

## Systematic review

**A narrative review on scientific evidence of mechanisms of naturopathy and yoga interventions for rheumatoid arthritis**Geetha B. Shetty<sup>1</sup>, Prashanth Shetty<sup>2</sup>, Balakrishna Shetty<sup>3</sup>, Abitone V. R.<sup>2</sup><sup>1</sup>Division of Nutrition and Dietetics, <sup>3</sup>Division of Basic Medical Sciences, <sup>2</sup>S.D.M College of Naturopathy and Yogic Sciences, Ujire, Karnataka, India*(Received: January 2024      Revised: February 2024      Accepted: February 2024)*Corresponding author: **Balakrishna Shetty**. Email: bksujire@gmail.com**ABSTRACT**

Rheumatoid arthritis (RA) is a chronic autoimmune systemic inflammatory disease, which has serious physical, psychological, and social consequences. Many RA patients continue to experience intolerable side effects from their treatments or an inadequate response, which leads to the disease progressing despite advancements in targeted biological and pharmacologic interventions. Examining the multi-modular, drugless approach of yoga and naturopathy to this autoimmune disease is equally important as it enables physicians to provide better care. Hence, the current review was undertaken to present an overview of the available scientific evidence on the mechanism of naturopathy and yoga therapeutic modalities in the management of RA. We searched PubMed and PubMed Central for pertinent English-language articles about the impact of yoga and naturopathy on RA. The results in this review are presented based on the therapeutic effect of yoga and various naturopathy treatment modalities with their mechanisms on RA. It shows naturopathy and yoga was effective in the management of RA due to its analgesic, anti-inflammatory, immunomodulatory and antioxidant effect.

**Keywords:** Rheumatoid arthritis; yoga therapy; naturopathy; diet therapy; acupuncture; hydrotherapy.**INTRODUCTION**

**R**heumatoid arthritis (RA) is a common autoimmune chronic systemic inflammatory disease characterized by poly articular joint involvement associated with extra-articular manifestations, including accelerated cardiovascular disease (1). It impacts between 0.1% and 2.0% of people globally. Different genetic and environmental factors influence the disease's prevalence both internationally and domestically (2). In developing countries like India, data on prevalence are scarce and underreported at between 0.28% to 0.7% of the general population with a remission rate of 20% (3). Sustained remission is an ultimate treatment goal in managing patients with rheumatoid arthritis which could be achieved by early diagnosis and management. Long-lasting morning stiffness, restricted range of motion (ROM), symmetrical joint deformity, ligamentous laxity, altered biomechanics and posture, pain, fatigue, malaise, fever, weight loss, neurological impairment, and decreased quality of life can all result from the progressive development of RA (4). Patients with RA often experience a major impact on physical, social, and emotional level (5).

Relieving pain and reducing inflammation is usually the first course of treatment. Conventional RA treatments currently in use are no longer regarded as curative or conclusive (6). Many RA patients are using complementary and alternative medicine (CAM) modalities in an attempt to alleviate their symptoms due to the negative consequences of traditional treatment. Research shows that between 28% and 90% of RA patients in the United States alone are thought to use CAM (7). Yoga and naturopathy are regarded

as the most common CAM modalities in Indian medical systems. The primary interventions used by naturopathic doctors include diet therapy, mud, hydrotherapy, massage, acupuncture, chromotherapy, magnet therapy, acupressure, and yoga therapy (7). Hence, the current review was undertaken to present an overview of the available evidence on the efficacy and mechanism of naturopathy and yoga therapeutic modalities in treating rheumatoid arthritis.

**METHODOLOGY**

Online databases viz., PubMed and PubMed Central were comprehensively searched for citations published between 1995 to 2023 using keywords related to different naturopathy and yoga treatment modalities. The list of keywords used were naturopathy, yoga therapy, hydrotherapy/Hot applications/cold applications, rheumatoid arthritis, magnet therapy, colour therapy, acupuncture, diet therapy/nutrition and physical therapy/exercise therapy using different Boolean queries. This review includes experimental papers, case studies, case series, systematic reviews, and English comments to the editor outlining the effects of different naturopathy and yoga treatment modalities on RA. The findings of studies included in the review are discussed based on their efficacy of each treatment with mechanisms in the management of RA.

**RESULTS AND DISCUSSION**

The findings of studies included in the review are discussed based on their efficacy of naturopathy and yoga by considering each treatment modality with mechanisms in the management of RA.

### Role of diet

Food intake is a modifiable risk factor for RA, possibly by modulating systemic inflammation. It has been shown in several studies that consuming fruits and vegetables help prevent RA (8). Besides being good providers of fibre, minerals, antioxidants, and other micronutrients, fruits and vegetables also have well-known anti-inflammatory properties. Interleukin-6 (IL-6), homocysteine, and C-reactive protein (CRP) have all been positively correlated with diets high in fat and processed meat, but they have been negatively correlated with diets high in whole grains and fruit (9). Studies have demonstrated that anti-inflammatory elements of a vegan diet, such as a high intake of fibre, can lower CRP by 33% (10).

Supplementation of diet with rich sources of omega -3 polyunsaturated fatty acids viz., flaxseed, flaxseed oil, canola oil, soybean oil, walnut, walnut oil, canola oil, and seeds (11) has been demonstrated to favourably alter the n-6/n-3 fatty acid ratio, reducing pain, inflammation, and disease activity in RA (12). They also alter the production of critical pro-inflammatory eicosanoids, prostaglandin E2, thromboxane B2, and leukotriene B4 toward a more anti-inflammatory profile (12).

In patients with RA, Vitamin D supplementation in the form of exposure to sunlight or consuming mushrooms, a rich source of Vitamin D may prevent and treat osteoporosis and its possible effects on disease activity, and pain relief (13). Consuming specific antioxidant micronutrients, especially  $\beta$ -cryptoxanthin and extra zinc, may prevent the onset of rheumatoid arthritis, according to a prospective cohort study (14). Because it increases inflammation, excessive oxidative stress is believed to play a crucial part in the pathophysiology of RA (15). Antioxidant intake, either by supplementation or diet, improves the clinical outcomes in RA by increasing erythrocyte antioxidant levels (16). Intake of foods rich in zinc, Flavonoids, Vitamin C, A and E,  $\alpha$ - and  $\beta$ -carotene, selenium, epigallocatechin gallate, resveratrol, oleuropein, quercetin was known to improve the outcomes of RA (17).

The delicate balance between inflammation and tolerance is disrupted in RA due to the modulation of innate and acquired immune responses by gut and oral microbiota. Diet, probiotics, prebiotics, antibiotics, exogenous enzymes, fecal microbiota transplantation, and other environmental factors can all have a positive impact on the gut microbiota (18). This microbe is essential for maintaining immunological homeostasis in RA because it forms the intestinal barrier. A Mediterranean diet rich in fruits, vegetables, cereal, legumes, olive oil, and other foods has been shown to have anti-inflammatory and antioxidant effects by altering gut microbiota and raising short-chain fatty acid levels (19).

### Role of yoga therapy in RA

The goal of the philosophical practice of yoga is to harmonize the body, mind, and spirit. The three main components of the yoga system are *asanas* (postures), *pranayama* (breathing exercises), and *dhyana* (meditation). Yoga can reverse harmful epigenetic alterations and improve RA symptoms while lowering the risk of relapse when used in conjunction with other healthy lifestyle practices or as part of a therapy regimen (20).

Symptomatically RA is presented with morning stiffness, tenderness, symmetrical joint pains, swelling, and fatigue, affecting the quality of life of an individual. Yoga modulates the endogenous opioid system through the release of endorphins (21). Endogenous opioids produced during sustained stretching of muscles in the practice of *yogasanas* help to relieve pain (22). Yoga has been proven to alleviate pain and strengthen muscle strength, supporting that yoga may positively affect mobility.

Auto-inflammation and autoimmunity are known to be triggered by psychological stress and depression. There is a reciprocal relationship between depression and the pathophysiology of RA because of the malfunctioning neuroendocrine system, systemic inflammation, accelerated immunological aging, oxidative DNA damage, and aberrant DNA damage sensing and repair machinery (23). Yoga most probably acts via the psycho-neuro-immunological axis, which creates a homeostatic balance between sympathetic and parasympathetic limbs of the autonomic nervous system and downregulates the HPA axis response during the aggressive symptomatic phase resulting in a reduction of its associated molecular and genetic markers and may help to normalize the flare and achieve remission in RA (20). In summary, sufficient evidence exists to suggest that yoga should be considered an add-on therapy for rheumatoid arthritis.

### Role of colour therapy in RA

Colour therapy or chromotherapy is therapeutic application of the seven colours available in the light spectrum of the sun rays for various diseases. The mode of application can include exposure to the coloured light, consumption of colour charged water (24). Though there is less evidence of how chromotherapy helps in RA, various researches on other ailments among humans and experimental models show how each colour application could affect RA's pathology and symptomatology. Irradiation with red colour (644 nm) increases the SOD activity by decreasing the activation energy required and eliminating free radicals, which undoubtedly increase immunity (25). Exposure to blue colour activates the S-nitrosylation signalling pathway required for inhibiting the IKK $\beta$  and NF- $\kappa$ B and thereby reduces oxidative stress and inflammation (26). Research has

demonstrated the analgesic effects of light-emitting diode (LED) photo-biomodulation for long-term illnesses like RA. Photo-biomodulation reduces muscle spasm and interstitial edema, suppresses central synaptic activity, modifies neurotransmitters, induces peripheral neural block, and has anti-inflammatory effects. These mechanisms account for the analgesic effect of photo-biomodulation. Furthermore, illumination heightens the synthesis of endogenous opioid neurotransmitters, elevates the threshold for pain, and stimulates local blood flow (27).

### **Role of hydrotherapy, balneotherapy, and mud therapy in RA**

Hydrotherapy and balneotherapy are techniques where there are an external or internal use of water in any of its forms (water, ice, steam) for health promotion or treatment of various diseases with various temperatures, pressure, duration, and site (28). Mud therapy is the application of natural products in the form of a wrap or bath that combine organic or inorganic compounds originating from geological, biological, or even both processes with a mixture of mineral or mineral-medicinal water (including seawater or salt water from lakes) (28).

Vasodilatation and enhanced cell oxygenation throughout the body are the results of hot applications. Hot applications also release  $\beta$ -endorphin, adrenocorticotrophic hormone (ACTH), and cortisol; the latter is particularly significant due to its anti-inflammatory properties and capacity to block the production of most cytokines. Keratinocytes release pro-opiomelanocortin (POMC), a common precursor of different endorphins, in response to thermal stimuli, which reduces pain (29). The hydrotherapy group's decreased joint loading due to buoyancy may be the cause of their decreased joint tenderness (30).

Pain is hypothesized to be less felt when the affected body part is submerged in water due to sensory overflow caused by the pressure and temperature of the water on the skin. Additionally, hot stimuli may affect muscle tone and lessen spasms in the muscles (31). Hot and cold water contrast baths cause sporadic vasoconstriction and vasodilation, which results in a vascular pumping effect. This improves healing by increasing tissue blood flow and oxygenation, and it also improves tissue waste-product transportation, which lowers oedema (32).

Mud-bath therapy raises levels of plasma beta-endorphins and secretes prolactin, growth hormone, cortisol, and corticotropin. Recent research has shown that thermal mud-pack therapy reduces circulating levels of key mediators of inflammation and pain, including prostaglandin E2 (PGE2), leukotriene B4 (LTB4), interleukin-1b (IL-1b), and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ). Increased insulin-like growth factor-1 (IGF1) promotes the anabolism of cartilage and the

production of transforming growth factor- $\beta$  (TGF- $\beta$ ), a powerful cytokine that modulates the immune system and reduces inflammation. TGF- $\beta$  is also involved in bone remodelling, fibrosis, and tissue healing. Studies indicate that Matrix Metallo Protease-3 (MMP-3) is correlated with systemic inflammation in RA, in contrast to its role in osteoarthritis on cartilage degradation. Its exact function in RA-related joint damage is still unknown (33).

Balneotherapy, also called mineral baths or spa therapy, uses different types of mineral water compositions like sulphur, radon, carbon dioxin, etc. The mineral water composition or mud minerals would be absorbed through the skin (34). Epsom salt is a magnesium sulphate mineral with a high level of sulphate, and magnesium is known for alleviating pain, inflammation, and oedema (35). Sulfurous and sulfated mineral-medicinal waters contain H<sub>2</sub>S, a hormetin that has the ability to actively penetrate skin. As an endogenous cell signaling molecule involved in the control of inflammation (via NF- $\kappa$ B) and oxidative stress, H<sub>2</sub>S plays vital physiological roles. Sulfur inhibits the generation of cytokines, particularly IL-2 and interferon-gamma (IFN- $\gamma$ ), by decreasing memory T cells' ability to multiply and generate cytokines, which modifies the immune response (36).

### **Role of acupuncture in RA**

Based on TCM theory, acupuncture has been used for thousands of years to treat a variety of clinical disorders, including "Bi" or RA-like conditions. It is considered an important component of TCM. As a group of diseases involving muscles, sinews, bones, and joints that are brought on by the invasion of wind, cold, dampness, or heat pathogens on the meridians, RA is classified as a "Bi" or impediment disease. This group of diseases is characterized by local pain, soreness, heaviness, or heat, as well as articular swelling, stiffness, and deformities. Acupuncture's anti-inflammatory, immune function-regulating, antioxidant, autonomic nervous system-modulating, and analgesic properties in RA patients may all contribute to its clinical efficacy (37).

The hypothalamo-pituitary axis, which controls the release of systemic glucocorticoids, which transactivate anti-inflammatory cytokines like IL-4 and IL-10, may be the cause of the anti-inflammatory effect of acupuncture in RA. Moreover, acupuncture modifies the sympathetic nervous system by stimulating the adrenal glands, which results in the release of catecholamines into the bloodstream. Through the prevention of systemic immunosuppression and susceptibility to secondary infections, this local supportive regulation of the immune system has anti-inflammatory effects (38).

Additionally, acupuncture creates tiny tears in the tissues under the skin, which may trigger the immune system. Axon reflex activation of A- $\delta$  and C-fibres

results in vasodilatation in small vessels, increased blood flow, and a triggered local inflammatory and anti-inflammatory response. These include mast cell involvement and the release of a vasoactive substance such as cGRP, histamine, SP, adenosine, prostaglandin, and bradykinin (39). The mechanisms mentioned above were evident from various clinical trials, which have shown a reduction in TNF- $\alpha$  and VEGF in serum and synovia, a decrease in pro-inflammatory cytokine of IL-1 and IL-6, and an increase in the inhibition cytokine of IL-4 and IL-10, reduction in blood RF, CRP, ESR, WBC and PLT, CRP after acupuncture (40).

Acupuncture, in accordance with the gate control theory, lowers pain input by stimulating the large-diameter (A-beta) pain inhibitory nerve fibers. Numerous bioactive substances, including opioids, serotonin, and norepinephrine, are released during acupuncture therapy via peripheral, spinal, and supraspinal mechanisms. Acupuncture-released opioids desensitize peripheral nociceptors and lower pro-inflammatory cytokines in the peripheral and spinal cord, both of which are important factors in chronic pain (41). In RA, electroacupuncture's (EA) analgesic mechanism is frequency-specific. EA that operates at a frequency of 2 Hz or higher releases endorphins and enkephalins, and at a frequency of 100 Hz or higher, releases dynorphins (42). Acupuncture alone or combined with other treatment modalities is beneficial to the clinical conditions of RA which can improve function and quality of life without adverse effects.

## CONCLUSION

One of the review's limitations is that it restricted the search to only publicly available online databases, which may have restricted access to real, field-based research. Additionally, pre-clinical and clinical studies establishing the scientific literature on the mechanisms of naturopathy and yoga therapeutic modalities in the treatment of rheumatoid arthritis were taken into consideration in the current review.

Overall, we found the practice of naturopathy and yoga therapeutic modalities safe with no adverse effects in RA. Though several studies are available elucidating the impact of different modalities, they lack methodological rigor. Considering the available scientific literature and their mechanism in RA patients suggests that naturopathy and yoga treatments either solely or in adjuvant to conventional therapy should be considered for alleviating pain and improving the quality of life among RA patients.

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## CONFLICT OF INTEREST

The authors have none to declare.

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