functionality, it also provides for better sleep and total-body homeostasis via its encouragement of healthy HPA axis function and substance P regulation [50, 51, 53, 90].

Cellular Repair

Predominant research suggests that a great deal of chronic disease is directly linked to cellular damage – often at the mitochondrial level.

In fact, Cleary confirms that, many times, "...organ failure is the result of energy failure on a cellular level because of oxidation damage of the mitochondrial membranes..." [91, p 164]. Furthermore, compelling evidence exists that ROS-induced mitochondrial damage may be a significant cause of physiologic dysfunction due to the subsequent loss of cellular energy [38]. Mitochondrial damage and dysfunction is common in CFS, FMS, and RA, producing a great deal of their characteristic biological markers, such as decreased ATP production and energy levels, continual free radical production and damage, and DNA fragmentation. Açai has been shown to combat these effects via its high concentration of niacin, a B vitamin essential for ATP production in the mitochondria, and an extremely high dose of the phospholipids and phytochemicals needed to repair damaged cell membranes [38, 77, 89, 92, 93].

DNA Repair Mediation

DNA damage represents perhaps one of the most imminent threats for cellular death and chronic disease in the human body. This damage often occurs in the form of fragmentation as a result of severe oxidative stress, prolonged inflammation, and compromised membrane integrity and is common to all three conditions [38, 77, 91, 93, 94]. The anti-inflammatory, antioxidant, and enzyme-like activity properties of açai provide strong evidence of its ability to prevent DNA damage and encourage the body's natural DNA repair cell cycle [71, 77, 78, 83].

Discussion

Treatment for inflammatory conditions varies depending upon the condition; however, research suggests, and patients confirm, that many of the mainstream modalities provide little relief, and most fail to attack the variety of underlying factors involved. In fact, most medications are aimed at treating the obvious symptoms, such as pain, sleep disturbances, and palpable inflammation [3, 5, 95, 96] rather than the pathologies behind them. According to Dr. Robert Shmerling of Harvard Medical School, "...it's hard to predict which, if any, medication will be helpful... because many medications may cause side effects and may not work...it's important to explore other treatment options" [95].

Front-line medications for FMS, CFS, and RA include non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), antidepressants, corticosteroids, sleep medications, muscle relaxants, and narcotics [5]. Though these drugs may provide short-term relief from symptoms, many carry dangerous side effects and prove themselves ineffective after a relatively abbreviated period of time. For example, researchers and physicians from Harvard Medical School warn that certain anti-inflammatories boast some severe risks: "...infection, rupture of tendons around the joint, thinning of the skin near the injection site, and damage to the blood supply of the underlying bone, which can result in bone death" [97]. DMARDs, often given in the treatment of RA, often inflict such side effects as "...nausea and vomiting, rash, mild hair loss, headache, mouth sores, and muscle aches." Some patients undergoing treatment for these conditions also experience gastrointestinal bleeding, vital organ damage, decreased immune function, sepsis, lung disease, hepatitis B reactivation, encephalopathy, and muscle wasting [5].

Ongoing medical research indicates that ensuring optimal vitamin D levels and incorporating powerful antioxidants into mainstream treatment for FMS, CFS, and RA could prove useful [43]. The literature confirms that açai is quite adept in its ability to remedy many of the biological abnormalities characteristic of all three conditions, and though few human trials have been conducted, current research

suggests that the supplement carries no known side effects or drug interactions [98, 99].

Açaí, now considered part of the “superfood family,” sits among some of the most powerful natural foods in terms of the promotion of health and wellness. Boasting an ORAC value of 1,027, açaí is not only an effective antioxidant and inflammatory mediator, it also is more adept at promoting DNA repair, preventing cellular damage, and protecting cellular integrity than many of its superfood counterparts [76, 77, 100-102].

Considerations for Future Research

Certainly, further research should be conducted with regard to açaí, proper dosage guidelines, the most effective form of administration (i.e., flakes versus extract versus pulp), and optimal preparation techniques. An in-depth examination of patient-specific disease factors would be necessary to identify a target population for generalization, including age, disease severity, other health-related factors, and lifestyle components that may affect disease progression and/or severity. Carefully controlled observational studies or randomized, double-blind, controlled studies would be appropriate to begin to assess açaí's true potential as a front-line option in the integrative treatment and management of acute and chronic inflammatory conditions.

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