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Triangular relation of food processing, nutrition, and osteoarthritis: A solution for the management and prevention of osteoarthritis?

Arashi Shahid [a,b], Ammar B. Altemimi [c,d], Iahtisham -Ul-Haq [e], Muhammad Inam-ur-Raheem [a,**], Roshina Rabail [a], Muhammad Hamdan Rashid [a], Sadia Kafeel [a], Muhammad Saad Akram [a], Amin Mousavi Khaneghah [f,g,*], Rana Muhammad Aadil [a,***]

[a] *National Institute of Food Science and Technology, University of Agriculture, Faisalabad, 38000, Pakistan*
[b] *Sydney Musculoskeletal Health, Kolling Institute, Faculty of Medicine and Health, The University of Sydney, Sydney, 2065, NSW, Australia*
[c] *Food Science Department, College of Agriculture, University of Basrah, Basrah, 61004, Iraq*
[d] *College of Medicine, University of Warith Al-Anbiyaa, Karbala, 56001, Iraq*
[e] *Kauser Abdulla Malik School of Life Sciences, Forman Christian College (A Chartered University), Punjab, Pakistan*
[f] *Faculty of Biotechnologies (BioTech), ITMO University, 191002, 9 Lomonosova, Street, Saint Petersburg, Russia*
[g] *Halal Research Center of IRI, Iran Food and Drug Administration, Ministry of Health and Medical Education, Tehran, Iran*

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ABSTRACT

Osteoarthritis (OA) is the most common and prevalent degenerative disorder of the joints. To manage OA using a dietary approach, it is crucial to have accurate knowledge of the nutritional content and bioavailability of OA-related foods. However, the increasing dominance of food processing techniques and technologies in the food sector is a significant concern for nutrition, disease, health, and well-being, leading to imprecise nutrient intake estimation. Increased consumer health awareness regarding the therapeutic potential of diet modification in OA management has led to the requirement to assess the effect of food processing approaches on nutritional quality. This review aims to provide a comprehensive understanding of the existing evidence of the effect of different food technologies on OA-related modifiable factors like bioavailability, nutritional and bioactive content, weight management, and inflammation. Scientific evidence supports the effectiveness of nonthermal food technologies over conventional food technologies, specifically ultrasound processing, irradiation, high-pressure, carbon dioxide, electric field, microwave processing, high hydrostatic pressure, and cold plasma; and other food technologies, including food fortification, biofortification, decaffeination processing, nanotechnology, fat replacers, and food excipients, have a tremendous potential to significantly improve diet-based OA management after overcoming their limitations and health-related safety concerns. Specifically, nanotechnology and food excipients are two rapidly emerging technologies that can improve OA management by improving bioavailability and providing sustained nutrient delivery. However, further randomized controlled trials in humans are needed to understand the effects of novel food processing technologies on OA-related foods and their effectiveness for treating and/or preventing OA.

1. Introduction

Osteoarthritis (OA), the most prevalent degenerative joint disorder, characterized by excessive synovial inflammation, sclerosis cartilage, degradation, and abnormal bone growth, is a leading cause of disability worldwide among older adults. Inflammatory cytokines, particularly interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α), are involved in OA onset and progression (Shahid, Inam-ur-Raheem, Aadil,

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* Corresponding author. Faculty of Biotechnologies (BioTech), ITMO University 191002, 9 Lomonosova, Street, Saint Petersburg, Russia.
** Corresponding author.
*** Corresponding author.

E-mail addresses: raheemuaf@uaf.edu.pk (M. Inam-ur-Raheem), mousavi@itmo.ru, mousavi.amin@gmail.com (A. Mousavi Khaneghah), muhammad.aadil@uaf.edu.pk (R.M. Aadil).

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& Israr, 2022.). Over 560 million people worldwide suffer from OA, which places an enormous financial and health burden on the global and national healthcare systems (Liem et al., 2020). About 18% of women and 9.6% of men over 60 years old suffer from OA symptoms, with a quarter of these people unable to do basic daily tasks (Thomas et al., 2018). Its prevalence is expected to increase globally, leading to a greater burden on the world economy and health system by 2050 (Steinmetz et al., 2023). Australia's annual OA-related medical expenses exceed $2.1 billion (Cooper et al., 2022). OA has no effective cure; its treatment mainly focuses on managing the symptoms. Although OA is an age-related disorder, obesity, diet, and nutrition are modifiable risk factors (Thomas et al., 2018). Clinical guidelines recommend exercise and diet therapy, including weight loss, as the first line of OA treatment (Lim et al., 2022). Evidence suggests that losing 5%–10% of body weight can improve OA-related symptoms and function (Chu et al., 2018). Many pieces of research elucidated that a diet rich in antioxidants, polyphenols, flavonoids, specific minerals, vitamins, and fatty acids may play a crucial role in attenuating the OA onset and progression (Cooper et al., 2022; Thomas et al., 2018). Moreover, Thomas et al. (2018) summarized the dietary interventions related to OA. They concluded that weight reduction in obese or overweight patients, dietary management of cholesterol and fat, and achieving an adequate level of vitamins E, C, A, K, and D from dietary sources (vegetables, fruits, nuts, and milk) may be beneficial in OA management (Thomas et al., 2018). However, numerous food processing methods decrease the nutritional quality of food, as most fruits and vegetables are not often eaten raw. Food undergoes various processing stages, commercially or domestically, that alter its composition, bioaccessibility, and bioavailability (Zheng & Xiao, 2022).

Food processing procedures primarily convert raw materials into food or other products appropriate for human or animal consumption. Some other specific goals include preserving nutrient composition or improving nutrient bioavailability, increasing the availability of foods not typically available during certain seasons, and enabling food production with a broader range of aromas, flavors, or textures. Another objective of food processing is to extend the shelf life of food and products by killing or inhibiting the growth of pathogens or contaminating microorganisms (Ifie & Marshall, 2018). Growing evidence has revealed that food processing can alter food's polyphenol and nutrient content, either positively or negatively (Zheng & Xiao, 2022). Different processing methods affect the quality, quantity, bioavailability, and bioaccessibility of treated food samples' vitamins, minerals, antioxidants, and polyphenols. While many food processing methods can cause phenolic compounds to degrade, others can increase their bioavailability and absorption. The demand for safe and high-quality food items has led to the development of numerous novel food processing technologies during the past few decades. Consumers today have high standards for sensory quality, usability, and nutritional value (Arfaoui, 2021). Because conventional thermal processing has unfavorable effects on quality metrics, the need for minimally processed, high-nutrition quality, and fresh-like foods can be satisfied via nonthermal technologies. Nonthermal processing techniques are considered safe and environment-friendly because they cause no or minimal loss to nutritional or sensory attributes of food. However, these nonthermal food processing techniques have limitations (Jadhav et al., 2021). Ultra-processed food consumption is associated with higher energy intake and weight gain (Crimarco et al., 2021). Another prospective observational study concluded that a higher intake of ultra-processed food is associated with a high gain in body mass index and an increased risk of weight gain and obesity (Beslay et al., 2020).

Since the weight loss and nutritional content of food, such as vitamins, minerals, fatty acids, and polyphenols, play an important role in OA onset and progression as well as management; it is imperative to contemplate the effect of food processing on nutritional quality, quantity, and bioavailability. In addition to food processing, it is also crucial to consider the effect of other food technologies (ingredient-modified processing, food fortification, food enrichment, preservatives, and additives) on OA management by exploring their impact on OA-related modifiable factors such as weight, inflammation, nutritional content, and bioavailability of bioactive compounds. The recent review focuses on summarizing the impact of household and industrial food processing methods on dietary content, bioaccessibility, and bioavailability of beneficial nutrients in OA management. For data collection, keywords like 'osteoarthritis' AND 'innovative food processing techniques, osteoarthritis dietary guidelines' AND 'osteoarthritis-related bioactive compounds' OR 'OA-related food and food processing' were searched in various search engines such as Science Direct, Wiley, Scopus, and Google Scholar. All possible research and review articles from the past ten years were collected and extended back to 2000 to get information on OA, obesity, and food processing technologies like food replacers or thermal processing, which have been collected and thoroughly studied. To the best of our knowledge, this is the first manuscript that focuses on how food-processing technologies affect OA-related factors and how these innovative food-processing techniques can be used to improve OA-related diet therapy that can be helpful to attenuate OA. This comprehensive review can pave the way for the effective use of food processing technologies to manage or attenuate OA. Before introducing the topic, a glance at the pathophysiology of OA and the role of a diet-based approach in OA is provided.

2. Pathogenesis of OA

OA is a disorder that involves the entire joint, including the joint capsule, chondral menisci, synovium, cartilage, and bone. OA is generally understood as a non-inflammatory arthropathy involving the remodeling of bone and cartilage. However, certain investigations have consistently shown some degree of inflammation in this disease (Korotkyi et al., 2020; Steves et al., 2016). OA synovial fluid contains chemokines, cytokines, and other inflammatory mediators produced locally by chondrocytes and synovium. It is evident that the elevated levels of cytokines such as matrix metalloproteinases (MMPs), IL-1, IL-6, TNF-α, and other y-chain cytokines like IL-2, IL-7 and IL-15, as well as chemokines, are involved in the pathogenesis of OA (Arican et al., 2022). Another group of cytokines (IL-4, IL-10, and IL-13) is known for its anti-inflammatory nature and plays a pivotal role in OA pathogenesis (Shahid, Inam-ur-Raheem, Aadil, & Israr, 2022). The role of inflammatory and anti-inflammatory cytokines in OA pathogenesis via intracellular and extracellular signaling pathways is still under investigation (Kapoor et al., 2011; Korotkyi et al., 2020; Wojdasiewicz et al., 2014). The molecular signaling pathways in the pathogenesis of OA are delineated in Fig. 1.

3. Evidence of the therapeutic effects of nutrients and phytochemicals in OA

A diet enriched with nutrients, antioxidants, polyphenols, and bioactive compounds has a strong positive association with OA progression and onset (Table 1). Understanding the chemical and nutritional constituents of food (fruits, vegetables, meat, and other foods) and how bioactive compounds in a typical diet affect joint health could provide a novel strategy to attenuate the onset and progression of OA. The antioxidant-enriched diet is receiving more attention in OA management due to its anti-inflammatory, chondroprotective, and cartilage-protective properties. The vast body of literature suggested that antioxidants such as vitamins C, D, and E, β-cryptoxanthin, ellagic acid, epigallocatechin 3-gallate, ferulic acid, quercetin, vitamins and minerals, eicosapentaenoic acid, docosahexaenoic acid, gingerol, anthocyanins, and curcumin can alleviate OA symptoms and attenuate its progression (Davidson et al., 2016; Hung et al., 2017; Shahid, Inam-ur-Raheem, Aadil, & Israr, 2022). The presumptive mechanism of action of a high intake of polyphenols against OA is delineated in Fig. 2. The Mediterranean and DASH diets, rich in fruits, vegetables, whole

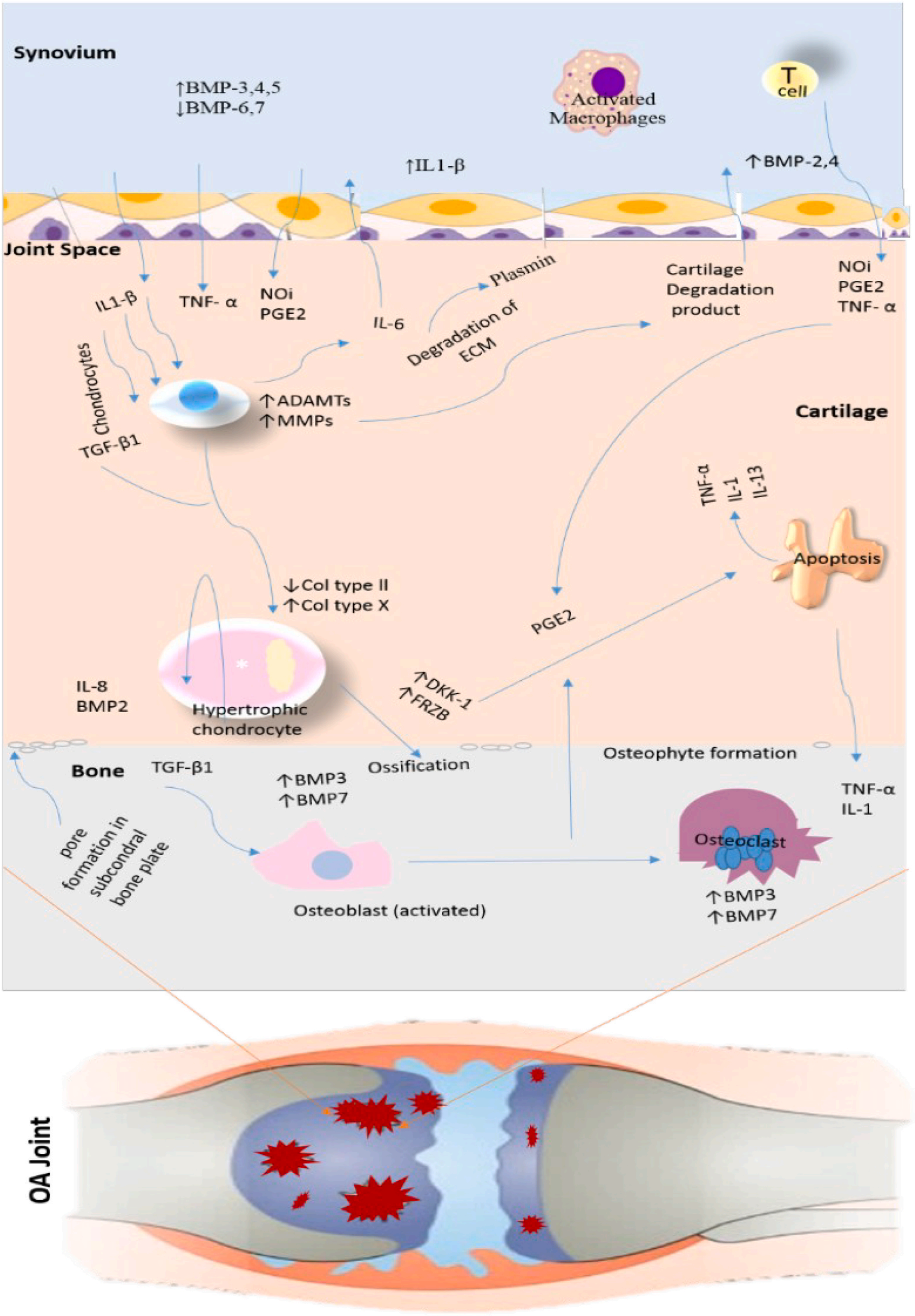

Fig. 1. Contextual molecular signaling pathways in the pathogenesis of OA.

Table 1
Therapeutic potential of anti-OA nutrients, phytochemicals, and foods in OA.

Anti-OA agents	Bioactive compound	Food	Model	Duration	Dose	Outcomes	Mechanism/signal pathway	References
Polyphenols	Sulforaphane	Cruciferous vegetables	H_2O_2-induced OA mouse chondrocytes	24 h 48 h	0.0, 12.5, 25.0, 50.0, 100, and 200 μM) of sulforaphane for 24 h and 48 h	Sulforaphane activated the SIRT1 signaling pathway *in vivo*, which had an anti-apoptotic effect on chondrocytes and mitigated OA	Inhibited chondrocyte apoptosis Down-regulation of Bax, Bcl-2, 78-kDa glucose-regulated protein, C/EBP homologous protein, and cleaved caspase 3 Endoplasmic reticulum stress and apoptosis in H_2O_2-exposed chondrocytes were alleviated	Chen et al. (2021)
	Ellagic acid	Berries, pomegranates, and nuts	OA-induced human chondrocytes	24 h	12.5, 25, or 50 μM Penetrated for 24 h	Ellagic acid may have therapeutic potential for OA treatment	IL-1β-induced expression of prostaglandin E2 (PGE2), inducible nitric oxide cyclooxygenase-2 (COX-2), synthase (iNOS), tumor necrosis factor-alpha (TNF-α), nitric oxide (NO), and interleukin-6 (IL-6) were down-regulated by ellagic acid	Lin et al. (2020)
	Ellagic acid	Fruits and nuts	IL-1β induced OA in C28/I2 human chondrocytes	24 h	Cell cultured with different concentrations of ellagic acid	Ellagic acid may reduce oxidative stress and provide a protective effect on chondrocytes	Ellagic acid up-regulated the nuclear factor erythroid 2-related factor 2 (Nrf2) expression. Targeted the heme oxygenase-1 attenuated the OA	Zhu et al. (2022)
	Ellagic acid	Berries, pomegranates, and nuts	Rats	8 weeks	40 mg/kg	Ellagic acid prevents the OA progression	Attenuated the PGE2, NOS, NO, COX-2 induced expression of IL-1β	Lin et al. (2020)
	Curcumin	Turmeric	Surgery-induced OA mice	8 weeks	Daily 50 mM curcumin injected intraperitoneally after surgery	Curcumin exerts protection on OA	Suppressed the expression of TNF-a, and IL-1b, at both RNA and protein levels	Sun et al. (2017)
	Quercetin	Fruits and vegetables	OA inducted by surgery of rats	12 weeks	50 and 100 mg/kg intraperitoneally	Quercetin blocks the IRAK1/NLRP3 signaling pathway to attenuate IL-1-induced cartilage degradation and inflammation and in OA	Both doses down-regulated the expression of IL-1β, TNF-α, NLRP3, IL-18, and caspase 3 IRAK1, NLRP3, and caspase-3 expression suppressed only in the high-dose group	Li et al. (2021)
	Epigallocatechin 3-gallate (EGCG)	Green tea	Surgically induced OA in mice	4–8 weeks	25 mg/kg intraperitoneally	EGCG showed a palliative effect and considerably reduced the progression of OA illness	MMP-13, MMP-8, MMP-3, MMP-1, ADAMTS5, and pain expression decrease	Leong et al. (2014)
Vitamins	Ascorbic acid	–	Chondrosarcoma cell line (SW1353)	24 h	100 μM	Treatment with vitamin C effectively shields cells from MIA-induced cell death	Attuentated the expression of MMP-13, MMP-1, MMP-3, IL-17A, IL-6, TNF-α, Bax, and cytochrome *c*. Increase the procaspase-9 and Procaspase-3 expression	Chiu et al. (2017)
	Ascorbic acid	–	Monosodium iodoacetate induced OA rat model	2 weeks	100, 200 and 300 mg/kg	100 mg/kg dose is more suitable for the prevention of OA progress than	MMP-13 IL-6, TNF-α, and levels reduced	Chiu et al. (2017)

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Table 1 (*continued*)

Anti-OA agents	Bioactive compound	Food	Model	Duration	Dose	Outcomes	Mechanism/signal pathway	References
						the 200 or 300 mg/kg dosages		
	Vitamin D	–	400 subjects having both vitamin D deficiency and symptomatic knee OA	2 years	50,000 IU compounded vitamin D3 capsule monthly	These capsules can significantly lengthen the amount of time needed to develop end-stage OA	The deficiency of vitamin D can lower the rate of cartilage loss	Cao et al. (2012)
	Vitamin E	–	Seventy-two patients with late-stage knee OA	2 months	400 IU of vitamin	These vitamins help lessen oxidative stress and alleviate clinical symptoms in late-stage osteoarthritic patients	Down-regulate the expression of nitric oxide macrophages, protein kinase C, nitrotyrosine Stain and decrease the swelling and inflammation	Tantavisut et al. (2017)
Food	–	Apple	Surgically induced OA model of rats	4 weeks and 8 weeks	480, 300 mg/kg body weight/day	Apple polyphenols may improve synovial conditions in OA and suppress OA progression	Down regulated the expression of matrix metalloproteinase (MMP)-13, and tumor necrosis factor (TNF)-α Superoxide dismutase (SOD) activity was enhanced	Kobayashi et al. (2022)
	–	Strawberry	Obese humans with knee OA	12 weeks	50 g/day beverage of freeze-dried strawberries	Dietary strawberries may offer significant analgesic and anti-inflammatory benefits in obese people with developed knee OA.	MMP-3, IL-6, and IL-1β were significantly diminished	Schell et al. (2017)
	–	Blueberries	Individuals with symptomatic knee OA	4 months	Freeze-dried blueberry powder (40 g)	Everyday consumption of whole blueberries may improve gait and performance in people with symptomatic knee OA by reducing pain, stiffness, and difficulty in completing daily tasks	IL-13 expression increased while MCP-1 concentration decreased	Du et al. (2019)
	–	Pomegranate	Knee OA patients	6 weeks	200 ml/day pomegranate juice	Pomegranate juice consumption decreases the breakdown of cartilage enzymes and increases antioxidant status in osteoarthritic individuals	A significant increase in GPx MMP-1 and MMP-13 were down-regulated	Ghoochani et al. (2016)
	–	Garlic	76 postmenopausal overweight or obese women having KOA	12 weeks	1000 mg odorless garlic tablet	Garlic has a therapeutic potential to manage the OA	In the garlic group, the WOMAC overall score, stiffness, pain, and physical function all considerably improved	Salimzadeh et al. (2018)
	–	Ginger	90 patients with kOA	12 weeks	500 mg/day	Ginger effectively attenuated the pain in patients with KOA	Pain scores declined	Alipour et al. (2017)
	–	Spinach	Monosodium iodoacetate-induced osteoarthritic rats	28 days	250 and 500 mg/kg/day	500 mg/kg/day dose was more effective for restoration of the cartilage as a therapeutic treatment	Down-regulate glutathione S-transferase (GST) activity and cartilage oligomeric matrix protein Up-regulation of aggrecan and TIMP2	(D. Choudhary et al., 2018)
	–	Cashew nut	Monosodium iodoacetate-	21 days	100 mg/kg	Cashew nuts decreased pain	Restores the lipid peroxidation, catalase	Fusco et al. (2020)

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Table 1 (*continued*)

Anti-OA agents	Bioactive compound	Food	Model	Duration	Dose	Outcomes	Mechanism/signal pathway	References
			induced osteoarthritic rats			intensity, restored the pro-oxidant/antioxidant balance, and restricted tissue damage and joint inflammation.	(CAT), glutathione (GPx) activity, and glutathione (GSH) levels. Significantly ameliorated histological and radiographic alteration related to OA	
Other nutrients	Polycan	Aureobasidium pullulans SM-2001	partial medial meniscectomy, and anterior cruciate ligament transection-induced osteoarthritic rats	48 days	Polycan (85, 42.5, and 21.25 mg/kg/day) orally	42.5 mg/kg dose of polycan for 48 days is the optimal dose to alleviate the OA	Reduced histological cartilage damage and low articular stiffness were noted	Kim et al. (2012)
	D-002 (mixture of beeswax alcohols)	Beeswax	OA patients	8 weeks	(50–100 mg/day)	D-002 (50–100 mg/day) for 6 was well tolerated. D-002 improves OA symptoms reduced total WOMAC score, pain, and joint stiffness	D-002 can inhibit the cyclooxygenase (COX) and 5-lipooxygenase (5-LOX) enzymes and has an anti-inflammatory effect.	Puente et al. (2014)
	Lactobacillus casei Glucosamine hydrochloride (Gln) Type II collagen (CII) Mixture (*L. casei*, CII, Gln,; 5	–	MIA-induced OA Female Wistar rats	Oral feeding began 14 days before MIA injection into the articular cartilage and lasted for up to 8 weeks	L. casei: 2 × 1010 cfu/kg, 500 mg/kg Glucosamine hydrochloride: 250 mg/kg CII/Gln: CCII, 250 mg/kg; Gln, 250 mg/kg Mixture: *L. casei*, 2 × 1010 cfu/kg, 500 mg/kg; CII, 250 mg/kg; Gln, 250 mg/kg	*L. casei* with CII and glucosamine hydrochloride effectively reduced lymphocyte infiltration, reduced pain and cartilage destruction in OA than glucosamine or *L. casei* alone	Down-regulated the TNF-α, IFN-γ, IL-17, IL-2, IL-6, and matrix metalloproteinase (MMP13, MMP3, and MMP1) While up-regulated IL-4 and IL-10 expression	So et al. (2011)

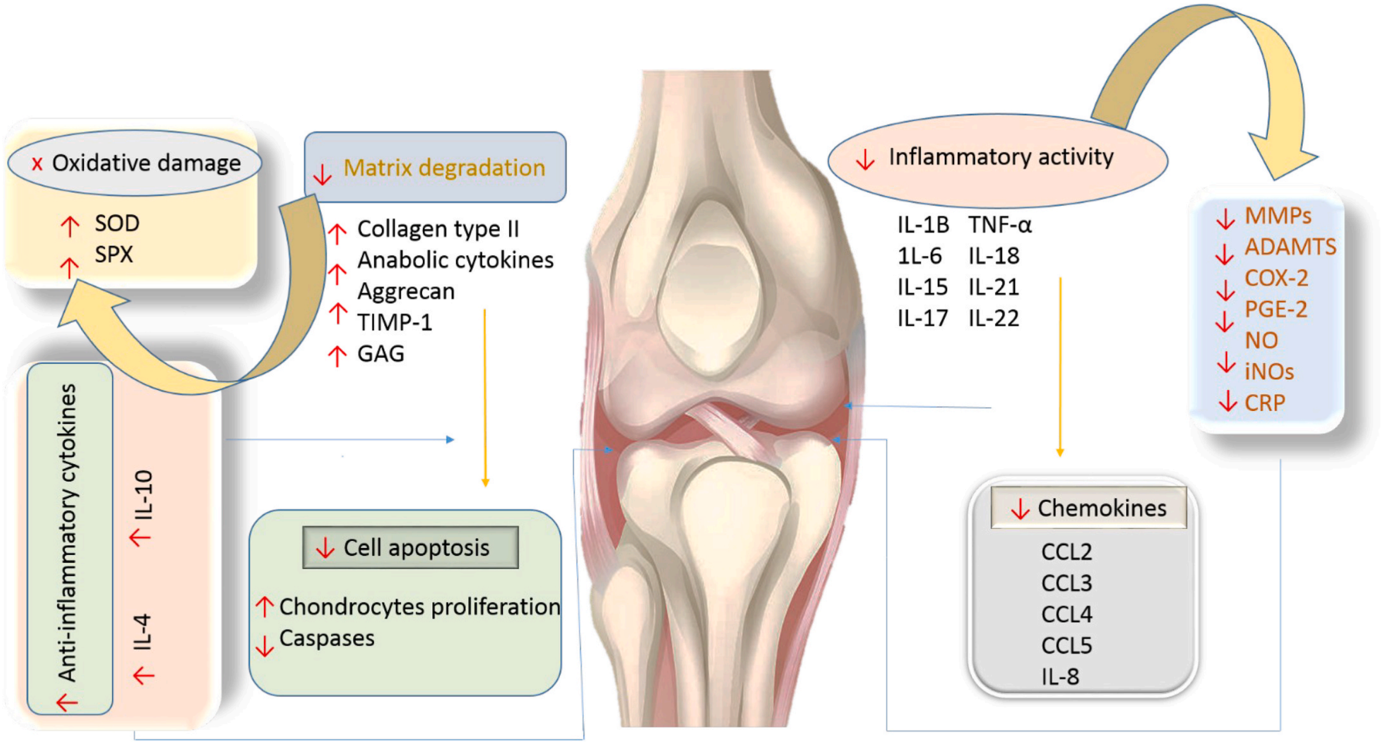

Fig. 2. Molecular mechanism of polyphenol in OA.

grains, nuts, lentils, beans, and olive oil (OO), positively correlate with OA attenuation. In contrast, a diet rich in trans and saturated fats is associated negatively with this disease (Dyer et al., 2016; Shahid, Inam-ur-Raheem, Aadil, & Israr, 2022; Vina & Kwoh, 2018). A review conducted in 2022 summarized the evidence-based key nutrients for OA and reported that the consumption of refined carbohydrates and high-sugar food, linoleic acid, purine diets, high-calorie diets, trans fat, saturated fatty acids, and monosodium glutamate can exacerbate OA-related symptoms and progression. In contrast, fish, fish oil, vegetables (dark green leafy vegetables, particularly spinach, broccoli, cabbage, dark lettuce, and parsley), fruits (particularly strawberries, pomegranate, guava leaves, mango, guava, avocado, and grapes), nuts (particularly peanut, peanut leaves, walnut, cashew, and pistachio), and spice and condiments (particularly garlic, turmeric, ginger, and cinnamon) are evidence-based superlative foods for OA (Shahid et al., 2022, 2024). Numerous pieces of research supported the positive effect of OO on OA. This effect is possibly due to its phytochemicals, which include phenolic compounds, hydroxytyrosol, oleuropein, tyrosol, tocopherol, and carotenoids, which have antibacterial, antioxidant, and anti-inflammatory properties (Montaño et al., 2016; Musumeci et al., 2013). The phenolic compounds of OO scavenge-free radicles lower oxidative stress, interact with the inflammatory cascade and avert osteoclast proliferation in the subchondral bone (Chin & Pang, 2017). High consumption of fruits is also inversely linked to the size of the tibial plateau bone and the bone marrow lesions, which is consistent with the fact that fruit is a significant source of nutrients, including vitamin C. Data also suggests the beneficial effect of zeaxanthin, β-cryptoxanthin, lutein, and vitamin E on the pathogenesis of OA progression (Davidson et al., 2016; Hung et al., 2017; Shahid, Inam-ur-Raheem, Aadil, & Israr, 2022). Consumption of different fruits or fruit parts has a palliative effect on health (Abbas & Alkheraije, 2023; Bebas et al., 2023; A. N. Choudhary & Tahir, 2023; Dalal et al., 2023; Turan et al., 2023; Ur-Rehman et al., 2023). Among these, guava fruit and leaves are cited widely for their therapeutic and pharmacological properties, mainly due to their high level of antioxidants, polyphenols, essential oils, vitamins, minerals, and polysaccharides (Shahid, Inam-ur-Raheem, Aadil, & Israr, 2022), which have the potential to ameliorate the OA (Kawasaki et al., 2018).

A study evaluated the therapeutic effect of spinach extract on monosodium iodoacetate-induced osteoarthritic rats. The animals were fed 500 and 250 mg/kg extract for 28 days. *In vitro*, cell-based, and cell-free assays corroborated spinach extract's anti-inflammatory and antioxidant potential against OA. The histological analysis also supported the chondroprotective properties of spinach extract. The author deduced that spinach extract could alleviate the monosodium iodoacetate-induced OA and can be a promising therapy for treating OA (Choudhary et al., 2018). Sulforaphane is a bioactive compound commonly present in cruciferous vegetables such as cabbage and broccoli. It has the potential to attenuate OA by inhibiting inflammatory and pro-inflammatory cytokines. It slows down the expression of cartilage-degrading proteinases and protects chondrocytes and cartilage by inhibiting NF-κB in human articular chondrocytes. However, it does not affect histone deacetylase inhibition or Nrf2 activation (Davidson et al., 2016). Parsley contains copious amounts of apigenin flavonoids and vitamins A, K, and C, and its anti-OA potential was investigated by orally administering 200 mg/kg/day of extract to OA-induced albino rats. The study's findings suggested that parsley extract has therapeutic potential for OA treatment (Aml & Rezq, 2016).

Various clinical trials evinced the anti-osteoarthritic activity of eicosapentaenoic acid, α-linolenic, and docosahexaenoic acid. Fish, fish oil, hazelnuts, walnuts, olives, sesame, and canola are copious reservoirs of omega-3 fatty acids (Durmuş, 2019). Researchers conducted a 16-week randomized, double-blind control trial to investigate the effect of fish oil (EPA 400 mg + DHA 200 mg) on OA. The findings of that trial evinced that fish oil significantly reduced OA-related chronic pain (Kuszewski et al., 2020).

4. Effect of food technology and processing on OA-related nutrients and bioactive compounds

Food processing improves nutritional value, safety, taste, and shelf-life. Although processing has many advantages, it can also be harmful and reduce the nutritional value of food. Various food processing techniques like thermal, nonthermal, pasteurization, food excipient, nanotechnology, ingredient modification technologies, food fortification, and bio-fortification not only affect the sensory attributes of food but also the nutritional composition and bioavailability of bioactive compounds, subsequently influencing the diet therapy to manage the OA (Augustin et al., 2016; Shahid, Inam-ur-Raheem, Aadil, & Israr, 2022). Therefore, more than understanding and knowing the nutritional composition of food is needed to address OA; it is crucial to comprehend which food processing technique impacts the nutrients and to what extent (Table 2). Fig. 3 instantiates the interrelation of food, OA, and food processing.

4.1. Thermal treatment/cooking and its impact on OA-related nutrients

The food type, amount consumed, and preparation methods primarily influence the nutritional status. During thermal processing, food undergoes various changes that modify its nutritional content and bioactive compounds, ultimately affecting health (Palermo et al., 2014; Ribas-Agustí et al., 2018).

Cooking is as old as human civilization, and it is a method of preparing food by applying heat to make it edible. Before consumption, food is cooked by heat processing methods such as pressure, boiling, sautéing, blanching, boiling, roasting, microwaving, steaming, or frying (Fabbri & Crosby, 2016). Heat treatment or cooking can cause the loss of vitamins, minerals, antioxidants, and phytochemicals in food through thermal degradation (Oral & Kaban, 2023), while matrix softening enhances the extractability of bioactive compounds (Palermo et al., 2014). This modification leads to imprecise nutrient intake estimation. Therefore, it is indispensable to provide nutritional information on how and which cooking method enhances nutrient retention, extractability, and loss (Palermo et al., 2014).

4.1.1. Thermal treatment/cooking and OA-related nutrients of vegetables

Burette et al. investigated the effect of microwaving, steaming, and boiling on the nutritional and physical characteristics of sweet potatoes, cauliflowers, and carrots with anti-OA nutrient components (Buratti et al., 2020). Nutritional quality was assessed, and principal component analysis was used to analyze the texture parameters and e-sense data. Boiling improved carotene accessibility while negatively affecting ascorbic acid, total phenolic content, and antioxidant activity. Steaming resulted in the loss of ascorbic acid, but it increased total phenolics and carotenoids. While microwaving caused a slight reduction in ascorbic acid levels, increased total phenolics, and did not affect carotenoids content. According to Guillén et al. (2017), the antioxidant components from boiled peppers (*Capsicum annum* L.) leached into the cooking water. Different cooking methods (microwaving, stir-frying, or boiling) significantly altered cooked food's ascorbic acid, total phenol, and radical-scavenging activity. However, various studies have suggested that steaming is the best method to avoid losing water-soluble components (Nicoletto et al., 2018; Rennie & Wise, 2010). A study assessed the effect of steaming, boiling, blanching, and microwaving cooking on true retention and content of ascorbic acid, vitamin K, vitamin E, and β-carotene. After microwaving, vitamin C retention was higher, while boiling resulted in the lowest retention. Cooked vegetables have a higher availability of fat-soluble vitamin levels (α-tocopherol and β-carotene) than their fresh counterparts, but it depends on the type of vegetable. In contrast to spinach and chard, microwave cooking caused a significant loss of vitamin K in crown daisy and mallow (Lee et al., 2018).

Heat treatment/cooking affects the vitamins and minerals and the polyphenols, the largest dietary antioxidants known for their capacity to neutralize free radicals (Cory et al., 2018). These non-nutrient

Table 2
Role of food technologies in diet-based OA management by affecting OA-related factors.

OA-related factors	Food technology/ intervention	Compound	Model	Processing parameters	Duration	Outcomes	Conclusion	References
Dietary fat	High intake of dietary fat is a risk factor for the development of OA and is associated with alterations in cartilage degradation *in vivo*							Brunner et al. (2012)
	Fat substitute	Nano-cellulose	–	1% weight of aqueous dispersion of cellulose nanofiber and its palm oil pickering emulsion at the ratio of 1:1 (water: oil, v:v) is a fat substitute that can replace 30% and 50% of the original fat	–	Using cellulose nanofiber and palm oil pickering emulsion to replace fat led to low-fat content, higher lightness values, higher moisture content, and lower cooking loss	For the development of low-fat meat products, cellulose nanofiber, and its pickering emulsion can serve as viable fat substitutes	(Yanan Wang et al., 2018)
	Fat replacer	Microcrystalline cellulose (MCC) or carboxymethyl cellulose (CMC) are non-digestible fibers	–	MCC or CMC aqueous dispersion was used to replace the 10% weigh of the ground beef at the concentration of 0.5–3.0 wt%	–	MCC has a fat-like mouthfeel in fried beef patties Patties with MCC (>1%) were juicer and softer than controls CMC is not suitable as a fat replacer in concentrations of more than 0.5% weight	Microcrystalline cellulose results in a reduction of fat by around 50% in patties.	Gibis et al. (2015)
	Fat replacer	Wheat and oat bran-based fat replacers in the form of gels	–	Gel-based fat substitutes made from wheat and oat bran were used to replace 30–50% of the fat in cookies	–	The sensory qualities of the full-fat cookies were preserved in the cookie formulation at a level of 30% wheat bran gel and had higher dietary fiber, phenolic content, and minerals than 30% oat bran gel-containing cookies	The use of wheat bran gels at a concentration of 30% resulted in the formulation of cookies having more nutritional value but low-fat	Milićević et al. (2020)
	Fat replacer (FR)	Sweet potato starch treated with citric acid as a fat replacer	–	Citric acid treatment (0, 1, and 2%) fat replacer was investigated in low-fat (1%), medium-fat (6%), and high-fat (11%) ice creams	60 days of storage	Medium-fat and low-fat ice creams containing 1% FR were found to be quite acceptable Overrun, acidity and hardness values of ice cream samples decreased throughout 60 days of storage	Sweet potato starch treated with citric acid turned out to be a promising substitute for fat in making ice cream	Surendra Babu et al. (2018)
	Fat replacer	Protein-based fat replacers or modified tapioca starch, Inulin, and maltodextrin	–	The low-fat (2%) and reduced-fat (4%) coconut milk ice cream The control sample contained 8% fat	–	Simplesse® 100, inulin, and maltodextrin-added reduced-fat ice creams did not differ substantially from the control	Low-fat and reduced-fat coconut milk can be made by replacing the fat with inulin and Simplesse® 100	Fuangpaiboon and Kijroongrojana (2017)
Caloric content	Calorie restriction (CR) mitigates OA by decreasing weight-bearing burden on joints and improving systemic inflammation							Radakovich et al. (2019)
	Fat replacer	Inulin	–	12%, 9%, 6%, and 3% inulin as a fat replacer was	23 days of storage	Significant energy content reductions of up	Sausages incorporated with 6% inulin-citrate	Nowak et al. (2007)

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Table 2 (*continued*)

OA-related factors	Food technology/ intervention	Compound	Model	Processing parameters	Duration	Outcomes	Conclusion	References
				added to the final product		to 47.5% were achieved when inulin (12%) was used to replace fat	showed low energy content (22%) compared to control sausages and were microbiologically stable for 23 days of storage	
	Fat replacer	Inulin, hydroxypropyl methylcellulose, and maltodextrin	–	Fat replacement (100%, 75%, 50%, 25%, and 0%) using inulin, hydroxypropyl methylcellulose, and maltodextrin	–	Similar mean overall acceptability scores (6.26 ± 1.37 and 6.40 ± 1.36 respectively) were obtained for the 75% fat-replacement snacks made from maltodextrin and inulin as compared to the control	These snacks products are an excellent source of protein and dietary fiber and provide low calories (≤25% less than reference food) than control and commercial	Colla and Gamlath (2015)
	Fat replacer	Oleogel developed with ethyl cellulose and behenic acid	–	As a fat replacer, ethyl cellulose-based oleogel with behenic acid used at different concentrations	–	The combination of ethyl cellulose and behenic acid at particular ratios (2:4 and 1:5 wt %) enhanced the oleogel's characteristics	In developing low-caloric food products, the oleogel developed with ethyl cellulose and behenic acid has good potential	Ahmadi et al. (2020)
Micronutrient deficiency	High consumption of vitamin E, vitamin D, vitamin K, vitamin A, vitamin C, and n-3 fatty acids are recommended to combat OA							Thomas et al. (2018)
	Fortification	Vitamin A	Lactating mothers, their infants and children, and cohorts of children and women	Fortification of unbranded palm oil with retinyl palmitate	–	Fortified oil improved vitamin A intakes	Vitamin A fortified oil intake contributed, on average, 38, 40%, 26 %, 35%, and 29 % of the daily recommended nutrient intake for children (5–9 years), (24–59 months), (12–23 months), non-lactating and lactating women, respectively. At endline, serum retinol was 2–19% higher than at the baseline	Jus'at et al. (2015)
	Fortification	Vitamin A	Postpartum Moroccan women	Fortification of cooking oil with vitamin A	6 months/ week	Serum retinol concentration was high in the fortified oil group compared to the non-fortified oil group	Fortification appears to be a long-term solution to overcome the vitamin A deficiency problem, especially in low-income regions	Atalhi et al. (2020)
	Fortification	Vitamin D	65 subjects from both sexes	D-fortified sunflower oil unfortified sunflower oil (500 IU/30g)	12 weeks	The level of serum 25(OH)D increased significantly accompanied by a significant reduction in iPTH Significant reduction in weight and waist	Cooking oil could be a useful tool for mass fortification campaigns to combat vitamin D deficiency, which could improve several cardiometabolic risk factors	Nikooyeh et al. (2020)

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Table 2 (*continued*)

OA-related factors	Food technology/ intervention	Compound	Model	Processing parameters	Duration	Outcomes	Conclusion	References
						circumference was also noted		
Polyphenols and antioxidants content of foods	Polyphenols may help to mitigate OA because of their anti-inflammatory and antioxidant effects							Valsamidou et al. (2021)
	Cold plasma	Anthocyanin content (Pomegranate juice)	–	Cold atmospheric gas phase plasma Treatment time (3,5,7 min) Treated juice volume (3,4,5 cm^3) Gas flow (0.75, 1, 1.25 dm3/min)	–	The anthocyanin content increased from 21% to 35%	Cold plasma was shown to be an excellent treatment Treatment at 3 min, 5 cm^3 sample volume, and 0.75 dm3/min gas flow was most effective	Kovačević et al. (2016)
	UV-Irradiation and thermal pasteurization	Ascorbic acid, and total phenolic content (Pineapple)	–	UV-irradiation: Wavelength 254 nm (53.42 mJ/ cm^2, 4.918 s) Thermal pasteurization: 80 °C for 10 min stored at 4^0C for 13 weeks	13 weeks	Ascorbic acid and total phenolic compound increased in UV irradiated samples	As a thermal pasteurization substitute technology, UV irradiation holds a great potential in producing products of high nutritional values	Chia et al. (2012)
	Gamma-irradiation	Vitamin C, anthocyanin, ellagic acid, gallic acid, pyrogallol, chlorogenic, and catechol (Strawberry fruit)	–	0, 300, 600, 900 Gy	–	600 Gy treated samples had the highest antioxidant and total phenolic content and activity, followed by 300 Gy Anthocyanin contents increased during storage Ascorbic acid decreased in all treatments	Irradiation increase the Phenylalanine ammonia-lyase (PAL) activity responsible for phenolic compound production (ellagic acid, gallic acid, pyrogallol, chlorogenic, and catechol)	Maraei and Elsawy (2017)
	Ultrasound	Vitamin C, and antioxidants (Strawberry fruit)	–	33 kHz, 60 W (0, 10, 20, 30, 40, 60, min)	–	Antioxidant potential decreases after 60 min exposure Vitamin C and antioxidant activity are better retained between 30 and 40 min	Ultrasound treatment can be used as a minimal processing	Gani et al. (2016)
	Thermosonication	Anthocyanin, carotenoid, total flavonols, TPC, and TFC (Spinach juice)	–	600 W, 400 W, and 200 W, 30 kHz, at 60 ± 1 °C for 20 min Pasteurization: 60 ± 1 °C for 30 min	–	Bioactive compounds, anthocyanins value, and phenolic compounds activity significantly high at 600 W, 30 kHz TPC and TFC increased in all treatments except pasteurization	High intensity thermosonication treatment increased the bioactive, antioxidant compounds (anthocyanin, carotenoid, and total flavonols) and their activity	Manzoor et al. (2021)
Bioavailability	Nano-particle colloidal dispersion	Curcumin	Individuals with knee OA	Surface-controlled water-dispersible curcumin named Theracurmin®	Theracurmin containing 180 mg/day of curcumin for 8 weeks	The bioavailability of Theracurmin is 27-fold higher than that of curcumin powder knee pain Visual analog scale (VAS) scores were considerably	For the treatment of knee OA in humans, Theracurmin has a modest potential	Nakagawa et al. (2014)

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Table 2 (*continued*)

OA-related factors	Food technology/ intervention	Compound	Model	Processing parameters	Duration	Outcomes	Conclusion	References
						lower in the Theracurmin group than in the placebo group		
	Excipient food technology	*Boswellia serrata* and bromelain	Individuals with various types of OA	Formulation of gastro-resistant food supplement of *Boswellia serrata* and bromelain using excipient	6 months	Seven out of the ten quality-of-life questions and the overall quality-of-life score both showed considerable improvements	Using those supplements may be an effective non-pharmacological approach for people with various kinds of OA to improve their quality of life	Italiano et al. (2020)
	Excipient food technology	*Curcuma* extract (Flexofytol®)	Individuals with OA	The galenic form of curcumin, in a specially made excipient, is used (4–6 capsules/ day)	6 months	Flexofytol® reduced patient discomfort related to OA, increased articular mobility, and improve quality of life within the first six weeks	Flexofytol® is an appropriate treatment option for patients with joint pain	Appelboom et al. (2014)
	Excipient food technology	Next Generation Ultrasol Curcumin (NGUC)	Monosodium iodoacetate (MIA)-induced knee OA in rats	20 mg/kg of curcuminoids in 100 mg/kg of NGUC and 40 mg/kg of curcuminoids in 200 mg/kg of NGUC excipients (phospholipids and monoglyceride) were used to develop NGUC	4 weeks	Reduction in IL-1β, IL-6, TNF-α, CRP, and COMP, and expressions of NFκB, COX-2, MMP-3, and 5-LOX, were noted Increased levels of antioxidant enzymes, e.g., CAT, GPX, and SOD, were noted	NGUC's bioavailability was 64.7 times higher, and it lessens the severity of MIA-induced OA in rats than natural turmeric extract	Yabas et al. (2021)

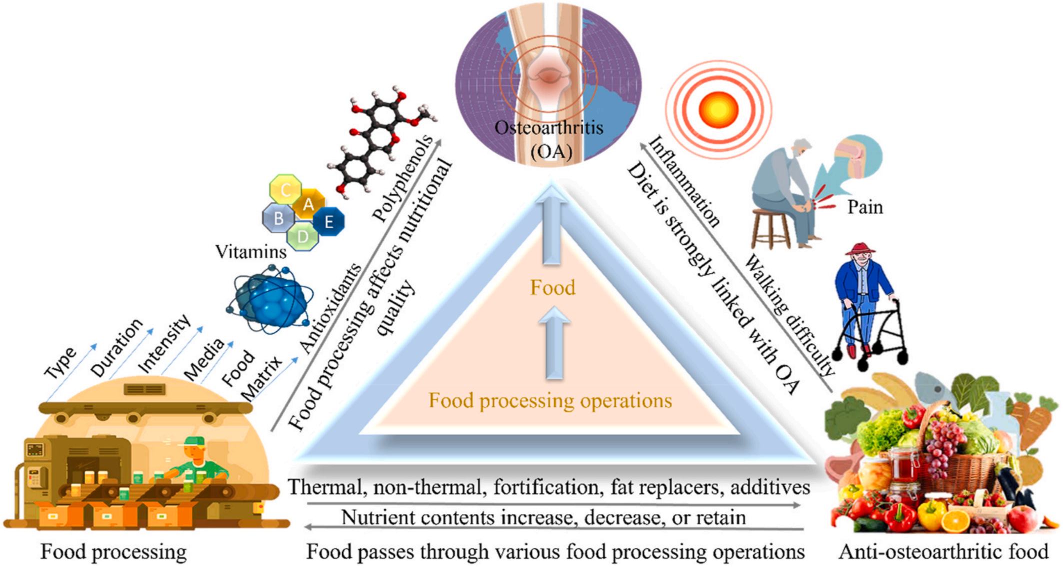

Fig. 3. Triangular relation of food, OA, and food processing technologies/operations.

compounds have antioxidant and anti-inflammatory properties that benefit OA management (Cory et al., 2018). The cooking/heating method applied to polyphenols mainly decides the fate of these compounds. Heat causes cell walls to burst, increasing the availability of the bound phenolics by allowing them to move to other areas (D'Archivio et al., 2010). At the same time, the heating process can damage some polyphenols through oxidation (Maghsoudlou et al., 2019). According to thermal treatment studies, the boiling method unfavorably alters the samples' polyphenol composition; steaming or frying can conserve these compounds (Ribas-Agustí et al., 2018). The underlying cause could be the water-soluble nature of phenolic compounds, which seep into the surrounding media during heating.

Nevertheless, the matrix's and polyphenol's chemical characteristics determine how temperature affects the phenolic compounds. Heat treatment causes the tissue to break down, allowing nutrients and bioactive components to enter the boiling water (Minatel et al., 2017). Frying showed detrimental effects on leafy vegetables (*Passiflora edulis, Gymnema lactiferum, Centella asiatica, Olax zeylanica,* and *Cassia auriculata)*. Depending on the type of leafy vegetable, boiling and steaming showed varying effects on polyphenols, carotenoids, and antioxidant characteristics (Gunathilake et al., 2018). *Centella asiatica* possesses anti-osteoarthritic activity and can be a novel food for OA (Micheli et al., 2020). Spinach is another green leafy vegetable that is a rich source of polyphenols, antioxidants, and nutrients and shows chondroprotective potential (Choudhary et al., 2018). Other green vegetables like cauliflower, cabbage, and broccoli also showed anti-osteoarthritic properties due to the sulforaphane compound (Davidson et al., 2016). Microwaving, steaming, boiling, and microwaving effects evolved on thirteen frozen (−20 °C after blanching) vegetables, including mushrooms, green and yellow French beans, hashed spinach, peas, brussels sprouts, broccoli, cauliflower, leek, zucchini, whole leaf branches, carrots, and salsify, and the impact of these thermal treatments on carotenoids, folate, and vitamin C content was characterized. The results revealed that cooking methods significantly impacted but varied depending on the vegetable and phytochemical characteristics. Generally, boiling is less suited, whereas pressure cooking, steaming, and microwaving could be the greatest approaches to maintaining nutritional quality (Coe & Spiro, 2022). Boiling resulted in a significant loss of total vitamin C, about 51% and 68% folates, an insignificant loss of lutein (15%), and about 9% loss of beta-carotene on a fresh weight basis. On a dry weight basis, it continued to be less suited for folates and vitamins, causing the loss of 65% and 44%, respectively, but not for carotenoids because it enhanced the extractability of lutein to 9% and carotene (20%) (Bureau et al., 2015). Sweet potatoes are a rich source of bioactive compounds well-known for their anti-inflammatory and anti-osteoarthritic properties like anthocyanin, chlorogenic acid, neochlorogenic acid, β-carotene, and ferulic acid (Jokioja et al., 2020). The effects of boiling, baking, steaming, and microwaving were assessed on four varieties of sweet potatoes. Boiling showed the most deleterious impact, decreasing the neochlorogenic acid (69%), chlorogenic acid (29%), and trans-ferulic acid (29%) in the 414-purple variety from Croatia, Slovakia, and Beauregard variety from Croatia, respectively. On the contrary, these treatments increased the total anthocyanins, total polyphenols, and total antioxidant activity in all samples (Musilova et al., 2020).

4.1.2. Thermal treatment/cooking and OA-related nutrients of fruits

It is evident from studies that heat processing treatments affect the bioavailability of macronutrients, micronutrients, and polyphenols (Jing et al., 2017; Luo et al., 2013). Lycopene, naringenin, and chlorogenic acid, commonly found in tomatoes, have anti-inflammatory and chondroprotective properties and can alleviate OA-related symptoms (Wang et al., 2017; Zada et al., 2021; Zhan et al., 2021). Naringenin attenuates the expression of Bax, MMP, and MMP13, restores type 11 collagen expression and protects the chondrocytes (Pan et al., 2022). Chlorogenic acid down-regulates the expression of IL-1β-mediated inflammation, PGE-2, COX-2, NF-κB, MMP-13, and iNOs, and protects the chondrocytes and type 11 collagen (Liu et al., 2017). However, heat treatments can affect these compounds. In a randomized controlled trial, researchers found that the naringenin glucuronide concentration in plasma and urine excretion was significantly higher in the tomato sauce group than in the raw tomato group, indicating that heating can improve the bioavailability of nutrients and antioxidants (Martínez-Huélamo et al., 2015). Another study evaluated the impact of heat by subjecting the tomatoes to different cooking methods. Stir-frying for 4.5 min (230 °C) and microwaving for 40 s (560 W) significantly affected the total phenolic compounds (TPC) and total flavonoid compounds (TFC). However, the stir-fried technique was more detrimental to TPC than microwaving. However, compared to microwave cooking and stir-frying, the losses from boiling were less considerable (Thanuja et al., 2019). Baking, proofing (the step when dough is allowed to rise), and cooking reduced the anthocyanin content of blueberries, while non-significant change in procyanidin content was seen. These treatments resulted in a decrease in oligomer content and a significant increase in procyanidin and chlorogenic content. While caffeic acid, quercetin, and ferulic acid content remained constant during these treatments (Rodriguez-Mateos et al., 2014). The effect of baking on the bioavailability of blueberry polyphenols (phenolic acids, anthocyanins, and procyanidins) was evaluated. Processing decreased the anthocyanin content by 42% and significantly increased the chlorogenic acid, flavanol trimmers, and dimers (23%, 28%, and 26%), respectively. At the same time, no effect has been observed on total polyphenolic content. The author assessed the bioavailability of total phenolic content by assessing 22 metabolites' plasma levels. The findings revealed that the bioavailability of phenolic compounds in the unprocessed blueberry drink remained unaffected. However, baking significantly decreased the contents of sinapic acids, hippuric acid, salicylic acid, and benzoic acid while increasing the levels of hydroxy hippuric acid, ferulic acid, and m-hydroxyphenyl acetic acid (Rodriguez-Mateos et al., 2014). Grape seeds are rich in numerous polyphenols that possess therapeutic and pharmacological activities for various diseases, including OA (Tanideh et al., 2020). Kim et al. (2006) evaluated the effects of various temperatures (200, 150, 100, and 50 °C) on grape seeds (whole and powdered forms). The results showed that heating the entire grape seed extract for 40 min at 150 °C yielded the highest TPC and radical scavenging activity (RSA). While heating the powdered grape seed extract for 10 min at 100 °C yielded the highest value. Gas chromatography-mass spectrometry (GC-MS) analysis identified several new low-molecular-weight phenolic compounds (o-cinnamic acid, azelaic acid, and 3,4-dihydroxy) produced in whole grape seed extract after heating at 150 °C for 40 min. According to the results of the high-performance liquid chromatography analysis, heat treatment considerably increased the gallocatechin gallate and caffeine in grape seed extract. This study concluded that thermal processing and duration affected the antioxidant activity of grape seed extraction (Kim et al., 2006). Intern microwave treatment resulted in 18% and 16% flavonol losses for quercetin 4′-glucoside (QmG) and quercetin 3,4′-diglucoside (QdG). Meanwhile, moderate microwave heating did not affect the flavonol content. Boiling the onion for 30 min leached the quercetin glycosides (29% QMG and 37% QdG) into the water. The effects of boiling for 60 min were severe. It caused the degradation of quercetin derivatives at rates of 44% and 53% for QmG and QdG, respectively. Frying treatment was more damaging than boiling, followed by roasting. Meanwhile, microwave roasting causes more damage than oven roasting (Rodrigues et al., 2009). Another study endorsed that the duration of the heat process affects the nutritional value of food. To preserve the nutritional quality of vegetables, limiting the heat (cooking) exposure to no more than 7.5 min is important; steaming is the best method to preserve the flavor compared to boiling (Poelman et al., 2013).

4.1.3. Thermal treatment/cooking and OA-related nutrients of fish, fish oil, and meat

Fish and fish oil are the best sources of omega-3 fatty acids, including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and their inverse relation with inflammation and pain is explicated by numerous studies related to OA (Durmuş, 2019; Kuszewski et al., 2020; Mehler et al., 2016; Wann et al., 2010). Leounge et al. (2018) assessed the effect of different cooking techniques and heat on salmon. Researchers found that different cooking techniques did not affect the arachidonic acid (AA), adrenic acid (AdA), EPA, and DHA in the salmon but significantly decreased PUFA content. Pan frying and oven baking triggered lipid oxidation and generated the by-product of lipid oxidation during cooking. Salmon cooked in a pan had the highest concentrations of

4-HHE and 4-HNE, followed by oven-baked, boiled, and raw salmon. Except for pan frying and oven baking, no other cooking technique produced salmon's enzymatic/bioactive oxidized PUFA products (Leung et al., 2018). Another study also showed that heat treatments (boiling, frying, and roasting) generally did not decrease DHA and EPA levels; however, only frying slightly decreased DHA and EPA levels (Gladyshev et al., 2006). Baking and grilling treatments caused the loss of thiamin (vitamin B1), riboflavin (vitamin B_2), and niacin (vitamin B_3). However, nicotinic acid was lost more during cooking. By grilling, average vitamin B loss was 45%, 38%, 45%, 46%, and 70% for vitamin B1, B2, nicotinamide, total vitamin B3, and nicotinic acid, respectively. The average vitamin B loss during baking was 52%, 57%, 54%, 55%, and 66%, respectively (Çatak et al., 2022). The overall loss of vitamins B3 and B6 during beef cooking through convection, radiation, and/or contact with a hot surface was estimated using heat transfer, juice loss, and heat denaturation models. This analysis concluded that vitamin B3 is highly heat-resistant, while vitamin B6 is denatured only at extremely high temperatures or during prolonged treatments (Kondjoyan et al., 2018).

4.1.4. *Other factors related to thermal treatment/cooking*

In addition to cooking methods, another factor that affects the nutritional composition of food and triggers different physio-chemical reactions is the cooking medium, e.g., oil medium, water medium, or no medium. Compared to raw samples, no medium (microwaving) and water medium (steaming and boiling) significantly increased the eggplant's antioxidant capacity and total phenolic content. Steaming and microwaving significantly increased the total polyphenol content compared to boiling. Microwaving for 10 min was the most effective method for improving the total antioxidant properties, compared to microwaving for 5 and 15 min. The antioxidants and phenolic compounds leach into the water during steaming and boiling, which could explain this phenomenon. In contrast, during microwave cooking, antioxidants and phenolic compounds remained preserved in food (Chumyam et al., 2013). Among oil mediums, different oils affect the nutritional quality of food differently (Ambra et al., 2022). Chio et al. (2007) elucidated the effect of phenol-spiked sunflower and olive oil by frying the 201-g sliced potatoes for 6 min at 175 °C. Results revealed that phenol-spiked sunflower oil fried potatoes had higher TPC, especially oleuropein, than phenol-spiked olive oil fried potatoes, suggesting that sunflower oil might be a better choice than OO if one wants to increase the PC content of food (Chiou et al., 2007). Another study showed that air-fried canola oil potatoes had a significantly higher phenolic content than potatoes in soybean oil and OO. This study also suggested that the air-frying technique is a healthier alternative to deep-frying, as it reduces the fat content by 70%, reduces the calorie content to 45 kcal/100 g, and causes less fat oxidation (Santos et al., 2017).

Pasteurization and drying are also thermal treatments. Currently, pasteurization refers to the process of heating milk or milk products at specific time-temperature combinations, most frequently at 72 °C for 15 s, which effectively destroys harmful pathogens (O'Callaghan et al., 2019, chap. 7). In the dairy industry, pasteurization is a prevalent thermal treatment. This treatment kills harmful bacteria and pathogens in milk and beverages and extends their shelf life (Dubey et al., 2022; Mandi et al., 2019). Nevertheless, nowadays, pasteurization application is also used for fruit juices. Pasteurization kills bacteria and pathogens and affects the overall nutrition quality, including antioxidants, polyphenols, and phenolic compounds. Various studies have shown that thermal processing deteriorates the nutritional value of food by denaturing bioactive compounds through ionization, hydrolysis, and oxidation reactions (Ignat et al., 2011; Paniwnyk, 2017; Putnik et al., 2017). Efforts are underway to develop novel pasteurization techniques, including nonthermal ones, to mitigate these nutritional losses.

4.2. *Nonthermal technologies and their impact on nutrition concerning OA*

Thermal processing offers numerous benefits, but its detrimental impact on nutritional quality is substantial. Numerous nutrients are heat sensitive and cause the loss of those nutrients during heat processing, resulting in low-quality food (Ignat et al., 2011; Paniwnyk, 2017; Putnik et al., 2017). Nonthermal technologies like high-pressure processing, ultrasound processing, high-pressure carbon dioxide, electric field, microwave processing, high-pressure homogenization, cold pasteurization, high hydrostatic pressure, and supercritical are promising processing methods that can minimize nutrition loss. Researchers have extensively studied these innovative technologies in the context of almost all food products and production to understand their effect on nutritional and sensory qualities and their application at the industrial level (Jadhav et al., 2021; Putnik et al., 2019). These nonthermal treatments improve the taste and textural qualities of the food, preserve the nutrients, decrease the microbial load, and extend the shelf life (Choudhary & Bandla, 2012; Jadhav et al., 2021; Thirumdas et al., 2015). These technologies do not use direct heat and process the samples at almost room temperature, e.g., ultrasound, which uses the mechanical sound waves that oscillate in the medium generated by molecular motions. These ultrasound waves (low-and high-intensity waves) have a frequency of around 20 kHz and are inaudible to the human ear. Nonthermal technology is still in its early stages in the food industry, although it is already well-established in other industries like the medical and biomedical fields (Gallo et al., 2018). The food industry employs the ultrasound technique for various purposes, including meat tenderization, dispersion, activation or deactivation of enzymes, improving the extraction, dissolution, crystallization, homogenization, emulsification, preservation, stabilization, aging and oxidation, hydrogenation, ripening, degassing, and atomization (Arvanitoyannis et al., 2017; Bhargava et al., 2021; Chavan et al., 2022; Chemat & Khan, 2011; Ojha et al., 2017; Villamiel et al., 2017).

The ultrasound enhances the efficiency of extracting bioactive compounds from plant and animal sources. The ultrasound extraction improved the bioactive compounds' physical and chemical characteristics and yield. For instance, ultrasound is a proven technique for oil extraction from flaxseed, olive, and soybean, which have anti-OA potential (Cavallo et al., 2020; Juliano et al., 2017). The use of ultrasound waves during drying improves not only the physical and sensory quality of fruits and vegetables but also the nutritional quality (minerals, vitamins, and antioxidants) of the dried product (Fan et al., 2017; Huang et al., 2020; Zhang & Abatzoglou, 2020). The combined cold plasma treatment and antimicrobial washing decreased the *P. digitatum* load without compromising the nutritional (ascorbic acid, total polyphenols, and antioxidant capacity) and sensory properties. It showed less ripening damage than untreated oranges. Cold plasma treatment for 6 min (7.2 log CFU/mL) inactivates the *Bacillus* spp. in blueberry juice (Hou et al., 2019), whey grapes (Amaral et al., 2018), cloudy apple juice (Illera et al., 2019), tomato juice (Starek et al., 2019), sour cherry nectar, tomato, apple, and orange juice (Dasan & Boyaci, 2018) without deteriorating the nutritional quality and enhances the retention of bioactive compounds and improves the color (Kovačević et al., 2016). Cold plasma works with various reactive species that cause lipid oxidation during storage, a disadvantage of this technology. The malondialdehyde (MDA), a by-product of lipid oxidation, increases the risk of OA (Vyas et al., 2015). Researchers have detected it in stored samples treated with cold plasma samples (Gao et al., 2019; S. Sharma, 2020). To overcome this disadvantage, high-lipid foods should be exposed to cold plasma treatment for a minimum, or adding antioxidants to that food can be helpful (Gavahian et al., 2018; Sarangapani et al., 2017). Supercritical carbon dioxide is ideal for food storage and preservation, as well as oil extraction, antioxidants, and polyphenols, because it is non-toxic and can be easily separated from the final product (Deotale et al., 2021). The growing body of evidence suggests that bioactive compounds like quercetin, ellagic acid, lycopene, carotenoids, resveratrol, curcumin, and anthocyanins can alleviate the inflammation in OA joints by suppressing the inflammatory and pro-inflammatory cytokines and mediators (IL-1β, TNF-α, and NFκβ) (Ansari et al., 2020; Shen et al., 2012; Sirše, 2022; Valsamidou et al., 2021). However, high temperatures can quickly destroy these bioactive compounds due to their sensitivity to oxygen and heat. Supercritical technology makes it possible to extract the bioactive compounds without compromising their quality because the presence of carbon dioxide and the extremely low temperature during the supercritical extraction technique preclude the presence of oxygen. Several studies reported the efficiency of supercritical technology to extract the functional compounds from feijoa leaves (isoquercetin, gallic acid, and catechin) (Santos et al., 2021), selective extraction of carotenoids and chlorophylls, carnosic acid, and rosmarinic acid from rosemary (Lefebvre et al., 2021), oil from corn germ (Rebolleda et al., 2012), apple seed (Ferrentino et al., 2020), olives (Al-Otoom et al., 2014), ginger (Salea et al., 2017), green coffee (de Oliveira et al., 2014), and bioactive compounds (astaxanthin, lycopene, quercetin, carotenoids, and anthocyanins) from seaweed and microalgae, and cape blueberry pulp (Gallego et al., 2019; Torres-Ossandón et al., 2018). These findings suggest the supremacy of supercritical extraction over conventional solvent extraction (Jadhav et al., 2021). This technology reduces the microbes and bacterial load by decreasing pH, causing cell rapture, and inactivating the bacteria and microbes. When pomegranate juice was stored for 28 days after being treated with supercritical carbon dioxide, bacteria growth was below the detection level, and the total phenolic content increased by 22%. Conversely, the total phenolic content decreased by 15% in juice treated with conventional pasteurization (Bertolini et al., 2020). The results from liquid food (Smigic et al., 2019), coconut water (Cappelletti et al., 2015), sports drinks (Cappelletti et al., 2015), and ground beef (Yu & Iwahashi, 2019) preserved in a supercritical fluid also supported that supercritical carbon enhances the polyphenolic compounds and preserves the nutritional profile that ultimately benefits the OA patients. Consequently, this technology is widely employed in the food industry to protect and store fruits, vegetables, and juices (Silva et al., 2020).

Irradiation, including X-rays and gamma rays, is employed effectively in the food sector to store, preserve, and inactivate pathogen microbes (Shalaby et al., 2016). These irradiation rays can penetrate deep into food, damage the nuclei aid, unfold the DNA strand, and cause oxidative damage to microbial pathogen cells, thereby reducing the microbial load (Bashir et al., 2021). Irradiation is effectively used for microbial inactivation in ready-to-cook chicken (Fallah et al., 2010), food grains (Bashir et al., 2017), fresh pasta (Cassares et al., 2020), and for enhancing the sensory and physical characteristics of food like grape juice (Mesquita et al., 2020), apple juice (Lim & Ha, 2021), garlic bulb (Sharma et al., 2020) and wheat (Bhat et al., 2020). Moreover, it causes no significant nutritional and sensory changes compared to conventional preservation. Despite the numerous advantages of irradiation technology, it is important to note that vitamins B1 and C are sensitive to irradiation and loss during irradiation treatment preservation (Witrowa-Rajchert et al., 2009; Woodside, 2015). While vitamin C is widely recognized for its anti-OA potential, which alleviates OA and OA-related symptoms by attenuating oxidative damage within articular cartilage (Marks, 2024). High-intensity irradiation also causes damage to lipids. Nevertheless, this loss is much less than conventional drying, cooking, freezing, and preservation (Witrowa-Rajchert et al., 2009; Woodside, 2015).

Pulsed electric field (PEF), a high-field intensity pulse applied to food for a short time, is extensively employed in the food sector because of its ability not to cause undesirable sensory or nutritional changes in treated food (Niu et al., 2020). It inactivates microbes such as E.coli in orange, coconut, and pineapple juice and inactivates the spoilage enzymes in pine nuts, apples, and carrot juice (Liang et al., 2017; Niu et al., 2020). The extended literature on the use of PEF in the extraction of bioactive compounds from anti-OA-related food, e.g., cyanobacteria (Chittapun et al., 2020), apple peel (Wang et al., 2020), cinnamon (Pashazadeh et al., 2020), and tomato (Pataro et al., 2020) elucidated its ability to preserve and improve these bioactive compounds and their bioactivity. Besides that, various studies have also explored its operation in freezing and dehydration. The PEF treatment reduces the time required for drying and freezing and maintains thawed and dehydrated food's color and textural properties (Jadhav et al., 2021). A study conducted in 2020 on PEF-treated spry dried red bell pepper juice powder showed higher retention of vitamin C but a lower level of total phenolic content (Rybak et al., 2020). Another study conducted to elucidate the PEF treatment effect on the phenolic compounds of carrots explicated that after 24 h of treatment, a significant increase in ferulic acid, p-OH-benzoic, total phenolic, and chlorogenic acid was noted (López-Gámez et al., 2020). More research is needed to understand and untangle the discrepancies in the reported effects of PEF treatment on total phenolic content.

High hydrostatic pressure (HHP) produces pressure on food by the water. During this treatment, exposure to HHP destroys mold, yeast, and gram-positive and gram-negative bacteria from exposed food. HHP-treated samples have fresh-like attributes because this technology effectively preserves the texture, nutritional, and sensory quality of food (Cap et al., 2020). This technology is highly effective in extracting anthocyanins, antioxidants, phenolics, and flavonoid compounds (de Jesus et al., 2020), which have therapeutic potential in alleviating the OA (Deligiannidou et al., 2020; Pomilio et al., 2024). Extraction of neutraceutical compounds from different foods, e.g., egg yolk, gooseberry juice, pomace of grapes, tomato waste, and red microalgae, demonstrated the effectiveness of HPP technology (Jadhav et al., 2021). HHP-treated fermented juices showed a substantially higher level of antioxidants and phenolic compounds than untreated samples (Rios-Corripio et al., 2020). This implies that future treatments for OA may utilize HHP-treated bioactive compounds or foods.

Pulsed ultraviolet technology (UV), an economical technology, is extensively employed by food industries to increase shelf life and destroy pathogens. Despite that, pulsed UV reduces the toxins and improves the activity and levels of bioactive compounds (Fenoglio et al., 2020). Thus, this technology can be considered safe for anti-osteoarthritic diet processing because it improves and preserves nutritional quality. A study conducted by Jagadeesh et al. (2011) reported that mature green tomatoes treated with UV-C (3.7 KJ/m2) in storage had significantly higher levels of ascorbic acid and total phenolic content but low levels of lycopene content compared to untreated samples. Recently, a study on pulsed UV-treated tomatoes (360 min, 365 nm) found a significantly high increase in flavonoids, lycopene, lutein, β-carotene, carotenoids, and phenolic compounds. This suggests that A-range ultraviolet irradiation has excellent potential to increase the antioxidant compounds and their activity in post-harvested tomatoes (Dyshlyuk et al., 2020). Despite its tremendous benefits, this technology also has some limitations, such as adversely affecting the texture of solid food and reducing its color. Ozone gas (O3) is highly reactive, but the food industry widely uses it for its ability to inactivate food toxins and kill bacteria and microbes. This gas sterilizes the equipment because of its effective antibacterial and antimicrobial activity (Porto et al., 2020; Tiwari et al., 2010). Nevertheless, this unstable gas reacts quickly with food components and causes undesirable changes like color reduction and lipid oxidation (Giménez et al., 2021). There is a great need for thorough studies and research regarding the limitations of nonthermal technologies to reduce undesirable changes and improve food acceptability.

4.3. Nanotechnology

Nanotechnology is another novel technology with various applications in food and nutrition, including detecting food pathogens and microorganisms, modifying the texture, taste, and color of food, enhancing nutrition quality, creating a nutrient delivery vehicle, and assisting in explicating nutrient physiology and metabolism. The field of nano-science technology has grown extensively into various domains of research, such as food agriculture, nutraceuticals, and pharmacy, and is aiding in the combat of numerous diseases and disorders, including OA (Arshad et al., 2021; Naeem et al., 2023; Xiao et al., 2022). Nanotechnology offers an avenue to improve OA treatment by using targeted therapeutics (antioxidants), smart scaffolds, and novel visco-supplements (Fig. 4) (Table 3) (Lawson et al., 2021). Nanotechnology significantly improves antioxidant therapy in OA treatment (González-Rodríguez et al., 2017). Phytochemicals can potentially prevent and treat various diseases, including OA (Amirkhizi et al., 2022; Guan et al., 2019; Mozafari et al., 2009). An expanding body of literature explicated that consumption of dietary polyphenols (quercetin, epigallocatechin gallate, soy isoflavones, phytosterols, resveratrol, anthocyanins, and rosmarinic) mitigates the OA onset and progression, and protects the cartilage by attenuating the inflammatory cytokines and IL-1β, NF-κB, and TNF-α (Amirkhizi et al., 2022; Calabrese et al., 2021; Guan et al., 2019). Unfortunately, these phytochemicals have extremely low solubility, bioavailability, and stability, leading to rapid degradation before reaching their target cells or tissues. Accumulated research explicated that nanotechnology improves phytochemicals' stability, bioavailability, and solubility, particularly quercetin, curcumin, epigallocatechin gallate, and resveratrol. It prevents the premature degradation of phytochemicals, increases the circulation time, and improves the cellular uptake, target specificity, and their bioactivities (Wang et al., 2014). Nanochitin slows down fat digestion, making it helpful in producing high-satiety foods that aid in weight loss, a crucial factor of OA. Nevertheless, it decreases fat-soluble vitamin bioaccessibility, which is not ideal from a nutritional perspective (Zhou et al., 2020). Many bioactive compounds and vitamins can degrade quickly due to their high sensitivity to acidity and the enzymatic activity of the stomach and duodenum. Nanocapsules, nanosized powders, or nano-cochleate can be used as carriers to increase the delivery or bioavailability of antioxidants, coenzyme Q10, flavors, essential oils, vitamins, minerals, and phytochemicals in the human system. Vitamin spray-dispersed nano-droplets improve the absorption and bioavailability of nutrients like curcumin, iron, and folic acid. These are efficient approaches to distributing nutrients effectively without changing the color or taste of food (Nile et al., 2020; Ognik et al., 2016; Singh et al., 2017).

Vitamins D, E, C, β-carotene, and calcium, indispensable in OA pathophysiology and treatment, have received significant attention in nanotechnology (Zhou et al., 2020). Curcumin has an anti-OA potential, but its absorption is limited because a minimal amount of those molecules can cross the intestinal barrier to become part of the circulation. Theracurmin, nanoparticle colloidal dispersion, had a 27-fold higher bioavailability in humans than curcumin powder. A short-term, randomized, double-blind, placebo-controlled prospective study of eight weeks was conducted to ascertain the clinical effect of Theracurmin on knee osteoarthritic patients. Knee pain visual analog scale (VAS) scores were significantly lower in the Theracurmin group than in the placebo group (Nakagawa et al., 2014). The potential of acid-activated curcumin polymer micelles as therapeutics for OA was appraised using a mouse model of monoidoacetate acid (MIA)-induced knee OA (KOA), and results manifested that acid-activated curcumin polymer micelles hold remarkable potential as a therapeutic agent for OA (Kang et al., 2020). Although nanomaterials have GRAS (Generally Recognized as Safe) status, the safety and health issues associated with their use cannot be overlooked. Focusing on the potential for nanoparticles to migrate from packaging materials into food, the use of cytotoxic agents, and their effects on consumer health, many studies have raised safety concerns

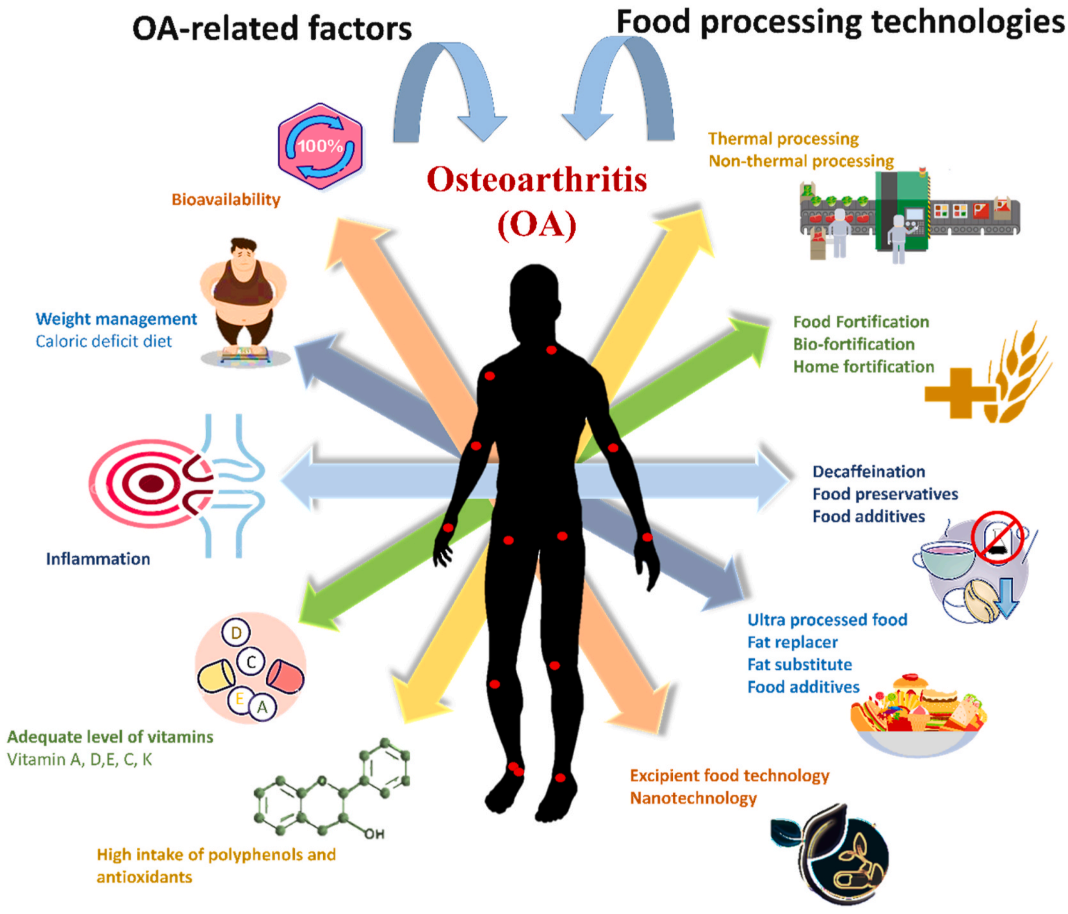

Fig. 4. Visual representation of food processing techniques of effects on OA-related factors.

Table 3
Preclinical/clinical studies and evidence supporting the efficacy of nanotechnology in OA therapy.

Category	Nanocarrier	Composition/Formulation	Animal model/cell line	OA induction	Drug delivery route	Study Duration	Outcomes	References
Gene therapy	Matrix metalloproteinase 13 Short interfering RNA (MMP13 siRNA)	siRNA loaded nanoparticles (siNPs) encapsulated in poly (lactic-co-glycolic acid) (PLGA) based microPlates (μPLs) to formulate siNP-μPLs against MMP13 (siMMP13-μPLs)	Mice	Post-traumatic OA induction by repetitive mechanical joint loading	1 intra-articular injection	28 days	MMP13 gene expression was down regulated by 65%–75%, which attenuate the development of osteophytes, meniscal degeneration, and cartilage deterioration	Bedingfield et al. (2021)
	G5-AHP/miR-140	A multifunctional gene vector G5-AHP with microRNA-140 (miR-140) were employed to make G5-AHP/miR-140 then construct the nano-microns combined with monodisperse-gelatin-methacryloyl hydrogel microspheres (MS)	Mice	OA induction by destabilizing the medial meniscus by surgery	1 intra-articular injection of PBS, MS@G5-AHP/miR-NC, G5-AHP/miR-140, and MS@G5-AHP/miR-140, after every 2 weeks	12 weeks	OARSI scores were lower in the G5-AHP/miR-140 and MS@G5-AHP/miR-140 groups than PBS group. The MS@G5-AHP/miR-140 group performed the best in terms of GAS level, indicating superior cartilage thickness retention.	Li et al. (2022)
	p5RHH-siRNA	p5RHH peptide that was synthesized by GenScript is an ationic amphipathic peptide and p5RHH–siRNA polyplexes were prepared	Mice	OA induction by destabilizing the medial meniscus by surgery	5 intra-articular injections of p5RHH–siRNA nano-complex were injected first, immediately after surgery then at 1, 2, 4 and 6 weeks	6 weeks	IL-1-induced MMP-13 and ADAMTS-4 and 5 expressions in chondrocytes were knockdown by these intra-articular injections	Duan et al. (2021)
	CircRNA3503 with small extracellular vesicles (sEVs)	From synovium mesenchymal stem cells, sEVs were derived and produced circRNA3503-loaded sEVs. Poly gels (PLEL) were used as sEVs carrier	*In vitro*: Osteoarthritic human synovial membrane and articular cartilage cells In vivo: Rats	*In vitro*: IL-1β (10 ng/mL) or TNF-α 10 ng/mL for human cells *In vivo*: Sham surgery	*In vivo*: After surgery, PLEL@sEVs were injected by intra-articular injection every 4th week	–	PLEL@circRNA3503-OE-sEVs is a highly successful therapeutic approach to halt the progression of OA. Additionally, circRNA3503-OE-sEVs increased chondrocyte regeneration to slow down the loss of chondrocytes over time.	Tao et al. (2021)
	Peptide-WNT16 mRNA nano complex	Peptide was incubated with WNT16 mRNA to form a nano complex and stabilized this complex with hyaluronic acid (HA)	Osteoarthritic human cartilage explants	–	–	48 h	Peptide-WNT16 mRNA nano complex inhibits canonical -catenin/WNT3a signalling, increasing the synthesis of lubricin and reducing chondrocyte death.	Yan et al. (2020)
	NPs-YCWP NPs: miR365 antagomir/AAT	miR365 antagomir/AAT (NPs) complex was made by miRNA365 antagomir and AAT then YCWP and NPs used to develop oral drug delivery. Fluorescently labelled yeast cell particle made by *S. cerevisiae* SAF-Mannan was used	Mice	Post-traumatic osteoarthritis model by surgical destabilization of the medial meniscus	Oral administration of 06/YCWP with 100 pmol miR365 antagomir every day	50 days	Histological staining, gene, and protein expression results showed that the OA symptoms were alleviated by the biodegradable miR365 antagonist/NPs-YCWP.	Zhang et al. (2020)
Drug delivery system	Polylactic acid (PLA) and chitosan hydrochloride (CS-HCl) nano complex	Etoricoxib-loaded bio-adhesive hybridized nanoparticles were formulated using PLA and (CS-HCl) in the presence of Captex®200, Tween®80, and polyvinyl alcohol	MC3T3-E1 normal bone cell line	–	–	28 days	This nanoparticle formulation enhanced the ALP activity, calcium ion binding and deposition. This nano complex showed strong binding capacity with naturally occurring HA	Salama et al. (2020)
	Kartogenin conjugated chitosan (CHI-KGN)	Kartogenin was conjugated with low and molecular-weight chitosan in the presence of a catalyst	Rat	Surgery	Intra-articular injections at weeks 6 and 9 after ACLT OA induction	14 weeks	Less degenerative alterations were observed in CHI-KGN NPs or CHI-KGN MPs treated OA rats. In conclusion, polymer-drug conjugates such as CHI-KGN NPs or MPs can be effective IA drug delivery systems for treating OA.	Kang et al. (2014)
	Micelles	Drug-loaded hydrogen peroxide-sensitive nano-micelle	Activated macrophages and BMSCs	–	–	7 days	These drug-loaded nano-micelles reduced the joint inflammation, up-regulated bone marrow mesenchymal	Wu et al. (2021)

(*continued on next page*)

Table 3 (*continued*)

Category	Nanocarrier	Composition/Formulation	Animal model/cell line	OA induction	Drug delivery route	Study Duration	Outcomes	References
							stem cells to regenerate cartilage and caused the BMSCs to develop into chondrocytes	
	Liposomal gel	Lipogel of diclofenac	OA patients	–	Applied on knees	6 weeks	Diclofenac liposomal gel was superior in reducing the symptoms of OA in the knee.	Bhatia et al. (2020)
	Thermo-responsive poly nano-particles loaded with KAFAK drug	pNIPAM shell prepared and then copolymerized with KAFAK drug	Cartilage plugs from bovine knee	The elimination of native aggrecan was used to replicate OA-like circumstances	Nano-particles and IL-1β were added every 2 days	8 Days	These thermosensitive drugs loaded nano-particles suppressed the IL-16 expression.	McMasters et al. (2017)
	Bisphosphate nanoparticle with clodronate drug	Clodronate drug embedded with amino bisphosphate nanoparticles	*In vivo*: OA patients *In vitro*: Circulating progenitor cells	–	*In vivo*: 200 mg weekly administrated through intra-muscular injection In vitro: 50 nM–100 nM	*In vivo*: 6 months	Compared to clodronate alone, drug-loaded NPs more effectively increased SOX9 expression and alleviate the OA pain. It also improved physical and mental health	Valenti et al. (2017)
	Berberine chloride-loaded chitosan nanoparticles	The ionic cross-linking method was used to develop these nanoparticles	Rat	Knee OA induced surgically	0.6 mg/ml BBR-loaded CNs injected by intra-articular injection and blood obtained at different hours after administration of nanoparticles	10 weeks	These nanoparticles increased anti-apoptotic activity and showed high retention time in synovial fluid. Because of their spherical shape, these nano-particles showed great stability	Zhou et al. (2015)
	Gold nanoparticles with chondroitin sulfate	Gold nanoparticles synthesized and combined with chondroitin sulfate (CS) to form an AuNps-CS complex	Goat chondrocytes	Collagenase	Specific concentrations of AuNps and CS were added	–	Collagen and GAG production is greatly enhanced, and chondrocyte proliferation and extracellular matrix formation also increased	Dwivedi et al. (2015)
	Nano-curcumin	A specific evaporation technique was employed to synthesize the nano-curcumin complex	Rat	Mono-iodoacetate	200 mg kg^{-1} curcumin and nanocurcumin were gavaged for 2 weeks	2 weeks	Nano-curcumin enhanced the chondroprotective potential of curcumin, enhanced the cellularity and slow down the degeneration of cartilage	Niazvand et al. (2017)

related to nanomaterials (Athinarayanan et al., 2014; Bradley et al., 2011; Jain et al., 2018). While developing nano-food products, the transparency of safety and health issues should be the priority. Thus, more research and mandatory testing related to the usage safety of nano-food products are required before they enter the market.

4.4. Ingredient-modified food processing

4.4.1. Fat-modified food

Obesity has emerged as a serious health concern in developed countries, and it has a strong association with OA. Even though obesity and overweight are modifiable, these are still the most decisive and determinant risk factors for OA, especially for KOA (Raud et al., 2020; Shahid, Inam-ur-Raheem, Aadil, & Israr, 2022). A 5% increase in body mass index increases the risk of KOA by 35% (Raud et al., 2020). The actual reason is that excessive body weight increases the mechanical load on joints, which damages the cartilage and cartilage mayhem (Kulkarni et al., 2016). Besides that, white adipose tissue produces leptin and adipokine, and elevated leptin is strongly associated with low-grade inflammation and cartilage degradation (Thomas et al., 2018). Adipokine contributes to OA pathogenesis because it is crucial in maintaining healthy bones and cartilage and is directly linked to inflammation and adiposity (Azamar-Llamas et al., 2017). A caloric-restricted diet with low fat is frequently advised to lose weight and improve joint health (Radakovich et al., 2019). Even though many have started choosing low-fat and fat-free diets, research shows that cutting back on fat is one of the healthiest but most difficult habits to keep up because reduced-fat and fat-free foods have poorer mouthfeel, flavor, texture, and sensory properties (Hsieh & Ofori, 2007). Therefore, the focus has been on substituting dietary fat in traditional foods with new components with similar sensory qualities usually attributed to dietary fat. Nowadays, fat replacers (FRs) successfully solve this problem by reducing high fat and high caloric content while maintaining the flavor, taste, mouthfeel, texture, and organoleptic attributes of food (Colla et al., 2018).

The FRs used as dietary fat substitutes can be carbohydrate-based, fat-based (also known as fat substitutes), or protein-based. They have different functions and structures, can replace one or more functions of fat, and provide a lower caloric value than the original fat (M et al., 2021; Colla et al., 2018). FRs can be synthetic fat substitutes (FS), fat mimetics (FMs), fat analogs, and fat extenders. Carbohydrate-based FRs include starch-derived FRs (resistant starch, maltodextrin, polydextrose), cellulose-based FRs (microcrystalline cellulose, MC gums), dietary fiber-based FRs (pectin, inulin, b-glucan, bacterial cellulose, and Z-trim), and gum-based FRs (locust bean gum and guar gum). Protein-FRs can be classified as animal-based or plant-based protein-fat replacers. Fat-based FRs, also referred to as fat substitutes, are used in food products to mimic the properties of traditional fats while reducing calorie content. Structured lipids, sugar polyesters, esterified propoxylated glycerol, dailkyl dihexadecymalonate, and trialkoxytricarballate are examples of fat-based FRs (Tur & Bibiloni, 2016). B-glucan is a polymer commonly found in oats, barley, and yeast cell walls. Its preparation is used as a substitute for vegetable oil in low-fat food products such as salad dressings, ice creams, yogurts, cheese, and mayonnaise. Furthermore, b-glucans have gained widespread recognition for their therapeutic potential and nowadays are under light for OA treatment (El Khoury et al., 2012). Kim and his collaborators investigated the efficacy of polycan, a beta-1,3-1,6-glucan originated from Aureobasidium pullulans SM-2001, in the treatment of OA caused by partial medial meniscectomy (PMM) and anterior cruciate ligament transection (ACLT). Cartilage proliferation, the maximum extension angle of each knee, cartilage histopathology, and the change in circumference were evaluated. The study's result showed that 84 days of continuous oral treatment with three different doses of polycan (21.25, 42.5, and 85, 42.5 mg/kg) significantly reduced articular stiffness and histological cartilage damage compared to OA controls, suggesting that 42.5 mg/kg of polycan is the ideal dose for treating OA (Kim et al., 2012). A double-blind, placebo-controlled 8-week trial evaluated the efficacy of beta-1,3/1,6-glucans on osteoarthritic dogs and elucidated that daily consumption of 800 ppm beta-1,3/1,6-glucans significantly reduced the pain, stiffness, and lameness and improved the locomotion and activity of dogs compared with placebo. The author suggested that 800 ppm beta-1,3/1,6-glucans in dry food for dogs would be worthwhile in treating OA (Beynen & Legerstee, 2010). Chia seeds and oats are antioxidants and polyunsaturated fatty acid-rich foods that possess anti-inflammatory properties and have been well known for their therapeutic potential, especially for OA (Kim et al., 2021; Mohamed et al., 2020). Polyphenols like avenanthramide, avenasterol, avenacoside, and β-glucan are major components of oats that attenuate inflammation (Kim et al., 2021). Avenanthramide C extracted from oats and β-glucan are promising candidates for attenuating OA progression (Tran et al., 2021). There is increasing interest in using oat and chia emulsion gels as substitutes for animal fat. It not only reduces fat and calories, but it also improves the nutritional content of food and minimizes nutrient loss during cooking. Including chia emulsion gel in reduced-fat fresh sausages improved the polyunsaturated and monounsaturated fatty acid content (Pintado et al., 2018). To develop healthier fat, Beeswax and ethyl cellulose oleogels were prepared using linseed oil, OO, and fish oil as fat replacers. Both olegels exhibited high nutritional value because of the high nutritional profile of these compounds. For example, OO: 45% MUFA, particularly 72% of oleic acid; linseed oil: 68% PUFA, most representative ones n-3 fatty acids; and fish oil: 35% PUFA, most abundantly EPA (18.7%) and DHA (12%) (Chin & Pang, 2017; Loef et al., 2019; Mendoza et al., 2013; Puente et al., 2014). Ethyl cellulose oleogel had a detrimental effect on sensory parameters, while beeswax oleogel had no discernible effect (Gómez-Estaca et al., 2019). Another study used oleogels made from beeswax and sesame oil as full or partial FRs in beef burger formulation, also substantiating the potential of wax olegoels as FRs in meat product development (Moghtadaei et al., 2018).

Inulin, an oligomer, forms a gel or cream at 40%–45% concentration, giving it a fatty cream feel. It has properties like durability against freeze-thaw, strong water binding, and suppression of syneresis in mayonnaise and salad dressings. Inulin with a degree of polymerization (DP) of 25 or below replaces high-performance fat in fat-reduced table spreads, cheese, meat, meat substitutes, fillings, and frozen sweet sauces (M et al., 2021). This oligomer is under discussion to understand the anti-osteoarthritic role of inulin (Korotkyi et al., 2020). Furthermore, polydextrose (Beynen et al., 2011; Reuter et al., 2015), xanthan gum (Li et al., 2019), and microcrystalline cellulose (Setu et al., 2014) are also FRs that have an ameliorative effect on OA. Z-trim, which stands for zero calories, is a carbohydrate-based FR that can replace some glycemic elements (starches, sugars, and syrups) and fat. It offers a fiber-like structure made of aqueous gel without imparting any taste. It significantly reduces the calories depending on how much fat and carbohydrates are replaced in meal formulations. It contributes zero calories, which is why it has been commonly used in dairy and bakery products since its discovery in 1996, and more focus is given now to using it in meat and meat products to replace meat or meat fat (Schmiele et al., 2015; Summo et al., 2020).

FRs are granted GRAS status by the Food and Drug Administration (FDA), except for olestra and polydextrose. Olestra is a synthetic fat made up of vegetable oil and sucrose that digestive enzymes cannot hydrolyze in the gut, cannot be absorbed due to its enormous molecular size, and remains undigested. It does not add any calories or fat to the meal, but its excessive use may cause fatty and watery stool and cause the loss of fat-soluble vitamins. A labeling disclaimer is always necessary when polydextrose is present in products because it can have a laxative effect (Hsieh & Ofori, 2007). Therefore, more research and work are required to address these issues and increase the applicability and acceptance of fat replacement technology. Despite the limitations of FRs, accumulating evidence suggests that FRs can help to reduce and control weight, which is a significant risk factor for osteoarthritic and non-osteoarthritic individuals, concurrently allowing them to enjoy their food while managing the OA through diet therapy.

4.4.2. Decaffeination processing

Caffeine, an alkaloid, is a stimulating compound naturally found in tea leaves, yerba mate leaves, cacao beans, guarana beans, cola nuts, and coffee beans. It can be produced synthetically and incorporated into foods, beverages, pills, and dietary supplements. It has no nutritional value, but it is one of the most often ingested substances, with an average daily intake of 120 mg. However, excessive consumption of caffeine-containing beverages is linked to various health issues, including OA. There is plenty of evidence that caffeine consumption negatively affects the physiology of articular cartilage and raises a person's risk of developing OA (Choi et al., 2017; Luo et al., 2015; Shangguan et al., 2017; Tan et al., 2012, 2018). Caffeine consumption negatively affects the articular cartilage by reducing the cartilage ECM (extracellular matrix) component synthesis, decreasing the tidemark, diminishing chondrocyte proliferation, and leading to an irregular cartilage surface. Caffeine consumption buildup of cholesterol in chondrocytes reduces the quality of chondrocytes (Guillán-Fresco et al., 2020). Numerous experimental studies investigated caffeine consumption's effect on rats' articular cartilage. These studies found that prenatal caffeine consumption, even below the threshold for clinical intoxication, severely damaged the articular cartilage of fetal rats. Histological studies specifically showed that parental caffeine exposure affected rat offspring rigorously. The unevenly distributed chondrocytes and irregularly surfaced cartilage were observed in the tangential zone of joints (Luo et al., 2015; Reis et al., 2018; Shangguan et al., 2017; Tan et al., 2012, 2018). It is important to note that parental caffeine's negative effect on the fetal rats' articular cartilage persisted into adulthood (Shangguan et al., 2017; Tan et al., 2018). Due to its deliberately devastating effect on OA onset and evaluation, caffeine intake should be avoided or mentored carefully, especially for persons with a slow metabolism (pregnant women and children) and those with OA or a high predisposition to having OA (Guillán-Fresco et al., 2020). However, advances in food technology have significantly contributed to the development of caffeine-free beverages.

Decaffeination can be executed using solvent extraction, supercritical carbon dioxide, and water decaffeination. Commonly used organic solvents are methylene chloride (DCM) and ethyl acetate (EA), while the water decaffeination process does not use any solvent (Pietsch, 2017, chap. 10). Supercritical carbon dioxide decaffeination has gained popularity due to its benefits, including its safety, non-flammability, and exceptional selectivity. During decaffeination, some volatile aroma precursors may also be removed along with caffeine, leading to a low, plain, and thin taste even after roasting (Muchtaridi et al., 2021; Pietsch, 2017, chap. 10). These decaffeination methods have some shortcomings, but water decaffeination is better than other methods due to its ability to maintain the taste of coffee while removing caffeine. In contrast, solvent extraction and carbon dioxide decaffeination are capital-intensive methods due to high-cost agents and show some health concerns. However, health concerns are associated with solvents such as methylene chloride, despite not being proven to cause cancer in humans but in mice at specific concentrations (Hsieh & Ofori, 2007).

Therefore, microbial decaffeination methods (caffeine degradation by bacteria, fungi, or enzymes) were employed as an alternative to conventional decaffeination processes. Fungi species (*Penicillium and Aspergillus)* and bacterial species *(Pseudomonas and Serratia genus*) are effective caffeine degraders. However, studies have shown fungi species are less efficient at decaffeination than bacteria. Demethylases and oxidases are enzymes responsible for the caffeine-degrading ability of bacteria and fungi. Researchers isolated and purified these enzymes to make this process more efficient by using them in caffeine degradation. However, these isolated enzymes are unstable and do not provide efficient results (Lukman et al., 2023). Studies related to genetic modification found that bacteria use N-demethylation and C-8 oxidation metabolic pathways for decaffeination. The discovery of these two catabolic pathways (N-demethylation and C-8 oxidation) can pave the way for numerous biotechnology applications that can be used for OA management (Lin et al., 2023; Vega et al., 2021). A review conducted in 2022 found that the most effective approach for making caffeine-free coffee species is to use CRISPR-Cas9 and A. tumefaciens-mediated transformation (AMT). This process involved genome editing and deleting two key genes in the caffeine biosynthesis pathways. These two genes are XMT (7-methylxanthine methyltransferase) and DXMT (3, 7-dimethylxanthine methyltransferase), which are crucial for caffeine synthesis (Leibrock et al., 2022).

4.5. Food fortification

Micronutrient deficiency is widespread, particularly in middle and low-income countries, affecting cognitive and physical health and enhancing the global disease burden. A low nutrient-dense food intake, a high processed diet intake, infection, or blood loss can cause micronutrient deficiency. According to estimates, micronutrient deficiencies contribute to 7.3% of the world disease burden, with vitamin A and iron deficiency ranking among the top 15 leading causes of morbidity in more than a million children each (Ahmed et al., 2012; Black et al., 2013). The United Nations Food and Agriculture Organization (FAO) and World Health Organization (WHO) employed various strategies to combat this micronutrient deficiency. Nonetheless, only food fortification has been proven to combat micronutrient deficiency successfully. Food fortification can be defined as adding vitamins and minerals to frequently consumed foods to enhance diets and prevent and control micronutrient deficiencies. It is a risk-free, cost-effective, and most appropriate nutritional intervention to combat nutritional deficiencies, particularly deficiencies related to vitamin D, vitamin A, folic acid, iron, and zinc deficiencies. The extended literature suggested an inverse relation between vitamin D, A, and B9 and OA progression. A low serum vitamin D level is associated with a high incidence of radiographic OA, narrower joint space, severe knee pain, and poor physical function (Tripathy et al., 2020). Magnetic resonance imaging (MRI) revealed that vitamin D deficiency is positively linked with the medial and lateral tibial bone area in women. In older men and women, serum 25(OH)D level was significantly and positively associated with knee cartilage volume. A five-year longitudinal study also explicated the significant association of vitamin D with OA. Results showed that a higher baseline serum level of vitamin D decreases cartilage volume loss and is associated with bone protective factors (Wang et al., 2023).

Food fortification of staple foods with vitamins D, A, B9, and B12 could assist in curbing OA onset and progression. Vitamin-D-fortified foods like fortified milk, fortified spreads, and fortified cereals are helpful to cope with vitamin D deficiency (available at DBA, the Association of UK Dieticians, https://www.bda.uk.com/resource/vitamin-d.html) and at Rheumatology online. To combat vitamin A deficiency, 29 developing countries are fortifying their foods with vitamin A (Mason et al., 2014). More than 40 countries mandated vitamin A and D fortification in sugar, margarine, and edible oil (Olson et al., 2021). In October 2019, the Rwandan government initiated the fortification of five staple foods, namely wheat flour and maize flour, with vitamin B12, vitamin B1, vitamin B3, vitamin B9, vitamin A, zinc, and iron, edible oils and sugar with vitamin A, and salt with iodine (Olson et al., 2021). Whiting and colleagues summarized different studies of food fortification to evaluate the effect of food fortification on bone health and metabolism. The findings of this review indicate that calcium and vitamin D have been the subjects of most studies of fortification and bone health, and these nutrients positively affect bone remodeling (Whiting et al., 2016).

Biofortification, another type of food fortification, increases the micronutrient content of staple crops through plant breeding, agronomically, or mineral fertilizers. Biofortification programs focus primarily on increasing provitamin, carotenoid, zinc, and iron content in food crops; some biofortification projects also focus on amino acids and protein. Biofortification projects include biofortification of vitamin A in cassava, potatoes, and corn, iron-biofortified rice, sweet potatoes, beans, and maize, and zinc-biofortified sweet potatoes, rice, wheat, beans, and rice. Genetic engineering enables the cultivation of micronutrient-enriched crops, which can help combat OA and many other comorbidities (de Brauw et al., 2019; Van Der Straeten et al., 2020).

Point-of-use fortification, also known as home fortification, is the addition of vitamins and minerals to cooked food or when it is ready to be eaten. It is a key approach to combating micronutrient deficiencies, particularly iron. Single-dose powdered vitamin and mineral packets sprinkled onto food that do not change the flavor, color, or taste (Organization, 2016). Most countries use a 15-micronutrient-powdered formulation for children (Suchdev et al., 2020). Formulating micronutrient supplements or powders designed explicitly for OA can be a safe and cost-effective approach to combating OA progression and onset, especially for individuals predisposing to OA.

4.6. Excipient food technology

The food or nutrients, regardless of whether they are hydrophilic or lipophilic, must be released from the food matrix, be bioaccessible after digestion, and reach the target tissue of action to improve health and mitigate the diseases, including OA, through an appropriate diet (Sensoy, 2021). Therefore, developing practical methods for enhancing the bioavailability profile of nutrients and bioactive compounds is of utmost importance. In this regard, excipient is a novel development that increases the bioavailability of orally consumed bioactive substances. An excipient is a non-bioactive component added to a dietary or pharmaceutical preparation to improve the bioavailability of co-ingested bioactive components (Ionova & Wilson, 2020). Non-integrated excipient foods refer to the co-ingestion of bioactive-rich food with the excipient food formulation. Integrated excipient foods contain the dispersion of bioactive compounds into the excipient food formulations. They can be consumed as independent functional foods, such as drinks, desserts, sauces, dressings, or yogurt fortified with nutraceuticals like omega-3 fatty acids, carotenoids, or polyphenols (McClements et al., 2015). This innovation can improve overall health and effectively combat OA by increasing the bioavailability of OA-related bioactive nutrients. For instance, eating a salad with a specially formulated salad dressing may boost the bioaccessibility of carotenoids, a proven anti-osteoarthritic compound. Various food ingredients, such as lipids that promote intestinal absorption, antioxidants that prevent chemical oxidation, enzyme inhibitors that slow metabolism, permeation enhancers that improve absorption, and efflux inhibitors, may be present in this dressing. The excipient foods enhance the bioavailability of carotenoids and oil-soluble vitamins in salads when consumed with fat-containing. A potential excipient food can be an edible coating that improves the bioavailability of flavonoids, phytosterols, or vitamins. Cream, yogurt, and ice creams can be potential excipient foods to enhance the bioavailability of berries, fruit flavonoids, and vitamins (McClements & Xiao, 2014). OO is a component of excipient food that increases carrots' α and β carotene content. According to pharmacokinetic studies, adding OO to carrots during cooking increases carotene extractability and solubilization (Rinaldi de Alvarenga et al., 2019), whereas adding it to tomato sauce improves the solubilization of phenolics (Martínez-Huélamo et al., 2015).

In addition to fat-based excipients, there are carbohydrate-based, protein-based, mineral-based, and food additive-based excipients that improve the bioavailability of bioactive compounds. The food excipients, carbohydrates, protect the EGCG from degradation in aqueous solutions like sugar. Food additives such as xylitol/vitamin C and xylitol/citric acid improve the absorption of the total catechin of green tea in the intestinal tract (Shpigelman et al., 2013). Various pieces of knowledge revealed that incorporating lipid droplets in starch-based hydrogels enhanced lipid and carotenoid digestion (Mun, Kim, & McClements, 2015; Mun, Kim, & McClements, 2015). Pectin also functions as a food excipient by altering the carotenoid bioaccessibility and lipid digestion, depending on the type of pectin (Verrijssen et al., 2015). The bioavailability of anthocyanins in blueberry juice can be improved by incorporating soybean flour (Ribnicky et al., 2014).

Curcumin has an anti-OA potential but cannot be used to its full potential because of the low bioavailability of curcumin in its native form. The galenic form of curcumin in a specific excipient is developed using a very thin dispersion of curcumin to maximize its bioavailability. This particular form of curcumin was evaluated for its anti-osteoarthritic potential and concluded that this new preparation of curcumin is a potential neutraceutical approach for OA (Appelboom et al., 2014). Another novel formulation of curcumin was prepared with a combination of established excipients, monoglycerides, and phospholipids, which have high intestinal absorption and solubility. This formulation of curcumin was evaluated for its anti-osteoarthritic potential, indicating that its substantially high bioavailability significantly improves the pathophysiology of OA (Yabas et al., 2021). A study was conducted to assess the efficacy of an excipient food technology-derived gastro-resistant food supplement formulation containing the combination of bromelain and *Boswellia serrata*. This study evinced that this food supplement significantly improved the quality of life of patients suffering from different forms of OA (Italiano et al., 2020).

Contrary to enhancing the bioavailability characteristic of food through excipients, many food combinations likewise reduced the bioavailability of bioactives.

Contrary to improving the bioavailability of food through excipients, many food combinations can decrease the bioavailability of bioactive compounds. For instance, milk proteins, particularly sodium caseinate, can dramatically reduce the bioaccessibility of flavan-3-ols. The low bioavailability of ferulic acid due to its polysaccharide binding restricts its extraction and absorption in the small intestine (Bohn et al., 2015). The crosstalk of evidence suggests that excipient food technology could be a novel way to boost the effectiveness of medications, dietary supplements, and nutraceuticals to curb OA and OA-related symptoms.

4.7. Other food processing factors and their effect on OA

4.7.1. Food additives and preservatives

Food additives and preservatives are chemicals commonly used in foods to enhance the color, taste, aroma, and shelf life and prevent deterioration from the exposure of microorganisms, oxygen, and enzymes. Despite their effect on health, food industries have employed more and more food additives and preservatives to enhance food attributes. Most of these chemicals are classified as GRAS, but a few additives and preservatives have deleterious effects on health and are still a regular part of food products. For instance, monosodium glutamate (MSG/E621) is a flavor enhancer that makes food palatable. Many restaurants commonly use it, and it is frequently used in home cooking. This flavor enhancer can lead to obesity by altering the leptin-mediated hypothalamic signaling cascade. As previously discussed, OA is directly linked to obesity and inflammation; therefore, MSG/E621 could increase OA predisposition and OA-induced comorbidities. A critical literature review corroborated that MSG/E621 consumption has a linear relationship with obesity and inflammation (Kazmi et al., 2017; Niaz et al., 2018). An extended and augmented body of literature elucidates the drastic role of phosphorous-based food additives in bone metabolism. The phosphorous-based food additives significantly elevate the circulating osteocalcin, fibroblast growth factor 23 (FGF23), and osteopontin while drastically lowering the sclerostin concentration compared to baseline values, which negatively links with bone and mineral metabolism (Gutiérrez et al., 2015). Growing evidence suggests that continuously high intakes of phosphorous can disrupt bone and mineral metabolism and cause bone loss, leading to bone-related disorders (Vorland et al., 2017). To date, no standard scientific research has evaluated the effect of commonly used food additives and preservatives on OA. Hence, in future work, scientists should consider elucidating the role of food additives and preservatives in bone and mineral metabolism with a specific reference to OA.

5. Conclusion and future perspectives

The crosstalk of this review confirmed that food processing and other related factors, such as additives, preservatives, the type of processing, the duration of treatment, and the food matrix, can affect OA diet-based management by affecting the nutritional content of OA-related foods. The non-thermal food technologies, specifically ultrasound processing, irradiation, high-pressure, carbon dioxide, electric field, microwave processing, high hydrostatic pressure, and cold plasma, and other food technologies, including food fortification, biofortification, decaffeination processing, nanotechnology, fat replacers, and food excipients, have a great potential to significantly improve diet-based OA management, specifically nanotechnology and food excipients. Despite being safe, these novel technologies have some limitations, such as concerns about health-related safety, degradation of nutritional quality, and significant cost. Extensive research is needed to overcome these limitations, safety issues, affordability, accessibility, and research gaps to design an effective diet-based OA management guideline. Additionally, the limited number of studies on food processing and OA indicate that future preclinical and clinical research, especially randomized controlled trials in humans, should focus on evaluating the effect of the novel food technologies and their combined impact on OA-related foods, which can pave the way for the development of safe and nutritious anti-OA foods and food products with maintained or improved color, texture, flavor, and mouthfeel for OA patients, focusing on personalized nutrition.

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CRediT authorship contribution statement

Arashi Shahid: Conceptulazion and drafted the article. Developed the theoretical framework and visualizations and wrote the manuscript. **Ammar B. Altemimi:** Reviewed and edited the manuscript. **Iahtisham-Ul-Haq:** Reviewed and edited the manuscript. Provided critical feedback and provided help in drafting the article. **Muhammad Inam-ur-Raheem and Rana Muhammad Aadil:** Conceptulazion. Supervised the manuscript, reviewed and edited the draft, provided critical feedback, and helped shape the manuscript. **Roshina Rabail:** Provided help drafting the article by giving critical feedback and guidelines. Reviewed the article. **Muhammad Hamdan Rashid:** Data collection. **Sadia Kafeel:** Data collection. **Muhammad Saad Akram:** Data collection. **Amin Mousavi Khaneghah:** Conceptulazion, Provided help drafting the article by giving critical feedback and guidelines. **Rana Muhammad Aadil:** Supervised the manuscript, reviewed and edited the draft, provided critical feedback, and helped shape the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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