www.foodandfeed.fins.uns.ac.rs
FOOD AND FEED RESEARCH
Journal of the Institute of Food Technology – FINS
University of Novi Sad
ISSN
2217-5369
(print version ceased in 2023)
2217-5660 (online)

UDK 613.2:612.392:616.72-002.77
https://doi.org/ 10.5937/foodandfeedresearch0-67296

Review

EXPLORING FUNCTIONAL FOODS AND BIOACTIVE COMPOUNDS IN RHEUMATOID ARTHRITIS MANAGEMENT: A NUTRIGENOMIC AND AI-DRIVEN PERSPECTIVE

Shirin Fargana Bava, Millicent Mabel M*, Irine Jerald, Monica Muniendra Babu, Selva Kumar TA

Rajalakshmi Engineering College, Department of Biotechnology, Thandalam, Chennai - 602105, India

Abstract: Systemic inflammation and gradual joint damage are the indications of rheumatoid arthritis (RA), a chronic inflammatory disease. While biologics and disease-modifying antirheumatic medications (DMARDs) continue to be the primary form of RA treatment, their long-term usage is often restricted because of their high cost and potential adverse effects. As a result, complementary approaches that integrate precision medicine-based nutritional interventions are gaining increasing scientific support. From a nutrigenomic and artificial intelligence approach, this review examines the function of bioactive substances and functional foods in the treatment of RA. Bioactive compounds (BCs) derived from cereals, legumes, fruits, vegetables, probiotics, and omega-3-rich foods, such as polyphenols, antioxidants, and essential fatty acids modulate immune response, oxidative stress, and inflammatory pathways involved in the pathophysiology of RA. However, genetic variants that impact nutrient absorption, metabolism, and bioavailability contribute to variability in clinical efficacy. Gene-nutrient interactions involving VDR, MTHFR, FADS, and HFE, which control vitamin D signalling, folate metabolism, fatty acid conversion, and iron homeostasis, respectively, are highlighted by nutrigenomic data. Predictive modelling of individual dietary responses to nutritional therapies is made possible by recent developments in Artificial intelligence (AI) and Machine learning (ML), which enable the combination of genetic, microbiome, and dietary data. Functional foods, nutrigenomics, and AI-driven analytics integrate to offer a potential foundation for creating individualised, long-term RA treatment plans.

Key words: *functional foods, chronic inflammatory disease, nutrigenomics, bioactive compounds, artificial intelligence, machine learning*

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterised by extra-articular involvement and inflammatory arthritis. It is a chronic disease with inflammation primarily targeting synovial joints, affecting approximately 1% of the world's population. It is caused by the interplay of various environmental and genetic factors, such as smoking (Gunes-Bayir et al., 2023; Klareskog et al., 2020). According to the Global Burden of Disease (GBD), the age-standardised prevalence rate of RA will increase to 0.21% globally in the year 2020, affecting more than 17.6 million people, representing a 14.1% increase since 1990 (Gao et al., 2024).

Corresponding author: Phone: +91 9176170575
E-mail address: millicentmable.m@rajalakshmi.edu.in

Epidemiological data further indicate that approximately 70% of individuals with RA are female, and more than half of the affected population is above the age of 55 (WHO, 2023).

Additionally, it affects extra-articular organs, including the gastrointestinal, renal, pulmonary, and cardiovascular systems (Ahmed et al., 2008). Current therapeutic strategies for RA primarily involve corticosteroids, biologics, DMARDs, and Non-Steroidal Anti-inflammatory Drugs (NSAIDs). While these medications can partially slow disease progression and reduce joint damage, long-term RA treatment, particularly with biologics and targeted therapies, imposes a significant financial burden (Shi et al., 2020; Mennini et al., 2017). India's healthcare system is distinguished by its combination of private and public providers. Most Indians receive their medical care in the private sector, where the expenses account for more than two-thirds of the total cost spent for health benefits in the public sector comparatively (Dieleman et al., 2017). The financial burden on lower-socioeconomic stratum households makes matters worse due to the high cost of care and a lack of health insurance (Kumar et al., 2011).

Regarding the use of Complementary and Alternative medicine (CAM) modalities as treatment methods for RA patients, the American College of Rheumatology in the position statement notes the increase in interest in CAM approaches among the population, and thus emphasises the necessity of conducting strict scientific investigation into any possible therapy for rheumatic diseases (Comella et al., 2015).

From that standpoint, one should consider nutrient intake and nutrition as potentially significant environmental risk factors influencing the occurrence and progression of the conditions under discussion (Pattison et al., 2004). The importance of nutrition science in connection with food and certain compounds that may either provoke or prevent inflammation due to their properties is emphasized (Calder et al., 2013).

Although the findings still remain inconclusive, there exist several investigations on links between dietary practices, including the consumption of fruits, vegetables, or meat, and the occurrence of the condition. Thus, it becomes clear that through investigating ways to use nutrition practices to decrease health care expenses, one might identify an effective approach to managing RA.

Immunopathological basis of rheumatoid arthritis

When susceptibility factors stimulate the formation of autoantibodies to produce the immune response, adaptive immunity is triggered towards peptidylarginine and peptidylcitrulline. Antigen-presenting cells (APCs) deliver these changes into the lymphatic tissues, where inflamematory cytokines (IL-6,8,17 etc.) are synthesised due to the activation of macrophages, APCs, and FLS. The immune response is further stimulated by immune complex and complement activation. Synthesis of cytokines and synovial vascular inflammation will lead to synovial inflammation and bone disintegration (Wójcik et al., 2021).

Genetics and epigenetics are one of the many complex features associated with the pathogenesis of RA. It involves an elaborate sequence of immunological and molecular events initiated by various genetic and environmental factors. Individuals who carry the risk genes, especially the alleles of HLA-DRB1, are more likely to develop autoimmune disorders in the case of exposure to certain environmental factors, including smoking, infections, or microbiome alterations (Sokolova et al., 2021). These environmental factors increase post-translational modifications of proteins via the citrullination process mediated by the peptidyl arginine deiminase (PAD) enzyme. This leads to citrullinated proteins. The immune system perceives the modified proteins as a neoantigen, which triggers the production of anti-citrullinated protein antibody (ACPA) with activation of auto-reactive B and T cells (Ding et al., 2023). Consequently, inflammation will be increased due to the immune reaction, resulting in immune cell infiltration and formation of an inflamamatory microenvironment. Inflammation leads to synovial hyperplasia and pannus formation, causing cartilage breakdown and bone erosion via osteoclast activation (Deshmukh, 2023). One of the most popular antipyretic and analgesic medications is NSAIDs. Its primary method of reducing inflammation is by blocking COX, which lowers the synthesis of prostaglandins. Regrettably, both selective and non-selective NSAIDs are linked to a significant risk of adverse events, such as cardiovascular and gastrointestinal problems, while new biologics are more expensive (Ge et al., 2022). All these events contribute to RA development. Understanding this complicated sequence of events

provides a scientific background for a nutraceutical approach to RA management along with drug therapy. Nutritional components are able to affect many factors involved in the above-mentioned pathophysiological pathway, including cytokine secretion, MAPK, NF-κB signaling and oxidative stress. For instance, polyphenols (resveratrol, quercetin) and omega-3 fatty acids affect the NF-KB and MAPK pathways; antioxidants found in fruits and millets lower oxidative stress levels, and curcumin and fucoidan block COX-2 and LOX activity.

This review aims to summarise the evidence regarding functional foods and bioactive compounds in RA management, evaluate gene-nutrient interactions influencing nutrient bioavailability and therapeutic response, and explore the role of artificial intelligence and machine learning in developing personalised nutrition strategies for RA patients.

MATERIALS AND METHODS

When susceptibility factors stimulate the formation of autoantibodies to produce the immune response, adaptive immunity is triggered towards peptidylarginine and peptidylcitrulline. Antigen-presenting cells (APCs) deliver these changes into the lymphatic tissues, where inflammatory cytokines (IL-6,8,17 etc.) are synthesised due to the activation of macrophages, APCs, and FLS. The immune response is further stimulated by immune complex and complement activation. Synthesis of cytokines and synovial vascular inflammation will lead to synovial inflammation and bone disintegration (Wójcik et al., 2021).

Genetics and epigenetics are one of the many complex features associated with the pathogenesis of RA. It involves an elaborate sequence of immunological and molecular events initiated by various genetic and environmental factors. Individuals who carry the risk genes, especially the alleles of HLA-DRB1, are more likely to develop autoimmune disorders in the case of exposure to certain environmental factors, including smoking and infections. The present review was conducted using the PRISMA 2020 guidelines that ensured transparency in the identification, screening, eligibility, and inclusion processes of selected articles. In addition, the topic covered by this review considered the involvement of functional foods and bioactive compounds in managing rheumatoid arthritis, along with genomic or artificial intelligence approaches.

Search strategy

A comprehensive literature search was conducted using Scopus, PubMed, Web of Science, ScienceDirect, and Google Scholar to identify relevant publications on rheumatoid arthritis, functional foods, nutrigenomics, personalised nutrition, and artificial intelligence. In PubMed, both MeSH terms and free-text keywords were used to enhance the retrieval of relevant literature. Search terms included “Rheumatoid Arthritis”, “Functional Foods”, “Nutrigenomics”, “Bioactive Compounds”, “Precision Nutrition”, “Artificial Intelligence”, “Machine Learning”, and “Gene–Diet Interactions”, combined using Boolean operators (AND, OR). Peer-reviewed original research articles, clinical studies, systematic reviews, meta-analyses, and recent review articles published between 2006 and 2026 were considered for inclusion. Additional information was obtained from reports, guidelines, and fact sheets published by recognised organisations such as FAO, WHO, and FSSAI. Reference lists of selected articles were also screened to identify further relevant studies.

Eligibility criteria

Eligibility criteria entailed studies that had been written in the English language, were related to rheumatoid arthritis, and looked into functional food items, bioactive components, immunelogical/inflammation-related pathways, gut microbiota, genomic linkages, and/or artificial intelligence-based techniques pertaining to nutritional therapies for RA. Both original research studies and clinically relevant reviews of the literature were taken into consideration. Duplicates, abstracts from conferences, editorials, commentaries, and studies not related to the topic of the present review were excluded.

Study selection

A flowchart of studies was designed using the PRISMA flow chart approach, which includes the number of records identified, screened, excluded and included, with reasons for exclusion at the full text stage of the search procedure. Duplicate articles were initially removed, and thereafter, the titles/abstracts were scrutinized for relevancy. Inclusion/exclusion criteria were applied to full-text articles considered for the present review.

Data extraction

Information extracted from every article selected for inclusion in the study included author, date of publication, research methodology used in the investigation, bioactive compounds under discussion or food items discussed, proposed mechanisms or theories explaining potential effects of certain substances on health, and relation to rheumatoid arthritis, genomics, or use of an AI-based approach.

Reporting considerations

The period of research covered included publiccations issued between 2001 and 2026, and a total number of 640 sources were found using the above-listed databases. After the exclusion of 145 duplicate papers, 495 studies were left for screening based on title and abstracts. 300 of those papers were not relevant, and therefore, they were not used further in the review process. 195 papers proceeded to the next stage of evaluation, but another 80 records were excluded because of low thematic relevance, non-scientific character of publications, unavailability of a complete paper, or lack of relevance to the review purpose, or microbiome alterations (Sokolova et al., 2021).

These environmental factors increase post-translational modifications of proteins via the citrullination process mediated by the peptidyl arginine deiminase (PAD) enzyme. This leads to citrullinated proteins. The immune system perceives the modified proteins as a neoantigen, which triggers the production of anti-citrullinated protein antibody (ACPA) with activation of autoreactive B and T cells (Ding et al., 2023). Consequently, inflammation will be increased due to the immune reaction, resulting in immune cell infiltration and formation of an inflammatory microenvironment. Inflammation leads to synovial hyperplasia and pannus formation, causing cartilage breakdown and bone erosion via osteoclast activation (Deshmukh, 2023). One of the most popular antipyretic and analgesic medications is NSAIDs. Its primary method of reducing inflammation is by blocking COX, which lowers the synthesis of prostaglandins. Regrettably, both selective and non-selective NSAIDs are linked to a significant risk of adverse events, such as cardiovascular and gastrointestinal problems, while new biologics are more expensive (Ge et al., 2022). All these events contribute to RA development. Understanding this complicated sequence of events provides a scientific background for a nutraceutical approach to RA management along with drug therapy. Nutritional components are able to affect many factors involved in the above-mentioned pathophysiological pathway, including cytokine secretion, MAPK, NF-κB signalling, and oxidative stress. For instance, polyphenols (resveratrol, quercetin) and omega-3 fatty acids affect the NF-KB and MAPK pathways; antioxidants found in fruits and millets lower oxidative stress levels, and curcumin and fucoidan block COX-2 and LOX activity.

This review aims to summarise the evidence regarding functional foods and bioactive compounds in RA management, evaluate gene-nutrient interactions influencing nutrient bioavailability and therapeutic response, and explore the role of artificial intelligence and machine learning in developing personalised nutrition strategies for RA patients.

FUNCTIONAL FOODS AND BIOACTIVE COMPOUNDS FOR RA MANAGEMENT

Definition and significance of functional foods

Functional foods are defined as foods with biologically active ingredients that offer health advantages beyond simple nutrition due to their correlation with physiological health benefits associated with the prevention of multiple chronic diseases (Alkhatib et al., 2017). These are referred to by various terminology, including nutraceuticals, designer foods, vita foods, pharma foods, medicinal foods, super foods and more (Essa et al., 2021). Another accepted definition is that they are “Foods that contain substances, in addition to nutrients, that may have potentially positive effects on health, beyond basic nutrition” (FAO, 2022). Functional foods encompass a wide range of food categories including cereals, legumes, seeds, vegetables, fruits, dairy products, beverages, fishes, herbs and spices. Each category offers unique health-promoting properties such as anti-inflammatory, immune-supportive, and disease-preventive effects. Additionally, they help prevent cancer, osteoporosis, high blood pressure, cholesterol, improve digestion, ease pain, and manage diabetes and depression (Das et al., 2011). Depending on the source, components, mechanism, chemical nature and properties, including live microorganisms such as probiotics (Fig. 1), which provide health benefits in addition to fundamental dietary elements.

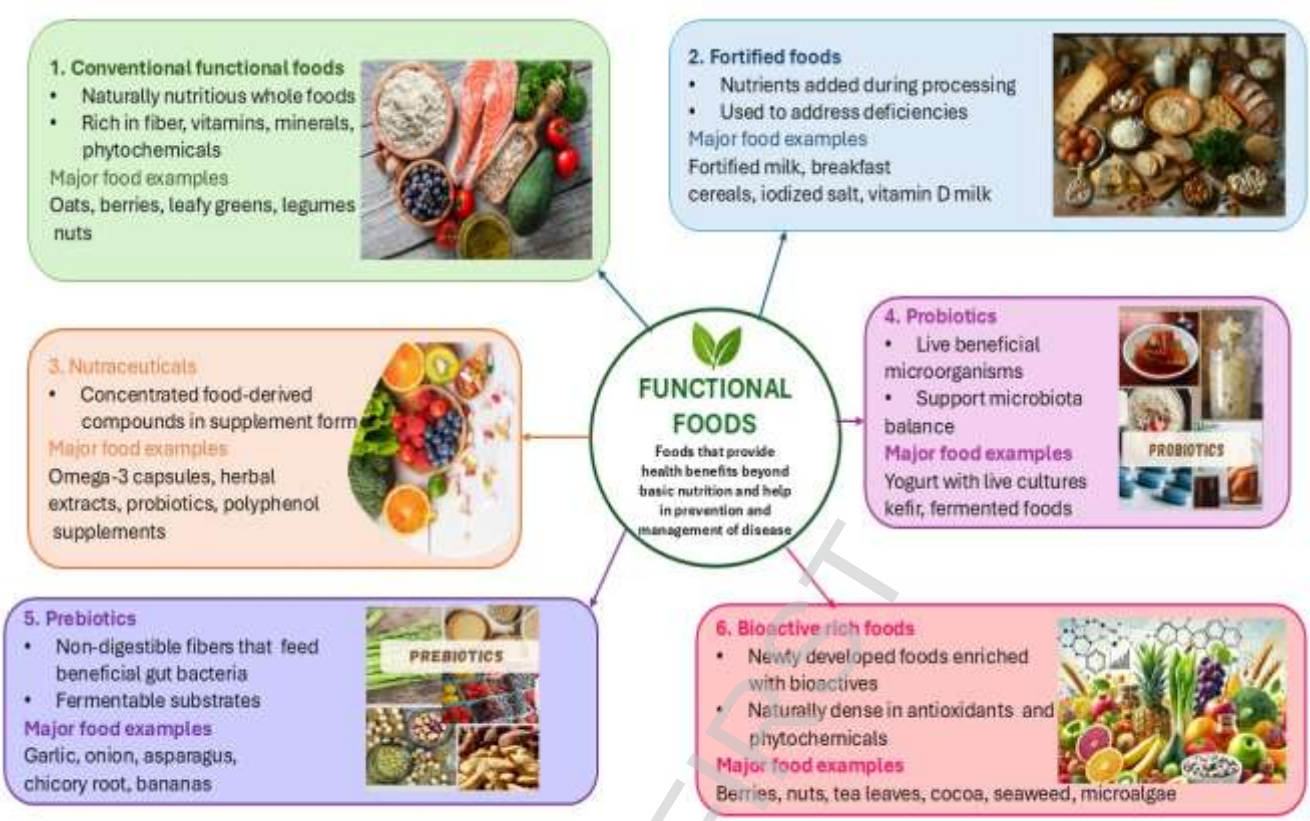

Figure 1. Categorization of functional foods

Overview of bioactive compounds from functional food that benefit RA management

Functional foods contain a wide range of Bioactive Compounds (BCs) that distinguish them from conventional food choices. These constituents, which range from vitamins, minerals, phytochemicals and essential fatty acids contains health-promoting properties that go beyond simple sustenance (Akhtar et al., 2023). Antioxidants, which neutralise dangerous free radicals and lower inflammation and oxidative stress, are abundant in many functional foods. Omega-3 fatty acids lessen the risk of heart disease and regulate cholesterol and are found in certain nutraceuticals (Bachheti et al., 2022). In addition to supporting digestive health, fibre, a prominent ingredient in functional foods, helps control body weight by increasing the feeling of satiety (Temple, 2022).

These natural dietary ingredients are either organic or inorganic substances that have the ability to modulate multiple metabolic pathways or processes, enhancing health and fostering wellbeing. Studies indicate a strong relationship between health, well-being, and functional dietary elements (Abuajah et al., 2014). Functional components thereby promote health at various stages of ailment control, which are linked to several progressive processes, from initiation to development. They can therefore be effectively utilised for treatment to prevent illnesses (Salehi et al., 2020).

Phytochemicals are physiologically active, nutrient-free substances derived from plants that function in the human body to postpone the onset of a number of chronic illnesses and more than 900 phytochemicals are identified in food (Busch et al., 2015). Mostly dietary polyphenols may help prevent the onset and symptoms of RA, based on the evidence from cell culture studies, animal models and clinical trials. They have been shown to lower plasma levels of inflammatory mediators as well as morning stiffness, discomfort and post-activity pain in RA patients (Christman & Gu, 2020).

For instance, allicin from garlic reduces synovial inflammation by inhibiting NF-κB activation and suppressing the production of proinflammatory cytokines including TNF-α and IL-6 (Borlinghaus et al., 2014). Ginger has gin-

gerol and shogaol, which decrease prostaglandin and leukotriene production, which are linked to joint inflammation by inhibiting COX-2 and 5-LOX enzymes. Clinical studies in RA patients have demonstrated reductions in pain scores and inflammatory markers with ginger supplementation (Gunathilake & Rupasinghe, 2014). Honey-derived polyphenols, including caffeic acid and kaempferol, reduce oxidative stress and suppress macrophage-mediated inflammatory signalling relevant to synovial pathology (Rao et al., 2017). Anthocyanins from berries such as blueberries and strawberries scavenge reactive oxygen species, downregulate NF-κB-driven cytokine expression, and have demonstrated cartilage-protective effects in preclinical arthritis models (Devore et al., 2012). The main bioactive component of turmeric, curcumin, decreases COX-2 expression, inhibits NF-κB and AP-1 transcription factors, and lowers blood levels of IL-1β, TNF-α and IL-6. DAS28 scores have significantly decreased in RA patients using curcumin supplements, according to many randomised controlled studies (Aggarwal & Sung, 2008). The benefits of green tea catechins, especially epigallocatechin-3-gallate (EGCG), include reducing cartilage degradation in collagen-induced arthritis models, lower matrix metalloproteinase activity in Fibroblast-like Synoviocytes (FLS), and blocks IL-6 mediated JAK/STAT signaling (Yang & Wang, 2016). Collectively, these phytochemicals illustrate how diverse BCs in functional foods converge on fundamental inflammatory pathways that are essential to RA pathogenesis.

Mechanism of action and therapeutic potential of BCs from food source

Cereals

One of the primary categories of functional food is cereals, which include wheat bran, oats, and maize. These foods are widely recognized for their high fiber content, which is crucial for maintaining digestive health and excluding conditions like constipation and diverticulitis (Khan et al., 2022). Along with lowering cholesterol and controlling blood sugar, fibre promotes cardiovascular health (Konstantinidi & Koutelidakis, 2019). Furthermore, certain grains include phytochemicals like phenolic acids that function as antioxidants and shield the body from oxidative stress, inflammation, and oxidative damage (Guo et al., 2021). Rice-derived natural peptide networks and zein peptides target TNF-α/IL-1β in chondrocytes and NF-κB in endothelial cells. Broken rice peptides inhibit NO/cytokines in LPS-macrophages, zein blocks TNF-α monocyte adhesion via NF-κB suppression and rapeseed peptides (LY/RALP/GHS) reduce ROS/lipid peroxides. Clinical studies indicate that rice-derived NPNs inhibit TNF-α and improve inflammatory status in ageing populations (human trial) (Kennedy et al., 2020).

Legumes

Because of their distinct nutritional profile, soybean and derivatives such as soy protein isolate, soy milk, soy oil, tofu and tempeh stand out within the legume family (Kumar et al., 2024). They are particularly noteworthy for having a high protein and isoflavone content, which improves heart health by lowering LDL cholesterol levels (Setchell & Lydeking-Olsen, 2003). Isoflavones, a kind of phytoestrogen that is prevalent in soybeans, play a major role in the metabolism of bone tissue, improving its density and preventing bone loss (Miedziaszczyk et al., 2023). Lunasin (43-aa soybean peptide) reduces IL-1β chondrocyte proliferation, type II collagen loss and inhibits synovial fibroblast proliferation/apoptosis via MMPs (Jia et al., 2015). Genistein suppresses FLS exosomes (Rab27/nSMase2/Mfge8/Dvl3/β-catenin/miR-221-3p) and enhances osteoblast mineralisation (Liu et al., 2025). Apart from soy, chia seed-derived peptides contain a high concentration of protein compared to cereals and are rich in polyphenols. It exhibits anti-inflammatory activity by attaching to immunological receptors, reduces NF-κB translocation, inhibits the inflammatory enzymes COX and nitric oxide synthase (NOS) (Mensah et al., 2024).

Seafoods and oils

Fatty fishes like mackerel, salmon, and tuna are rich in omega-3 fatty acids, which are vital for heart functionality, cognitive function, and decreasing inflammation. Omega-3 fatty acids like EPA and DHA are crucial for maintaining cardiovascular health because they lower blood pressure and the risk of heart attacks and strokes (Jovanovic et al., 2021). By stimulating blood valve relaxation and reducing arterial stiffness, alpha-linolenic acid (ALA), a kind of omega-3 fatty acid that is prevalent in flaxseed oil, may enhance blood flow and heart health (Thomas et al., 2015). In RA, EPA/DHA reduces pro-inflammatory eicosanoids (COX-2), cytokines (IL-1β/TNF-α/IL-6) via monocyte modulation

in combination with metformin targets like JAK/STAT, PI3K/AKT/mTOR, TLR and MAPK. Clinical trials have shown the reduction of DAS28/NSAIDs and plasma IL-1β in fish oil RCTs (El-Sayyad et al., 2021).

Vegetables

Sometimes called "leafy greens," the BCs found in leafy vegetables exhibit several biochemical properties (Sagar et al., 2018). Although they are only found in minimal levels, these metabolites are essential to the secondary metabolism of plants (Pateiro et al., 2023). Nutrient content and phytocompounds are abundant in leafy vegetables including spinach, tomatoes, onions, garlic, carrots and psyllium. These are essential sources of vitamins, minerals, and dietary fibers have antioxidant, anti-cancer and anti-inflammatory effects (Koss-Mikołajczyk et al., 2019). The lowest risk for cancer was found at 600 g/day consumption, while the lowest risk for stroke, CVD and mortality was found at 800 g/day of consumption (Aune et al., 2016). The body converts beta-carotene, a strong antioxidant found in carrots, into vitamin A, which is essential for immunity and ocular wellness. Lycopene is an acyclic isomer of β-carotene that raises glutathione/IL-10, decreases TNF--α/IL-6/myeloperoxidase, inhibits IL-1β induced NF-κB/STAT3 in chondrocytes, and activates NrF2 (Dixit et al., 2023). Psyllium's high fibre content promotes good digestion and blood sugar regulation. Leafy greens like spinach and kale are rich in minerals like calcium and iron, as well as vitamins A, C, and K. These substances inhibit cytokines, synovial hyperplasia, and inflammation in CIA rats by targeting the MAPK pathways (Wickramasinghe et al., 2020). Quercetin and Organosulfur compounds found in garlic and onions demonstrates the ability to target cytokine production, T/B cell modulation, decrease pro-inflammatory genes and boost Treg induction, lowering the risk of cardiovascular disease (Ried et al., 2018).

Fruits

Citrus fruits such as lemon, oranges, and grapefruit are rich in vitamin C content, flavonoids (quercetin, rutin, and kaempferol, naringin, hesperidin), coumarins, terpenoids (limonoids and carotenoids), carotenoids (α- and β-carotene, violaxanthin, lutein) and pectin. Kaempferol inhibits the activation of NF-κβ and phosphorrylation of ERK1/2, p38, and JNK by lowering the levels of cytokine IL-1 β (Aruoma et al., 2012). It acts as a powerful antioxidant that is essential for scavenging free radicals in the body, shielding cells from oxidative damage, and lowering inflammation (Baiano & Del Nobile, 2015). Avocados are a great source of oleic acid and other good monounsaturated fats that lowers cholesterol and prevents breast cancer. It contains vitamin E, a carotenoid called lutein, which prevents prostate cancer from developing. Also, the high potassium content of avocados is associated with lowering blood pressure (Mezzomo & Ferreira, 2016).

Raspberry extract has anthocyanins and ellagitannins that protect cartilage and reduce inflammation in explants/CIA rats. An in vivo study reported that mangiferin from mangoes downregulates IL-1β, IL-6, and TNF-α, inhibits NF-κB signalling, and activates ERK1/2. Fig contains ficin and polyphenols, which reduce oxidative stress and improve histology in CFA rats. Bell peppers contain capsaicin that targets COX-2 pathways and shows a reduction in IL-6/TNF-α in CFA rats (Bala & Gupta, 2026). Magnesium, calcium, manganese, phosphorus, and copper are the minerals that are abundant in pears. According to Carluccio *et al*. (2016), these minerals help to prevent the loss of bone mineral, which is beneficial in preventing diseases like osteoporosis (Carluccio *et al*., 2016).

Dairy foods

Probiotics, calcium, and vitamin D are present in abundance in yoghurt and other fermented dairy products. By balancing the intestinal flora, probiotic bacteria present in these foods help to preserve gut health, facilitating digestion and nutrient absorption (Ratajczak et al., 2021). Probiotics may also lower the chance of developing several chronic conditions, such as irritable bowel syndrome and inflammatory bowel disease.

Calcium and vitamin D, which are essential for strong bones, osteoporosis prevention, and tooth development, are found in dairy products (Ivanov *et al*., 2021). They modulate RA related signalling pathways primarily via gut-immune modulation, producing SCFAs (butyrate/acetate) that inhibit NF-κB/TLR4, restore Th17/Treg balance, enhance epithelial barriers (Zo-1/TJs), and suppress cytokines (TNF-α/IL-6/IL-17/IL-12) while boosting IL-10/Tregs. Strains like *Lactobacillus casei*, *Bifidobacterium adolescentis*, *L. helveticus*, and *Parabacteroides histicola* show preclinical/clinical efficacy (Ferro et al., 2021).

Though the immunomodulatory and anti-inflammatory potential of functional foods and bioactive compounds is demonstrated, their clinical efficacy is inconsistent across patients. This variability is mainly attributed to the individual's genetic architecture rather than the patients' therapeutic response to dosages, its formulations or the severity of the disease. The cytokine suppression achieved in one patient by following one particular dietary intervention may not be effective for another due to inherited variations in the absorption process, metabolization and bioconversion of nutrients in to active form. Hence, knowledge about gene-nutrient interaction is important for translating the functional food therapy into consistent, personalized clinical approaches for RA management.

GENOMIC INSIGHTS IN NUTRIENT ABSORPTION AND METABOLISM

The relationship between the human genome and nutrient metabolism is highly individualised compared to traditional guidelines. In the context of RA, understanding how genomic variation shapes nutrient absorption, metabolism, and bioavailability is critical, as the efficacy of functional foods and their bioactive compounds as therapeutic agents is substantially modulated by the genetic architecture of the individual patient.

Nutritional science is presently using high-throughput "omics" scientific technologies, such as proteomics, metabolomics, transcriptmics, microbiomics, and genomics, to determine the underlying mechanisms of the detrimental effects of certain nutrients and to provide accurate dietary recommendations (Cassotta et al., 2021). Food choices and diet are the key environmental variables that interact with the genome, transcriptome, proteome, metabolome and microbiota. This lifelong interaction determines an individual's state of health and illness (Gioia et al., 2020).

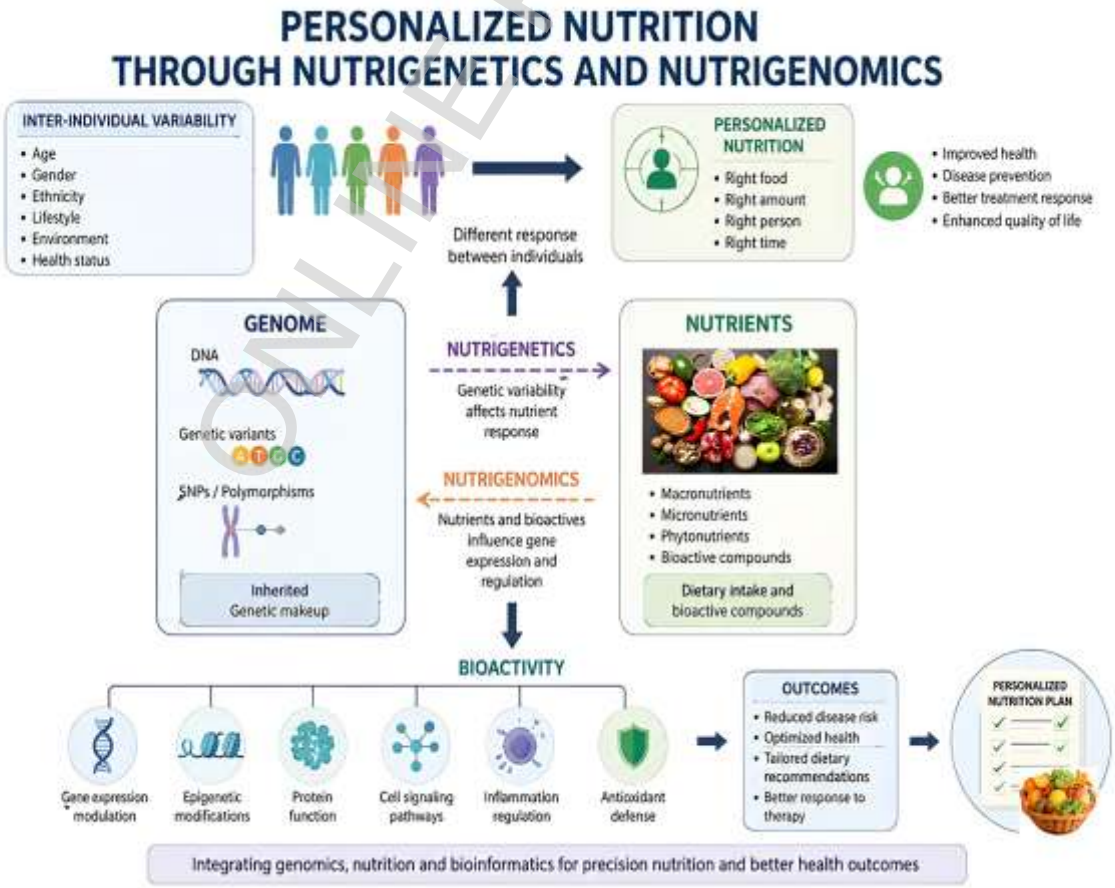

Figure 2. Personalized nutrition through nutrigenetics and nutrigenomics

Table 1.
Key genes and their nutrient - RA relevance

Gene	Nutrient affected	Mechanism	RA Relevance	References
VDR	Vitamin D	Receptor binding efficiency	Immune modulation, anti-inflammatory signaling	Bonetti et al., 2022
MTHFR	Folate, B12	Enzyme activity reduction	Homocysteine elevation, DNA methylation, oxidative stress	Shane et al., 2018
FADS1/FADS2	Omega-3 (EPA, DHA)	Desaturase activity, PUFA conversion	Pro- or anti-inflammatory eicosanoid balance	Coulson & Mutch, 2025
HFE	Iron	Intestinal absorption regulation	Oxidative injury in synovium, anaemia of inflammation	Stover, 2006
HLA-DRB1	Microbiome-mediated	Gut microbiota composition	Polyphenol bioavailability, gut-joint axis	Hu et al., 2025
APOE	Dietary lipids	Lipid transport and metabolism	Modulates lipid related inflammatory pathways and CVD risk in RA	Toga & Mazziotta, 2007
PPARG	Fatty acids, Polyphenols	Regulation of adipogenesis and inflammation	Influences inflammatory cytokine production and metabolic responses	Song et al., 2022
PPARA	Fatty acids, Polyphenols	Fatty acid oxidation and energy metabolism	Mediates anti-inflammatory effects of omega-3 fatty acids	Paradis et al., 2005
CYP2R1	Vitamin D	Encodes the primary hepatic 25-hydroxylase responsible for conversion of vitamin D to 25-hydroxyvitamin D [25(OH)D]	Genetic variants in CYP2R1 influence circulating vitamin D levels, potentially affecting immune regulation, inflammation, and susceptibility to autoimmune diseases including RA	Akter et al., 2026
NR1H3	Cholesterol-derived oxysterols, dietary lipids, omega-3 fatty acids	Regulates lipid metabolism, cholesterol homeostasis, and inflammatory responses	Activation of NR1H3 (LXRα) suppresses pro-inflammatory cytokine production and macrophage activation, suggesting a protective role in RA-associated inflammation	Mooijaart et al., 2007

In its broadest contemporary definition, nutrigenomics refers to the use of genomics, proteomics, transcriptomics, metabolomics, and epigenomics to clarify the molecular relationships between gene and nutrient. It also includes nutrigenetic studies that investigate relationships between genetic variants and diet in regulating disease risk (Sales et al., 2014), as depicted in Fig. 2. The integrated use of genetic polymorphisms into nutritional epidemiology research has direct therapeutic value for RA patients. This has made it possible for researchers to address several limitations, notably genetic variability that affecting absorption, distribution, metabolism, elimination and biotransformation of a nutrient or bioactive food component.

Single nucleotide polymorphisms and their role in nutrient metabolism and bioavailability

The most prevalent type of genetic variation in the human genome is represented by single nucleotide polymorphisms (SNPs), which are crucial for examining the variations in dietary responses across individuals. Nutrigenetics is presently employed to assess the genes involved in transport and metabolism of nutrients, elimination of toxins, and defense against oxidetive stress, which are pertinent to the pathophysiology of RA (Table 1).

Vitamin D receptor (VDR) gene polymorphism

Vitamin D is an immunomodulatory micronutrient with documented relevance to autoimmune inflammation. Variants in the vitamin D-related VDR gene have commonly been associated with the risk of a range of skeletal and non-skeletal health outcomes, as well as autoimmune illnesses including RA and systemic lupus erythematosus (Niforou et al., 2020). SNPs in the VDR gene influence vitamin D availability and are associated with an increased risk of osteoporosis in individuals with less calcium intake (Bonetti et al., 2022). Beyond bone health, reduced VDR signalling efficiency due to polymorphic variants is a particular concern in RA,

where immune dysregulation is the central pathological feature.

Methylene Tetrahydrofolate Reductase (MTHFR) gene and folate metabolism

The MTHFR gene encodes a key enzyme in folate metabolism. The C677T (rs1801133) SNP is a C to T transition at position 677, causes alanine to valine substitution, producing a thermostable protein with reduced activity. Individuals with the TT genotype show lower folate, higher homocysteine and increased disease risk (Molloy, 2011). The C677T polymorphism appears as T/T in 5-10% and C/T up to 40% of the general population. Together with A1298C, it reduces MTHFR activity, impairs folate accumulation, and elevates plasma homocysteine, a vascular disease risk factor (Shane et al., 2018). In RA, elevated homocysteine also amplifies systemic oxidative stress and endothelial dysfunction, compounding articular and cardiovascular comorbidities. Significantly folic acid supplementation can mitigate the negative health effects of these SNPs by decreasing plasma homocysteine levels (Farhud et al., 2010).

High Iron Fe (HFE) gene and iron absorption

Iron dysregulation is an underappreciated facet of RA-associated anaemia and inflammatory burden. The HFE gene carries a common Cys282Tyr polymorphism linked to hereditary haemochromatosis, an iron overload disorder that causes excess deposition in the liver, heart, and endocrine glands. The HFE protein regulates cellular iron balance and controls intestinal absorption by modulating transferrin receptor – transferrin interactions (Stover, 2006). Variants in HFE may therefore modulate iron-mediated oxidative injury in RA synovial tissue, while altering the bioavailability of dietary iron from functional foods.

Fatty Acid Desaturase (FADS) gene cluster: Omega-3 fatty acid metabolism and inflammatory signalling

The most clinically consequential genomic factor in the context of RA and functional food therapy is variation in FADS gene clusters like FADS1 and FADS2 genes. Their interactions activate key fatty acid desaturases that transform linoleic (LA) and alpha-linolenic acid (ALA) into their long-chain, highly unsaturated fatty acid (HUFA) counterparts. These gene-nutrient interactions impact the levels of n-6 and n-3 HUFA, which are subsequently transformed into a broad range of lipids with signalling roles, such as eicosanoids, docosanoids, other oxylipins, and endocannabinoids (Chilton et al., 2022).

Eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA) are two examples of n-3 long-chain polyunsaturated fatty acids (LC-PUFAs) that have potent anti-inflammatory capabilities. FADS1 and FADS2 genes mediate their shared pathway with n-6 PUFA production. Changes in LC-PUFA levels and FADS1/2 expression are linked to genetic variations in the FADS gene cluster (Coulson & Mutch, 2025).

SNPs in the FADS gene cluster affect endogenous conversion of α-linolenic acid (ALA) to EPA and DHA. Variant alleles in FADS1/2 reduce desaturase activity, lowering circulating levels of EPA. This has therapeutic relevance in rheumatoid arthritis, as uniform omega-3 supplementation may be inadequate. Patients with minor FADS allele defects may benefit more from direct EPA/DHA intake from marine sources rather than plant derived ALA (Wang et al., 2020).

Additionally, FADS1 and FADS2 genetic polymorphisms are linked to fatty acid metabolism by altering gene expression and DNA methylation. This implies that the connection between chromosomal diversity and PUFA availability is mediated by epigenetic processes (He et al., 2018). The epigenetic factors introduce additional complexity, such as dietary bioactive compounds such as curcumin and resveratrol, which modulate DNA methylation patterns. This may indirectly influence fatty acid metabolism in FADS variant carriers.

Gut microbiome, genetic susceptibility, and nutrient bioavailability

Factors affecting nutrition absorption do not only include variations in the metabolic enzymes. The genetic makeup of the patient will impact the nature of the gut microbiota and hence will influence the availability of the bioactive compounds in the food consumed. Some of the susceptibility alleles associated with RA include the HLA-DRB1, PTPN22 and PADI4 alleles and are identified through genome-wide association studies (GWAS).

Surprisingly, even individuals who are asymptomatic but carry the HLA-DRB1 susceptibility

allele present unique changes in the gut microbiota, where there is an increase in abundance of Lachnospiraceae, Clostridiaceae and Bifidobacterium longum (Hu et al., 2025). These changes in microbiota composition influence the ability of the gut to convert polyphenols and flavonoids, among others to biologically available forms. Also, previous studies investigated the impact of a Mediterranean Diet enriched with fermented foods on gut microbiota and rheumatoid arthritis (RA) outcomes. It aims to explore how dietary interventions can improve disease activity and inflammation in RA patients, bridging the gap between nutrition and disease management (Charneca et al., 2025).

Dietary components like fibres, polysaccharides, and resistant starch are identified as influential in combating RA by modulating gut microbiota and impacting immune responses (Shan et al., 2025). To facilitate adaptive barrier responses in the mucosal tissue, hypoxia-inducible factor (HIF) is critical in the regulation of tight junction proteins such as claudin-1.

Maintenance of gut barrier integrity and regulation of iron intake require HIF-2α, whose expression is specific to the mucosal epithelium (Das et al., 2019). Disruption of this pathway, particularly due to the associated inflammation, could impair the ability of the gut to absorb iron, zinc and lipophilic bioactive compounds.

Epigenetic modulation of nutrient-gene interactions in RA

Beyond static SNP-based genome variation from diet, the additional epigenetic reprogramming of RA synoviocytes influences the translation of genetic mechanisms to immunological effects. Phytochemicals or any other bioactive components, including secondary metabolites of the plant, inhibit the expression of inflammatory or catabolic mediators, thus avoiding the onset of inflammatory arthritis. Besides this, phytonutrients also regulate the remodelling of the histones and non-coding RNAs involved in inflammatory pathways, including the DNA methylation epigenetic modification (Villagrán-Andrade et al., 2024).

Some of the gene variations include FTO, APOE and MTHFR, whose presence changes the way people respond to either macronutrients or micronutrients in terms of oxidative stress and inflammation, among others. With the use of various epigenetic mechanisms, which include DNA methylation, histone modification and miRNA, phytonutrients such as polyphenols, Omega-3 Fatty Acids and vitamins play an important role in controlling gene expression (Antony, 2025).

Clinical implications towards genotype-guided nutritional therapy in RA

Numerous research works confirm the shift towards personalized diet and nutritional therapy in order to prevent or treat RA in a genotype-guided manner. Application of multiple omics technologies allows finding novel biomarkers associated with the intake of particular foods. In addition, this makes human nutrition studies possible and, thus, provides the opportunity to develop preventative measures for RA among vulnerable populations. It can also enhance the effectiveness of existing treatment strategies (Cassotta et al., 2021).

PREDICTIVE AI IN NUTRIGENOMICS FOR RA

Application of nutrigenomic discoveries in the development of dietary strategies for RA patients is currently limited by methodological issues such as classical statistical techniques. While GWAS helped gain substantial knowledge about the genetics of complex disorders, prediction of the disease and/or traits' outcomes on the basis of such studies is currently impossible because of statistical models' limitations (Agrawal et al., 2025).

Recent studies addressed the integration of artificial intelligence (AI) in nutrition, highlighting its potential to enhance public health through innovative solutions in dietary assessment and disease prevention. This integration is significant as it can optimise dietary recommenddations and improve individual nutritional outcomes, which are crucial for managing health issues like diabetes (Theodore Armand et al., 2024). However, recent advances in AI and ML offer unprecedented opportunities for solving the issue.

Nutrition for Precision Health (NPH), being an initiative of the NIH All of Us Research Program, is dedicated to the development of AI-based predictive algorithms for food response at the individual level. With the use of genetics, microbiome, metabolomics and lifestyle factors, this program aims to shift from a "one size fits all" diet model to personalised nutrition (NIH, 2025).

Multi-SNP nutrigenomic models through machine learning architectures

The primary strength of ML compared to conventional statistics is the capability of modelling nonlinear, multi-dimensional relationships between multiple genotypes, diets and immunelogical outcomes all at once. ML methods are increasingly used in nutrigenomics to study complex interactions between genes and dietary variables, which can then be used to make tailored recommendations about nutrition. CNNs and other forms of deep learning are particularly suitable for analysing genomic and microbiome data as biological indicators of nutrition sensitivity and improving biomarker discovery scaling and precision (Doussiere et al., 2026; Yu et al., 2018).

In addition, gradient-boosted machine learning models like XGBoost can iteratively refine their predictions, giving them an edge in the face of class imbalance and large feature spaces typical of RA genomic datasets. ML polygenic scoring of RA risk has shown remarkable results. 60-70% of variation in RA susceptibility is attributable to genetics. ML studies have successfully created predictive models using SNPs combined with traditional risk factors, whereby the best results were obtained using the XGBoost algorithm, as measured by key metrics such as area under the curve and F-1 scores (Xu & Wu, 2025; Shi et al., 2024).

Critically, utilizing each SNP as a separate predictor may be advantageous since treating SNPs as predictors does not rely on assumptions about additivity, whereas poly-genic risk scores do. Therefore, this method could more effectively capture polygenic liability of RA (Dubey et al., 2024). This distinction is especially important for nutrigenomic modelling, where the joint effects of multiple low-penetrance variants on fatty acid metabolism or folate bioavailability cannot be captured by additive linear models.

PRS-Net is an interpretable geometric deep learning framework that deconvolutes genome-wide polygenic risk scores at single-gene resolution. It leverages graph neural networks to capture gene-gene interactions through message passing. This approach enhances disease prediction, including RA (Wang, 2025).

AI integration of multi-omics data for holistic dietary prediction

AI-driven nutrigenomic profiling, integrated with multi-omics and computational biology, enables precision nutrition with high accuracy in predicting individual metabolic responses (Hsu et al., 2025). A process known as deep phenotyping, which evaluates observable traits resulting from a combination of genetic, epigenetic, societal, environmental, and behavioural influences, is made possible by integrating data from demographic profiles, genomic and omics-based sources, and lifestyle metrics. This allows for the development of precise nutrition strategies tailored to individual health needs (Mahdavi, 2025; Wani et al., 2026). For RA patients, deep phenotyping unifies HLA-DRB1 genotype, microbiome, cytokines, nutrients and diet into an AI model delivering real-time, genotype-aware dietary recommendations.

Large-scale trials like PREDICT validated multi-omics AI nutrition, achieving approx. 60% accuracy in forecasting individual glycemic and lipid variability (Mukherjee et al., 2024). The FOOD4ME trial showed genotype-guided nutrition led to greater, sustained 24-month reductions in BMI and cholesterol versus general advice (Celis-Morales et al., 2016). Translating this paradigm to RA-specific functional food research represents one of the most promising frontiers in the field.

AI for bioactive compound discovery and functional food optimisation for RA

AI is instrumental in accelerating the bioactive compound discovery process for the treatment of RA and optimizing functional food products to minimize inflammation. Several recent studies describe AI applications in virtual screening, predictive modeling, and peptide characterization for RA target compounds such as TNF-α (Nabi et al., 2024). AI models conduct virtual screening on natural compounds using RA targets (TNF-α, TYK2, IL-6) and predict bioactivity (pIC50), thereby identifying hits such as Imperiageniline and Gelsemine. Multi-target virtual screening and molecular dynamics simulations identify Rutaecarpine and Hecogenin as potential candidates (Mansouri et al., 2025). AI models transform peptide discovery from a traditional screening process to a predictive modelling framework by selecting rice-derived NPNs to inhibit TNF-α and increase strength in inflammaging populations. This results in early identification of bioactive compounds, enabling efficient development of functional ingredients for alleviating RA symptoms (Kennedy et al., 2020). Explainable

AI (XAI) addresses the "black box" problem of AI algorithms by providing explanations to the decision-making process, connecting genomic information (for example, SNPs in RA patients) with diet recommendations and health outcomes. It is vital for nutrigenomic research in RA because of the complexity of gene-diet interactions, requiring trust from physicians and regulators (Toussaint et al., 2023). While traditional deep learning makes predictions based on nutrient responses, explainable AI techniques such as SHAP (SHapley Additive exPlanations) provide insights into variant-specific dietary recommendations. Table 2 describes the AI-nutrigenomics workflow in Functional food therapy (Wang et al., 2025).

Patients' perspective regarding AI in rheumatology care

In Germany, a country-wide survey conducted among 778 patients suffering from a rheumatic disorder showed high interest in AI applications, especially when dealing with symptom checkers, treatment advice, and Chabot.

Even though the majority of patients (26.8%) did not apply AI to their healthcare practice, 57.8% were still ready to do so and appreciated physician-assisted diagnosis performed by using AI solutions. The most important advantages that were mentioned include better access to information and rapidness of disease identification, yet some disadvantages were also found, such as wrong application of artificial intelligence and lack of human touch, in addition to data confidentiality issues. Cluster analysis resulted in identifying three main groups, namely AI-skilled, AI-practical, and AI-pessimistic, that depended mainly on demographic variables such as age and education (Labinsky et al., 2025).

PERSONALIZED APPROACHES IN RA MANAGEMENT

In contrast to the traditional "treat-to-target" concept that implies similar therapeutic goals for different patients with a heterogeneous clinical presentation, personalised RA management considers individual characteristics such as genotypes, multifactorial biomarker profiles, and severity of comorbid conditions, microbiota composition, and dietary traits, thus facilitating a patient-specific intervention strategy. This approach is more holistic in comparison with the conventional disease activity-based management. It not only utilizes consolidated "treat-to-target" approach, but also factors linked to improved quality of life of patients, including dietary regimen. This approach may reduce the risk of adverse effects while improving treatment outcomes and preventing the occurrence of flare-ups by up to 30-50% (Dey et al., 2024).

Table 2.
The AI-nutrigenomics pipeline for RA functional food therapy

AI methodology	Nutrigenomic application in RA	Key advantages	References
XGBoost	SNP-based prediction of nutrient risk	High dimensionality; handles stratification	Xu & Wu, 2025
Random Forest	Prediction of treatment response and identification of nutrient related biomarkers	Handles high-dimensional genomic data; robust against overfitting	Kennedy et al., 2020
Artificial Neural Network (ANN)	Modelling complex interactions and patient-specific responses	Captures non-linear relationships	Agrawal et al., 2025
Deep Learning Models	Multi-SNP interaction; FADS pathway risk	Captures non-linear gene-diet	Wang et al., 2022
Graph Neural Network (GNN)	Analysis of disease interactions	Identifies biological network relationship effectively	Doussiere et al., 2026
Transformer Models	Multi-omics + dietary data integration	Contextual reasoning across heterogeneous data	Mukherjee et al., 2024
Polygenic Risk Score (PRS) Based Models	Risk stratification and identification of genetically susceptible individuals	Supports personalized prevention strategies	Wang, 2025
Explainable AI (SHAP)	Genomic recommendations	Clinical-regulatory transparency	Wang et al., 2025
Multi-Omics Integration Platform	Integration of genomics, transcriptomics, metabolomics, microbiome and dietary information	Enables comprehensive precision nutrition approach	Cassotta et al., 2021
Clinical Decision Support System (CDSS)	Decision support administered directly to patients through health records	Facilitates translation of research findings into clinical practice	Sutton et al., 2020

Genetic profiling based on identification of specific single-nucleotide polymorphisms (SNPs), specifically SNPs in MTHFR and VDR genes, enables optimised dosage of folates and vitamin D. This is primarily due to the influence of folate levels in determining the efficacy and toxicity of methotrexate (MTX), which remains the first-line DMARD. Previous studies have demonstrated that individualisation of nutritional intervention according to one's metabolic capacity helps to enhance the effectiveness of MTX therapy by 20-40% and, at the same time, to reduce the risk of adverse effects associated with MTX administration, such as gastrointestinal problems or hepatotoxicity (Wang et al., 2022). As far as the economic costs of RA are concerned, they are associated mainly with expensive biologic agents and indirect costs associated with disabilities. Personalised treatment strategies might help to stabilise the disease in its early stage, thereby reducing the use of expensive biologic therapies and JAK inhibitors for RA-related healthcare. Consequently, improved disease control and lower DAS28 scores may help maintain patient productivity. This approach may help reduce work disability and productivity loss among patients with RA and prevent "presenteeism" syndrome (Dey et al., 2024). Moreover, personalization of RA therapy includes pharmacological interventions and socio-environmental factors that influence the disease treatment. Hence, these frameworks, such as the chronic care model or ecological model of health, may prove helpful (Ohta & Sano, 2023).

CLINICAL EVIDENCE OF FUNCTIONAL FOODS IN RA

Clinical evidence of the role of functional foods in RA comes from RCTs and animal experiments where there is evidence of the anti-inflammatory effect mediated through bioactive agents such as omega-3s, polyphenols, and probiotics, resulting in DAS28 score reduction by 0.5-1.5 points. Though a promising strategy in combination with DMARDs, evidence of their efficacy differs across the type of functional food, with PUFAs and dietary intervention having more supporting evidence (Alwarith et al., 2019). Clinical trials with personalized dietary advice for early-stage RA patients show insignificant yet encouraging results of lower levels of inflammation markers, lipids profile, and higher levels of micronutrients such as vitamin C, iron, fibre, and folate after six months than the standardized diet. Individuals adhering to personalized intervention during clinical trial showed significant improvement in physical activity and nutrition intake which could be beneficial for future treatment (Van Den Bruel et al., 2025). Some of the clinical and observational studies regarding functional foods and bioactive compounds in rheumatoid arthritis are summarized in Tab. 3 below.

There is growing clinical evidence supporting the use of functional foods as adjuvant therapies in RA. However, substantial heterogeneity has been observed across studies (I^2 = 60%- 80%), attributable to variations in dosing, formulations, and patient baseline characteristics. For instance, the use of omega-3 results in variable effects on DAS28 (1-10 g of EPA and/or DHA daily). A major limitation of many studies is the small sample size, which is less than 100 participants, leading to an increased probability of Type II errors and CIs. Only 20% of RCTs had a sample size of more than 50 participants. Furthermore, challenges remain in the standardisation and bioavailability of functional food ingredients. Hence, well-designed and standardised clinical studies are required to establish an efficient and safe intervention of functional foods in the management of RA.

LIMITATIONS

Considerable interest has emerged in the use of functional foods, nutrigenomics, and artificial intelligence for RA management, but there are very limited clinical studies. Moreover, these studies exhibit substantial clinical and methodological heterogeneity because most studies have a relatively small sample size, limited duration of intervention, and variable outcome measures. Variations in dietary compositions, bioactive compounds' concentration, patient characteristics, and analytical methodologies used in research further create challenges in the interpretation of the study. In addition to this, there are several other limitations, such as the lack of standardized biomarkers availability in nutrigenomics studies, inadequate external validation by predictive models, and the longitudinal integration of clinical data for AI applications. Addressing these challenges and limitations is essential for a well-established personalised nutrient strategy for RA management.

Table 3.
Clinical evidence of functional foods in RA

Functional food / Compound	**Study type**	**Effect size**	**Key findings**	**Relevance to RA**	**References**
Omega-3 fatty acids (EPA/DHA)	Randomized clinical trials	DAS28 WMD -0.47, NSAID ↓ 20%	Reduced joint pain, morning stiffness, and NSAID use	Anti-inflammatory via eicosanoid modulation	Kostoglou-Athanassiou et al., 2020
Curcumin (turmeric)	Clinical trial	DAS28 WMD -1.47 (95% CI -2.39 to -0.55)	Reduced DAS28 score and inflammatory cytokines	Inhibits NF-κB and inflammatory signalling	Zhang & Niu, 2025
Mediterranean diet	Longitudinal cohort study	HR - 0.17, CI [0.08 -0.37]	Improved physical function and reduced disease activity	High antioxidants and anti-inflammatory nutrients	Alawadhi et al., 2023
Probiotics (Lactobacillus spp.)	Clinical intervention study	CRP SMD -0.97 ($p<0.01$), DAS28 -0.6	Reduced CRP levels and improved gut microbiota balance	Modulates gut-immune axis	Paul et al., 2021
Polyphenols (green tea catechins)	Experimental + clinical evidence	DAS28 WMD -1.76 (95%CI -2.71, -0.81)	Reduced oxidative stress and inflammatory markers	Antioxidant and immune regulatory effects	Long et al., 2023
Vitamin D	Observational + clinical studies	DAS28/CRP (r = - 0.13)	Low vitamin D associated with increased RA severity	Immunomodulatory via VDR signaling	Charoenngam, 2021
Resveratrol	Randomized controlled clinical trials	DAS28 WMD -1.8	Reduced inflammatory cytokines and oxidative stress	Suppression of NF-kB signaling and oxidative damage	Khojah et al., 2018
Quercetin	Randomized controlled clinical trials	DAS28 – 1.4 ($p<0.05$)	Reduced joint inflammation and oxidative stress	Antioxidant and anti-inflammatory activity	Javadi et al., 2016
Genistein	Preclinical + experimental studies	$P<0.05$	Downregulation of inflammatory mediators	Modulation of cytokine signaling pathways	Moosavian et al., 2020
Allicin	Randomized, double-blind, placebo-controlled trial	DAS28 5.20 ± 0.82 ($P<0.001$)	Reduced inflammatory responses and oxidative stress	Antioxidant and immune modulatory effects	
Plant-based diets	Review and clinical evidence	-	Improved inflammatory status and quality of life	Reduced pro inflammatory dietary load	Alwarith et al., 2019
Dietary fibre and prebiotic rich foods	Clinical and observational studies	-	Improved gut microbiota and reduced inflammation	Production of short-chain fatty acids and immune regulation. Supports microbiome targeted nutrition	Das et al., 2019; Ferro et al., 2021

FUTURE RESEARCH DIRECTIONS

While the above findings indicate a clear shift toward a more integrative approach to RA care with an increased focus on functional foods, nutrigenomics, and AI, many translational barriers persist. First, multi-omics clinical trials that are needed to evaluate the combined effects of genomic, transcriptomic, metabolomics, gut microbiome, and dietary parameters interaction on treatment efficacy should be conducted to provide prospective intervention designs. Specifically, standard criteria for biospecimen handling and outcome reporting are crucial for such trials to increase their translational potential (Gong et al., 2024; Xue et al., 2025). Second,

validation of AI models in independent populations of RA patients is necessary for clinical practice to confirm the robustness of the results and ensure minimal data quality and explainability biases in real-life settings. Indeed, recent findings indicate that machine learning based on metabolomic profiles could be successfully externally validated, showing its applicability to future nutrigenomics investigations (Tang et al., 2025). Third, nutrigenomic biomarkers should be standardised through a consensus panel involving all factors, including inflammation, nutrient metabolism, gut microbiome activity, and treatment response. Such measures would support the principles of reproducibility and interlaboratory comparability known to be critical for successful translational studies in nutrition science (Nourazarain & Vaziri, 2025). Fourth, longitudinal trials lasting 6 to 12 months are required for dietary interventions in RA patients to assess sustained changes, adherence, relapse prevention, and safety of such treatments (Raad et al., 2024).

CONCLUSION

The current approach to the management of RA represents a profound paradigm shift from population-level standardised treatment through a "treat-to-target" approach towards a highly specialised and personalised model. Although pharmacologic treatments still remain the backbone of the therapy, the prohibitive cost of biological agents and adverse effects of chronic administration requires introduction of sustainnable and complementary treatment methods. Functional foods and bioactive substances derived from diverse dietary sources, including polyphenolic substances and antioxidants from plants or omega-3 fatty acids isolated from marine animals, have demonstrated considerable potential in managing inflammation and oxidative stress related to RA. Another important finding from the literature is that the efficacy of nutrition-related therapies depends greatly on the genetic makeup of the patients. Specific mutations in the genes encoding vitamin D receptor (VDR), methylene tetrahydrofolate reductase (MTHFR), and fatty acid desaturases (FADS) affect the availability and uptake of certain nutrients, consequently affecting the response to nutritional interventions. The emergence of AI/ML technologies represents another significant driver of this paradigm shift. Through the use of advanced neural networks and machine learning approaches such as GNN and XGBoost, a clinician can move beyond correlation coefficients and develop predictive analytics that would take into account the high dimensionality of complex interactions between multi-omics data and dietary phenotypes. Concurrently, advances in nutrigenomic studies, including genomic profiling, targeted prediction of phytochemical targets, and AI-based design of functional foods, are contributing to the development of personalised nutrient treatment. Patients' attitude towards personalised medicine and rapid advances in technologies supports the transition from the concept of conventional nutrition towards precision nutrition in RA management, which also incorporates socioenvironmental determinants of health.

AUTHORS' CONTRIBUTION

Conceptualization, literature search, data curation, methodology, writing-original draft preparation, visualization, S.F.B.; Review & editing, data curation, M.M.M.; Writing, I.J.; Writing – review, visualization, investigation, M.M.B.; Writing – review & editing, validation, supervision, conceptualization; S.K.T.

All authors have read and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

No new data were generated or analyzed in this study. Data sharing is not applicable to this article.

FUNDING

No funding was received for this manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Abuajah, C. I., Ogbonna, A. C., & Osuji, C. M. (2014). Functional components and medicinal properties of food: A review. *Journal of Food Science and Technology*, 52(5), 2522–2529. https://doi.org/10.1007/s13197-014-1396-5

Aggarwal, B. B., & Sung, B. (2008). Pharmacological basis for the role of curcumin in chronic diseases: an age-old spice with modern targets. *Trends in Pharmacological Sciences*, *30*(2), 85–94. https://doi.org/10.1016/j.tips.2008.11.002

Agrawal, K., Goktas, P., Kumar, N., & Leung, M. (2025). Artificial intelligence in personalized nutrition and food manufacturing: a comprehensive review of methods, applications, and future directions. *Frontiers in Nutrition*, *12*, 1636980. https://doi.org/10.3389/fnut.2025.1636980

Ahmed, S., Marotte, H., Kwan, K., Ruth, J. H., Campbell, P. L., Rabquer, B. J., Pakozdi, A., & Koch, A. E. (2008). Epigallocatechin-3-gallate inhibits IL-6 synthesis and suppresses transsignaling by enhancing soluble gp130 production. *Proceedings of the National Academy of Sciences*, *105*(38), 14692–14697. https://doi.org/10.1073/pnas.0802675105

Akhtar, S., Gupta, A. K., Varshney, A., Rawat, M., Choudhary, A., Kandpal, R., Jha, A. K., Mishra, S., Naik, B., Kumar, V., Ranjan, R., Rather, M. A., Rustagi, S., & Preet, M. S. (2023). Comprehensive review of sustainable utilization of Arenga obtusifolia Griff. as a food. *Journal of Agriculture and Food Research*, *15*, 100945. https://doi.org/10.1016/j.jafr.2023.100945

Akter, S., Ibrahim, M. N. B., Mahmud, Z., Tamanna, S., Shawon, M. S. H., Ansari, F., & Howlader, M. Z. H. (2026). Genetic association and computational analysis of CYP2R1 gene polymorphisms rs2060793 and rs12794714 with vitamin D deficiency and acute myocardial infarction in the Bangladeshi population: A case control study. *PLoS ONE*, *21*(6), e0350994. https://doi.org/10.1371/journal.pone.0350994

Alawadhi, B., Alsaber, A., Shatawan, I., Al-Herz, A., Setiya, P., Saleh, K., Al-Awadhi, A., Hasan, E., Al-Kandari, W., Mokaddem, K., Ghanem, A., Attia, Y., Hussain, M., Alhadhood, N., Ali, Y., Tarakmeh, H., Aldabie, G., AlKadi, A., Alhajeri, H., & Aldei, A. (2023). Adherence to the Mediterranean diet is associated with a reduced DAS28 index among patients with rheumatoid arthritis: Case study from KRRD. *International Journal of Rheumatic Diseases*, *26*(12), 2430–2440. https://doi.org/10.1111/1756-185x.14928

Alkhatib, A., Tsang, C., Tiss, A., Bahorun, T., Arefanian, H., Barake, R., Khadir, A., & Tuomilehto, J. (2017). Functional foods and lifestyle approaches for diabetes prevention and management. *Nutrients*, *9*(12), 1310. https://doi.org/10.3390/nu9121310

Alwarith, J., Kahleova, H., Rembert, E., Yonas, W., Dort, S., Calcagno, M., Burgess, N., Crosby, L., & Barnard, N. D. (2019). Nutrition interventions in rheumatoid arthritis: the potential use of plant-based diets. A review. *Frontiers in Nutrition*, 6, 141. https://doi.org/10.3389/fnut.2019.00141

Antony, J. (2025). Recent trends in nutrigenomics and personalized diet: A mini review. *International Journal of Biology Sciences*, *7*(8), 191–195. https://doi.org/10.33545/26649926.2025.v7.i8c.465

Aruoma, O. I., Landes, B., Ramful-Baboolall, D., Bourdon, E., Neergheen-Bhujun, V., Wagner, K., & Bahorun, T. (2012). Functional benefits of citrus fruits in the management of diabetes. *Preventive Medicine*, *54*, S12–S16. https://doi.org/10.1016/j.ypmed.2012.02.012

Aune, D., Giovannucci, E., Boffetta, P., Fadnes, L. T., Keum, N., Norat, T., Greenwood, D. C., Riboli, E., Vatten, L. J., & Tonstad, S. (2016). Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality—a systematic review and dose-response meta-analysis of prospective studies. *International Journal of Epidemiology*, *46*(3), 1029–1056. https://doi.org/10.1093/ije/dyw319

Bachheti, R. K., Worku, L. A., Gonfa, Y. H., Zebeaman, M., Deepti, N., Pandey, D. P., & Bachheti, A. (2022). Prevention and treatment of cardiovascular diseases with plant phytochemicals: A review. *Evidence-based Complementary and Alternative Medicine*, *2022*, 1–21. https://doi.org/10.1155/2022/5741198

Baiano, A., & Del Nobile, M. A. (2015). Antioxidant Compounds from vegetable matrices: biosynthesis, occurrence, and extraction systems. *Critical Reviews in Food Science and Nutrition*, *56*(12), 2053–2068. https://doi.org/10.1080/10408398.2013.812059

Bala, V. C., & Gupta, A. K. (2026). Phytochemicals as a promising approach to rheumatoid arthritis: current perspectives. *BIO Integration*, *7*(1) e9. doi.org. https://doi.org/10.15212/bioi-2025-0142

Bonetti, G., Kiani, A. K., Donato, K., Kaftalli, J., Herbst, K. L., Stuppia, L., Fioretti, F., Nodari, S., Perrone, M., Chiurazzi, P., Bellinato, F., Gisondi, P., & Bertelli, M. (2022). Polymorphisms, diet and nutrigenomics. *Journal of Preventive Medicine and Hygiene*, *63*(2 Suppl 3), E125–E141. https://doi.org/10.15167/2421-248/jpmh2022.63.2s3.2754

Borlinghaus, J., Albrecht, F., Gruhlke, M., Nwachukwu, I., & Slusarenko, A. (2014). Allicin: chemistry and biological properties. *Molecules*, *19*(8), 12591–12618. https://doi.org/10.3390/molecules190812591

Busch, C., Burkard, M., Leischner, C., Lauer, U. M., Frank, J., & Venturelli, S. (2015). Epigenetic activities of flavonoids in the prevention and treatment of cancer. *Clinical Epigenetics*, *7*(1), 64. https://doi.org/10.1186/s13148-015-0095-z

Calder, P., Ahluwalia, N., Albers, R., Bosco, N., Bourdet-Sicard, R., Haller, D., Holgate, S., Jönsson, L., Latulippe, M., Marcos, A., Moreines, J., M'Rini, C., Müller, M., Pawelec, G., Van Neerven, R., Watzl, B., & Zhao, J. (2013). A consideration of biomarkers to be used for evaluation of inflammation in human nutritional studies. *British Journal of Nutrition*, *109*(S1), S1–S34. https://doi.org/10.1017/s0007114512005119

Carluccio, F., Lenucci, M., Piro, G., Siems, W., & Luño, J. (2016). Integrated medicine with vegetable derived antioxidant and vitamin D - effects on oxidative stress and bone mineral metabolism of aged patients with renal disease. *Functional Foods in Health and Disease*, *6*(6), 379. https://doi.org/10.31989/ffhd.v6i6.269

Cassotta, M., Forbes-Hernandez, T. Y., Cianciosi, D., Zabaleta, M. E., Cano, S. S., Dominguez, I., Bullon, B., Regolo, L., Alvarez-Suarez, J. M., Giampieri, F., & Battino, M. (2021). Nutrition and rheumatoid arthritis in the 'Omics' era. *Nutrients*, *13*(3), 763. https://doi.org/10.3390/nu13030763

Celis-Morales, C., Livingstone, K. M., Marsaux, C. F. M., Macready, A. L., Fallaize, R., O'Donovan, C. B., Woolhead, C., Forster, H., Walsh, M. C., Navas-Carretero, S., San-Cristobal, R., Tsirigoti, L., Lambrinou, C. P., Mavrogianni, C., Moschonis, G., Kolossa, S., Hallmann, J., Godlewska, M., Surwiłło, A., Mathers, J. C. (2016). Effect of personalized nutrition on health-related behaviour change: evidence from the Food4me European randomized

controlled trial. *International Journal of Epidemiology*, *46*(2), dyw186. https://doi.org/10.1093/ije/dyw186

Charneca S, Hernando A, Almada-Correia I, Polido-Pereira J, Vieira A, Sousa J, Almeida AS, Motta C, Barreto G, Eklund KK, Alonso-Pérez A, Gómez R, Cicci F, Mauro D, Pinho SS, Fonseca JE, Costa-Reis P, Guerreiro CS. (2025) TASTY trial: protocol for a study on the triad of nutrition, intestinal microbiota and rheumatoid arthritis. *Nutrition Journal*. Apr 7;.*24*(1), 52. https://doi.org/10.1186/s12937-025-01089-6.

Charoenngam, N. (2021). Vitamin D and rheumatic diseases: A review of clinical evidence. *International Journal of Molecular Sciences*, *22*(19), 10659. https://doi.org/10.3390/ijms221910659

Chilton, F. H., Manichaikul, A., Yang, C., O'Connor, T. D., Johnstone, L. M., Blomquist, S., Schembre, S. M., Sergeant, S., Zec, M., Tsai, M. Y., Rich, S. S., Bridgewater, S. J., Mathias, R. A., & Hallmark, B. (2022). Interpreting clinical trials with omega-3 supplements in the context of ancestry and FADS genetic variation. *Frontiers in Nutrition*, *8*, 808054. https://doi.org/10.3389/fnut.2021.808054

Christman, L. M., & Gu, L. (2020). Efficacy and mechanisms of dietary polyphenols in mitigating rheumatoid arthritis. *Journal of Functional Foods*, *71*, 104003. https://doi.org/10.1016/j.jff.2020.104003

Comella, N. F., Matilla, M. F., & Cuesta, J. A. C. (2015). Have complementary therapies demonstrated effecttiveness in rheumatoid arthritis? *Reumatología Clínica*, *12*(3), 151–157. https://doi.org/10.1016/j.reuma.2015.10.011

Coulson, M., & Mutch, D. M. (2025). Molecular insights into the functional roles of variants in the FADS gene cluster on omega-3 long-chain polyunsaturated fatty acid synthesis. *Lifestyle Genomics*, *19*(1), 9–22. https://doi.org/10.1159/000549658

Das, L., Bhaumik, E., Raychaudhuri, U., & Chakraborty, R. (2011). Role of nutraceuticals in human health. *Journal of Food Science and Technology*, *49*(2), 173–183. https://doi.org/10.1007/s13197-011-0269-4

Das, N. K., Schwartz, A. J., Barthel, G., Inohara, N., Liu, Q., Sankar, A., Hill, D. R., Ma, X., Lamberg, O., Schnizlein, M. K., Arqués, J. L., Spence, J. R., Nunez, G., Patterson, A. D., Sun, D., Young, V. B., & Shah, Y. M. (2019). Microbial metabolite signaling is required for systemic iron homeostasis. *Cell Metabolism*, *31*(1), 115-130.e6. https://doi.org/10.1016/j.cmet.2019.10.005

Deshmukh, R. (2023). Rheumatoid arthritis: Pathophysiology, current therapeutic strategies and recent advances in targeted drug delivery system. *Materials Today Communications*, *35*, 105877. https://doi.org/10.1016/j.mtcomm.2023.105877

Devore, E. E., Kang, J. H., Breteler, M. M. B., & Grodstein, F. (2012). Dietary intakes of berries and flavonoids in relation to cognitive decline. *Annals of Neurology*, *72*(1), 135–143. https://doi.org/10.1002/ana.23594

Dey, M., Busby, A., Isaacs, J. D., Pratt, A., Ndosi, M., Young, A., Lempp, H., & Nikiphorou, E. (2024). Personalised care packages for people with rheumatoid arthritis: a mixed-methods study. *RMD Open*, *10*(1), e003483. https://doi.org/10.1136/rmdopen-2023-003483

Dieleman, J. L., Campbell, M., Chapin, A., Eldrenkamp, E., Fan, V. Y., Haakenstad, A., Kates, J., Li, Z., Matyasz, T., Micah, A., Reynolds, A., Sadat, N., Schneider, M. T., Sorensen, R., Abbas, K. M., Abera, S. F., Kiadaliri, A. A., Ahmed, M. B., Alam, K., . . . Murray, C. J. L. (2017). Future and potential spending on health 2015–40: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. *The Lancet*, *389*(10083), 2005–2030. https://doi.org/10.1016/s0140-6736(17)30873-5

Ding, Q., Hu, W., Wang, R., Yang, Q., Zhu, M., Li, M., Cai, J., Rose, P., Mao, J., & Zhu, Y. Z. (2023). Signaling pathways in rheumatoid arthritis: implycations for targeted therapy. *Signal Transduction and Targeted Therapy*, *8*(1), 68. https://doi.org/10.1038/s41392-023-01331-9

Dixit, V., Kamal, S. W. J., Chole, P. B., Dayal, D., Chaubey, K. K., Pal, A. K., Xavier, J., Manjunath, B. T., & Bachheti, R. K. (2023). Functional foods: exploring the health benefits of bioactive compounds from plant and animal sources. *Journal of Food Quality*, *2023*, 1–22. https://doi.org/10.1155/2023/5546753

Doussiere, M., Aboud, A., Dequen, G., & Goëb, V. (2026). Artificial intelligence in rheumatology: from algorithms to clinical impact in osteoporosis and chronic inflammatory rheumatic diseases. *Journal of Clinical Medicine*, *15*(2), 491. https://doi.org/10.3390/jcm15020491

Dubey, S., Chan, A., Adebajo, A. O., Walker, D., & Bukhari, M. (2024). Artificial intelligence and machine learning in rheumatology. *Rheumatology*, *63*(8), 2040–2041. https://doi.org/10.1093/rheumatology/keae092

El-Sayyad, S. M., Ali, M. A., Kandil, L. S., Ragab, G. M., & Ibrahim, S. S. A. (2021). Metformin and omega-3 fish oil elicit anti-inflammatory effects via modulation of some dysregulated micro RNAs expression and signaling pathways in experimental induced arthritis. *International Immunopharmacology*, *92*, 107362. https://doi.org/10.1016/j.intimp.2020.107362

Essa, M. M., Bishir, M., Bhat, A., Chidambaram, S. B., Al-Balushi, B., Hamdan, H., Govindarajan, N., Freidland, R. P., & Qoronfleh, M. W. (2021). Functional foods and their impact on health. *Journal of Food Science and Technology*, *60*(3), 820–834. https://doi.org/10.1007/s13197-021-05193-3

(FAO) Food and Agricultural Organization of the United Nations. (2022). FAO terminology portal on functional foods. https://www.fao.org/faoterm/viewentry/en/?entryId=170967

Farhud, D., Yeganeh, M. Z., & Yeganeh, M. Z. (2010). Nutrigenomics and nutrigenetics. *Iranian Journal of Public Health*, *39*(4), 1–14. https://pubmed.ncbi.nlm.nih.gov/23113033

Ferro, M., Charneca, S., Dourado, E., Guerreiro, C. S., & Fonseca, J. E. (2021). Probiotic supplementation for rheumatoid arthritis: a promising adjuvant therapy in the gut microbiome era. *Frontiers in Pharmacology*, *12*, 711788. https://doi.org/10.3389/fphar.2021.711788

Gao, Y., Zhang, Y., & Liu, X. (2024). Rheumatoid arthritis: pathogenesis and therapeutic advances. *MedComm*, *5*(3), e509. https://doi.org/10.1002/mco2.509

Ge, J., Liu, Z., Zhong, Z., Wang, L., Zhuo, X., Li, J., Jiang, X., Ye, X., Xie, T., & Bai, R. (2022). Natural terpenoids with anti-inflammatory activities: potential leads for anti-inflammatory drug discovery. *Bioorganic Chemistry*, *124*, 105817. https://doi.org/10.1016/j.bioorg.2022.105817

Gioia, C., Lucchino, B., Tarsitano, M. G., Iannuccelli, C., & Di Franco, M. (2020). Dietary habits and nutrition in rheumatoid arthritis: can diet influence disease development and clinical manifestations? *Nutrients*, *12*(5), 1456. https://doi.org/10.3390/nu12051456

Gong, X., Su, L., Huang, J., Liu, J., Wang, Q., Luo, X., Yang, G., & Chi, H. (2024). An overview of multi-omics technologies in rheumatoid arthritis: applications in biomarker and pathway discovery. *Frontiers in Immunology*, *15*, 1381272. https://doi.org/10.3389/fimmu.2024.1381272

Gunathilake, K. P. P., & Rupasinghe, H. V. (2014). Inhibition of human low-density lipoprotein oxidation in vitro by ginger extracts. *Journal of Medicinal Food*, *17*(4), 424–431. https://doi.org/10.1089/jmf.2013.0035

Gunes-Bayir, A., Mendes, B., & Dadak, A. (2023). The integral role of diets including natural products to manage rheumatoid arthritis: a narrative review. *Current Issues in Molecular Biology*, *45*(7), 5373–5388. https://doi.org/10.3390/cimb45070341

Guo, H., Wu, H., Sajid, A., & Li, Z. (2021). Whole grain cereals: the potential roles of functional components in human health. *Critical Reviews in Food Science and Nutrition*, *62*(30), 8388–8402. https://doi.org/10.1080/10408398.2021.1928596

He, Z., Zhang, R., Jiang, F., Zhang, H., Zhao, A., Xu, B., Jin, L., Wang, T., Jia, W., Jia, W., & Hu, C. (2018). FADS1-FADS2 genetic polymorphisms are associated with fatty acid metabolism through changes in DNA methylation and gene expression. *Clinical Epigenetics*, *10*(1), 113. https://doi.org/10.1186/s13148-018-0545-5

Hsu, C., Askar, S., Alshkarchy, S. S., Nayak, P. P., Attabi, K. a. L., Khan, M. A., Mayan, J. A., Sharma, M. K., Islomov, S., & Samarkhazan, H. S. (2025). AI-driven multi-omics integration in precision oncology: bridging the data deluge to clinical decisions. *Clinical and Experimental Medicine*, *26*(1), 29. https://doi.org/10.1007/s10238-025-01965-9

Hu, W., Li, R., & Zhang, Z. (2025). Natural compounds for the treatment of rheumatoid arthritis based on the 'gut-joint axis'. *Molecular Medicine Reports*, *33*(1), 1–24. https://doi.org/10.3892/mmr.2025.13756

Ivanov, I., Petrov, K., Lozanov, V., Hristov, I., Wu, Z., Liu, Z., & Petrova, P. (2021). Bioactive Compounds produced by the accompanying microflora in bulgarian yoghurt. *Processes*, *9*(1), 114. https://doi.org/10.3390/pr9010114

Javadi, F., Ahmadzadeh, A., Eghtesadi, S., Aryaeian, N., Zabihiyeganeh, M., Foroushani, A. R., & Jazayeri, S. (2016). The Effect of quercetin on inflammatory factors and clinical symptoms in women with rheumatoid arthritis: a double-blind, randomized controlled trial. *Journal of the American College of Nutrition*, *36*(1), 9–15. https://doi.org/10.1080/07315724.2016.1140093

Jia, S., Zhang, S., Yuan, H., & Chen, N. (2015). Lunasin inhibits cell proliferation via apoptosis and reduces the production of proinflammatory cytokines in cultured rheumatoid arthritis synovial fibroblasts. *BioMed Research International*, *2015*, 1–9. https://doi.org/10.1155/2015/346839

Jovanovic, S., Dietrich, D., Becker, J., Kohlstedt, M., & Wittmann, C. (2021). Microbial production of polyunsaturated fatty acids — high-value ingredients for aquafeed, superfoods, and pharmaceuticals. *Current Opinion in Biotechnology*, *69*, 199–211. https://doi.org/10.1016/j.copbio.2021.01.009

Kennedy, K., Keogh, B., Lopez, C., Adelfio, A., Molloy, B., Kerr, A., Wall, A. M., Jalowicki, G., Holton, T. A., & Khaldi, N. (2020). An artificial intelligence characterised functional ingredient, derived from rice, inhibits TNF-α and significantly improves physical strength in an inflammaging population. *Foods*, *9*(9), 1147. https://doi.org/10.3390/foods9091147

Khan, J., Khan, M., Ma, Y., Meng, Y., Mushtaq, A., Shen, Q., & Xue, Y. (2022). Overview of the composition of whole grains' phenolic acids and dietary fibre and their effect on chronic non-communicable diseases. *International Journal of Environmental Research and Public Health*, *19*(5), 3042. https://doi.org/10.3390/ijerph19053042

Khojah, H. M., Ahmed, S., Abdel-Rahman, M. S., & Elhakeim, E. H. (2018). Resveratrol as an effective adjuvant therapy in the management of rheumatoid arthritis: a clinical study. *Clinical Rheumatology*, *37*(8), 2035–2042. https://doi.org/10.1007/s10067-018-4080-8

Klareskog, L., Rönnelid, J., Saevarsdottir, S., Padyukov, L., & Alfredsson, L. (2020). The importance of differences; on environment and its interactions with genes and immunity in the causation of rheumatoid arthritis. *Journal of Internal Medicine*, *287*(5), 514–533. https://doi.org/10.1111/joim.13058

Konstantinidi, M., & Koutelidakis, A. E. (2019). Functional foods and bioactive compounds: A review of its possible role on weight management and obesity's metabolic consequences. *Medicines*, *6*(3), 94. https://doi.org/10.3390/medicines6030094

Koss-Mikołajczyk, I., Baranowska, M., Todorovic, V., Albini, A., Sansone, C., Andreoletti, P., Cherkaoui-Malki, M., Lizard, G., Noonan, D., Sobajic, S., & Bartoszek, A. (2019). Prophylaxis of non-communicable diseases: why fruits and vegetables may be better chemo preventive agents than dietary supplements based on isolated phytochemicals? *Current Pharmaceutical Design*, *25*(16), 1847–1860. https://doi.org/10.2174/1381612825666190702093301

Kostoglou-Athanassiou, I., Athanassiou, L., & Athanassiou, P. (2020). The effect of omega-3 fatty acids on rheumatoid arthritis. *Mediterranean Journal of Rheumatology*, *31*(2), 190. https://doi.org/10.31138/mjr.31.2.190

Kumar, A. S., Chen, L. C., Choudhury, M., Ganju, S., Mahajan, V., Sinha, A., & Sen, A. (2011). Financing health care for all: challenges and opportunities. *The Lancet*, *377*(9766), 668–679. https://doi.org/10.1016/s0140-6736(10)61884-3

Kumar, H., Guleria, S., Kimta, N., Dhalaria, R., Nepovimova, E., Dhanjal, D. S., Alomar, S. Y., & Kuca, K. (2024). Amaranth and buckwheat grains: nutritional profile, development of functional foods,

their pre-clinical cum clinical aspects and enrichment in feed. *Current Research in Food Science*, *9*, 100836. https://doi.org/10.1016/j.crfs.2024.100836

Labinsky, H., Klemm, P., Graalmann, L., Thiele, T., Hornig, J., Fink, D., Morf, H., Mucke, J., Kiltz, U., Pecher, A., Pfeil, A., Elling-Audersch, C., Bendzuck, G., Krusche, M., Hueber, A. J., & Knitza, J. (2025). Patient experiences, attitudes, and profiles regarding artificial intelligence in rheumatology: a German national cross-sectional survey study. *Rheumatology International*, *45*(12), 269. https://doi.org/10.1007/s00296-025-06023-x

Liu, J., Shi, J., Niu, S., Liu, Z., Cui, X., Song, Y., Tang, X., Fan, J., Xu, H., Yu, W., Zhu, M., Lu, B., Liao, N., Peng, D., Wang, Y., & Yu, L. (2025). Genistein alleviates rheumatoid arthritis by inhibiting fibroblast-like synovial exosome secretion regulated by the Rab27/nSMase2/Mfge8 pathway. *Food & Function*, *16*(4), 1407–1422. https://doi.org/10.1039/d4fo05730a

Long, Z., Xiang, W., He, Q., Xiao, W., Wei, H., Li, H., Guo, H., Chen, Y., Yuan, M., Yuan, X., Zeng, L., Yang, K., Deng, Y., & Huang, Z. (2023). Efficacy and safety of dietary polyphenols in rheumatoid arthritis: a systematic review and meta-analysis of 47 randomized controlled trials. *Frontiers in Immunology*, *14*. https://doi.org/10.3389/fimmu.2023.1024120

Mahdavi, S. (2025). Advancing nutritional genomics in the era of big data, multiomics and artificial intelligence. BMJ Nutrition Prevention & Health, *8*(2), 359–362. https://doi.org/10.1136/bmjnph-2025-001238

Mansouri, P., Najafipour, S., Kouhpayeh, S. A., Farjadfar, A., & Behmard, E. (2025). Multi-target drug discovery for rheumatoid arthritis: a comprehensive computational approach using bioactive compounds. *Scientific Reports*, *15*(1), 27516. https://doi.org/10.1038/s41598-025-12666-4

Mennini, F. S., Marcellusi, A., Gitto, L., & Iannone, F. (2017). Economic burden of rheumatoid arthritis in Italy: possible consequences on anti-citrullinated protein antibody-positive patients. *Clinical Drug Investigation*, *37*(4), 375–386. https://doi.org/10.1007/s40261-016-0491-y

Mensah, E. O., Nadtochii, L., Adadi, P., & Agyei, D. (2024). Chia derived bioactive peptides: extraction, characterization, pharmacological activities and potential food applications. *Food Bioscience*, *59*, 103975. https://doi.org/10.1016/j.fbio.2024.103975

Mezzomo, N., & Ferreira, S. R. S. (2016). Carotenoids functionality, sources, and processing by supercritical technology: A review. *Journal of Chemistry*, *2016*, 1–16. https://doi.org/10.1155/2016/3164312

Miedziaszczyk, M., Maciejewski, A., Idasiak-Piechocka, I., Karczewski, M., & Lacka, K. (2023). Effects of isoflavonoid and vitamin D synergism on bone mineral density - a systematic and critical review. *Nutrients*, *15*(24), 5014. https://doi.org/10.3390/nu15245014

Molloy, A. M. (2011). Genetic aspects of folate metabolism. *Subcellular Biochemistry*, *56*, 105–130. https://doi.org/10.1007/978-94-007-2199-9_7

Mooijaart, S. P., Kuningas, M., Westendorp, R. G. J., Houwing-Duistermaat, J. J., Slagboom, P. E., Rensen, P. C. N., & Van Heemst, D. (2007). Liver X receptor alpha associates with human life span. *The Journals of Gerontology Series A*, *62*(4), 343–349. https://doi.org/10.1093/gerona/62.4.343

Moosavian, S. P., Paknahad, Z., Habibagahi, Z., & Maracy, M. (2020). The effects of garlic *(Allium sativum)* supplementation on inflammatory biomarkers, fatigue, and clinical symptoms in patients with active rheumatoid arthritis: a randomized, double-blind, placebo-controlled trial. *Phytotherapy Research*, *34*(11), 2953–2962. https://doi.org/10.1002/ptr.6723

Mukherjee, A., Abraham, S., Singh, A., Balaji, S., & Mukunthan, K. S. (2024). From data to cure: a comprehensive exploration of multi-omics data analysis for targeted therapies. *Molecular Biotechnology*, *67*(4), 1269–1289. https://doi.org/10.1007/s12033-024-01133-6

Nabi, T., Riyed, T. H., & Ornob, A. (2024). Deep learning based predictive modeling to screen natural compounds against TNF-alpha for the potential management of rheumatoid arthritis: virtual screening to comprehensive in silico investigation. *PLoS ONE*, *19*(12), e0303954. https://doi.org/10.1371/journal.pone.0303954

Niforou, A., Konstantinidou, V., & Naska, A. (2020). Genetic variants shaping inter-individual differences in response to dietary intakes - a narrative review of the case of vitamins. *Frontiers in Nutrition*, *7*, 558598. https://doi.org/10.3389/fnut.2020.558598

Nourazarain, A., & Vaziri, Y. (2025). Nutrigenomics meets multi-omics: integrating genetic, metabolic, and microbiome data for personalized nutrition strategies. *Genes & Nutrition*, *20*(1), 30. https://doi.org/10.1186/s12263-025-00790-9

(NIH) nutrition for precision health, powered by the all of us research program. (2025). https://commonfund.nih.gov/nutritionforprecisionhealth

Ohta, R., & Sano, C. (2023). Integrating clinical and socio-environmental approaches in managing rheumatoid arthritis with social determinants of health: a case study of an elderly patient in rural Japan. *Cureus*, *15*(12), e50915. https://doi.org/10.7759/cureus.50915

Paradis, A., Fontaine-Bisson, B., Bossé, Y., Robitaille, J., Lemieux, S., Jacques, H., Lamarche, B., Tchernof, A., Couture, P., & Vohl, M. (2005). The peroxisome proliferator-activated receptor α Leu162Val polymorphism influences the metabolic response to a dietary intervention altering fatty acid proportions in healthy men. *American Journal of Clinical Nutrition*, *81*(2), 523–530. https://doi.org/10.1093/ajcn.81.2.523

Pateiro, M., Domínguez, R., Munekata, P. E. S., Nieto, G., Bangar, S. P., Dhama, K., & Lorenzo, J. M. (2023). Bioactive compounds from leaf vegetables as preservatives. *Foods*, *12*(3), 637. https://doi.org/10.3390/foods12030637

Pattison, D. J., Symmons, D. P. M., Lunt, M., Welch, A., Luben, R., Bingham, S. A., Khaw, K., Day, N. E., & Silman, A. J. (2004). Dietary risk factors for the development of inflammatory polyarthritis: evidence for a role of high level of red meat consumption. *Arthritis & Rheumatism*, *50*(12), 3804–3812. https://doi.org/10.1002/art.20731

Paul, A. K., Paul, A., Jahan, R., Jannat, K., Bondhon, T. A., Hasan, A., Nissapatorn, V., Pereira, M. L., Wilairatana, P., & Rahmatullah, M. (2021). Probiotics

and amelioration of rheumatoid arthritis: significant roles of lactobacillus casei and lactobacillus acidophilus. *Microorganisms*, *9*(5), 1070. https://doi.org/10.3390/microorganisms9051070

Raad, T., George, E., Griffin, A., Larkin, L., Fraser, A., Kennedy, N., & Tierney, A. (2024). Effects of a telehealth-delivered Mediterranean diet intervention in adults with rheumatoid arthritis (MEDRA): a randomised controlled trial. *BMC Musculoskeletal Disorders*, *25*(1), 631. https://doi.org/10.1186/s12891-024-07742-1

Rao, S., Hegde, S., Rao, P., Dinkar, C., Thilakchand, K., George, T., Baliga-Rao, M., Palatty, P., & Baliga, M. (2017). Honey mitigates radiation-induced oral mucositis in head and neck cancer patients without affecting the tumor response. *Foods*, *6*(9), 77. https://doi.org/10.3390/foods6090077

Ratajczak, A. E., Zawada, A., Rychter, A. M., Dobrowolska, A., & Krela-Kaźmierczak, I. (2021). Milk and dairy products: good or bad for human bone? practical dietary recommendations for the prevention and management of osteoporosis. *Nutrients*, *13*(4), 1329. https://doi.org/10.3390/nu13041329

Ried, K., Travica, N., & Sali, A. (2018). The Effect of kyolic aged garlic extract on gut microbiota, inflammation, and cardiovascular markers in hypertensives: The GarGIC Trial. *Frontiers in Nutrition*, *5*, 122. https://doi.org/10.3389/fnut.2018.00122

Sagar, N. A., Pareek, S., Sharma, S., Yahia, E. M., & Lobo, M. G. (2018). Fruit and vegetable waste: bioactive compounds, their extraction, and possible utilization. *Comprehensive Reviews in Food Science and Food Safety*, *17*(3), 512–531. https://doi.org/10.1111/1541-4337.12330

Salehi, B., Azzini, E., Zucca, P., Varoni, E. M., Kumar, N. V. A., Dini, L., Panzarini, E., Rajkovic, J., Fokou, P. V. T., Peluso, I., Mishra, A. P., Nigam, M., Rayess, Y. E., Beyrouthy, M. E., Setzer, W. N., Polito, L., Iriti, M., Sureda, A., Quetglas-Llabrés, M. M., . . . Sharifi-Rad, J. (2020). Plant-derived bioactives and oxidative stress-related disorders: A key trend towards healthy aging and longevity promotion. *Applied Sciences*, *10*(3), 947. https://doi.org/10.3390/app10030947

Sales, N. M. R., Pelegrini, P. B., & Goersch, M. C. (2014). Nutrigenomics: Definitions and advances of this new science. *Journal of Nutrition and Metabolism*, *2014*, 1–6. https://doi.org/10.1155/2014/202759

Setchell, K. D., & Lydeking-Olsen, E. (2003). Dietary phytoestrogens and their effect on bone: evidence from in vitro and in vivo, human observational, and dietary intervention studies. *American Journal of Clinical Nutrition*, *78*(3), 593S-609S. https://doi.org/10.1093/ajcn/78.3.593s

Shan L, Chelliah R, Rahman SME, Hwan Oh D. (2025). Unraveling the gut microbiota's role in rheumatoid arthritis: dietary pathways to modulation and therapeutic potential. *Critical Reviews in Food Science and Nutrition*. *65*(17):3291-3301. https://doi.org/10.1080/10408398.2024.2362412

Shane, B., Pangilinan, F., Mills, J. L., Fan, R., Gong, T., Cropp, C. D., Kim, Y., Ueland, P. M., Bailey-Wilson, J. E., Wilson, A. F., Brody, L. C., & Molloy, A. M. (2018). The 677C→T variant of MTHFR is the major genetic modifier of biomarkers of folate status in a young, healthy Irish population. *American Journal of Clinical Nutrition*, *108*(6), 1334–1341. https://doi.org/10.1093/ajcn/nqy209

Shi, Y., Shu, H., Wang, X., Zhao, H., Lu, C., Lu, A., & He, X. (2020). Potential advantages of bioactive compounds extracted from traditional chinese medicine to inhibit bone destructions in rheumatoid arthritis. *Frontiers in Pharmacology*, *11*. https://doi.org/10.3389/fphar.2020.561962

Shi, Y., Zhou, M., Chang, C., Jiang, P., Wei, K., Zhao, J., Shan, Y., Zheng, Y., Zhao, F., Lv, X., Guo, S., Wang, F., & He, D. (2024). Advancing precision rheumatology: applications of machine learning for rheumatoid arthritis management. *Frontiers in Immunology*, *15*, 1409555. https://doi.org/10.3389/fimmu.2024.1409555

Sokolova, M. V., Schett, G., & Steffen, U. (2021). Autoantibodies in rheumatoid arthritis: historical background and novel findings. *Clinical Reviews in Allergy & Immunology*, *63*(2), 138–151. https://doi.org/10.1007/s12016-021-08890-1

Song, Y., Li, S., & He, C. (2022). PPARΓ gene polymorphisms, metabolic disorders, and coronary artery disease. *Frontiers in Cardiovascular Medicine*, *9*, 808929. https://doi.org/10.3389/fcvm.2022.808929

Stover, P. J. (2006). Influence of human genetic variation on nutritional requirements. *American Journal of Clinical Nutrition*, *83*(2), 436S-442S. https://doi.org/10.1093/ajcn/83.2.436s

Sutton, R. T., Pincock, D., Baumgart, D. C., Sadowski, D. C., Fedorak, R. N., & Kroeker, K. I. (2020). An overview of clinical decision support systems: benefits, risks, and strategies for success. *Npj Digital Medicine*, *3*(1), 17. https://doi.org/10.1038/s41746-020-0221-y

Tang, J., Jiang, R., Gao, H., Xia, J., Ma, Y., Han, Z., Yu, H., Zhang, Y., Xie, F., Sheng, H., & Lin, J. (2025). Development and multi-center validation of machine learning models based on targeted metabolomics for rheumatoid arthritis. *Journal of Translational Medicine*, *23*(1), 1257. https://doi.org/10.1186/s12967-025-07265-w

Temple, N. J. (2022). A rational definition for functional foods: a perspective. *Frontiers in Nutrition*, 9, 957516. https://doi.org/10.3389/fnut.2022.957516

Theodore Armand TP, Nfor KA, Kim JI, Kim HC. (2024). Applications of artificial intelligence, machine learning, and deep learning in nutrition: a systematic review. *Nutrients*, *16*(7), 1073. https://doi.org/10.3390/nu16071073

Thomas, J., Thomas, C. J., Radcliffe, J., & Itsiopoulos, C. (2015). Omega-3 fatty acids in early prevention of inflammatory neurodegenerative disease: a focus on Alzheimer's disease. *BioMed Research International*, *2015*, 1–13. https://doi.org/10.1155/2015/172801

Toga, A. W., & Mazziotta, J. C. (2007). Computational neuroanatomy - a dependency on databases. *MSV*, *10*(12), 3–10. https://doi.org/10.3390/life10120330

Toussaint, P. A., Leiser, F., Thiebes, S., Schlesner, M., Brors, B., & Sunyaev, A. (2023). Explainable artificial intelligence for omics data: a systematic mapping study. *Briefings in Bioinformatics*, *25*(1), 1-16. https://doi.org/10.1093/bib/bbad453

Van Den Bruel, K., Kulyk, M., Neerinckx, B., & De Vlam, K. (2025). Nutrition and diet in rheumatoid arthritis, axial spondyloarthritis, and psoriatic arthritis: a

systematic review. *Frontiers in Medicine*, *12*, 1655165. https://doi.org/10.3389/fmed.2025.1655165

Villagrán-Andrade, K. M., Núñez-Carro, C., Blanco, F. J., & De Andrés, M. C. (2024). Nutritional epigenomics: bioactive dietary compounds in the epigenetic regulation of osteoarthritis. *Pharmaceuticals*, *17*(9), 1148. https://doi.org/10.3390/ph17091148

Wang, F., Zheng, J., Cheng, J., Zou, H., Li, M., Deng, B., Luo, R., Wang, F., Huang, D., Li, G., Zhang, R., Ding, X., Li, Y., Du, J., Yang, Y., & Kan, J. (2022). Personalized nutrition: A review of genotype-based nutritional supplementation. *Frontiers in Nutrition*, *9*, 992986. https://doi.org/10.3389/fnut.2022.992986

Wang, L., Sun, X., Liang, J., Ma, Z., Li, F., Hao, S., Liu, B., Guo, L., & Weng, X. (2025). Machine learning model interpretability using SHAP values: applied to the task of classifying and predicting the nutritional content of different cuts of mutton. *Food Chemistry X*, *29*, 102739. https://doi.org/10.1016/j.fochx.2025.102739

Wang, Y. (2025). RAGNet: transformer–GNN–enhanced cox–logistic hybrid model for rheumatoid arthritis risk prediction. In proceedings of the 2025 *International Conference on Health Informatization and Data Analytics*, 90–94. https://doi.org/10.1145/3759972.3760153

Wang, Y., Tang, Y., Ji, Y., Xu, W., Ullah, N., Yu, H., Wu, Y., & Xie, L. (2020). Association between FADS1 rs174547 and levels of long-chain PUFA: a meta-analysis. *British Journal of Nutrition*, *126*(8), 1121–1129. https://doi.org/10.1017/s0007114520005103

Wani, A. K., Bashir, S. M., Elboughdiri, N., Kriaa, K., Maatki, C., Hadrich, B., Singh, J., & Singh, R. (2026). Food metagenomics integrated with multi-Omics and AI: functional insights, microbiome engineering and predictive bioprocessing for sustainable food preservation. *Trends in Food Science & Technology*, *169*, 105566. https://doi.org/10.1016/j.tifs.2026.105566

Wickramasinghe, K., Mathers, J. C., Wopereis, S., Marsman, D. S., & Griffiths, J. C. (2020). From lifespan to healthspan: the role of nutrition in healthy ageing. *Journal of Nutritional Science*, *9*. https://doi.org/10.1017/jns.2020.26

(WHO) World Health Organization. (2023). Fact sheet on rheumatoid arthritis. https://www.who.int/news-room/fact-sheets/detail/rheumatoid-arthritis

Wójcik, P., Gęgotek, A., Žarković, N., & Skrzydlewska, E. (2021). Oxidative stress and lipid mediators modulate immune cell functions in autoimmune diseases. *International Journal of Molecular Sciences*, *22*(2), 723. https://doi.org/10.3390/ijms22020723

Xu, Y., & Wu, Q. (2025). Using machine learning and single nucleotide polymorphisms for improving rheumatoid arthritis risk prediction in postmenopausal women. *PLOS Digital Health*, *4*(4), e0000790. https://doi.org/10.1371/journal.pdig.0000790

Xue, M., Wang, H., Campos, F., Jackson, C. J., & March, L. (2025). Rheumatoid arthritis: biomarkers and the latest breakthroughs. *International Journal of Molecular Sciences*, *26*(21), 10594. https://doi.org/10.3390/ijms262110594

Yang, C., & Wang, H. (2016). Cancer preventive activities of tea catechins. *Molecules*, *21*(12), 1679. https://doi.org/10.3390/molecules21121679

Yu, K., Beam, A. L., & Kohane, I. S. (2018). Artificial intelligence in healthcare. *Nature Biomedical Engineering*, *2*(10), 719–731. https://doi.org/10.1038/s41551-018-0305-z

Zhang, F., & Niu, B. (2025). Effect of curcumin on inflammatory markers and disease activity in patients with rheumatoid arthritis: a meta-analysis. *Medicine*, *104*(48), e46177. https://doi.org/10.1097/md.0000000000046177

ISTRAŽIVANJE ULOGE FUNKCIONALNE HRANE I BIOAKTIVNIH SUPSTANCI U TERAPIJI REUMATOIDNOG ARTRITISA: PERSPEKTIVA ZASNOVANA NA NUTRIGENOMICI I VEŠTAČKOJ INTELIGENCIJI

Shirin Fargana Bava, Millicent Mabel M*, Irine Jerald, Monica Muniendra Babu, Selva Kumar TA
Rajalakšmi inženjerski koledž, Departman za biotehnologiju, Tandalam, Činaj, Indija

Sažetak: Sistemska inflamacija i postepeno oštećenje zglobova predstavljaju ključne indikacije reumatoidnog artritisa (RA), hronične inflamatorne bolesti. Iako biološki lekovi i lekovi koji modifikuju tok bolesti (DMARDs) ostaju osnovna terapijska strategija, njihova dugoročna primena često je ograničena visokim troškovima i potencijalnim neželjenim efektima. Kao posledica toga, komplementarni pristupi koji integrišu nutricionističke intervencije zasnovane na principima precizne medicine dobijaju sve veću naučnu podršku. Ovaj pregled, iz perspektive nutrigenomike i veštačke inteligencije, razmatra ulogu bioaktivnih supstanci i funkcionalne hrane u tretmanu RA. Bioaktivna jedinjenja (BCs) poreklom iz žitarica, mahunarki, voća, povrća, probiotika i namirnica bogatih omega-3 masnim kiselinama, kao što su polifenoli, antioksidansi i esencijalne masne kiseline, modulišu imunološki odgovor, oksidativni stres i inflamatorne puteve uključene u patofiziologiju RA. Međutim, genetske varijante koje utiču na apsorpciju, metabolizam i biodostupnost nutrijenata doprinose varijabilnosti kliničke efikasnosti. Nutrigenomski podaci ističu interakcije gena i nutrijenata koje uključuju VDR, MTHFR, FADS i HFE, a koji kontrolišu signalizaciju vitamina D, metabolizam folata, konverziju masnih kiselina i homeostazu gvožđa. Najnoviji napredak u oblasti veštačke inteligencije (AI) i mašinskog učenja (ML) omogućava prediktivno modelovanje individualnih dijetetskih odgovora na nutricionističke terapije kroz integraciju genetskih, mikrobiomskih i dijetetskih podataka. Funkcionalna hrana, nutrigenomika i analitika zasnovana na AI zajedno nude potencijalnu osnovu za kreiranje individualizovanih, dugoročnih terapijskih planova za RA.

Ključne reči: *funkcionalna hrana, hronična upalna stanja, nutrigenomika, bioaktivna jedinjenja, veštačka inteligencija, mašinsko učenje*

Received: *16 May 2026/* ***Received in revised form:*** *03 June 2026/* ***Accepted:*** *15 June 2026*

Available online: *August 2026*