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## Dietary approaches in the management of rheumatoid arthritis - A Review

Vijayalakshmi S<sup>1</sup> and Kripa KG<sup>2\*</sup><sup>1</sup>School of Hotel and Catering Management, Vels Institute of Science, Technology and Advanced Studies, Pallavaram, Chennai-600117 Tamil Nadu, India<sup>2</sup>Department of Biochemistry, School of Life Sciences, Vels Institute of Science, Technology and Advanced Studies, Pallavaram, Chennai-600117 Tamil Nadu, India

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### ABSTRACT

Rheumatoid arthritis (RA) patients may experience chronic pain and inflammations, deficiencies in nutrients are prone to develop stress and associated medical complications. Food allergy due to an impact on the immune system has also been highlighted in rheumatic patients. A therapeutic diet not only reduces discomfort and pain but may also protect joints. RA patients hence are to be recommended for a stable and healthy diet and this review article categorizes dietary approaches for arthritic patients and also discusses the mechanisms to inform the choice of nutrition therapy. Dietary approaches may include in this review: anti-inflammatory diet, gluten-free diet, elemental diet, Mediterranean diet etc., which are known to control pain and inflammation, thereby significantly reducing the severity of the disease. The recommended diets are critically analyzed and emphasized to supplement and manage the disease condition, boost their immune system and protect overall health.



### \* Corresponding Author

Name: K.G. Kripa  
 Phone: +91-9677195749  
 Email: kgkripa.sls@velsuniv.ac.in

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### INTRODUCTION

Nutrition professionals now recognize that diet approaches might confer optimum outcomes in the prevention and management of autoimmune diseases (M Hermann, 2017). The most common autoimmune diseases are Celiac disease, Crohn's disease, Multiple sclerosis, Rheumatoid arthritis, Systemic lupus erythematosus, Type-1 diabetes (Lette G and Rioux JD, 2008). Recently, nutritional science has geared significance in the field of research towards the use of food for their diversified health benefits for people with rheumatoid arthritis. Our review article show

some evidence of diet approaches in the management of RA.

Rheumatoid arthritis (RA) is an inflammatory disorder progressively affecting articular and extra-articular joints resulting in pain, disability and mortality (Heidari B, 2011). Individuals with the rheumatoid condition may experience difficulty in absorption of specific nutrients. NSAIDs and DMARDS, the drugs that have widespread usage in the treatment of RA have proven side effects including gastritis, nausea and vomiting, angular stomatitis and anorexia nervosa. Eventually, rheumatoid disease and its treatment can severely affect nutrition (Miggiano GA, Gagliardi L, 2005). Nonetheless the tremendous advancement in the field of medicine and the development of new drugs for the treatment of rheumatoid arthritis (RA), many patients are still interested in seeking a remedy to ease its symptoms with food and dietary supplements (M. Haugen *et al.*, 1999).

This review paper aims to congregate dietary approaches for RA patients and also discusses the mechanisms to inform the choice of nutrition therapy. Diet for them may include a variety of

approaches such as Anti-Oxidant diet, anti-inflammatory diet, gluten-free diet, Elemental diet, Mediterranean, Paleo diet and diet elimination therapy. In this review, the recommended diets are critically analyzed and emphasized to supplement in the diets of RA patients to obtain significant benefits in improving their nutritional status and controlling joint damage and inflammation and to sustain the quality of life of these patients.

### Nutritional Deficiencies in Patients with RA

Long-term exposure to RA medications may lead to nutritional deficiencies in patients. They often experience anemia and weight loss due to poor nutritional status. Other RA medications may be associated with conditions such as gastritis or peptic ulcer, anemia and loss of appetite. Specific micronutrient deficiencies observed in RA patients are those of folic acid, vitamin B6, vitamin B12, vitamin C, vitamin D, calcium, magnesium, zinc and selenium (C Koch, 2015, G. Vreugdenhil *et al.*, 1990 & Juturu *et al.*, 2010).

Certain important B vitamins such as B6, B12, and folate are often deficient in people with rheumatoid arthritis. Patients are receiving methotrexate, are mostly identified with folic acid deficiency. In a study conducted by Gough K. R *et al.*, 1964, on 46 RA patients, it was established that there was a significant increase in the incidence of megaloblastic anemia, the cause being a folic acid deficiency. Impaired vitamin B6 status results from inflammation. The low plasma pyridoxal 5'-phosphate levels seen in inflammation are suspect to be due to insufficient intake or excessive vitamin B6 excretion (Chiang E-P *et al.*, 2005). Vitamin B12 deficiency is a common condition associated with rheumatoid arthritis (N Iqtida, M.N. Chaudary, 2012). Rheumatoid arthritis patients also exhibit as apparent vitamin C deficiency as indicated by the low concentration of the vitamin in the blood (M. G. Hall *et al.*, 1938). Vitamin D deficiency is highly prevalent in patients with RA, and that vitamin D deficiency may be linked to disease severity in RA. As vitamin D deficiency has been linked to diffuse musculoskeletal pain, these results have severe clinical implications.

RA patients are often in a negative calcium balance due to inadequate dietary calcium and increased disease activity. Treatment with Glucocorticoids (GCs) can also reduce intestinal calcium absorption and worsen hypercalciuria (E.W.St. Clair *et al.*, 2004). Rheumatoid arthritis patients were found to have insufficient Mg intake (Zeng, C *et al.*, 2015) and malabsorption of zinc (K. D. Rainsford *et al.*, 1998). Low selenium level was noted down in severe RA patients (J R O'Dell *et al.*, 1991).

Thus, RA patients are always found to be deficient with respect to several nutrients and it is necessary to suggest to them that routine dietary supplementation with multivitamins and trace elements is essential.

### Anti-Oxidant Diet and Anti-inflammatory Diet

Earlier studies have revealed the effectiveness of specific non-enzymic antioxidants such as vitamins A, C and E in the treatment of rheumatoid arthritis. Diet rich in antioxidants may decrease free-radical damage in joint linings, which diminish swelling, pain and inflammation. Some important dietary antioxidants are vitamin A, vitamin C, vitamin E and selenium. RA patients are advised to include fresh fruits and vegetables, nuts and green tea as a means to achieve a high antioxidant status through diet (ME Elli and N Butler, 2016 & Juturu *et al.*, 2010).

Ground flaxseeds, as well as flaxseed oil, are one of the best plant-based sources of the anti-inflammatory omega-3 fatty acids. Salmon helps reduce joint pain and stiffness as well as signs of inflammation in people with rheumatoid arthritis. The potential of pumpkin seeds in the treatment and prevention of rheumatoid arthritis is linked to their strong anti-inflammatory properties. Dried pumpkin seeds can be eaten raw as a snack or added to salads or other sweet and savoury dishes. Studies suggest that Quercetin is a flavonoid and a powerful antioxidant that it can fight inflammation, in the joints of rheumatoid arthritis patients. Dietary sources of quercetin include capers, apples, lovage, red and yellow onions, broccoli, red grapes, tea, cherries, citrus fruits, chia seeds, and many berries including raspberries, lingonberries, and cranberries (HealWithFood.org's). Flavonoids can reduce inflammation, pain and swelling. Foods that are high in flavonoids include berries, green tea, grapes, broccoli and soy. Dark chocolate is also high in flavonoids. Blueberries contain flavonoids called anthocyanins that are known to possess potent anti-inflammatory properties (Mary Ellen Elli, Natalie Butler, 2016).

According to the Arthritis Foundation, fruits and vegetables are powerhouses of antioxidants and phytochemicals that help relieve pain and reduce inflammation. Oranges help to mitigate inflammation in RA. Berries are loaded with antioxidants and vitamin C. Kiwi help reduce inflammation due to its strong content of vitamin C. Apples and cherries contain antioxidant, that fight against inflammation. Parsley rich in beta-carotene and prunes is rich in antioxidants. Carrots are high in vitamin A and carotenoids. Broccoli is rich in beta-carotene and vitamin C. Pineapple is loaded with bromelain which it is a potent anti-

inflammatory phytochemical. Protein-rich beans reduce inflammation by replacing the body protein broken down by inflammation. Red grapes lower inflammation. Lycopene content in tomatoes relieves inflammation. Sweet potatoes are rich sources for Vitamin A, C and E. Papin in papaya has anti-inflammatory property. These fruits and vegetables have high levels of antioxidants and phytochemicals which play an active role in reducing inflammation (Carole Jacobs *et al.*, 2010). HealWithFood.org's suggests that the beneficial effects of selenium on RA are based on the role of this trace element in the antioxidant system of the body. Selenium is a key component of several enzymes involved in antioxidant defence mechanism. Combination of selenium-rich foods with foods high in vitamin E will give more benefits and selenium boosts the effectiveness of the vitamin E.

### Gluten-Free Vegan Diet

A study reports that the gluten, gut-derived antigens may have a role in the pathogenesis of rheumatoid arthritis. Coeliac disease associated with rheumatoid arthritis (Warjri S. *et al.*, 2015). A gluten-free diet may be a clinical benefit for certain RA patients as it may bring about a reduction in the immunoreactivity against specific food antigens. The Gluten-free vegan diet contained vegetables, root vegetables, nuts, fruits, buckwheat, millet, corn, rice, sunflower seeds and unshelled sesame seeds. This diet may be beneficial at least in some patients with RA as established by I. Hafström *et al.*, 2001.

### Elemental Diet

The elemental diet is the simplest formulation of pre-digested solutions that contain broken down macronutrients and it could be used to treat patients with active rheumatoid arthritis. The term "elemental diet" is applied to food and readily available nutrients including essential amino acids (no whole proteins), simple sugars and low fat supplemented with vitamins and trace elements with about 2% to 3 % of calories derived from long-chain triglycerides, proven to be less immunogenic and easily digestible (D Makola, 2005).

Elemental diets have an advantage over intravenous nutrition in that they are easier to administer and allow greater flexibility in the use of trace elements (R. I. Russell, 1975). This diet was as effective as a course of pre-digested oral prednisolone 15 mg daily in improving subjective clinical parameters (Podas, T *et al.*, 2007). Patients treated with an elemental diet showed reduced symptoms of RA (Khanna, S *et al.*, 2017).

The potential disadvantages of elemental diets are their unpalatability, gastrointestinal side effects like nausea, diarrhea and gastric retention, dehydration, hypoprothrombinemia, skin rashes, hyperglycemia and aspiration (R. I. Russell, 1975). There are also disagreements about how patients should be managed when they achieve remission. The reintroduction of normal foodstuffs is still controversial (Hunter, J. 2015).

### Mediterranean Diet

The Mediterranean-style diet (MedDiet) involves substantial intake of fruits, vegetables, and fish, and lower consumption of dairy, red meat, and sugars. (Hardman RJ *et al.*, 2016). Recently, Mediterranean diet is gaining significance as there are many biochemical studies that relate a high intake of foods typical to the Mediterranean food products and their ingredients to protection against many lifestyle-related diseases like cardiovascular disease, cancer, metabolic syndrome and dementia; confers quality health status; reduces mortality and increase life expectancy (Boskou D 2015 & Hardman RJ *et al.*, 2016).

A scientific investigation pioneered by Skoldstam, L *et al.*, 2003, discusses the efficacy of a Mediterranean diet (MD) versus an ordinary Western diet for suppression of disease activity in patients with rheumatoid arthritis (RA). The results indicated that patients with RA, subjected to a Mediterranean diet, there was a reduction in inflammatory activity, an increase in physical function, and improved vitality.



Figure 1: Mediterranean diet chart

### Diet Elimination Therapy

An elimination diet is the systematic elimination of foods or group of foods from the diet suspected in causing a food allergy which should be undertaken with the supervision of a physician and/or dietician. It is used as a means to diagnose an allergic reaction to foods (Encyclopedia of Children's Health Forum).

Food elimination diets therapy varies in their 3 main forms. 1. A single food exclusion diet excludes one suspected food (eggs). 2. A multifood exclusion

diet eliminates the most common food allergens: (Example, 6-food elimination diet-cow-milk protein, soy, wheat, eggs, peanuts, and seafood). 3. A "few foods diet" (also called an oligoantigenic diet) restricts a person's diet to only a few less commonly consumed foods (Example, lamb/venison, quinoa/rice, pear, and others with low allergenic potential) (Nigg, J. T., & Holton, K, 2014).

In RA patients, specific foods have been shown to aggravate the symptoms. Diet elimination therapy is a method of determining food hypersensitivities with these patients. The form of exclusion diet avoids a specific food or group of foods such as milk, meat or processed foods that are known to be prime allergy suspects. These foods are eliminated from the diet for a given period. Foods are then gradually reintroduced one at a time, to determine whether any of them causes a reaction (C Koch, 2015).

### **Balanced Diet and Supplementation of Nutrients**

A balanced diet may warrant an adequate intake of nutrients (Miggiano GA and Gagliardi L, 2005). Eventually, a well-balanced diet is recommended for optimal health for RA patients. They are to review with patient's recommendations such as the 2010 Dietary Guidelines for Americans while stressing that they achieve or maintain appropriate body weight and include plenty of fruits, vegetables, whole grains, and calcium-rich foods in their diets (K Duncan, 2015).

Nutritional supplements are defined as concentrated sources of nutrients or other substances with a nutritional or physiological effect that supplements the normal diet (Piccardi N, Manissier P. 2009). Although food is always the preferred source for vitamins and minerals, it may be essential to use supplementation to assist in counterbalancing the outlined deficiencies and improving nutritional status, relieve inflammation and pain for patients with RA. In view of this context, nutritional supplements may be used to improve the quality of life

### **Omega-3 to Omega-6 fatty acids**

Omega-3 to omega-6 fatty acids are found in fish oil, soya bean oil, flaxseed oil, sunflower oil, and sesame oil and these can decrease the production of TNF-alpha and IL-1 beta, thus providing a more favourable background environment for the effective application of drug therapies for RA. Omega-3 fatty acids may help reduce inflammation. Omega-3 fatty acids have the potential for sparing pharmaceuticals and decreasing the side effect profile and also reduce the risk of heart disease in RA patients (Marcolina, ST, 2006).

### **Bromelain**

Pineapple contains the proteolytic enzyme bromelain. Bromelain blocks the production of kinins, the compounds produced during inflammation that increase swelling and induce pain (JA. Duke, 1997). There is evidence that oral therapy with bromelain produces certain analgesic and anti-inflammatory effects in patients with rheumatoid arthritis, which is one of the most common autoimmune diseases (Pavan R *et al.*, 2012)

### **Gamma Linolenic Acid (GLA)**

Gamma linolenic acid is an essential fatty acid found in borage seed oil and black currant seed oil. The immune responses, inflammation, and joint tissue injury in RA may be controlled by treatment with GLA oil (Reed, G. W *et al.*, 2014 & L. J. Leventhal *et al.*, 1994).

### **Folic Acid**

The modest amounts of this vitamin are beneficial for the patients with RA who have the better-controlled disease because folic acid supplements allow them to tolerate MTX therapy (JE Baggott, SL Morgan, 2008). A study conducted by S. L. Whittle, R. A. Hughes (2004) that oral folic acid supplement of 5 mg was prescribed routinely for all patients receiving MTX for the treatment of RA. The results showed that the supplemental folic acid decreases the elevation in plasma homocysteine associated with the use of MTX. This may, in turn, reduce the risk of cardiovascular disease, which is over-represented amongst patients with RA.

### **Vitamin D**

Vitamin D deficiency is common among in patients with RA, and that vitamin D deficiency may be associated with disease severity in RA. Supplementation of this vitamin could possibly be used as an adjunct therapy with DMARDs in patients with active RA (Hajjaj-Hassouni, N *et al.*, 2017). Also, vitamin D supplementation may be needed for pain relief in patients with RA (Kostoglou-Athanassiou I *et al.*, 2012).

### **CONCLUSION**

Rheumatoid arthritis patients are at high risk of obesity, abnormal vitamin levels, and poor nutrient intakes. Rheumatoid arthritis patients require a stable, healthy diet for a number of different reasons. They may sustain their chronic pain and inflammation, remain undernourished, or endure medical complications without an appropriate diet. Considering the diet as part of RA treatment, the dietary approaches addressed in this review it is certain that nutrition plays a crucial role in the management of this autoimmune disease RA. However, the use of food as

conventional diet therapy should be carefully assessed due to the possibility of food-drug interactions. In this view, nutrition may serve as phytotherapy are used to manage rheumatoid arthritis. In conclusion, RA patients are encouraged to follow a stable and healthy diet that aids in managing disease condition, boosting their immune system and protecting overall health.

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