Current Obesity Reports (2022) 11:305–335
https://doi.org/10.1007/s13679-022-00490-0

METABOLISM (M DALAMAGA, SECTION EDITOR)

The Role of Nutrition on Meta-inflammation: Insights and Potential Targets in Communicable and Chronic Disease Management

Omar Ramos-Lopez[1] · Diego Martinez-Urbistondo[2] · Juan A. Vargas-Nuñez[3,4] · J. Alfredo Martinez[5,6,7]

Accepted: 27 August 2022 / Published online: 18 October 2022

Abstract

Purpose of Review Chronic low-grade inflammation may contribute to the onset and progression of communicable and chronic diseases. This review examined the effects and eventual mediation roles of different nutritional factors on inflammation.

Recent Findings Potential nutritional compounds influencing inflammation processes include macro and micronutrients, bioactive molecules (polyphenols), specific food components, and culinary ingredients as well as standardized dietary patterns, eating habits, and chrononutrition features. Therefore, research in this field is still required, taking into account critical aspects of heterogeneity including type of population, minimum and maximum intakes and adverse effects, cooking methods, physiopathological status, and times of intervention. Moreover, the integrative analysis of traditional variables (age, sex, metabolic profile, clinical history, body phenotype, habitual dietary intake, physical activity levels, and lifestyle) together with individualized issues (genetic background, epigenetic signatures, microbiota composition, gene expression profiles, and metabolomic fingerprints) may contribute to the knowledge and prescription of more personalized treatments aimed to improving the precision medical management of inflammation as well as the design of anti-inflammatory diets in chronic and communicable diseases.

Keywords Inflammation · Disease · Nutrition · Anti-inflammatory diets · Bioactive compounds · Personalized nutrition

Introduction

Inflammation is a pivotal component of innate immunity in response to endogenous and exogenous harmful stimuli (i.e., toxic chemicals, environmental agents, trauma, and pathogens/viral infection), which is physiologically challenged as a defense mechanism for injury removal and wound healing processes [1].

Based on timing and pathological features, inflammation can be acute and chronic [2]. Acute inflammation is usually of short duration (minutes to days) consisting of the migration of lymphocytes/neutrophils and macrophages to the inflammatory site, which stimulate the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin 6 (IL-6), and high motility group box-1 (HMGB-1) as well as cell aggregation and enzyme breakdown [3]. Moreover, the activation of NOD-like receptors (NLRs) such as NLRP3, NLRP1, and NLRC4 results in the recruitment of a highly regulated protein complex (known as inflammasome), whose activation initiates downstream inflammatory cytokine production,

This article is part of the Topical Collection on *Metabolism*

✉ Omar Ramos-Lopez
oscar.omar.ramos.lopez@uabc.edu.mx

1 Medicine and Psychology School, Autonomous University of Baja California, Universidad 14418, UABC, Parque Internacional Industrial Tijuana, 22390 Tijuana, Baja California, Mexico

2 Internal Medicine Department, Clinica Universidad de Navarra, 28027 Madrid, Spain

3 Servicio de Medicina Interna, Hospital Universitario Puerta de Hierro Majadahonda, 28222 Madrid, Spain

4 Department of Medicine, Facultad de Medicina, Universidad Autónoma de Madrid, 28029 Madrid, Spain

5 Precision Nutrition and Cardiometabolic Health, IMDEA Food Institute, CEI UAM+CSIC, 28049 Madrid, Spain

6 Department of Nutrition, Food Science, Physiology and Toxicology, Centre for Nutrition Research, University of Navarra, 31009 Pamplona, Spain

7 Spanish Biomedical Research Centre in Physiopathology of Obesity and Nutrition (CIBERobn), 28029 Madrid, Spain

mainly interleukin 1 beta (IL-1β) and interleukin 18 (IL-18) in response to cellular stress [4]. Other intermediaries encompass chemokines, lipid mediators, acute-phase proteins such as C-reactive protein (CRP), transcriptional factors including the nuclear factor kappa B (NF-κB), and major immune cell types [5].

However, uncontrolled acute inflammation may become a permanent condition leading to expanded tissue damage, hemodynamic changes, and organ failure [6]. In fact, chronic inflammation has been linked to the development of non-communicable diseases such as obesity and associated comorbidities [7]. In this regard, obesity leads to abnormal fat accumulation in adipocytes, immune cell infiltration, and pro-inflammatory milieu that disrupt the insulin signaling cascade inducing insulin resistance [8]. Besides, inflammation and oxidative stress interactions are critical to understand the physiopathology of obesity, involving impairments of endoplasmic reticulum functions, hypoxia in the adipose tissue, mitochondrial alterations, and reactive oxygen species overproduction [9]. Furthermore, gut microbiota seems to be implicated in the development of obesity-related low-grade inflammation involving lipopolysaccharides translocation and toll-like receptor 4 (TLR-4) binding, which trigger a state of blood endotoxemia [10]. The resulting unresolved immune activation not only affects local tissues, but also systemic physiology that is termed meta-inflammation [11].

Therefore, it is relevant to identify the triggers that activate pro-inflammatory cascades in order to identify potential targets as well as implement precision intervention strategies for health care [12]. In this context, cumulative population-based evidence supports the role of nutrition on inflammatory pathways [13]. In this critical review, the effects and eventual mediation of different nutritional factors on inflammation are discussed, including specific nutrients (types of carbohydrates, protein sources, structural fatty acids, micronutrients, and trace elements) and bioactive compounds (polyphenols); staple-characterized dietary patterns (i.e., Western, Mediterranean, and Nordic diets); therapeutic diets (i.e., DASH approach); common culinary ingredients (species and herbs); and chrononutrition features (Fig. 1). Moreover, the potential of prescribing personalized anti-inflammatory diets based on social, phenotypical, clinical, genetic/epigenetic, and metabolic/metabolomic characteristics with a precision medicine scope is postulated (Fig. 2).

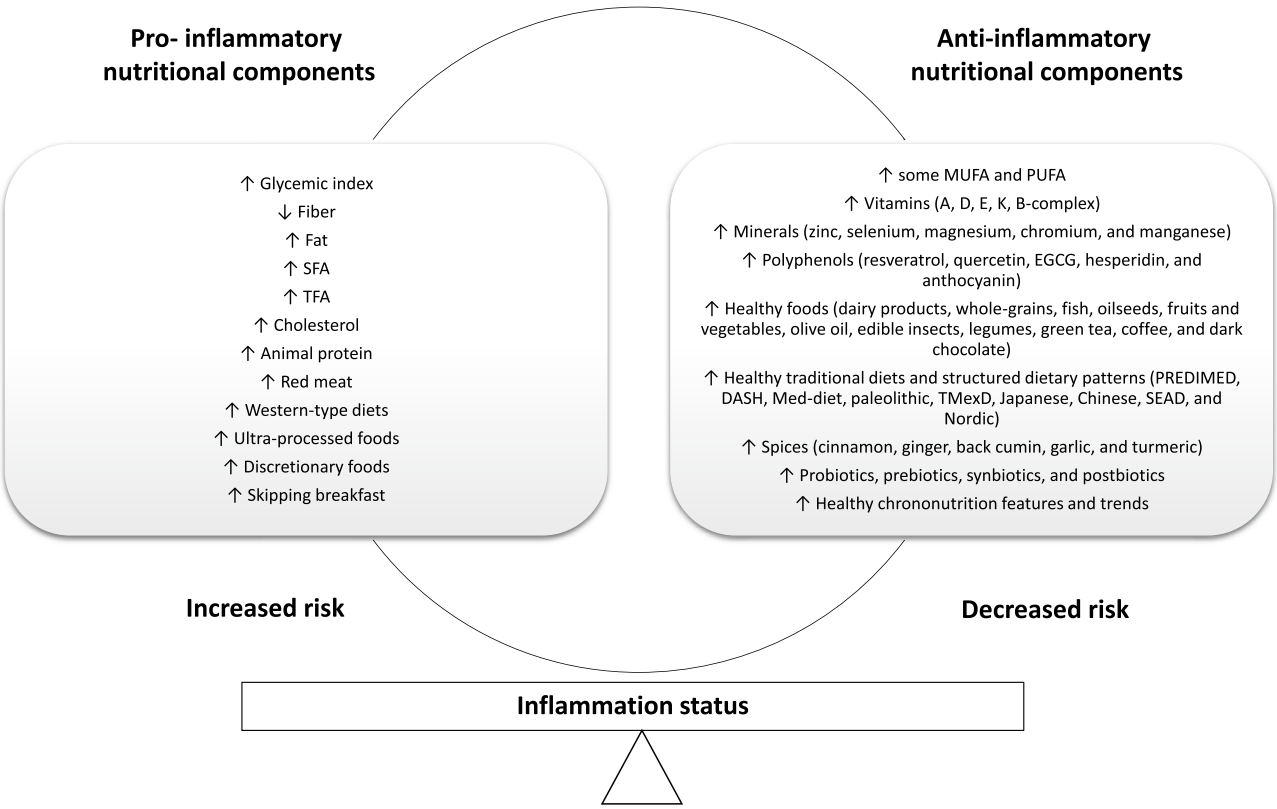

Fig. 1 Nutritional factors associated with inflammatory outcomes in humans. DASH, Dietary Approaches to Stop Hypertension; EGCG, epigallocatechin-3-gallate; Med-diet, Mediterranean diet; MUFA, monounsaturated fatty acids; PREDIMED, Prevención con Dieta Mediterránea; PUFA, polyunsaturated fatty acids; SEAD, Southern European Atlantic Diet; SFA, saturated fatty acids; TFA, trans fatty acids; TMexD, traditional Mexican diet

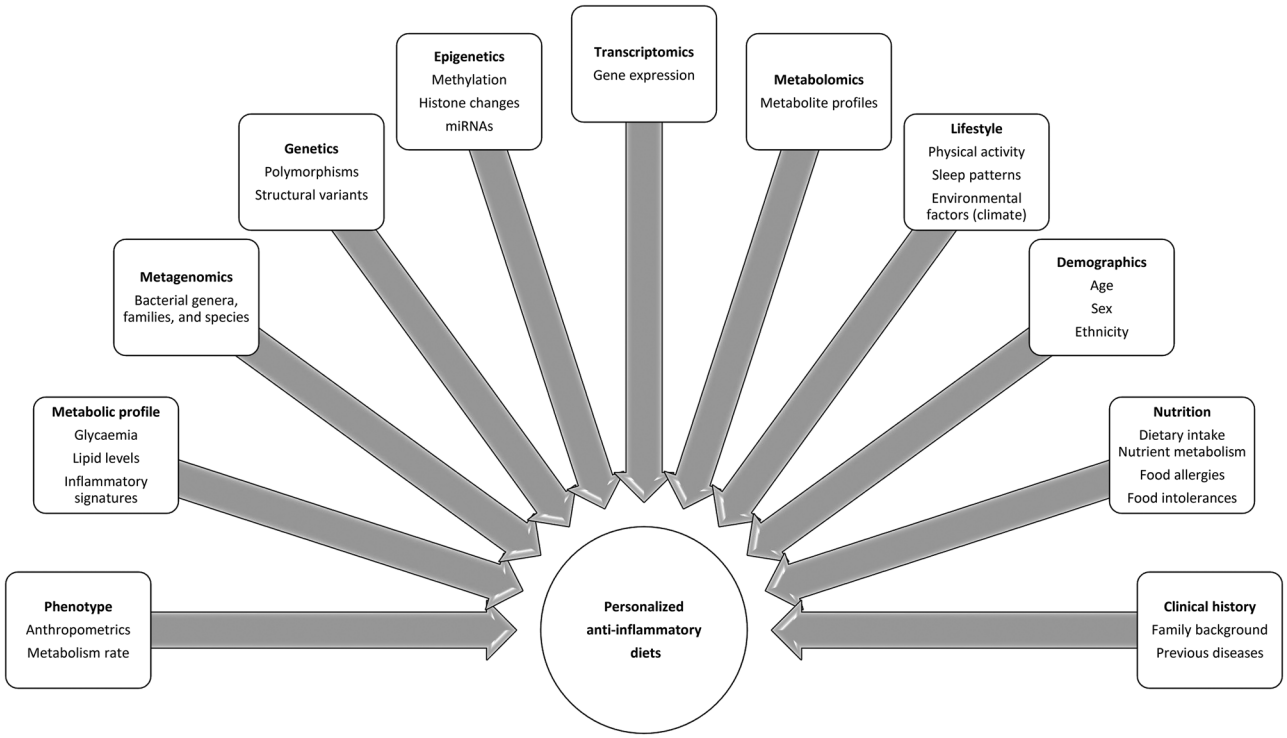

Fig. 2 Precision information for the prescription of personalized anti-inflammatory nutritional strategies

The Role of Nutrition on Inflammation

Macronutrients

Total Carbohydrates

Dietary carbohydrates exert differential effects on health depending on quantity and quality features [14]. Interestingly, a low-carbohydrate diet (20% of total energy) significantly improved the subclinical inflammatory state (lower serum levels of IL-1Ra and IL-6) in diabetic patients [15]. Notably, the adherence to a low-carbohydrate diet (35% of total energy) reduced the levels of inflammatory markers in women with obesity [16]. Also, it was found an overall favorable effect of a low-carbohydrate diet ($\leq$30 g/day) on inflammation in subjects with severe obesity [17]. Additionally, a very low carbohydrate diet (12% of total energy) resulted in relevant reductions in inflammation compared to a low-fat diet (24% of total energy), as reported elsewhere [18].

Glycemic Index

The glycemic index (GI) has been devised to physiologically assess the carbohydrate quality from different foods based on effects on postprandial plasma glucose concentrations [19]. Interestingly, a high-GI diet (based on cooked vermicelli pasta, GI = 35) significantly increased the activation rates of NF-κB in mononuclear cells in lean healthy subjects [20]. Indeed, the negative metabolic and inflammatory responses induced by a high-GI diet (GI > 70) were counteracted by a low-GI diet (GI < 55) in diabetic patients [21]. Furthermore, findings from the DIOGenes trial revealed that low-GI carbohydrates (15 points of difference regarding high-GI carbohydrates) may reduce low-grade inflammation in subjects with overweight or obesity following a weight maintenance diet after weight loss [22].

Fiber

Dietary fiber may provide health benefits involving some immunological mechanisms [23]. Accordingly, fiber intake equal or more than 15 g/1000 kcal has been associated with decreased blood CRP levels in diabetic patients [24]. Accordingly, a randomized intervention trial demonstrated that fiber intake (30 g/day) from a diet naturally rich in fiber or from a supplement can substantially reduce the circulating levels of CRP in lean normotensive participants [25]. Moreover, significant inverse linear associations were detected between dietary fiber intake (mean

16.8 g/day) and CRP serum concentrations in middle age adults [26].

Total Fat

Dietary fat elicit a number of essential functions in the organism; however, excessive fat consumption may lead to obesity and related low-grade inflammatory processes [27]. Indeed, clinical evidence indicates that high-fat diets (i.e., nearly 75% of total energy) cause overproduction of circulating free fatty acids and systemic inflammation [28]. Consistently, a low-fat diet (25% of energy needs) was associated with lower plasma IL-6 levels in diabetic patients [29].

Saturated Fatty Acids

There is increasing evidence concerning the fact that dietary saturated fatty acids (SFAs) act as an important link between obesity and inflammation [30]. Interestingly, subjects consuming more than 10% energy as saturated dietary fat had increased serum levels of CRP compared to subjects having a normal saturated fat intake (< 7% of caloric intake) in young Asian Indians [31]. Likewise, ingestion of SFA (100 mL of dairy cream with 70% saturated fat content) resulted in lipid-induced increases in plasma CRP in women independently of obesity status [32].

Monounsaturated Fatty Acids

Monounsaturated fatty acids (MUFAs) are assumed as a healthy type of fat, being the oleic acid (OA) the most commonly consumed MUFA in daily nutrition [33]. In this context, a cross-sectional epidemiologic study in Japanese population reported a significant inverse relationship between the intake of OA (mean 6.94% of total energy) and serum CRP concentrations [34]. Further controlled trials with different doses of MUFA for the treatment of inflammatory features are warranted.

Polyunsaturated Fatty Acids

In the last years, a plethora of evidence has supported the beneficial effects of polyunsaturated fatty acids (PUFAs) in the prevention of cardiovascular and other chronic diseases with an inflammatory basis [35]. In this context, the intakes of the n-3 PUFA eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were inversely associated with plasma levels of soluble TNF receptors 1 and 2 in healthy individuals [36]. Moreover, total dietary n-3 PUFAs inversely correlated with blood levels of CRP and IL-6 in women [37].

Additionally, some clinical trials have evaluated the effects of prescribing diets high in PUFA or through PUFA supplementation on inflammatory outcomes. For instance, fish oil supplementation (38.2 g/day EPA + DHA during 90 days) lowered the blood levels of pro-inflammatory markers in hypertensive patients [38]. Similarly, healthy young adults receiving n-3 PUFA (2.5 g/day, 2085 mg EPA and 348 mg DHA) for 12 weeks underwent a 14% decrease in serum IL-6 levels [39]. Likewise, low (1.25 g/day) or high (2.5 g/day) doses of n-3 PUFA supplementation for 4 months reduced inflammation responses (specifically serum IL-6 and TNF-α concentrations) in overweight adults [40].

Trans Fatty Acids

Trans fatty acids (TFAs) are mainly industrially formed by the hydrogenation of vegetable oils or from ruminant-derived foods including dairy products and meats [41]. TFA intake has been positively associated with plasma biomarkers of inflammation (including CRP, VCAM-1, E-selectin) in women [42]. In this same population, the consumption of TFA was positively associated with the plasma levels of soluble TNF receptors 1 and 2, mainly in women with higher body mass index [43]. Furthermore, serum CRP concentrations were elevated after TFA consumption (8% of total fat) in men [44].

Dietary Cholesterol

Excessive cholesterol may have deleterious effects on health including some processes affecting inflammation status [45]. For example, highest quartile of serum CRP concentrations (5.9 mg/L) was associated with higher intake of dietary cholesterol (189 mg/day) among Iranian adults [46]. Likewise, in a large representative Middle East population, positive correlations between dietary cholesterol and plasma CRP levels were found [47].

Protein Quantity and Quality

Both the quantity and quality of dietary protein are main determinants of nutritional values and body/endocrine homeostasis [48]. Among participants of the Framingham Heart Study Offspring cohort, dietary protein intake (particularly from plant sources) was inversely associated with serum markers of inflammation such as IL-6 and CRP [49]. Moreover, consuming high (30% of total energy) or low (10% of total energy) protein diets resulted in reduced blood CRP concentrations in morbidly obese individuals [50].

Regarding protein sources, diets characterized by higher intakes of animal protein (high levels of fatty and processed meats) were positively associated with certain blood pro-inflammatory markers such as CRP, IL-6, TNF-a, IL-8, serum amyloid A, and glycoprotein acetylation [51].

Furthermore, findings from the RESMENA dietary study (30% energy from protein) revealed positive associations between animal and meat protein intakes and inflammation, whereas vegetable- or fish-derived proteins had no significant influence on inflammatory status [52].

Micronutrients

Vitamins

Longitudinal and observational studies have shown some associations between dietary vitamin intakes and inflammatory features. For instance, consumption of vitamins C and E or carotene were inversely associated with the probability of having serum CRP concentrations > 3 mg/L in American adults [53]. In the cross-sectional KORA study, dose–response analyses revealed that participants, who regularly ingested more than 78 mg vitamin E/day, had 22% lower serum CRP levels than subjects who were not exposed to any extra vitamin E sources [54].

In addition, the intakes of dietary supplements containing vitamin E and C as well as B-complex vitamins (B1, B2, B3, B5, B6, B9, and B12) were associated with lower blood CRP levels in women [55]. Moreover, subjects in the upper tertile of changes in dietary vitamin K_1 (phylloquinone) intake (after 1-year of follow-up) showed a greater reduction in IL-6 and TNF-α plasma concentrations than those in the lowest tertile group [56]. Also, dietary B5 vitamin intake was inversely related to serum CRP concentrations in healthy Korean adults [57]. Furthermore, participants who consumed > 310 mg/day of dietary choline (commonly grouped within the B-complex vitamins) had lower blood concentrations of CRP, IL-6, and TNF-α in healthy adults [58]. Findings of clinical trials exploring the impact of vitamins on inflammation status are systematically summarized (Table 1). Some studies have found relevant benefits on lowering inflammation after vitamin supplementation.

Minerals and Trace Elements

Minerals and trace elements are essential for structural, immunological, and metabolic functions in the human organism [93]. In this regard, high magnesium consumption was related to lower plasma concentrations of potential markers of systemic inflammation (CRP, sTNF-R2, and IL-6) in postmenopausal women [94]. Similarly, magnesium intake from dietary sources was found to be inversely correlated with plasma IL-6 in women from the Nurses' Health Study cohort [95]. Likewise, a nested case–control study reported an opposite association concerning dietary manganese and circulating levels of serum pro-inflammatory cytokines in postmenopausal women [96]. Also, changes in lymphocyte proliferation and *IL-2R* expression have been reported to be early markers of mild zinc dietary deficiency in healthy men [97]. In addition, dietary copper intake has been directly associated with blood CRP concentrations in adults [98]. In turn, iron deficit may be exacerbated by the effects of obesity-related inflammation on gut iron absorption [99]. Furthermore, main outcomes regarding the anti-inflammatory effects of supplementation with certain minerals on humans are shown (Table 2).

Bioactive Compounds

Polyphenols

Polyphenols are a large family of bioactive molecules widely occurring in plant-based foods, with potent antioxidant and anti-inflammatory properties [136]. In this context, it was reported that total flavonoid intake was inversely associated with serum CRP concentration in American adults [137]. Also, inverse relationships between flavanone consumption and blood IL-6 concentrations were reported in a multiethnic cohort [138]. Likewise, higher isoflavone intake (highest quartile = 1.61–78.8 mg/day) was related to lower plasma CRP in healthy premenopausal women [139]. Besides, lower serum levels of IL-8 were found among women showing high intakes of flavones, flavanones, and total flavonoids (highest quintiles = 264 ng/L, 273 ng/L, and 276 ng/L, respectively) [140]. Moreover, elevated total flavonoids intake and tea consumption inversely correlated with CRP levels in Taiwanese [141]. Of note, a number of randomized clinical trials have tested the anti-inflammatory potential of several polyphenols, whose results are summarized (Table 3).

Specific Foods

Red Meat

Concerning implications on inflammation, greater total (median 54 g/day), unprocessed (median 47 g/day), and processed red meat intakes (median 4 g/day) have been associated with unfavorable plasma concentrations of inflammatory biomarkers (including CRP and ferritin) in women [168]. Within the Multiethnic Cohort Study, red and processed meat consumption positively correlated with serum CRP levels [169]. Likewise, the consumption of processed meat was associated with increased levels of serum CRP (difference of 38% for each 50 g/day higher intake) in British adults [170]. In adjusted models, red meat consumption was significantly associated with blood CRP in a large American sample [171].

Table 1 Clinical trials analyzing the anti-inflammatory effects of certain vitamins and bioactive compounds

Vitamin	Study design	Dose/duration	Population	Main finding	Reference
A (retinyl palmitate)	RCT	10 000 IU/week or placebo until 6 weeks postpartum	Pregnant and lactating women: Experimental group ($n=48$) Placebo group ($n=50$)	↑ IFN-gamma:IL10 ratio	[59]
A (retinyl palmitate)	RCT	25,000 IU/day or placebo for 6 months	Patients with multiple sclerosis: Experimental group ($n=18$) Placebo group ($n=17$)	NS effects on IL-1β, TNF-α, IFN-γ, IL-2, IL-6, IL-17, IL-10, IL-13, IL-4, and TGF-β	[60]
A (retinyl palmitate)	RCT	25,000 IU/day or placebo for 6 months	Patients with multiple sclerosis Experimental group ($n=18$) Placebo group ($n=17$)	↑ Plasma CRP	[61]
B1	RCT	3 capsules × 100 mg/day) or placebo for 6 weeks	Hyperglycemic subjects Experimental group ($n=12$) Placebo group ($n=12$)	NS effects on blood CRP	[62]
B2	CIS	100 mg/day for 3 weeks	Crohn's disease patients with low ($n=40$) or high ($n=30$) fecal calprotectin (FC) levels	↓ Plasma IL-2 in low FC ↓ Plasma CRP in high FC	[63]
C	RCT	500 mg twice a day or free of supplements (control) for 8 weeks	Adults with obesity and/or hypertension Experimental group ($n=31$) Control group ($n=33$)	↓ Serum CRP and IL-6	[64]
C	RCT	250 mg three times per week or free of supplements (control) for 2 months	Chronic hemodialysis patients Experimental group ($n=19$) Control group ($n=14$)	NS effects on blood CRP	[65]
C	RCT	200 mg/day for 3 months and no treatment in the next 3 months (group 1) No treatment in the first 3 months and 200 mg/day for the next 3 months (group 2)	Hemodialysis patients Group 1 ($n=48$) Group 2 ($n=52$)	↓ Plasma CRP after supplementation, but returned to basal state after supplementation was withdrawn	[66]
C	RCT	1000 mg/day or placebo for 2 months	Healthy nonsmokers subjects Experimental group ($n=128$) Placebo group ($n=138$)	↓ Blood CRP among individuals with CRP > or = 1.0 mg/L	[67]
C	RCT	12 g/50 mL (intravenous) every 12 h or placebo for 7 days	Critical patients with COVID-19 Experimental group ($n=27$) Placebo group ($n=29$)	↓ Serum IL-6	[68]
Choline	RCT	~400 mg choline/day from eggs or supplement sources for 4 weeks	Subjects with metabolic syndrome ($n=23$)	↓ Serum IL-6 with both sources of choline ↓ Blood CRP only with eggs	[69]
D	RCT	300,000 IU or placebo for 90 days	Patients with ulcerative colitis Experimental group ($n=46$) Placebo group ($n=40$)	↓ Blood CRP and ESR	[70]
D	RCT	100,000 IU bolus followed by 4000 IU daily or matching placebo for 16 weeks	Adults with overweight or obesity Experimental group ($n=28$) Placebo group ($n=26$)	NS effects on serum levels of CRP, TNF, MCP-1, IFN-α, IL-1β, IL-6, IL-8, IL-10, IL-12, IL-18, IL-23, IL-33 NS effects on NFκB activity in PBMCs	[71]

Table 1 (continued)

Vitamin	Study design	Dose/duration	Population	Main finding	Reference
D	RCT	2000 IU/day plus low-calorie diet or placebo plus low calorie diet for 8 weeks	Adults with overweight or obesity Experimental group ($n=30$) Placebo group ($n=29$)	↓ Plasma CRP and sICAM-1	[72]
D	RCT	50,000 IU/day plus low-calorie diet or placebo plus low-calorie diet for 12 weeks	Adults with obesity Experimental group ($n=22$) Placebo group ($n=22$)	↓ Serum IL-1β and TLR-4	[73]
D	RCT	7000 IU/day or placebo for 26 weeks	Adults with obesity Experimental group ($n=26$) Placebo group ($n=26$)	NS effects on blood CRP, IL-6, MCP-1, PAI-1, MMP-9, adiponectin, and leptin	[74]
D3	RCT	1000 IU/day (group 1); 2000 IU/day (group 2); or 4000 IU/day (group 3); or placebo for 3 months	African Americans Group 1 ($n=67$) Group 2 ($n=76$) Group 3 ($n=78$) Placebo ($n=71$)	NS effects on blood CRP, IL-6, IL-10, and sTNF-R2	[75]
D3	RCT	200,000 IU/day or placebo for 4 weeks	Women with overweight or obesity Experimental group ($n=14$) Placebo group ($n=15$)	↑ Plasma CRP and MDA	[76]
D3	RCT	200,000 IU/day or placebo for 4 weeks	Elderly women with vitamin D insufficiency Experimental group ($n=20$) Placebo group ($n=20$)	↓ Plasma CRP and AGP-A NS effects on blood MDA	[77]
D3	RCT	750 µg/day (group 1); 1500 µg/day (group 2); or placebo for 12 months	Older adults Group 1 ($n=215$) Group 2 ($n=215$) Placebo ($n=214$)	NS effects on blood CRP, IL-10, leptin, and adiponectin ↑ IL-6 in group 2 vs. placebo	[78]
E	RCT	1200 IU/day or placebo for 12 weeks	Patients with diabetic nephropathy Experimental group ($n=30$) Placebo group ($n=30$)	↓ Plasma TNF-α, MDA, MMP-2, MMP-9, and AGEs	[79]
E	RCT	600 IU/day or placebo for 10 weeks	Hemodialysis patients Experimental group ($n=25$) Placebo group ($n=24$)	↓ ICAM-1 and VCAM-1 NS effects on serum CRP and IL-6	[80]
Folic acid	RCT	5 mg/day or placebo for 4 weeks	Healthy cigarette smokers Experimental group ($n=12$) Placebo group ($n=12$)	↓ Plasma homocysteine, fibrinogen, and WCC	[81]
Folic acid	RCT	2.5 mg/day or placebo for 3 months	Healthy overweight volunteers Experimental group ($n=30$) Placebo group ($n=30$)	↓ Serum homocysteine, IL-8, MCP-1, and CRP	[82]
Folic acid	RCT	0.8 mg/day for 1 year or placebo	Men and postmenopausal women with homocysteine concentrations of 1.8 mg/L or higher Experimental group ($n=264$) Placebo group ($n=266$)	↓ Serum homocysteine NS effects on plasma CRP and sICAM-1	[83]

Table 1 (continued)

Vitamin	Study design	Dose/duration	Population	Main finding	Reference
Folic acid	RCT	1.25 mg/day or free of supplement (control) for 6 months	Patients with Alzheimer's disease Experimental group ($n=61$) Control group ($n=60$)	↓ TNFα protein and mRNA levels	[84]
Folic acid	RCT	400 µg/day or free of supplement (control) for 12 months	Patients with mild cognitive impairment Experimental group ($n=84$) Control group ($n=84$)	↓ Blood homocysteine, IL-6 and TNF-α	[85]
Folic acid plus vitamin B12	RCT	Folic acid 1.2 mg/day plus vitamin B12 50 µg/day or placebo for 6 months	Patients with Alzheimer's disease Experimental group ($n=60$) Placebo group ($n=60$)	↓ Serum homocysteine and TNF-α	[86]
Folic acid plus vitamin B12	RCT	400 µg/day folic acid (group 1); 25 µg/day vitamin B12 (group 2); 400 µg/day folic acid plus 25 µg vitamin B12 (group 3); or free of supplement (control) for 6 months	Participants with mild cognitive impairment Group 1 ($n=60$) Group 2 ($n=60$) Group 3 ($n=60$) Control ($n=60$)	↓ Blood homocysteine, IL-6, TNF-α, and MCP-1 (group 3 vs. control)	[87]
Folic acid plus vitamin B12	RCT	Folic acid (400 µg/day) plus vitamin B12 (500 µg/day) or placebo for 2 years	Elderly subjects with hyperhomocysteinemia Experimental group ($n=271$) Placebo group ($n=251$)	NS effects on plasma CRP, ICAM-1, VCAM-1, VEGF, and SAA	[88]
Folic acid plus vitamin B12 plus vitamin B6	RCT	Daily folic acid (2.5 mg), vitamin B6 (50 mg), vitamin B12 (1 mg), or matching placebo for 7.3 years	Women at increased risk of CVD Experimental group ($n=150$) Placebo group ($n=150$)	↓ Serum homocysteine NS effects on blood CRP, IL-6, fibrinogen, and ICAM-1	[89]
Folic acid plus vitamin B12 plus vitamin B6	RCT	Group 1: folic acid (0.8 mg/day)/vitamin B12 (0.4 mg/day)/vitamin B6 (40 mg/day); group 2: folic acid (0.8 mg/day)/vitamin B12 (0.4 mg/day); group 3: vitamin B6 (40 mg/day); or placebo for 6 months	Patients with suspected coronary artery disease Group 1 ($n=22$) Group 2 ($n=23$) Group 3 ($n=21$) Placebo ($n=24$)	↓ Serum homocysteine (groups 1 and 2) NS effects on blood CRP, IL-6, neopterin, and sCD40L	[90]
K_1 (phylloquinone)	RCT	10 mg/day or placebo for 8 weeks	Patients with definitive rheumatoid arthritis Experimental group ($n=29$) Placebo group ($n=29$)	NS effects on plasma IL-6	[91]
K_1 (phylloquinone)	RCT	500 µg/day or placebo during two periods of 6 weeks of duration	Postmenopausal women ($n=31$)	NS effects on blood IL-6, CRP, sICAM-1, sVCAM-1	[92]

RCT ranzomized controlled trial, *CIS* clinical intervention study, *NS* no significant, *FC* fecal calprotectin, *IU* international units, *MDA* malondialdehyde, *NF-kB* transcription nuclear factor kappa B, *CRP* C-reactive protein, *IL-6* interleukin 6, *TNF-α*, tumor necrosis factor alpha, *IL-8* interleukin 8, *IL-4* interleukin 4, *IL-10* interleukin 10, *IL-2* interleukin 2, *IL-1β* interleukin-1β, *TLR-4* toll-like receptor 4, *sTNF-R2* serum soluble tumor necrosis factor receptor 2, *IFN-γ* interferon gamma; *IL-17* interleukin 17, *IL-18* interleukin 18, *IL-13* interleukin 13, *IL-23* interleukin 23, *IL-33* interleukin 33, *TGF-β* transforming growth factor β, *ESR* erythrocyte sedimentation rate, *TNF* tumor necrosis factor, *MCP-1* monocyte chemoattractant protein-1, *IFN-α* interferon alpha, *PBMCs* peripheral blood mononuclear cells, *ICAM-1* intercellular adhesion molecule-1, *sICAM-1* soluble intercellular adhesion molecule-1, *VCAM-1* vascular cell adhesion molecule 1, *sVCAM-1* soluble vascular cell adhesion molecule 1, *PAI-1* plasminogen activator inhibitor-1, *MMP-2* matrix metalloproteinase-2, *MMP-9* matrix metalloproteinase-9, *AGP-A* alpha 1-acid glycoprotein, *AGEs* advanced glycation endproducts, *WCC* white cell count, *SAA* serum amyloid A, *VEGF* vascular endothelial growth factor; *sCD40L* soluble CD40 ligand

Table 2 Clinical trials analyzing the anti-inflammatory effects of certain minerals

Mineral	Study design	Dose/duration	Population	Main finding	Reference
Chromium	RCT	200 µg/day or placebo for 8 weeks	Patients with PCOS Experimental group ($n=30$) Placebo group ($n=30$)	↓ Plasma CRP and MDA	[100]
Chromium	RCT	200 µg/day or placebo for 8 weeks	20 patients with PCOS who were candidate for in vitro fertilization Experimental group ($n=20$) Placebo group ($n=20$)	↓ Blood CRP ↓ Gene expression of *IL-1* in PBMCs NS effects on gene expression of *IL-8*, *TNF-α*, *TGF-β*, and *VEGF* of in PBMCs	[101]
Chromium	RCT	400 µg/day or placebo for 3 months	Patients with NAFLD Experimental group ($n=23$) Placebo group ($n=23$)	↓ Serum TNF-α, CRP, and IL-6, and fetuin-A NS effects on blood IL-17	[102]
Chromium	RCT	400 µg/day (chromium picolinate); 400 µg/day (chromium dinicocysteinate; or placebo for 3 months	Patients with T2DM Chromium picolinate ($n=12$) Chromium dinicocysteinate ($n=18$) Placebo ($n=13$)	↓ Plasma TNF-α (chromium dinicocysteinate vs. placebo)	[103]
Chromium	RCT	1000 µg/day or placebo for 16 weeks	Patients with metabolic syndrome Experimental group ($n=33$) Placebo group ($n=30$)	NS effects on blood CRP	[104]
Chromium	RCT	400 µg/day (chromium picolinate); 400 µg/day (chromium dinicocysteinate; or placebo for 3 months	Patients with T2DM Chromium picolinate ($n=25$) Chromium dinicocysteinate ($n=24$) Placebo ($n=25$)	↓ Serum TNF-α (chromium dinicocysteinate vs. baseline)	[105]
Chromium + magnesium + zinc	RCT	300 mg/day magnesium plus 600 µg/day chromium plus 36 mg/day zinc or placebo for 24 weeks	Adults with metabolic syndrome Experimental group ($n=16$) Placebo group ($n=16$)	↓ Plasma CRP	[106]
Copper	RCT	2 mg/day or placebo for 8 weeks	Adults with moderately high cholesterol Experimental group ($n=35$) Placebo group ($n=35$)	NS effects on serum CRP and homocysteine	[107]
Iron	RCT	50 g/day meat; 20 g/day of fortified rice cereal (1.10 mg of iron); or 20 g/day of local rice cereal (0.04 mg of iron) for 1 year	6-month-old infants Meat group ($n=137$) Fortified cereal group ($n=140$) Local cereal group ($n=133$)	↑ Plasma CRP and AGP-A	[108]
Iron	RCT	50 mg for 4 day/week or identical placebo for 38 weeks	Children with iron deficiency Experimental group ($n=22$) Placebo group ($n=27$)	NS effects on gut inflammation (measured by fecal calprotectin concentration)	[109]
Iron	RCT	6 mg/kg/day iron plus placebo; or 6 mg/kg/day plus 18 mg/day vitamin E for 8 weeks	Iron-deficient infants and toddlers Iron plus placebo ($n=22$) Iron plus vitamin E ($n=14$)	NS effects on gut inflammation (measured by fecal calprotectin concentration) and blood levels of TNF-α and IL-4	[110]
Magnesium	RCT	500 mg/day or placebo for 4 weeks	Healthy overweight volunteers Experimental group ($n=7$) Placebo group ($n=7$)	NS effects on plasma CRP, IL-6, and TNF-α, sICAM-1, sVCAM-1, and E-selectin ↓ Gene expression of *C1q*, *C1QTNF9*, and *PPBP*	[111]
Magnesium	RCT	250 mg/day or placebo for 8 weeks	Middle-aged overweight women Experimental group ($n=35$) Placebo group ($n=34$)	NS effects on serum CRP, IL-6, and fibrinogen	[112]
Magnesium	RCT	320 mg/day or placebo for 7 weeks	Adults with poor sleep quality Experimental group ($n=46$) Placebo group ($n=49$)	↓ Blood CRP in participants with baseline values > 3.0 mg/L	[113]

Table 2 (continued)

Mineral	Study design	Dose/duration	Population	Main finding	Reference
Magnesium	RCT	300 mg/day or placebo for 6 months	COPD patients Experimental group ($n=25$) Placebo group ($n=24$)	↓ Plasma CRP NS effects on serum TNF-α	[114]
Magnesium	RCT	30 ml of MgCl(2) 5% solution (equivalent to 382 mg of magnesium) per day or placebo for 3 months	Subjects with prediabetes and hypomagnesemia Experimental group ($n=13$) Placebo group ($n=13$)	NS effects on CRP, IL-6, TNF-α, and IL-10 levels	[115]
Magnesium	RCT	30 mL of $MgCl_2$ 5% solution (equivalent to 382 mg of magnesium) per day or placebo for 3 months	Subjects with new diagnosis of prediabetes and hypomagnesemia Experimental group ($n=29$) Placebo group ($n=28$)	↓ Blood CRP	[116]
Magnesium and zinc	RCT	250 mg of magnesium oxide plus 220 mg of zinc sulfate or placebo twice a day for 12 weeks	Subjects with PCOS Experimental group ($n=30$) Placebo group ($n=30$)	↓ Plasma CRP and protein carbonyl ↓ Gene expression of *IL-1* and *TNF-α*	[117]
Na and K	RCT	Supplemental Na (3.0 g/day); supplemental K (2.8 g/day) or placebo for 4 weeks	Pre-hypertensive patients ($n=36$)	↓ Blood IL-8 (K supplementation)	[118]
Selenium	RCT	200 µg/day or placebo for 12 weeks	Patients with diabetic nephropathy Experimental group ($n=30$) Placebo group ($n=30$)	NS effects on plasma CRP, TGF-β, AGEs, protein carbonyl, and MDA	[119]
Selenium	RCT	200 µg/day or placebo for 12 weeks	Patients with CHF Experimental group ($n=26$) Placebo group ($n=27$)	NS effects on serum CRP	[120]
Selenium	RCT	200 µg/day or placebo for 12 weeks	Hemodialysis patients Experimental group ($n=40$) Placebo group ($n=40$)	↓ Blood MDA and IL-6 NS effects on homocysteine, ferritin, and transferrin	[121]
Selenium	RCT	200 µg/day or placebo for 6 weeks	Pregnant women with GDM Experimental group ($n=35$) Placebo group ($n=35$)	↓ Blood CRP and MDA	[122]
Selenium	RCT	200 µg/day or placebo for 8 weeks	Women with PCOS Experimental group ($n=32$) Placebo group ($n=32$)	↓ Serum CRP and MDA	[123]
Selenium	RCT	200 µg/day or placebo for 4 weeks	17 patients undergoing CABG surgery Experimental group ($n=17$) Placebo group ($n=16$)	↓ Plasma CRP and MDA	[124]
Selenium	RCT	200 µg/day or placebo for 8 weeks	Patients with T2DM and CHD Experimental group ($n=30$) Placebo group ($n=30$)	↓ Blood CRP	[125]
Selenium	RCT	200 µg or placebo twice daily for 14 days	Patients undergoing HSCT Experimental group ($n=37$) Placebo group ($n=37$)	NS effects on serum TNF-α, IL-1, and IL-6	[126]
Zinc	RCT	30 mg/day or placebo for 12 weeks	Women with premenstrual syndrome Experimental group ($n=30$) Placebo group ($n=30$)	NS effects on serum CRP	[127]

Table 2 (continued)

Mineral	Study design	Dose/duration	Population	Main finding	Reference
Zinc	RCT	45 mg/day or placebo for 6 months	Healthy elderly subjects Experimental group ($n=20$) Placebo group ($n=20$)	↓ Blood CRP, IL-6, MCP-1, VCAM-1, MDA, and secretory phospholipase A2 ↓ TNF-α, IL-1β, VCAM-1, and NF-kB activity in THP-1 cells and human aortic endothelial cells ↑ Anti-inflammatory proteins A20 and PPAR-α in THP-1 cells and human aortic endothelial cells	[128]
Zinc	RCT	15 mg/day or placebo for 12 weeks	Women with migraine Experimental group ($n=30$) Placebo group ($n=30$)	NS effects on plasma CRP	[129]
Zinc	RCT	25 mg/day or placebo for 3 months	18 adult SCD patients Experimental group ($n=18$) Placebo group ($n=18$)	↓TNF-α and IL-1β mRNAs in MNCs ↓ NF-kB binding in MNCs ↑ IL-2 and IL-2Ralpha mRNAs in phytohemagglutinin-p-stimulated MNCs	[130]
Zinc	RCT	25 mg/day or placebo for 12 weeks	Patients with major depression Experimental group ($n=20$) Placebo group ($n=17$)	NS effects on serum IL-6 and TNF-α	[131]
Zinc	RCT	30 mg/day or placebo for 8 weeks	Women with obesity Experimental group ($n=20$) Placebo group ($n=20$)	↓ Blood CRP and IL-6 NS effects on serum leptin and adiponectin levels	[132]
Zinc	RCT	30 mg/day or placebo for 15 weeks	Subjects with obesity Experimental group ($n=18$) Placebo group ($n=22$)	↓ Plasma CRP	[133]
Zinc	RCT	50 mg/day or placebo for 8 weeks	24 women with PCOS Experimental group ($n=24$) Placebo group ($n=24$)	NS effects on serum CRP	[134]
Zinc	RCT	20 mg/day or placebo for 8 weeks	Prepubescent children with metabolic syndrome Experimental group ($n=30$) Placebo group ($n=30$)	↓ Blood CRP	[135]

RCT randomized controlled trial, *NS* no significant, *PCOS* polycystic ovary syndrome, *COPD* chronic obstructive pulmonary disease, *SCD* sickle-cell disease, *CHF* congestive heart failure, *GDM* gestational diabetes mellitus, *CABG* coronary artery bypass grafting surgery, *T2DM* type 2 diabetes mellitus, *CHD* coronary heart disease, *NAFLD* non-alcoholic fatty liver disease, *HSCT* hematopoietic stem cell transplantation, *CRP* C-reactive protein, *IL-6* interleukin 6, *TNF-α* tumor necrosis factor alpha, *IL-8* interleukin 8, *IL-10* interleukin 10, *IL-1* interleukin 1, *IL-1β* interleukin-1β, *IL-2* interleukin 2, *IL-4* interleukin 4, *MDA* malondialdehyde, *PBMCs* peripheral blood mononuclear cells, *TGF-β* transforming growth factor beta, *VEGF* vascular endothelial growth factor, *IL-17* interleukin 17, *AGP-A* alpha 1-acid glycoprotein, *C1QTNF9* tumor necrosis factor related protein 9, *PPBP* pro-platelet basic protein, *TGF-β* transforming growth factor β, *AGEs* advanced glycation endproducts, *MCP-1* monocyte chemoattractant protein-1, *VCAM-1* vascular cell adhesion molecule 1, *NF-kB* transcription nuclear factor kappa B, *PPAR-α* peroxisome proliferator-activated receptor-alpha, *MNCs* mononuclear cells

Table 3 Clinical trials analyzing the anti-inflammatory effects of certain polyphenols

Polyphenol	Study design	Dose/duration	Population	Main finding	Reference
Anthocyanin	RCT	40 mg/day (group 1); 80 mg/day (group 2); 320 mg/day (group 3); or placebo for 12 weeks	Patients with dyslipidemia Group 1 ($n=44$) Group 2 ($n=40$) Group 3 ($n=42$) Placebo ($n=43$)	↓ Blood TNF-α and IL-6 (group 2 vs. baseline) ↓ Blood TNF-α and IL-6, and MDA (group 3 vs. groups 1 and 2)	[142]
Anthocyanin	OLCT	320 mg/day for 4 weeks	Patients with T2DM ($n=12$) Patients at risk of T2DM ($n=14$) Healthy individuals ($n=14$)	↓ Plasma TNF-α, IL-6, and IL-18 (patients with TD2M, pre vs. post intervention) NS effects on IL-1Rα, leptin, IL-8, and CRP in any group (pre vs. post intervention)	[143]
Anthocyanin	RCT	20 mg/day (group 1); 40 mg/day (group 2); 80 mg/day (group 3); 160 mg/day (group 4); 320 mg/day (group 5); or placebo for 14 days	Healthy young adults Group 1 ($n=20$) Group 2 ($n=19$) Group 3 ($n=19$) Group 4 ($n=19$) Group 5 ($n=19$) Placebo ($n=15$)	↓ Blood IL-10 (group 4 and 5 vs. placebo) ↓ IL-6 (groups 2 and 5 vs. placebo) NS effects on TNF-α in any group	[144]
Anthocyanin	RCT	640 mg/day or placebo for 4 weeks	Pre-hypertensive men Experimental group ($n=16$) Placebo group ($n=15$)	NS effects on serum CRP, IL-6, TNF-α, IL-4, MCP-1, P-selectin, ICAM, VCAM, and CD40L	[145]
Anthocyanin	RCT	320 mg/day or placebo for 28 days	Sedentary subjects Experimental group ($n=16$) Placebo group ($n=16$)	NS effects on blood CRP	[146]
EGCG	RCT	2 tablets 300 mg/day or placebo for 2 months	Patients with T2DM Experimental group ($n=25$) Placebo group ($n=25$)	NS changes in serum IL-6	[147]
EGCG	RCT	300 mg/day or placebo for 12 weeks	Pre-menopausal women with obesity Experimental group ($n=43$) Placebo group ($n=40$)	NS effects on blood CRP	[148]
Hesperidin	RCT	500 mg or placebo twice daily for 12 weeks	Patients with metabolic syndrome Experimental group ($n=25$) Placebo group ($n=24$)	↓ Plasma TNF-α	[149]
Hesperidin	RCT	600 mg/day or placebo for 4 weeks	Patients with myocardial infarction Experimental group ($n=38$) Placebo group ($n=37$)	NS effects on serum CRP, IL-6, and leptin	[150]
Hesperidin	RCT	500 mg/day or placebo for 6 weeks	Patients with T2DM Experimental group ($n=32$) Placebo group ($n=32$)	↓ Blood TNF-α, CRP, and IL-6	[151]
Hesperidin	RCT	30 g/day flaxseed plus lifestyle (group 1); 1 g/day hesperidin plus lifestyle (group 2); 30 g/day flaxseed plus 1 g/day hesperidin plus lifestyle (group 3); or lifestyle alone (control) for 12 weeks	Patients with NAFLD Group 1 ($n=24$) Group 2 ($n=22$) Group 3 ($n=25$) Control ($n=21$)	↓ NF-κB (groups 1 and 2 vs. control) ↓ Plasma CRP (groups 2 and 3 vs. control)	[152]

Table 3 (continued)

Polyphenol	Study design	Dose/duration	Population	Main finding	Reference
Hesperidin	RCT	1 g/day plus lifestyle or placebo (only lifestyle) for 12 weeks	Patients with NAFLD Experimental group ($n=25$) Placebo group ($n=25$)	↓ Serum TNF-α, CRP, and NF-κB	[153]
Quercetin	RCT	500 mg/day or placebo for 8 weeks	Post-myocardial infarction patients Experimental group ($n=44$) Placebo group ($n=44$)	NS changes in blood IL-6, CRP, and TNF-α	[154]
Quercetin	RCT	500 mg/day of quercetin plus 250 mg/day vitamin C (group 1); 500 mg/day of quercetin alone (group 2); 250 mg/day of vitamin C alone (group 3); or placebo for 8 weeks	Subjects with systematic and regular exercise Group 1 ($n=15$) Group 2 ($n=15$) Group 3 ($n=15$) Placebo ($n=15$)	↓ Plasma IL-6 and F2-isoprostane (group 1 vs. placebo)	[155]
Quercetin	RCT	100 mg/day (-)-epicatechin (group 1); 160 mg/day quercetin-3-glucoside (group 2); or placebo for 4 weeks	Pre-hypertensive adults Group 1 ($n=37$) Group 2 ($n=37$) Placebo ($n=37$)	↓ Serum IL-1β (group 2 vs. placebo)	[156]
Quercetin	RCT	500 mg/day or placebo for 8 weeks	Women with rheumatoid arthritis Experimental group ($n=25$) Placebo group ($n=25$)	↓ Blood TNF-α	[157]
Quercetin	RCT	500 mg/day (group 1); 1000 mg/day (group 2); or placebo for 12 weeks	Women Group 1 ($n=38$) Group 2 ($n=40$) Placebo ($n=42$)	NS effects on plasma IL-6, TNF-α, and blood leucocyte subsets (groups 1 and 2 vs. placebo)	[158]
Quercetin	RCT	50 mg/day (group 1); 100 mg/day (group 2); or 150 mg/day (group 3) for 2 weeks	Healthy volunteers Group 1 ($n=11$) Group 2 ($n=12$) Group 3 ($n=11$)	NS effects on serum TNF-α	[159]
Quercetin	RCT	500 mg/day or placebo for 8 weeks	Women with rheumatoid arthritis Experimental group ($n=20$) Placebo group ($n=20$)	NS effects on blood CRP, MDA, and ox-LDL	[160]
Quercetin	RCT	162 mg/day or placebo for 6 weeks	Overweight-to-obese subjects with pre-hypertension Experimental group ($n=68$) Placebo group ($n=68$)	NS effects on serum CRP and TNF-α	[161]
Resveratrol	RCT	480 mg/day or placebo for 4 weeks	Patients with T2DM and chronic periodontitis Experimental group ($n=21$) Placebo group ($n=22$)	NS effects on blood IL-6 and TNF-α	[162]
Resveratrol	RCT	500 mg/day or placebo for 12 weeks	Patients with NAFLD Experimental group ($n=25$) Placebo group ($n=25$)	↓ Plasma IL-6, CRP, cytokeratin-18, and NF-κB	[163]
Resveratrol	RCT	500 mg/day or placebo for 6 weeks	Patients with ulcerative colitis Experimental group ($n=25$) Placebo group ($n=25$)	↓ Serum TNF-α, CRP, and NF-κB	[164]

Table 3 (continued)

Polyphenol	Study design	Dose/duration	Population	Main finding	Reference
Resveratrol	RCT	500 mg/day or placebo for 30 days	Adult smokers Experimental group ($n=25$) Placebo group ($n=25$)	↓ CRP	[165]
Resveratrol	RCT	800 mg/day or placebo for 8 weeks	Patients with T2DM Experimental group ($n=25$) Placebo group ($n=20$)	NS effects on blood TNF-α, IL-6, CRP, and IL-1β NS effects on expression of genes *NF-κB*, *TLR2*, and *TLR4*	[166]
Resveratrol	RCT	500 mg/day or placebo for 4 weeks	CKD patients Experimental group ($n=9$) Placebo group ($n=11$)	NS changes in plasma TNF-α, CRP, IL-6, and NF-κB	[167]

RCT randomized controlled trial, *OLCT* open-label clinical trial, *NS* no significant, *CKD* chronic kidney disease, *NAFLD* non-alcoholic fatty liver disease, *T2DM* type 2 diabetes mellitus, *EGCG* epigallocatechin-3-gallate, *CRP* C-reactive protein, *IL-6* interleukin 6, *TNF-α*, tumor necrosis factor alpha, *IL-4* interleukin 4, *IL-8* interleukin 8, *IL-18* interleukin 18, *IL-1β* interleukin-1β, *NF-kB* transcription nuclear factor kappa B, *IL-1Rα* interleukin-1R alpha, *MCP-1* monocyte chemotactic protein, *ICAM* intercellular adhesion molecule, *VCAM* vascular cell adhesion molecule, *CD40L* CD40 ligand, *MDA* malondialdehyde, *ox-LDL* oxidized low density lipoprotein, *TLR2* toll-like receptor 2, *TLR4* toll-like receptor 4

Dairy Products

In a cross-sectional study in Brazilians, increased yogurt consumption (median 10 g/day) appeared to exert an anti-inflammatory effect, whereas cheese consumption (median 10.7 g/day) could have potentiated a pro-inflammatory status [172]. In normal-weight adolescents, total dairy product and milk intakes were inversely associated with the serum concentrations of IL-6 [173]. Also, findings from the ATTICA study showed lower blood levels of CRP, IL-6, and TNF-α among individuals weekly consuming between 11 and 14 servings of dairy products compared to those consuming fewer than 8 servings per week [174].

Fish

Findings from the ATTICA study revealed independent associations between habitual fish consumption (> 300 g of fish per week) and lower inflammatory marker levels among healthy adults, including reduced CRP, IL-6, TNF-a, serum amyloid A, and white blood cell counts [175]. During a 6-year follow-up, fish consumption (about 100 g/week) decreased endothelial dysfunction and low-grade inflammation in healthy adults [176]. Furthermore, a high frequency of fish intake was associated with lower peripheral white blood cell counts (a marker of chronic inflammation) in an apparently healthy Japanese population [177]. In fact, the neutrophil/lymphocyte ratio (a marker of systemic inflammation) significantly decreased as the weekly frequency of fish intake (0 day, 1–2 days, 3–4 days, or 5–7 days) increased [178].

Edible Insects

In recent years, edible insects are being recognized as high-value food products with anti-inflammatory and antioxidant properties [179]. For example, cricket consumption (25 g/day) was associated with reduced systemic inflammation via microbiota modulation in healthy adults [180]. However, more research in humans is required to confirm these findings in order to recommend the habitual consumption of edible insects as an anti-inflammatory therapy.

Fruits and Vegetables

Inverse associations were found between the intakes of fruits and vegetables and serum CRP levels in Iranian females [181]. Besides, Chinese women consuming high amounts of cruciferous vegetables (highest quintile > 140.6 g/day)

showed decreased circulating levels of TNF-α, IL-1β, and IL-6 [182]. In a randomized crossover trial, the consumption of cruciferous vegetables (14 g/kg body weight) during 14 days consistently reduced circulating IL-6 in in healthy young adults [183].

Oilseeds and Extra Virgin Olive Oil

In the multi-ethnic study of atherosclerosis, frequent nut and seed consumption (especially five or more times/week) was associated with lower levels of inflammatory markers, including IL-6 and CRP [184]. Moreover, in two large cohorts of Americans, subjects with a nut intake of five or more times/week had significantly lower blood concentrations of CRP and IL-6 compared to individuals in the frequency categories of never or almost never [185]. Likewise, a systematic review and meta-analysis of randomized controlled trials revealed that intakes of flaxseed and associated nutritional derivatives systematically reduced circulating CRP levels in obese subjects [186]. Using the same approach, acute high-oleic peanut consumption systematically led to stronger moderation of postprandial TNF-α concentrations in overweight/obese men [187].

Additionally, it has been shown that the incorporation of almonds (56 g/day during 4 weeks) into a healthy diet could improve inflammation and oxidative stress in Chinese diabetic patients [188]. A randomized trial also found that the consumption of almonds (10–20% isoenergetic replacement of control diet with almonds for 4 weeks) lowered serum CRP levels in healthy adults [189]. Indeed, plasma levels of TNF-α and IL-6 decreased after almond feeding (56 g/day for 90 days) in adolescents and young adults [190].

Furthermore, it has been reported that a daily dose of 50 mL of extra virgin olive oil (EVOO), administered over two periods of 3 weeks, decreased the plasma levels of IL-6 and CRP in stable coronary heart disease patients [191]. Besides, EVOO (50 mL) exerted acute postprandial anti-inflammatory and antioxidant effects in normolipemic, healthy subjects [192].

Cereals and Whole Grains

Interestingly, the intake of cereal fiber was inversely associated with lower blood levels of CRP and TNF-R2 in diabetic women [193]. Moreover, concomitant reductions in serum TNF-α and increased plasma IL-10 were found after the consumption of whole-grain wheat (70 g/day during 8 weeks) in subjects with overweight and obesity [194]. In addition, findings from the GRAANDIOOS study showed that whole-grain wheat consumption (98 g/day for 12 weeks) may promote liver and inflammatory resilience in subjects with overweight/obesity and mild hypercholesterolemia [195].

Legumes

Soy food consumption has been inversely related to circulating levels of inflammatory markers such as IL-6, TNFα, and soluble TNF receptors 1 and 2 in middle-aged Chinese women [196]. Consistently, a 6-week nutritional trial with a legume-enriched diet (a total of 24 packs of 65 g were consumed during the all the intervention phase) significantly reduced CRP concentrations in diabetic patients compared with a habitual diet [197]. Moreover, a legume-based hypocaloric diet (160–235 g/day for 8 weeks) consistently reduced pro-inflammatory status and improved metabolic features in overweight/obese subjects [198].

Green Tea and Coffee

In obese women, green tea extract (450 mg/day) supplementation during 8 weeks improved oxidative stress biomarkers and reduced IL-6 circulating levels [199]. Also, green tea consumption (379 mg/day) by 3 months reduced serum CRP and TNF-α concentration in obese, hypertensive patients [200]. Furthermore, high coffee consumption (8 cups/day) exerted beneficial effects on subclinical inflammation in habitual coffee drinkers [201]. Consistently, coffee consumption was inversely associated with markers of inflammation and endothelial dysfunction in healthy and diabetic women [202]. Among older non-Hispanic Whites, heavy coffee drinkers (equal or more than 2.5 cups/day) presented lower systemic inflammation [203]. On the other hand, analyses from the ATTICA study reported an increase on inflammation markers (including IL-6, TNF-α, and CRP) after moderate-to-high coffee consumption (> 200 mL coffee/d), emphasizing the importance of the dose in outcomes [204].

Dark Chocolate

Available evidence suggests that regular consumption of dark may reduce inflammation, especially in consumers of up to 1 serving (20 g) of dark chocolate every 3 days [205]. In a randomized parallel clinical trial, diabetic patients, who received dark chocolate (30 g of 84% dark chocolate during 8 weeks) along with a healthy lifestyle, had lower levels of inflammatory markers (CRP, TNF-α, and IL-6) compared with those subjects who only followed general lifestyle guidelines [206]. Indeed, acute dark chocolate intake (50 g) elicited anti-inflammatory outcomes both by increasing IL-10 expression and by attenuating the intracellular pro-inflammatory stress response [207]. Moreover, healthy women presented lower blood levels of CRP after the ingestion of dark chocolate (100 g per day during one week), which was not detected in men [208].

Spices and Culinary Ingredients

Over the past several decades, several investigations have ascertained the efficacious role of spices and herbs in preventing and combating various chronic diseases [209]. The diverse range of health properties of these culinary ingredients are attributed to bioactive constituents such as sulfur-containing molecules, tannins, alkaloids, and phenolic diterpenes, with potential anti-inflammatory properties [210]. Findings of clinical trials exploring the impact of spices on inflammation status are summarized (Table 4).

Probiotics, Prebiotics, Synbiotics, and Postbiotics

Probiotics, prebiotics, and synbiotics are either beneficial microorganisms, substrates (polysaccharides and oligosaccharides), or combinations that eventually may also alleviate inflammatory symptoms [240]. In diabetic patients, probiotic and synbiotic supplementation is recommended to decrease inflammatory manifestations by consistently reducing the circulating levels of CRP and TNF-α [241]. Regarding bowel disease, it has been recently reported that the use of probiotics (based on *Lactobacillus* and *Bifidobacterium*) and synbiotics can promote anti-inflammatory reactions and balance the intestinal homeostasis [242].

In addition, the anti-inflammatory effects of short-chain fatty acids (nonviable bacterial products known as postbiotics) are mediated by inhibiting the NF-κB pathway, Treg cell differentiation, and pro-inflammatory cytokine blockade in gut epithelial cells [243]. For example, *Lactobacillus casei DG* and derived postbiotics suppressed IL-8, IL-1α, IL-6, and TLR-4 expression levels in colonic mucosa from patients with irritable bowel syndrome [244].

Dietary Patterns

Traditional Healthy Diets

Overall, plant-based diets have shown to improve the obesity-related inflammation status [245]. Remarkably, the beneficial effect of the vegetarian diet on blood CRP and IL-6 levels was mediated by BMI in North Americans [246]. In addition, a systematic review and meta-analysis revealed that vegetarian-based dietary patterns also lowered immune biomarkers such as fibrinogen and total leukocyte concentrations [247].

A systematic review of observational and intervention trials revealed a beneficial influence of the Nordic diet (based on staple foods from Nordic countries) on low-grade inflammation amelioration [248]. Potential mechanisms include the downregulation of pro-inflammatory genes in individuals with features of the metabolic syndrome, particularly *TNFRSF1A* and *RELA* [249].

The Southern European Atlantic Diet (SEAD) is the traditional diet of Northern Portugal and Galicia, Spain, which is characterized by greater intakes of fish, milk, potatoes, fruit, vegetable and olive oil, and red wine [250]. Overall, SEAD adherence has been associated with reduced plasma concentrations of inflammatory markers (predominately CRP) and lowered cardio-metabolic risk [251].

Regarding Asian regions, a healthy Japanese dietary pattern (rich in mushrooms, seaweed, soyabean products and potatoes, vegetables, fish/shellfish, and fruits) seems to exert anti-inflammatory effects and improve mental health in local consumers [252]. Likewise, several herbs from traditional Chinese medicine have shown to suppress pro-inflammatory pathways and control inflammation-associated diseases [253].

Furthermore, the traditional Mexican diet (TMexD) has shown to reduce the risk of systemic inflammation and insulin resistance in women of Mexican descent [254]. Specific foods of the TMexD include maize, beans, chili, squash, tomato, nopal, and onion, which are high in fiber, vitamins, minerals, and capsaicinoids, with potential anti-inflammatory and antioxidant properties [255].

In a pooled cross-sectional study, a Paleolithic diet (based on the consumption of diversity of vegetables and fruits, lean meat, fish, nuts, and sources of calcium) was associated with lower levels of systemic inflammation and oxidative stress in humans [256].

Moreover, the consumption of the DASH eating pattern (characterized by high consumption of fruits and vegetables, low-fat dairy products, and complex carbohydrates) during 6 weeks reduced the circulating levels of CRP among adolescents with metabolic syndrome [257]. In female adults, the DASH diet was cross-sectionally associated with lower serum CRP levels, but not with IL-17A concentrations in Iranians [258]. Quantitative estimations revealed that the DASH diet reduced CRP by 13% after 4 weeks of follow-up [259].

Findings from the PREDIMED trial have shown the anti-inflammatory effect of the Med-diet (rich in vegetables and fruits, fiber, and vitamins C and E) since it downregulates cellular and circulating inflammatory biomarkers involved in atherogenesis development [260]. In this cohort, the Med-Diet reduced the serum CRP and IL-6 levels as well as endothelial and monocytary adhesion molecules and pro-inflammatory chemokines [261]. Additionally, the Med-diet (including EVOO and vegetables) decreased the plasma concentrations of TNFR60 in patients at high cardiovascular risk after 1 year of follow-up [262]. In the long term (3 years), the PREDIMED trial confirmed the anti-inflammatory effect of the Med-diet by decreasing the levels of IL-1β, IL-6, IL-8, and TNF-α compared to a control low-fat diet [263].

Table 4 Clinical trials analyzing the anti-inflammatory effects of certain spices and culinary ingredients

Spice/ingredient	Study design	Dose/duration	Population	Main finding	Reference
Black cumin (*Nigella sativa*)	RCT	2 capsules/day (500 mg each) or placebo for 8 weeks	Patients with rheumatoid arthritis Experimental group ($n=23$) Placebo group ($n=16$)	↑ Serum IL-10 ↓ MDA and nitric oxide NS effects on blood TNF-α	[211]
Black cumin (*Nigella sativa*)	RCT	1000 mg oil/day or placebo for 8 weeks	Patients with Behcet's disease Experimental group ($n=47$) Placebo group ($n=42$)	NS effects on blood TNF-α, IL-10, CRP, and MDA	[212]
Black cumin (*Nigella sativa*)	RCT	3 g/day plus a low-calorie diet or placebo plus low-calorie diet for 8 weeks	45 women with obesity Experimental group ($n=45$) Placebo group ($n=45$)	↓ Blood CRP and TNF-α NS effects on serum IL-6	[213]
Cardamom	RCT	3 g day^{-1} or identical placebo for 8 weeks	Pre-diabetic subjects Experimental group ($n=40$) Placebo group ($n=40$)	↓ Blood CRP, CRP:IL-6 ratio, and MDA	[214]
Cinnamon	RCT	3 g/day or placebo for 8 weeks	Adult patients with T2DM Experimental group ($n=20$) Placebo group ($n=19$)	NS effects on reduction of SIRT1, IL-6, CRP, and TNF-α levels ↓ Plasma NF-kB	[215]
Cinnamon	RCT	3 glasses/day of black tea plus either 3 g/day of cardamom (group 1); 3 g/day cinnamon (group 2); 3 g/day ginger (group 3); 3 g/day of saffron (group 4); or control (only 3 glasses of black tea) for 8 weeks	Adult patients with TD2M Group 1 ($n=42$) Group 2 ($n=40$) Group 3 ($n=41$) Group 4 ($n=42$) Control ($n=39$)	NS effects on serum CRP (groups 1, 2, 3, and 4 vs. control)	[216]
Cinnamon	RCT	3 g/day of cinnamon (group 1); 3 g/day of ginger (group 2); or placebo for 6 weeks	Iranian female athletes ($n=60$)	NS effects on plasma IL-6 (groups 1 and 2 vs. placebo)	[217]
Cinnamon	RCT	2 capsules/day (each capsule contain 750 mg of cinnamon) or placebo for 12 weeks	Patients with NAFLD Experimental group ($n=23$) Placebo group ($n=22$)	↓ Serum CRP	[218]
Cinnamon powder	RCT	4 capsules/day of 500 mg of cinnamon powder or placebo for 8 weeks	Women with rheumatoid arthritis Experimental group ($n=18$) Placebo group ($n=18$)	↓ Blood CRP and TNF-α	[219]
Cinnamon powder	RCT	3 capsules/day (each containing 600 mg of cinnamon) or placebo	Patients with migraine Experimental group ($n=21$) Placebo group ($n=22$)	↓ Blood IL-6 and nitric oxide	[220]
Clove buds	RCT	1 capsule/day (250 mg of clovinol) or placebo for 2 weeks	Male social drinkers Experimental group ($n=8$) Placebo group ($n=8$)	↓ Serum CRP, IL-6, and lipid peroxidation	[221]
Cumin essential oil	RCT	75-mg cumin essential oil or placebo thrice daily for 8 weeks	Patients with metabolic syndrome Experimental group ($n=22$) Placebo group ($n=22$)	↓ Blood MDA NS effects on CRP and TNF-α	[222]
Garlic extracts	RCT	3.6 g/day or placebo for 6 weeks	Healthy adults with obesity Experimental group ($n=24$) Placebo group ($n=24$)	↓ Blood IL-6 and TNF-α (borderline)	[223]

Table 4 (continued)

Spice/ingredient	Study design	Dose/duration	Population	Main finding	Reference
Garlic extracts	RCT	400 mg twice a day or placebo for 8 weeks	Peritoneal dialysis patients Experimental group ($n=19$) Placebo group ($n=21$)	↓ Serum IL-6, CRP, and ESR	[224]
Garlic powder	RCT	2.1 g/day or placebo for 3 months	Overweight and smoking subjects Experimental group ($n=28$) Placebo group ($n=26$)	NS effects on serum TNF-α and CRP	[225]
Garlic powder	RCT	300 mg/day or placebo for 8 weeks	Hemodialysis patients Experimental group ($n=70$) Placebo group ($n=70$)	↓ Plasma homocysteine and oxLDL	[226]
Garlic powder	RCT	400 mg/day or placebo for 15 weeks	Patients with NAFLD Experimental group ($n=47$) Placebo group ($n=51$)	↓ Blood CRP	[227]
Ginger	RCT	2 tablets/day (1 g ginger in each) or placebo for 2 months	Adult patients with T2DM Experimental group ($n=32$) Placebo group ($n=32$)	↓ Blood CRP and TNF-α NS effects on serum IL-6	[228]
Ginger	RCT	4 tablets 500 mg (2 g) ginger or placebo twice a day for 8 weeks	Adult patients with T2DM and chronic periodontitis Experimental group ($n=21$) Placebo group ($n=21$)	↓ Plasma CRP, IL-6, and TNF-α	[229]
Green cardamom	RCT	Two 500 mg capsules three times/day or placebo for 3 months	Overweight or obese patients with NAFLD Experimental group ($n=43$) Placebo group ($n=44$)	↓ Serum CRP, TNF-α, IL-6, and Sirt1	[230]
green cardamom plus low-calorie diet	RCT	3 g/day plus low-calorie diet or placebo (only low-calorie diet) during 16 weeks	Obese women with PCOS Experimental group ($n=99$) Placebo group ($n=95$)	↓ Serum CRP, TNF-α, and IL-6 ↓ Expression levels of *TNF-α* and *CRP* genes	[231]
Green cumin essential oil	RCT	50 mg/day (group 1); 100 mg/day (group 2); or placebo for 8 weeks	Adult patients with type 2 diabetes Group 1 ($n=33$) Group 2 ($n=33$) Placebo group ($n=33$)	NS effects on blood CRP, TNF-α, and adiponectin (groups 1 and 2 vs. placebo)	[232]
Herbal formulation	RCT	Curcumin (300 mg), gingerols (7.5 mg), and piperine (3.75 mg) or naproxen twice a day for 4 weeks	Patients with knee osteoarthritis Herbal formulation ($n=30$) Naproxen ($n=30$)	NS effects on plasma prostaglandin E2 levels	[233]
Onion	RCT	1 capsule of peel extracts (100 mg quercetin/day) or placebo for 12 weeks	Healthy overweight and obese women Experimental group ($n=18$) Placebo group ($n=19$)	NS effects on plasma leptin, TNF-α, IL-4, and visfatin	[234]
Turmeric (curcumin)	RCT	1 g/day or placebo for 4 weeks	Sulfur mustard-exposed patients Experimental group ($n=46$) Placebo group ($n=50$)	↓ Serum IL-8 and CRP NS effects on IL-6	[235]
Turmeric (curcumin)	RCT	2 g/day or placebo for 8 weeks	Patients with NAFLD Experimental group ($n=32$) Placebo group ($n=32$)	↓ Plasma MDA	[236]

Table 4 (continued)

Spice/ingredient	Study design	Dose/duration	Population	Main finding	Reference
Turmeric (curcumin)	RCT	500 mg/day or placebo for 8 weeks	Women with moderate physical activity levels Experimental group ($n=32$) Placebo group ($n=33$)	↓ Blood MDA, CRP, and LDH	[237]
Turmeric (curcumin)	RCT	500 mg/day or placebo for 10 weeks	Overweight and obese adolescent girls Experimental group ($n=30$) Placebo group ($n=30$)	↓ Serum IL-6 and CRP	[238]
Turmeric (curcumin)	RCT	1500 mg/day plus lifestyle or placebo (only lifestyle) for 12 weeks	Patients with NAFLD Experimental group ($n=25$) Placebo group ($n=25$)	NS effects on NF-kB activity	[239]

RCT randomized controlled trial, *NS* no significant, *T2DM* type 2 diabetes mellitus, *NAFLD* non-alcoholic fatty liver disease, *PCOS* polycystic ovary syndrome, *MDA* malondialdehyde, *NF-kB* transcription nuclear factor kappa B, *CRP* C-reactive protein, *IL-6* interleukin 6, *TNF-α* tumor necrosis factor alpha, *IL-8* interleukin 8, *IL-4* interleukin 4, *IL-10* interleukin 10, *SIRT1* sirtuin 1, *ESR* erythrocyte sedimentation rate, *oxLDL* oxidized LDL, *LDH* lactate dehydrogenase

Westernized Diets and Ultra-processed/Discretionary Foods

Overall, the adoption of Western-type diets (WTD), with high contents of unhealthy fats, refined grains, sugars, and salt, evokes a state of chronic metabolic inflammation [264]. In this regard, a WTD showed positive associations with markers of inflammation and endothelial dysfunction in women from the Nurses' Health Study I cohort [265]. Also, a comparable WTD score positively correlated with CRP and IL-6 pro-inflammatory markers among Iranian women [266].

Interestingly, positive associations were found between the consumption of ultra-processed foods (UPF), which contain high amounts of free sugars, total fats, SFA, TFA, and sodium, and serum CRP levels among Brazilian women [267]. Likewise, Brazilian adolescents in the upper tertile of UPF (≥ 30% of total energy) had increased circulating IL-8 concentrations when compared with adolescents in tertile 1 (≤ 15.9% of total energy) of UPF [268].

Furthermore, a poor diet quality (considering habitual discretionary food consumption such as sweets, cakes, soft drinks, and fried potatoes) was associated with increased inflammation measured as plasma CRP and erythrocyte sedimentation rates in Swedish patients with rheumatoid arthritis [269].

Chrononutrition Patterns

Recent progress in the analysis of circadian rhythms and nutrition (referred as "chrononutrition") has revealed that the time of day when food is consumed may affect metabolic homeostasis and immune function [270]. In this context, a significant association between breakfast skipping and elevated serum CRP concentrations was reported in Chinese adults with poor diet quality [271]. In a randomized controlled crossover trial, breakfast skipping induced a higher activation of the NLRP3 inflammasome in human peripheral blood mononuclear cells and monocytes [272].

Intermittent fasting (IF), where individuals fast on consecutive or alternate days, has improved systemic inflammation in males with obesity [273]. Nevertheless, a transient elevation of biomarkers of macrophage infiltration in adipose tissue (CD40 +) and skeletal muscle (CD163 +) were found after IF in women with overweight or obesity [274].

Available evidence suggests that time-restricted eating (TRE), an alternative chrononutritional approach based on the consolidation of the total calorie intake during the active phase of the day, may modulate a variety of metabolic disease risk factors including exacerbated inflammation [275]. Indeed, it has been postulated that TRE as part of a periodized nutrition plan could be beneficial for reducing inflammation and induce a protective effect on some components of the immune system [276].

Interestingly, greater reductions in blood CRP levels were found in patients with metabolic syndrome after following an alternate day fasting (ADF), which consists of a "fast day," where caloric intake is limited, alternating with a "feed day," where food is consumed ad libitum [277]. Moreover, ADF reduced the plasma levels of sICAM-1 (an age-associated inflammatory marker) in healthy non-obese subjects [278].

Additionally, it has been reported that late eating, which refers to delay in the timing of meals (commonly the main meal of the day or the dinner) may increase the risk for developing cardiometabolic diseases [279]. In fact, late eating was associated with abdominal obesity, inflammatory

biomarkers such as IL-6 and CRP, and circadian-related disturbances in children [280].

Personalized Anti-inflammatory Nutritional Strategies

The integrative analysis of precision variables (age, sex, body phenotype, habitual dietary intake, physical activity levels, and lifestyle) together with personalized issues (genetic background, epigenetic signatures, microbiota composition, gene expression profiles, and metabolomic fingerprints) may contribute to the prescription of more personalized treatments seeking to improve the nutritional and medical management of inflammation (Fig. 2). For example, there is evidence that genetic variation may predispose to inflammatory conditions through interactions with environmental factors, such as diet, modulating the individual susceptibility to developing inflammation-related chronic and acute diseases [281]. Also, epigenetic signatures (including DNA methylation, miRNA expression, and histone modifications) play a fundamental role in inflammatory gene transcription [282]. Of note, a microbiota-based regression model has been able to predict the obesity-related inflammatory status in humans, which could be a useful tool in the precision management of inflammobesity [283]. Moreover, the expressions of genes with pro- and anti-inflammatory effects ultimately determine the outcome of inflammation [284]. Furthermore, metabolomics is an integrative approach that can be used to dissect the local and systemic metabolic consequences of inflammation, providing novel insights into the regulation of inflammatory diseases [285]. The application of these instruments are helping to elucidate unique and specific inflammo-metabotypes, expanding our understanding of the complexity and diversity of human metabolism [286]. Overall, these novel scientific insights are leading to the design and implementation of precision medicine/nutrition strategies for the prevention and control of prevalent chronic diseases with an inflammatory background [287].

Concluding Remarks

Nutrition is critical for life and well-being not only by contributing to disease prevention, health maintenance, and morbid conditions management, but also as a defense against endogenous and exogenous harmful factors including inflammation/oxidative stress or immune system dysfunctions. On the one hand, pro-inflammatory nutritional factors include the high consumption of foods rich in simple carbohydrates (fructose), SFA, TFA, cholesterol, and animal protein as well as habitually skipping breakfast and late overeating. On the other hand, potential anti-inflammatory compounds encompass MUFA, PUFA, antioxidant vitamins and minerals, bioactive molecules (polyphenols), specific foods (dairy products, whole-grains, fish, oilseeds, fruits and vegetables, edible insects, legumes, green tea, and coffee), culinary spices (cinnamon, ginger, back cumin, garlic, and turmeric) and some chrononutrition features including intermittent fasting and time-restricted eating (Fig. 1). Because inconsistencies and discrepancies between studies exist, further research in this field is still required, taking into account critical aspects of heterogeneity including type of population (ancestry), minimum and maximum levels and adverse effects, cooking methods, physiopathological status, and times of intervention. However, current evidence is contributing to the understanding of the relationship between nutrition and meta-inflammation, providing novel insights and potential targets for the control and management of communicable and non-communicable diseases.

Author Contribution Conceptualization: Omar Ramos-Lopez and J. Alfredo Martinez; formal analysis and investigation: Diego Martinez-Urbistondo and Juan A. Vargas-Nuñez; writing: Omar Ramos-Lopez and J. Alfredo Martinez. All authors have read and approved the final manuscript.

Funding Thi study received support from the "FACINGLCOVID-CM project. Funding REACT EU Program (Comunidad de Madrid and The European Regional Development Fund. ERDF. European Union)" and from the "Fundación Española Medicina Interna (FEMI 2020): Nutrición de precisión en pacientes con enfermedades autoinmunes sistémicas y con síndrome metabólico." Also, Metacategorización personalizada de procesos inflamatorios asociados a síndrome metabólico, enfermedades autoinmunes y virales para medicina de precisión (METAINFLAMACIÓN, Ref: Y2020/BIO-6600) is gratefully acknowledged.

Declarations

Competing Interests All authors reported no conflict of interest.

References

1. Medzhitov R. Inflammation 2010: new adventures of an old flame. Cell. 2010;140:771–6. https://doi.org/10.1016/j.cell.2010.03.006.
2. Sherwood ER, Toliver-Kinsky T. Mechanisms of the inflammatory response. Best Pract Res Clin Anaesthesiol. 2004;18:385–405. https://doi.org/10.1016/j.bpa.2003.12.002.
3. Kumar R, Clermont G, Vodovotz Y, Chow CC. The dynamics of acute inflammation. J Theor Biol. 2004;230:145–55. https://doi.org/10.1016/j.jtbi.2004.04.044.
4. Lukens JR, Dixit VD, Kanneganti TD. Inflammasome activation in obesity-related inflammatory diseases and autoimmunity. Discov Med. 2011;12:65–74.
5. Bennett JM, Reeves G, Billman GE, Sturmberg JP. Inflammation-nature's way to efficiently respond to all types of challenges: implications for understanding and managing "the epidemic" of chronic diseases. Front Med (Lausanne). 2018;5:316. https://doi.org/10.3389/fmed.2018.00316.

6. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, Li Y, Wang X, Zhao L. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2017;9:7204–18. https://doi.org/10.18632/oncotarget.23208.
7. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. Arch Med Sci. 2017;13:851–63. https://doi.org/10.5114/aoms.2016.58928.
8. Chen L, Chen R, Wang H, Liang F. Mechanisms linking inflammation to insulin resistance. Int J Endocrinol. 2015;2015:508409. https://doi.org/10.1155/2015/508409.
9. Bondia-Pons I, Ryan L, Martinez JA. Oxidative stress and inflammation interactions in human obesity. J Physiol Biochem. 2012;68:701–11. https://doi.org/10.1007/s13105-012-0154-2.
10. Al Bander Z, Nitert MD, Mousa A, Naderpoor N. The gut microbiota and inflammation: an overview. Int J Environ Res Public Health. 2020;17:7618. https://doi.org/10.3390/ijerph17207618.
11. Li C, Xu MM, Wang K, Adler AJ, Vella AT, Zhou B. Macrophage polarization and meta-inflammation. Transl Res. 2018;191:29–44. https://doi.org/10.1016/j.trsl.2017.10.004.
12. Rossi JF, Lu ZY, Massart C, Levon K. Dynamic immune/inflammation precision medicine: the good and the bad inflammation in infection and cancer. Front Immunol. 2021;12: 595722. https://doi.org/10.3389/fimmu.2021.595722.
13. Ricordi C, Garcia-Contreras M, Farnetti S. Diet and inflammation: possible effects on immunity, chronic diseases, and life span. J Am Coll Nutr. 2015;34(Suppl 1):10–3. https://doi.org/10.1080/07315724.2015.1080101.
14. Slavin J, Carlson J. Carbohydrates. Adv Nutr. 2014;5:760–1. https://doi.org/10.3945/an.114.006163.
15. Jonasson L, Guldbrand H, Lundberg AK, Nystrom FH. Advice to follow a low-carbohydrate diet has a favourable impact on low-grade inflammation in type 2 diabetes compared with advice to follow a low-fat diet. Ann Med. 2014;46:182–7. https://doi.org/10.3109/07853890.2014.894286.
16. Tavakoli A, Mirzababaei A, Sajadi F, Mirzaei K. Circulating inflammatory markers may mediate the relationship between low carbohydrate diet and circadian rhythm in overweight and obese women. BMC Womens Health. 2021;21:87. https://doi.org/10.1186/s12905-021-01240-5.
17. Seshadri P, Iqbal N, Stern L, Williams M, Chicano KL, Daily DA, McGrory J, Gracely EJ, Rader DJ, Samaha FF. A randomized study comparing the effects of a low-carbohydrate diet and a conventional diet on lipoprotein subfractions and C-reactive protein levels in patients with severe obesity. Am J Med. 2004;117:398–405. https://doi.org/10.1016/j.amjmed.2004.04.009.
18. Forsythe CE, Phinney SD, Fernandez ML, Quann EE, Wood RJ, Bibus DM, Kraemer WJ, Feinman RD, Volek JS. Comparison of low fat and low carbohydrate diets on circulating fatty acid composition and markers of inflammation. Lipids. 2008;43:65–77. https://doi.org/10.1007/s11745-007-3132-7.
19. Esfahani A, Wong JM, Mirrahimi A, Srichaikul K, Jenkins DJ, Kendall CW. The glycemic index: physiological significance. J Am Coll Nutr. 2009;28(Suppl):439S-445S. https://doi.org/10.1080/07315724.2009.10718109.
20. Dickinson S, Hancock DP, Petocz P, Ceriello A, Brand-Miller J. High-glycemic index carbohydrate increases nuclear factor-kappaB activation in mononuclear cells of young, lean healthy subjects. Am J Clin Nutr. 2008;87:1188–93. https://doi.org/10.1093/ajcn/87.5.1188.
21. Gomes JMG, Fabrini SP, Alfenas RCG. Low glycemic index diet reduces body fat and attenuates inflammatory and metabolic responses in patients with type 2 diabetes. Arch Endocrinol Metab. 2017;61:137–44. https://doi.org/10.1590/2359-3997000000206.
22. Gögebakan O, Kohl A, Osterhoff MA, van Baak MA, Jebb SA, Papadaki A, Martinez JA, Handjieva-Darlenska T, Hlavaty P, Weickert MO, Holst C, Saris WH, Astrup A, Pfeiffer AF, DiOGenes. Effects of weight loss and long-term weight maintenance with diets varying in protein and glycemic index on cardiovascular risk factors: the diet, obesity, and genes (DiOGenes) study: a randomized, controlled trial. Circulation. 2011;124:2829–38. https://doi.org/10.1161/CIRCULATIONAHA.111.033274.
23. Anderson JW, Baird P, Davis RH Jr, Ferreri S, Knudtson M, Koraym A, Waters V, Williams CL. Health benefits of dietary fiber. Nutr Rev. 2009;67:188–205. https://doi.org/10.1111/j.1753-4887.2009.00189.x.
24. Vitale M, Masulli M, Rivellese AA, Babini AC, Boemi M, Bonora E, Buzzetti R, Ciano O, Cignarelli M, Cigolini M, Clemente G, Citro G, Corsi L, Dall'Aglio E, Del Prato S, Di Cianni G, Dolci MA, Giordano C, Iannarelli R, Iovine C, Lapolla A, Lauro D, Leotta S, Mazzucchelli C, Montani V, Perriello G, Romano G, Romeo F, Santarelli L, di Cola RS, Squatrito S, Tonutti L, Trevisan R, Turco AA, Zamboni C, Riccardi G, Vaccaro O. Influence of dietary fat and carbohydrates proportions on plasma lipids, glucose control and low-grade inflammation in patients with type 2 diabetes-The TOSCA.IT Study. Eur J Nutr. 2016;55:1645–51. https://doi.org/10.1007/s00394-015-0983-1.
25. King DE, Egan BM, Woolson RF, Mainous AG 3rd, Al-Solaiman Y, Jesri A. Effect of a high-fiber diet vs a fiber-supplemented diet on C-reactive protein level. Arch Intern Med. 2007;167:502–6. https://doi.org/10.1001/archinte.167.5.502.
26. Ning H, Van Horn L, Shay CM, Lloyd-Jones DM. Associations of dietary fiber intake with long-term predicted cardiovascular disease risk and C-reactive protein levels (from the National Health and Nutrition Examination Survey Data [2005-2010]). Am J Cardiol. 2014;113:287–91. https://doi.org/10.1016/j.amjcard.2013.09.020.
27. Lichtenstein AH, Kennedy E, Barrier P, Danford D, Ernst ND, Grundy SM, Leveille GA, Van Horn L, Williams CL, Booth SL. Dietary fat consumption and health. Nutr Rev. 1998;56:S3-19. https://doi.org/10.1111/j.1753-4887.1998.tb01728.x.
28. Tan BL, Norhaizan ME. Effect of high-fat diets on oxidative stress, cellular inflammatory response and cognitive function. Nutrients. 2019;11:2579. https://doi.org/10.3390/nu11112579.
29. Davis NJ, Crandall JP, Gajavelli S, Berman JW, Tomuta N, Wylie-Rosett J, Katz SD. Differential effects of low-carbohydrate and low-fat diets on inflammation and endothelial function in diabetes. J Diabetes Complications. 2011;25:371–6. https://doi.org/10.1016/j.jdiacomp.2011.08.001.
30. Zhou H, Urso CJ, Jadeja V. Saturated fatty acids in obesity-associated inflammation. J Inflamm Res. 2020;13:1–14. https://doi.org/10.2147/JIR.S229691.
31. Arya S, Isharwal S, Misra A, Pandey RM, Rastogi K, Vikram NK, Dhingra V, Chatterjee A, Sharma R, Luthra K. C-reactive protein and dietary nutrients in urban Asian Indian adolescents and young adults. Nutrition. 2006;22:865–71. https://doi.org/10.1016/j.nut.2006.05.002.
32. González F, Considine RV, Abdelhadi OA, Acton AJ. Inflammation triggered by saturated fat ingestion is linked to insulin resistance and hyperandrogenism in polycystic ovary syndrome. J Clin Endocrinol Metab. 2020;105:e2152–67. https://doi.org/10.1210/clinem/dgaa108.
33. Schwingshackl L, Hoffmann G. Monounsaturated fatty acids, olive oil and health status: a systematic review and meta-analysis of cohort studies. Lipids Health Dis. 2014;13:154. https://doi.org/10.1186/1476-511X-13-154.
34. Yoneyama S, Miura K, Sasaki S, Yoshita K, Morikawa Y, Ishizaki M, Kido T, Naruse Y, Nakagawa H. Dietary intake of fatty acids and serum C-reactive protein in Japanese. J Epidemiol. 2007;17:86–92. https://doi.org/10.2188/jea.17.86.
35. Shahidi F, Ambigaipalan P. Omega-3 polyunsaturated fatty acids and their health benefits. Annu Rev Food Sci Technol. 2018;9:345–81. https://doi.org/10.1146/annurev-food-111317-095850.

36. Pischon T, Hankinson SE, Hotamisligil GS, Rifai N, Willett WC, Rimm EB. Habitual dietary intake of n-3 and n-6 fatty acids in relation to inflammatory markers among US men and women. Circulation. 2003;108:155–60. https://doi.org/10.1161/01.CIR.0000079224.46084.C2.
37. Lopez-Garcia E, Schulze MB, Manson JE, Meigs JB, Albert CM, Rifai N, Willett WC, Hu FB. Consumption of (n-3) fatty acids is related to plasma biomarkers of inflammation and endothelial activation in women. J Nutr. 2004;134:1806–11. https://doi.org/10.1093/jn/134.7.1806.
38. Yang B, Ren XL, Li ZH, Shi MQ, Ding F, Su KP, Guo XJ, Li D. Lowering effects of fish oil supplementation on proinflammatory markers in hypertension: results from a randomized controlled trial. Food Funct. 2020;11:1779–89. https://doi.org/10.1039/c9fo03085a.
39. Kiecolt-Glaser JK, Belury MA, Andridge R, Malarkey WB, Glaser R. Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial. Brain Behav Immun. 2011;25:1725–34. https://doi.org/10.1016/j.bbi.2011.07.229.
40. Kiecolt-Glaser JK, Belury MA, Andridge R, Malarkey WB, Hwang BS, Glaser R. Omega-3 supplementation lowers inflammation in healthy middle-aged and older adults: a randomized controlled trial. Brain Behav Immun. 2012;26:988–95. https://doi.org/10.1016/j.bbi.2012.05.011.
41. Allison DB, Egan SK, Barraj LM, Caughman C, Infante M, Heimbach JT. Estimated intakes of trans fatty and other fatty acids in the US population. J Am Diet Assoc. 1999;99:166–74. https://doi.org/10.1016/S0002-8223(99)00041-3.
42. Lopez-Garcia E, Schulze MB, Meigs JB, Manson JE, Rifai N, Stampfer MJ, Willett WC, Hu FB. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. J Nutr. 2005;135:562–6. https://doi.org/10.1093/jn/135.3.562.
43. Mozaffarian D, Pischon T, Hankinson SE, Rifai N, Joshipura K, Willett WC, Rimm EB. Dietary intake of trans fatty acids and systemic inflammation in women. Am J Clin Nutr. 2004;79:606–12. https://doi.org/10.1093/ajcn/79.4.606.
44. Baer DJ, Judd JT, Clevidence BA, Tracy RP. Dietary fatty acids affect plasma markers of inflammation in healthy men fed controlled diets: a randomized crossover study. Am J Clin Nutr. 2004;79:969–73. https://doi.org/10.1093/ajcn/79.6.969.
45. Andersen CJ. Impact of dietary cholesterol on the pathophysiology of infectious and autoimmune disease. Nutrients. 2018;10:764. https://doi.org/10.3390/nu10060764.
46. Mazidi M, Heidari-Bakavoli A, Khayyatzadeh SS, Azarpazhooh MR, Nematy M, Safarian M, Esmaeili H, Parizadeh SM, Ghayour-Mobarhan M, Kengne AP, Ferns GA. Serum hs-CRP varies with dietary cholesterol, but not dietary fatty acid intake in individuals free of any history of cardiovascular disease. Eur J Clin Nutr. 2016;70:1454–7. https://doi.org/10.1038/ejcn.2016.92.
47. Khayyatzadeh SS, Kazemi-Bajestani SMR, Bagherniya M, Mehramiz M, Tayefi M, Ebrahimi M, Ferns GA, Safarian M, Ghayour-Mobarhan M. Serum high C reactive protein concentrations are related to the intake of dietary macronutrients and fiber: findings from a large representative Persian population sample. Clin Biochem. 2017;50:750–5. https://doi.org/10.1016/j.clinbiochem.2017.03.016.
48. Wu G. Dietary protein intake and human health. Food Funct. 2016;7:1251–65. https://doi.org/10.1039/c5fo01530h.
49 Hruby A, Jacques PF. Dietary protein and changes in biomarkers of inflammation and oxidative stress in the Framingham Heart Study Offspring Cohort. Curr Dev Nutr. 2019;3:nzz019. https://doi.org/10.1093/cdn/nzz019.
50. Koelman L, Markova M, Seebeck N, Hornemann S, Rosenthal A, Lange V, Pivovarova-Ramich O, Aleksandrova K. Effects of high and low protein diets on inflammatory profiles in people with morbid obesity: a 3-week intervention study. Nutrients. 2020;12:3636. https://doi.org/10.3390/nu12123636.
51. Yeh KL, Kautz A, Lohse B, Groth SW. Associations between dietary patterns and inflammatory markers during pregnancy: a systematic review. Nutrients. 2021;13:834. https://doi.org/10.3390/nu13030834.
52. Lopez-Legarrea P, de la Iglesia R, Abete I, Navas-Carretero S, Martinez JA, Zulet MA. The protein type within a hypocaloric diet affects obesity-related inflammation: the RESMENA project. Nutrition. 2014;30:424–9. https://doi.org/10.1016/j.nut.2013.09.009.
53. Floegel A, Chung SJ, von Ruesten A, Yang M, Chung CE, Song WO, Koo SI, Pischon T, Chun OK. Antioxidant intake from diet and supplements and elevated serum C-reactive protein and plasma homocysteine concentrations in US adults: a cross-sectional study. Public Health Nutr. 2011;14:2055–64. https://doi.org/10.1017/S1368980011000395.
54. Schwab S, Zierer A, Schneider A, Heier M, Koenig W, Kastenmüller G, Waldenberger M, Peters A, Thorand B. Vitamin E supplementation is associated with lower levels of C-reactive protein only in higher dosages and combined with other antioxidants: The Cooperative Health Research in the Region of Augsburg (KORA) F4 study. Br J Nutr. 2015;113:1782–91. https://doi.org/10.1017/S0007114515000902.
55. Scheurig AC, Thorand B, Fischer B, Heier M, Koenig W. Association between the intake of vitamins and trace elements from supplements and C-reactive protein: results of the MONICA/KORA Augsburg study. Eur J Clin Nutr. 2008;62:127–37. https://doi.org/10.1038/sj.ejcn.1602687.
56. Juanola-Falgarona M, Salas-Salvadó J, Estruch R, Portillo MP, Casas R, Miranda J, Martínez-González MA, Bulló M. Association between dietary phylloquinone intake and peripheral metabolic risk markers related to insulin resistance and diabetes in elderly subjects at high cardiovascular risk. Cardiovasc Diabetol. 2013;12:7. https://doi.org/10.1186/1475-2840-12-7.
57. Jung S, Kim MK, Choi BY. The long-term relationship between dietary pantothenic acid (vitamin B5) intake and C-reactive protein concentration in adults aged 40 years and older. Nutr Metab Cardiovasc Dis. 2017;27:806–16. https://doi.org/10.1016/j.numecd.2017.05.008.
58. Detopoulou P, Panagiotakos DB, Antonopoulou S, Pitsavos C, Stefanadis C. Dietary choline and betaine intakes in relation to concentrations of inflammatory markers in healthy adults: the ATTICA study. Am J Clin Nutr. 2008;87:424–30. https://doi.org/10.1093/ajcn/87.2.424.
59. Cox SE, Arthur P, Kirkwood BR, Yeboah-Antwi K, Riley EM. Vitamin A supplementation increases ratios of proinflammatory to anti-inflammatory cytokine responses in pregnancy and lactation. Clin Exp Immunol. 2006;144:392–400. https://doi.org/10.1111/j.1365-2249.2006.03082.x.
60. Bitarafan S, Mohammadpour Z, Jafarirad S, Harirchian MH, Yekaninejad MS, Saboor-Yaraghi AA. The effect of retinyl-palmitate on the level of pro and anti-inflammatory cytokines in multiple sclerosis patients: a randomized double blind clinical trial. Clin Neurol Neurosurg. 2019;177:101–5. https://doi.org/10.1016/j.clineuro.2019.01.003.
61. Jafarirad S, Siassi F, Harirchian MH, Amani R, Bitarafan S, Saboor-Yaraghi A. The effect of vitamin a supplementation on biochemical parameters in multiple sclerosis patients. Iran Red Crescent Med J. 2013;15:194–8. https://doi.org/10.5812/ircmj.3480.
62. Alaei-Shahmiri F, Soares MJ, Zhao Y, Sherriff J. The impact of thiamine supplementation on blood pressure, serum lipids and C-reactive protein in individuals with hyperglycemia: a randomised, double-blind cross-over trial. Diabetes Metab Syndr. 2015;9:213–7. https://doi.org/10.1016/j.dsx.2015.04.014.

63. von Martels JZH, Bourgonje AR, Klaassen MAY, Alkhalifah HAA, Sadaghian Sadabad M, Vich Vila A, Gacesa R, Gabriëls RY, Steinert RE, Jansen BH, Bulthuis MLC, van Dullemen HM, Visschedijk MC, Festen EAM, Weersma RK, de Vos P, van Goor H, Faber KN, Harmsen HJM, Dijkstra G. Riboflavin supplementation in patients with Crohn's disease [the RISE-UP study]. J Crohns Colitis. 2020;14:595–607. https://doi.org/10.1093/ecco-jcc/jjz208.
64. Ellulu MS, Rahmat A, Patimah I, Khaza'ai H, Abed Y. Effect of vitamin C on inflammation and metabolic markers in hypertensive and/or diabetic obese adults: a randomized controlled trial. Drug Des Devel Ther. 2015;9:3405–12. https://doi.org/10.2147/DDDT.S83144.
65. Fumeron C, Nguyen-Khoa T, Saltiel C, Kebede M, Buisson C, Drüeke TB, Lacour B, Massy ZA. Effects of oral vitamin C supplementation on oxidative stress and inflammation status in haemodialysis patients. Nephrol Dial Transplant. 2005;20:1874–9. https://doi.org/10.1093/ndt/gfh928.
66. Zhang K, Li Y, Cheng X, Liu L, Bai W, Guo W, Wu L, Zuo L. Cross-over study of influence of oral vitamin C supplementation on inflammatory status in maintenance hemodialysis patients. BMC Nephrol. 2013;14:252. https://doi.org/10.1186/1471-2369-14-252.
67. Block G, Jensen CD, Dalvi TB, Norkus EP, Hudes M, Crawford PB, Holland N, Fung EB, Schumacher L, Harmatz P. Vitamin C treatment reduces elevated C-reactive protein. Free Radic Biol Med. 2009;46:70–7. https://doi.org/10.1016/j.freeradbiomed.2008.09.030.
68. Zhang J, Rao X, Li Y, Zhu Y, Liu F, Guo G, Luo G, Meng Z, De Backer D, Xiang H, Peng Z. Pilot trial of high-dose vitamin C in critically ill COVID-19 patients. Ann Intensive Care. 2021;11:5. https://doi.org/10.1186/s13613-020-00792-3.
69. DiBella M, Thomas MS, Alyousef H, Millar C, Blesso C, Malysheva O, Caudill MA, Fernandez ML. Choline intake as supplement or as a component of eggs increases plasma choline and reduces interleukin-6 without modifying plasma cholesterol in participants with metabolic syndrome. Nutrients. 2020;12:3120. https://doi.org/10.3390/nu12103120.
70. Sharifi A, Hosseinzadeh-Attar MJ, Vahedi H, Nedjat S. A randomized controlled trial on the effect of vitamin D3 on inflammation and cathelicidin gene expression in ulcerative colitis patients. Saudi J Gastroenterol. 2016;22:316–23. https://doi.org/10.4103/1319-3767.187606.
71. Mousa A, Naderpoor N, Johnson J, Sourris K, de Courten MPJ, Wilson K, Scragg R, Plebanski M, de Courten B. Effect of vitamin D supplementation on inflammation and nuclear factor kappa-B activity in overweight/obese adults: a randomized placebo-controlled trial. Sci Rep. 2017;7:15154. https://doi.org/10.1038/s41598-017-15264-1.
72. Cheshmazar E, Hosseini AF, Yazdani B, Razmpoosh E, Zarrati M. Effects of vitamin D supplementation on omentin-1 and spexin levels, inflammatory parameters, lipid profile, and anthropometric indices in obese and overweight adults with vitamin D deficiency under low-calorie diet: a randomized placebo controlled trial. Evid Based Complement Alternat Med. 2020;2020:3826237. https://doi.org/10.1155/2020/3826237.
73. Lotfi-Dizaji L, Mahboob S, Aliashrafi S, Vaghef-Mehrabany E, Ebrahimi-Mameghani M, Morovati A. Effect of vitamin D supplementation along with weight loss diet on meta-inflammation and fat mass in obese subjects with vitamin D deficiency: a double-blind placebo-controlled randomized clinical trial. Clin Endocrinol (Oxf). 2019;90:94–101. https://doi.org/10.1111/cen.13861.
74. Wamberg L, Kampmann U, Stødkilde-Jørgensen H, Rejnmark L, Pedersen SB, Richelsen B. Effects of vitamin D supplementation on body fat accumulation, inflammation, and metabolic risk factors in obese adults with low vitamin D levels - results from a randomized trial. Eur J Intern Med. 2013;24:644–9. https://doi.org/10.1016/j.ejim.2013.03.005.
75. Chandler PD, Scott JB, Drake BF, Ng K, Manson JE, Rifai N, Chan AT, Bennett GG, Hollis BW, Giovannucci EL, Emmons KM, Fuchs CS. Impact of vitamin D supplementation on inflammatory markers in African Americans: results of a four-arm, randomized, placebo-controlled trial. Cancer Prev Res (Phila). 2014;7:218–25. https://doi.org/10.1158/1940-6207.CAPR-13-0338-T.
76 Pessoa Mamede LCG, de Lima RLFC, Silva AS, Rodrigues Pita JCL, Galdino Gomes NI, de Sena EA, Moraes Nobrega RP, Scarano Alcântara JO, Fontes de Souza JH, Cardoso GA, de Brito Alves JL, Rodrigues Gonçalves MDC. Effects of a single oral megadose of vitamin D3 on inflammation and oxidative stress markers in overweight and obese women: a randomized, double-blind, placebo-controlled clinical trial. Diabetes Metab Syndr Obes. 2021;14:525–34. https://doi.org/10.2147/DMSO.S285597.
77 de Medeiros Cavalcante IG, Silva AS, Costa MJ, Persuhn DC, Issa CT, de Lunafreire TL, da Conceição Rodrigues Gonçalves M. Effect of vitamin D3 supplementation and influence of BsmI polymorphism of the VDR gene of the inflammatory profile and oxidative stress in elderly women with vitamin D insufficiency: vitamin D3 megadose reduces inflammatory markers. Exp Gerontol. 2015;66:10–6. https://doi.org/10.1016/j.exger.2015.03.011.
78. Waterhouse M, Tran B, Ebeling PR, English DR, Lucas RM, Venn AJ, Webb PM, Whiteman DC, Neale RE. Effect of vitamin D supplementation on selected inflammatory biomarkers in older adults: a secondary analysis of data from a randomised, placebo-controlled trial. Br J Nutr. 2015;114:693–9. https://doi.org/10.1017/S0007114515002366.
79. Khatami PG, Soleimani A, Sharifi N, Aghadavod E, Asemi Z. The effects of high-dose vitamin E supplementation on biomarkers of kidney injury, inflammation, and oxidative stress in patients with diabetic nephropathy: a randomized, double-blind, placebo-controlled trial. J Clin Lipidol. 2016;10:922–9. https://doi.org/10.1016/j.jacl.2016.02.021.
80. Pirhadi-Tavandashti N, Imani H, Ebrahimpour-Koujan S, Samavat S, Hakemi MS. The effect of vitamin E supplementation on biomarkers of endothelial function and inflammation among hemodialysis patients: a double-blinded randomized clinical trial. Complement Ther Med. 2020;49: 102357. https://doi.org/10.1016/j.ctim.2020.102357.
81. Mangoni AA, Arya R, Ford E, Asonganyi B, Sherwood RA, Ouldred E, Swift CG, Jackson SH. Effects of folic acid supplementation on inflammatory and thrombogenic markers in chronic smokers. A randomised controlled trial. Thromb Res. 2003;110:13–7. https://doi.org/10.1016/s0049-3848(03)00295-0.
82. Solini A, Santini E, Ferrannini E. Effect of short-term folic acid supplementation on insulin sensitivity and inflammatory markers in overweight subjects. Int J Obes (Lond). 2006;30:1197–202. https://doi.org/10.1038/sj.ijo.0803265.
83. Durga J, van Tits LJ, Schouten EG, Kok FJ, Verhoef P. Effect of lowering of homocysteine levels on inflammatory markers: a randomized controlled trial. Arch Intern Med. 2005;165:1388–94. https://doi.org/10.1001/archinte.165.12.1388.
84. Chen H, Liu S, Ji L, Wu T, Ji Y, Zhou Y, Zheng M, Zhang M, Xu W, Huang G. Folic acid supplementation mitigates Alzheimer's disease by reducing inflammation: a randomized controlled trial. Mediators Inflamm. 2016;2016:5912146. https://doi.org/10.1155/2016/5912146.
85. Ma F, Wu T, Zhao J, Song A, Liu H, Xu W, Huang G. Folic acid supplementation improves cognitive function by reducing the levels of peripheral inflammatory cytokines in elderly Chinese

subjects with MCI. Sci Rep. 2016;6:37486. https://doi.org/10.1038/srep37486.
86. Chen H, Liu S, Ge B, Zhou D, Li M, Li W, Ma F, Liu Z, Ji Y, Huang G. Effects of folic acid and vitamin B12 supplementation on cognitive impairment and inflammation in patients with Alzheimer's disease: a randomized, single-blinded, placebo-controlled trial. J Prev Alzheimers Dis. 2021;8:249–56. https://doi.org/10.14283/jpad.2021.22.
87. Ma F, Zhou X, Li Q, Zhao J, Song A, An P, Du Y, Xu W, Huang G. Effects of Folic Acid and Vitamin B12, Alone and in combination on cognitive function and inflammatory factors in the elderly with mild cognitive impairment: a single-blind experimental design. Curr Alzheimer Res. 2019;16:622–32. https://doi.org/10.2174/1567205016666190725144629.
88. van Dijk SC, Enneman AW, Swart KM, van Wijngaarden JP, Ham AC, de Jonge R, Blom HJ, Feskens EJ, Geleijnse JM, van Schoor NM, Dhonukshe-Rutten RA, de Jongh RT, Lips P, de Groot LC, Uitterlinden AG, van den Meiracker TH, Mattace-Raso FU, van der Velde N, Smulders YM. Effect of vitamin B12 and folic acid supplementation on biomarkers of endothelial function and inflammation among elderly individuals with hyperhomocysteinemia. Vasc Med. 2016;21:91–8. https://doi.org/10.1177/1358863X15622281.
89. Christen WG, Cook NR, Van Denburgh M, Zaharris E, Albert CM, Manson JE. Effect of combined treatment with folic acid, vitamin B6, and vitamin B12 on plasma biomarkers of inflammation and endothelial dysfunction in women. J Am Heart Assoc. 2018;7: e008517. https://doi.org/10.1161/JAHA.117.008517.
90. Bleie Ø, Semb AG, Grundt H, Nordrehaug JE, Vollset SE, Ueland PM, Nilsen DW, Bakken AM, Refsum H, Nygård OK. Homocysteine-lowering therapy does not affect inflammatory markers of atherosclerosis in patients with stable coronary artery disease. J Intern Med. 2007;262:244–53. https://doi.org/10.1111/j.1365-2796.2007.01810.x.
91. Shishavan NG, Gargari BP, Jafarabadi MA, Kolahi S, Haggifar S, Noroozi S. Vitamin K1 supplementation did not alter inflammatory markers and clinical status in patients with rheumatoid arthritis. Int J Vitam Nutr Res. 2018;88:251–7. https://doi.org/10.1024/0300-9831/a000276.
92. Kristensen M, Kudsk J, Bügel S. Six weeks phylloquinone supplementation produces undesirable effects on blood lipids with no changes in inflammatory and fibrinolytic markers in postmenopausal women. Eur J Nutr. 2008;47:375–9. https://doi.org/10.1007/s00394-008-0737-4.
93. Mehri A. Trace elements in human nutrition (II) - an update. Int J Prev Med. 2020;11:2. https://doi.org/10.4103/ijpvm.IJPVM_48_19.
94. Chacko SA, Song Y, Nathan L, Tinker L, de Boer IH, Tylavsky F, Wallace R, Liu S. Relations of dietary magnesium intake to biomarkers of inflammation and endothelial dysfunction in an ethnically diverse cohort of postmenopausal women. Diabetes Care. 2010;33:304–10. https://doi.org/10.2337/dc09-1402.
95. Song Y, Li TY, van Dam RM, Manson JE, Hu FB. Magnesium intake and plasma concentrations of markers of systemic inflammation and endothelial dysfunction in women. Am J Clin Nutr. 2007;85:1068–74. https://doi.org/10.1093/ajcn/85.4.1068.
96. Gong JH, Lo K, Liu Q, Li J, Lai S, Shadyab AH, Arcan C, Snetselaar L, Liu S. Dietary manganese, plasma markers of inflammation, and the development of type 2 diabetes in postmenopausal women: findings from the Women's Health Initiative. Diabetes Care. 2020;43:1344–51. https://doi.org/10.2337/dc20-0243.
97. Pinna K, Kelley DS, Taylor PC, King JC. Immune functions are maintained in healthy men with low zinc intake. J Nutr. 2002;132:2033–6. https://doi.org/10.1093/jn/132.7.2033.
98. Bo S, Durazzo M, Gambino R, Berutti C, Milanesio N, Caropreso A, Gentile L, Cassader M, Cavallo-Perin P, Pagano G. Associations of dietary and serum copper with inflammation, oxidative stress, and metabolic variables in adults. J Nutr. 2008;138:305–10. https://doi.org/10.1093/jn/138.2.305.
99. Cepeda-Lopez AC, Osendarp SJ, Melse-Boonstra A, Aeberli I, Gonzalez-Salazar F, Feskens E, Villalpando S, Zimmermann MB. Sharply higher rates of iron deficiency in obese Mexican women and children are predicted by obesity-related inflammation rather than by differences in dietary iron intake. Am J Clin Nutr. 2011;93:975–83. https://doi.org/10.3945/ajcn.110.005439.
100. Jamilian M, Bahmani F, Siavashani MA, Mazloomi M, Asemi Z, Esmaillzadeh A. The effects of chromium supplementation on endocrine profiles, biomarkers of inflammation, and oxidative stress in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. Biol Trace Elem Res. 2016;172:72–8. https://doi.org/10.1007/s12011-015-0570-6.
101. Amiri Siavashani M, Zadeh Modarres S, Mirhosseini N, Aghadavod E, Salehpour S, Asemi Z. The effects of chromium supplementation on gene expression of insulin, lipid, and inflammatory markers in infertile women with polycystic ovary syndrome candidate for in vitro fertilization: a randomized, double-blinded, placebo-controlled trial. Front Endocrinol (Lausanne). 2018;9:726. https://doi.org/10.3389/fendo.2018.00726.
102. Moradi F, Kooshki F, Nokhostin F, Khoshbaten M, Bazyar H, Pourghassem GB. A pilot study of the effects of chromium picolinate supplementation on serum fetuin-A, metabolic and inflammatory factors in patients with nonalcoholic fatty liver disease: a double-blind, placebo-controlled trial. J Trace Elem Med Biol. 2021;63: 126659. https://doi.org/10.1016/j.jtemb.2020.126659.
103. Saiyed ZM, Lugo JP. Impact of chromium dinicocysteinate supplementation on inflammation, oxidative stress, and insulin resistance in type 2 diabetic subjects: an exploratory analysis of a randomized, double-blind, placebo-controlled study. Food Nutr Res. 2016;60:31762. https://doi.org/10.3402/fnr.v60.31762.
104. Iqbal N, Cardillo S, Volger S, Bloedon LT, Anderson RA, Boston R, Szapary PO. Chromium picolinate does not improve key features of metabolic syndrome in obese nondiabetic adults. Metab Syndr Relat Disord. 2009;7:143–50. https://doi.org/10.1089/met.2008.0048.
105. Jain SK, Kahlon G, Morehead L, Dhawan R, Lieblong B, Stapleton T, Caldito G, Hoeldtke R, Levine SN, Bass PF 3rd. Effect of chromium dinicocysteinate supplementation on circulating levels of insulin, TNF-α, oxidative stress, and insulin resistance in type 2 diabetic subjects: randomized, double-blind, placebo-controlled study. Mol Nutr Food Res. 2012;56:1333–41. https://doi.org/10.1002/mnfr.201100719.
106. Kim HN, Kim SH, Eun YM, Song SW. Effects of zinc, magnesium, and chromium supplementation on cardiometabolic risk in adults with metabolic syndrome: a double-blind, placebo-controlled randomised trial. J Trace Elem Med Biol. 2018;48:166–71. https://doi.org/10.1016/j.jtemb.2018.03.022.
107. DiSilvestro RA, Joseph EL, Zhang W, Raimo AE, Kim YM. A randomized trial of copper supplementation effects on blood copper enzyme activities and parameters related to cardiovascular health. Metabolism. 2012;61:1242–6. https://doi.org/10.1016/j.metabol.2012.02.002.
108. Ma J, Sun Q, Liu J, Hu Y, Liu S, Zhang J, Sheng X, Hambidge KM. The effect of iron fortification on iron (Fe) status and inflammation: a randomized controlled trial. PLoS ONE. 2016;11: e0167458. https://doi.org/10.1371/journal.pone.0167458.
109. Dostal A, Baumgartner J, Riesen N, Chassard C, Smuts CM, Zimmermann MB, Lacroix C. Effects of iron supplementation on dominant bacterial groups in the gut, faecal SCFA and gut inflammation: a randomised, placebo-controlled intervention trial in South African children. Br J Nutr. 2014;112:547–56. https://doi.org/10.1017/S0007114514001160.
110. Tang M, Frank DN, Sherlock L, Ir D, Robertson CE, Krebs NF. Effect of vitamin E with therapeutic iron supplementation on iron

repletion and gut microbiome in US iron deficient infants and toddlers. J Pediatr Gastroenterol Nutr. 2016;63:379–85. https://doi.org/10.1097/MPG.0000000000001154.
111. Chacko SA, Sul J, Song Y, Li X, LeBlanc J, You Y, Butch A, Liu S. Magnesium supplementation, metabolic and inflammatory markers, and global genomic and proteomic profiling: a randomized, double-blind, controlled, crossover trial in overweight individuals. Am J Clin Nutr. 2011;93:463–73. https://doi.org/10.3945/ajcn.110.002949.
112. Moslehi N, Vafa M, Rahimi-Foroushani A, Golestan B. Effects of oral magnesium supplementation on inflammatory markers in middle-aged overweight women. J Res Med Sci. 2012;17:607–14.
113. Nielsen FH, Johnson LK, Zeng H. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. Magnes Res. 2010;23:158–68. https://doi.org/10.1684/mrh.2010.0220.
114. Zanforlini BM, Ceolin C, Trevisan C, Alessi A, Seccia DM, Noale M, Maggi S, Guarnieri G, Vianello A, Sergi G. Clinical trial on the effects of oral magnesium supplementation in stable-phase COPD patients. Aging Clin Exp Res. 2021. https://doi.org/10.1007/s40520-021-01921-z.
115. Simental-Mendía LE, Rodríguez-Morán M, Reyes-Romero MA, Guerrero-Romero F. No positive effect of oral magnesium supplementation in the decreases of inflammation in subjects with prediabetes: a pilot study. Magnes Res. 2012;25:140–6. https://doi.org/10.1684/mrh.2012.0322.
116. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. Oral magnesium supplementation decreases C-reactive protein levels in subjects with prediabetes and hypomagnesemia: a clinical randomized double-blind placebo-controlled trial. Arch Med Res. 2014;45:325–30. https://doi.org/10.1016/j.arcmed.2014.04.006.
117. Afshar Ebrahimi F, Foroozanfard F, Aghadavod E, Bahmani F, Asemi Z. The effects of magnesium and zinc co-supplementation on biomarkers of inflammation and oxidative stress, and gene expression related to inflammation in polycystic ovary syndrome: a randomized controlled clinical trial. Biol Trace Elem Res. 2018;184:300–7. https://doi.org/10.1007/s12011-017-1198-5.
118. Gijsbers L, Dower JI, Schalkwijk CG, Kusters YH, Bakker SJ, Hollman PC, Geleijnse JM. Effects of sodium and potassium supplementation on endothelial function: a fully controlled dietary intervention study. Br J Nutr. 2015;114:1419–26. https://doi.org/10.1017/S0007114515002986.
119. Bahmani F, Kia M, Soleimani A, Mohammadi AA, Asemi Z. The effects of selenium supplementation on biomarkers of inflammation and oxidative stress in patients with diabetic nephropathy: a randomised, double-blind, placebo-controlled trial. Br J Nutr. 2016;116:1222–8. https://doi.org/10.1017/S0007114516003251.
120. Raygan F, Behnejad M, Ostadmohammadi V, Bahmani F, Mansournia MA, Karamali F, Asemi Z. Selenium supplementation lowers insulin resistance and markers of cardio-metabolic risk in patients with congestive heart failure: a randomised, double-blind, placebo-controlled trial. Br J Nutr. 2018;120:33–40. https://doi.org/10.1017/S0007114518001253.
121. Salehi M, Sohrabi Z, Ekramzadeh M, Fallahzadeh MK, Ayatollahi M, Geramizadeh B, Hassanzadeh J, Sagheb MM. Selenium supplementation improves the nutritional status of hemodialysis patients: a randomized, double-blind, placebo-controlled trial. Nephrol Dial Transplant. 2013;28:716–23. https://doi.org/10.1093/ndt/gfs170.
122. Asemi Z, Jamilian M, Mesdaghinia E, Esmaillzadeh A. Effects of selenium supplementation on glucose homeostasis, inflammation, and oxidative stress in gestational diabetes: randomized, double-blind, placebo-controlled trial. Nutrition. 2015;31:1235–42. https://doi.org/10.1016/j.nut.2015.04.014.
123. Razavi M, Jamilian M, Kashan ZF, Heidar Z, Mohseni M, Ghandi Y, Bagherian T, Asemi Z. Selenium supplementation and the effects on reproductive outcomes, biomarkers of inflammation, and oxidative stress in women with polycystic ovary syndrome. Horm Metab Res. 2016;48:185–90. https://doi.org/10.1055/s-0035-1559604.
124. Kamali A, Amirani E, Asemi Z. Effects of selenium supplementation on metabolic status in patients undergoing for coronary artery bypass grafting (CABG) surgery: a randomized, double-blind, placebo-controlled trial. Biol Trace Elem Res. 2019;191:331–7. https://doi.org/10.1007/s12011-019-1636-7.
125. Farrokhian A, Bahmani F, Taghizadeh M, Mirhashemi SM, Aarabi MH, Raygan F, Aghadavod E, Asemi Z. Selenium supplementation affects insulin resistance and serum hs-CRP in patients with type 2 diabetes and coronary heart disease. Horm Metab Res. 2016;48:263–8. https://doi.org/10.1055/s-0035-1569276.
126. Daeian N, Radfar M, Jahangard-Rafsanjani Z, Hadjibabaie M, Ghavamzadeh A. Selenium supplementation in patients undergoing hematopoietic stem cell transplantation: effects on pro-inflammatory cytokines levels. Daru. 2014;22:51. https://doi.org/10.1186/2008-2231-22-51.
127. Jafari F, Amani R, Tarrahi MJ. Effect of zinc supplementation on physical and psychological symptoms, biomarkers of inflammation, oxidative stress, and brain-derived neurotrophic factor in young women with premenstrual syndrome: a randomized, double-blind, placebo-controlled trial. Biol Trace Elem Res. 2020;194:89–95. https://doi.org/10.1007/s12011-019-01757-9.
128. Bao B, Prasad AS, Beck FW, Fitzgerald JT, Snell D, Bao GW, Singh T, Cardozo LJ. Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: a potential implication of zinc as an atheroprotective agent. Am J Clin Nutr. 2010;91:1634–41. https://doi.org/10.3945/ajcn.2009.28836.
129. Mazaheri M, Aghdam AM, Heidari M, Zarrin R. Assessing the effect of zinc supplementation on the frequency of migraine attack, duration, severity, lipid profile and hs-CRP in adult women. Clin Nutr Res. 2021;10:127–39. https://doi.org/10.7762/cnr.2021.10.2.127.
130. Bao B, Prasad AS, Beck FW, Snell D, Suneja A, Sarkar FH, Doshi N, Fitzgerald JT, Swerdlow P. Zinc supplementation decreases oxidative stress, incidence of infection, and generation of inflammatory cytokines in sickle cell disease patients. Transl Res. 2008;152:67–80. https://doi.org/10.1016/j.trsl.2008.06.001.
131. Ranjbar E, Shams J, Sabetkasaei M, M-Shirazi M, Rashidkhani B, Mostafavi A, Bornak E, Nasrollahzadeh J. Effects of zinc supplementation on efficacy of antidepressant therapy, inflammatory cytokines, and brain-derived neurotrophic factor in patients with major depression. Nutr Neurosci. 2014;17:65–71. https://doi.org/10.1179/1476830513Y.0000000066.
132. Kim J, Ahn J. Effect of zinc supplementation on inflammatory markers and adipokines in young obese women. Biol Trace Elem Res. 2014;157:101–6. https://doi.org/10.1007/s12011-013-9885-3.
133. Khorsandi H, Nikpayam O, Yousefi R, Parandoosh M, Hosseinzadeh N, Saidpour A, Ghorbani A. Zinc supplementation improves body weight management, inflammatory biomarkers and insulin resistance in individuals with obesity: a randomized, placebo-controlled, double-blind trial. Diabetol Metab Syndr. 2019;11:101. https://doi.org/10.1186/s13098-019-0497-8.
134. Jamilian M, Foroozanfard F, Bahmani F, Talaee R, Monavari M, Asemi Z. Effects of zinc supplementation on endocrine outcomes in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. Biol Trace Elem Res. 2016;170:271–8. https://doi.org/10.1007/s12011-015-0480-7.
135. Kelishadi R, Hashemipour M, Adeli K, Tavakoli N, Movahedian-Attar A, Shapouri J, Poursafa P, Rouzbahani A. Effect of zinc supplementation on markers of insulin resistance, oxidative stress, and inflammation among prepubescent children with metabolic

syndrome. Metab Syndr Relat Disord. 2010;8:505–10. https://doi.org/10.1089/met.2010.0020.
136. Landete JM. Updated knowledge about polyphenols: functions, bioavailability, metabolism, and health. Crit Rev Food Sci Nutr. 2012;52:936–48. https://doi.org/10.1080/10408398.2010.513779.
137. Chun OK, Chung SJ, Claycombe KJ, Song WO. Serum C-reactive protein concentrations are inversely associated with dietary flavonoid intake in U.S. adults. J Nutr. 2008;138:753–60. https://doi.org/10.1093/jn/138.4.753.
138. Rohrmann S, Shvetsov YB, Morimoto Y, Wilkens LR, Monroe KR, Le Marchand L, Franke AA, Kolonel LN, Maskarinec G. Self-reported dietary flavonoid intake and serum markers of inflammation: the multiethnic cohort. Cancer Causes Control. 2018;29:601–7. https://doi.org/10.1007/s10552-018-1034-z.
139. Filiberto AC, Mumford SL, Pollack AZ, Zhang C, Yeung EH, Perkins NJ, Wactawski-Wende J, Schisterman EF. Habitual dietary isoflavone intake is associated with decreased C-reactive protein concentrations among healthy premenopausal women. J Nutr. 2013;143:900–6. https://doi.org/10.3945/jn.112.173187.
140 Landberg R, Sun Q, Rimm EB, Cassidy A, Scalbert A, Mantzoros CS, Hu FB, van Dam RM. Selected dietary flavonoids are associated with markers of inflammation and endothelial dysfunction in U.S. women. J Nutr. 2011;141:618–25. https://doi.org/10.3945/jn.110.133843.
141. Hsieh CT, Wang J, Chien KL. Association between dietary flavonoid intakes and C-reactive protein levels: a cross-sectional study in Taiwan. J Nutr Sci. 2021;10: e15. https://doi.org/10.1017/jns.2021.8.
142. Zhang H, Xu Z, Zhao H, Wang X, Pang J, Li Q, Yang Y, Ling W. Anthocyanin supplementation improves anti-oxidative and anti-inflammatory capacity in a dose-response manner in subjects with dyslipidemia. Redox Biol. 2020;32: 101474. https://doi.org/10.1016/j.redox.2020.101474.
143. Nikbakht E, Singh I, Vider J, Williams LT, Vugic L, Gaiz A, Kundur AR, Colson N. Potential of anthocyanin as an anti-inflammatory agent: a human clinical trial on type 2 diabetic, diabetic at-risk and healthy adults. Inflamm Res. 2021;70:275–84. https://doi.org/10.1007/s00011-021-01438-1.
144. Guo Y, Zhang P, Liu Y, Zha L, Ling W, Guo H. A dose-response evaluation of purified anthocyanins on inflammatory and oxidative biomarkers and metabolic risk factors in healthy young adults: a randomized controlled trial. Nutrition. 2020;74: 110745. https://doi.org/10.1016/j.nut.2020.110745.
145. Hassellund SS, Flaa A, Kjeldsen SE, Seljeflot I, Karlsen A, Erlund I, Rostrup M. Effects of anthocyanins on cardiovascular risk factors and inflammation in pre-hypertensive men: a double-blind randomized placebo-controlled crossover study. J Hum Hypertens. 2013;27:100–6. https://doi.org/10.1038/jhh.2012.4.
146. Thompson K, Hosking H, Pederick W, Singh I, Santhakumar AB. The effect of anthocyanin supplementation in modulating platelet function in sedentary population: a randomised, double-blind, placebo-controlled, cross-over trial. Br J Nutr. 2017;118:368–74. https://doi.org/10.1017/S0007114517002124.
147. Bazyar H, Hosseini SA, Saradar S, Mombaini D, Allivand M, Labibzadeh M, Alipour M. Effects of epigallocatechin-3-gallate of Camellia sinensis leaves on blood pressure, lipid profile, atherogenic index of plasma and some inflammatory and antioxidant markers in type 2 diabetes mellitus patients: a clinical trial. J Complement Integr Med. 2020;18:405–11. https://doi.org/10.1515/jcim-2020-0090.
148. Mielgo-Ayuso J, Barrenechea L, Alcorta P, Larrarte E, Margareto J, Labayen I. Effects of dietary supplementation with epigallocatechin-3-gallate on weight loss, energy homeostasis, cardiometabolic risk factors and liver function in obese women: randomised, double-blind, placebo-controlled clinical trial. Br J Nutr. 2014;111:1263–71. https://doi.org/10.1017/S0007114513003784.
149. Yari Z, Movahedian M, Imani H, Alavian SM, Hedayati M, Hekmatdoost A. The effect of hesperidin supplementation on metabolic profiles in patients with metabolic syndrome: a randomized, double-blind, placebo-controlled clinical trial. Eur J Nutr. 2020;59:2569–77. https://doi.org/10.1007/s00394-019-02105-2.
150. Haidari F, Heybar H, Jalali MT, Ahmadi Engali K, Helli B, Shirbeigi E. Hesperidin supplementation modulates inflammatory responses following myocardial infarction. J Am Coll Nutr. 2015;34:205–11. https://doi.org/10.1080/07315724.2014.891269.
151. Homayouni F, Haidari F, Hedayati M, Zakerkish M, Ahmadi K. Blood pressure lowering and anti-inflammatory effects of hesperidin in type 2 diabetes; a randomized double-blind controlled clinical trial. Phytother Res. 2018;32:1073–9. https://doi.org/10.1002/ptr.6046.
152. Yari Z, Cheraghpour M, Alavian SM, Hedayati M, Eini-Zinab H, Hekmatdoost A. The efficacy of flaxseed and hesperidin on non-alcoholic fatty liver disease: an open-labeled randomized controlled trial. Eur J Clin Nutr. 2021;75:99–111. https://doi.org/10.1038/s41430-020-0679-3.
153. Cheraghpour M, Imani H, Ommi S, Alavian SM, Karimi-Shahrbabak E, Hedayati M, Yari Z, Hekmatdoost A. Hesperidin improves hepatic steatosis, hepatic enzymes, and metabolic and inflammatory parameters in patients with nonalcoholic fatty liver disease: a randomized, placebo-controlled, double-blind clinical trial. Phytother Res. 2019;33:2118–25. https://doi.org/10.1002/ptr.6406.
154. Dehghani F, Sezavar Seyedi Jandaghi SH, Janani L, Sarebanhassanabadi M, Emamat H, Vafa M. Effects of quercetin supplementation on inflammatory factors and quality of life in post-myocardial infarction patients: a double blind, placebo-controlled, randomized clinical trial. Phytother Res. 2021;35:2085–98. https://doi.org/10.1002/ptr.6955.
155. Askari G, Ghiasvand R, Feizi A, Ghanadian SM, Karimian J. The effect of quercetin supplementation on selected markers of inflammation and oxidative stress. J Res Med Sci. 2012;17:637–41.
156. Dower JI, Geleijnse JM, Gijsbers L, Schalkwijk C, Kromhout D, Hollman PC. Supplementation of the pure flavonoids epicatechin and quercetin affects some biomarkers of endothelial dysfunction and inflammation in (pre)hypertensive adults: a randomized double-blind, placebo-controlled, crossover trial. J Nutr. 2015;145:1459–63. https://doi.org/10.3945/jn.115.211888.
157. Javadi F, Ahmadzadeh A, Eghtesadi S, Aryaeian N, Zabihiyeganeh M, Rahimi Foroushani A, Jazayeri S. The effect of quercetin on inflammatory factors and clinical symptoms in women with rheumatoid arthritis: a double-blind, randomized controlled trial. J Am Coll Nutr. 2017;36:9–15. https://doi.org/10.1080/07315724.2016.1140093.
158. Heinz SA, Henson DA, Nieman DC, Austin MD, Jin F. A 12-week supplementation with quercetin does not affect natural killer cell activity, granulocyte oxidative burst activity or granulocyte phagocytosis in female human subjects. Br J Nutr. 2010;104:849–57. https://doi.org/10.1017/S000711451000156X.
159. Egert S, Wolffram S, Bosy-Westphal A, Boesch-Saadatmandi C, Wagner AE, Frank J, Rimbach G, Mueller MJ. Daily quercetin supplementation dose-dependently increases plasma quercetin concentrations in healthy humans. J Nutr. 2008;138:1615–21. https://doi.org/10.1093/jn/138.9.1615.
160. Javadi F, Eghtesadi S, Ahmadzadeh A, Aryaeian N, Zabihiyeganeh M, Foroushani AR, Jazayeri S. The effect of quercetin on plasma oxidative status, C-reactive protein and blood pressure in women with rheumatoid arthritis. Int J Prev Med. 2014;5:293–301.
161. Brüll V, Burak C, Stoffel-Wagner B, Wolffram S, Nickenig G, Müller C, Langguth P, Alteheld B, Fimmers R, Stehle P, Egert S. No effects of quercetin from onion skin extract on serum leptin

and adiponectin concentrations in overweight-to-obese patients with (pre-)hypertension: a randomized double-blinded, placebo-controlled crossover trial. Eur J Nutr. 2017;56:2265–75. https://doi.org/10.1007/s00394-016-1267-0.
162. Javid AZ, Hormoznejad R, Yousefimanesh HA, Haghighi-Zadeh MH, Zakerkish M. Impact of resveratrol supplementation on inflammatory, antioxidant, and periodontal markers in type 2 diabetic patients with chronic periodontitis. Diabetes Metab Syndr. 2019;13:2769–74. https://doi.org/10.1016/j.dsx.2019.07.042.
163. Faghihzadeh F, Adibi P, Rafiei R, Hekmatdoost A. Resveratrol supplementation improves inflammatory biomarkers in patients with nonalcoholic fatty liver disease. Nutr Res. 2014;34:837–43. https://doi.org/10.1016/j.nutres.2014.09.005.
164. Samsami-Kor M, Daryani NE, Asl PR, Hekmatdoost A. Anti-inflammatory effects of resveratrol in patients with ulcerative colitis: a randomized, double-blind, placebo-controlled pilot study. Arch Med Res. 2015;46:280–5. https://doi.org/10.1016/j.arcmed.2015.05.005.
165. Bo S, Ciccone G, Castiglione A, Gambino R, De Michieli F, Villois P, Durazzo M, Cavallo-Perin P, Cassader M. Anti-inflammatory and antioxidant effects of resveratrol in healthy smokers a randomized, double-blind, placebo-controlled, cross-over trial. Curr Med Chem. 2013;20:1323–31. https://doi.org/10.2174/0929867311320100009.
166. Khodabandehloo H, Seyyedebrahimi S, Esfahani EN, Razi F, Meshkani R. Resveratrol supplementation decreases blood glucose without changing the circulating CD14+CD16+ monocytes and inflammatory cytokines in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. Nutr Res. 2018;54:40–51. https://doi.org/10.1016/j.nutres.2018.03.015.
167. Saldanha JF, Leal VO, Rizzetto F, Grimmer GH, Ribeiro-Alves M, Daleprane JB, Carraro-Eduardo JC, Mafra D. Effects of resveratrol supplementation in Nrf2 and NF-κB expressions in nondialyzed chronic kidney disease patients: a randomized, double-blind, placebo-controlled, crossover clinical trial. J Ren Nutr. 2016;26:401–6. https://doi.org/10.1053/j.jrn.2016.06.005.
168. Ley SH, Sun Q, Willett WC, Eliassen AH, Wu K, Pan A, Grodstein F, Hu FB. Associations between red meat intake and biomarkers of inflammation and glucose metabolism in women. Am J Clin Nutr. 2014;99:352–60. https://doi.org/10.3945/ajcn.113.075663.
169. Chai W, Morimoto Y, Cooney RV, Franke AA, Shvetsov YB, Le Marchand L, Haiman CA, Kolonel LN, Goodman MT, Maskarinec G. Dietary red and processed meat intake and markers of adiposity and inflammation: the multiethnic cohort study. J Am Coll Nutr. 2017;36:378–85. https://doi.org/10.1080/07315724.2017.1318317.
170. Papier K, Hartman L, Tong TYN, Key TJ, Knuppel A. Higher meat intake is associated with higher inflammatory markers, mostly due to adiposity: results from UK Biobank. J Nutr. 2021:nxab314. https://doi.org/10.1093/jn/nxab314.
171. Mazidi M, Kengne AP, George ES, Siervo M. The association of red meat intake with inflammation and circulating intermediate biomarkers of type 2 diabetes is mediated by central adiposity. Br J Nutr. 2021;125:1043–50. https://doi.org/10.1017/S0007114519002149.
172. Gadotti TN, Norde MM, Rogero MM, Fisberg M, Fisberg RM, Oki E, Martini LA. Dairy consumption and inflammatory profile: a cross-sectional population-based study, São Paulo, Brazil. Nutrition. 2018;48:1–5. https://doi.org/10.1016/j.nut.2017.10.003.
173. Abreu S, Agostinis-Sobrinho C, Santos R, Moreira C, Lopes L, Gonçalves C, Oliveira-Santos J, Sousa-Sá E, Rodrigues B, Mota J, Rosário R. Association of dairy product consumption with metabolic and inflammatory biomarkers in adolescents: a cross-sectional analysis from the LabMed study. Nutrients. 2019;11:2268. https://doi.org/10.3390/nu11102268.
174. Panagiotakos DB, Pitsavos CH, Zampelas AD, Chrysohoou CA, Stefanadis CI. Dairy products consumption is associated with decreased levels of inflammatory markers related to cardiovascular disease in apparently healthy adults: the ATTICA study. J Am Coll Nutr. 2010;29:357–64. https://doi.org/10.1080/07315724.2010.10719852.
175. Zampelas A, Panagiotakos DB, Pitsavos C, Das UN, Chrysohoou C, Skoumas Y, Stefanadis C. Fish consumption among healthy adults is associated with decreased levels of inflammatory markers related to cardiovascular disease: the ATTICA study. J Am Coll Cardiol. 2005;46:120–4. https://doi.org/10.1016/j.jacc.2005.03.048.
176. van Bussel BC, Henry RM, Schalkwijk CG, Ferreira I, Feskens EJ, Streppel MT, Smulders YM, Twisk JW, Stehouwer CD. Fish consumption in healthy adults is associated with decreased circulating biomarkers of endothelial dysfunction and inflammation during a 6-year follow-up. J Nutr. 2011;141:1719–25. https://doi.org/10.3945/jn.111.139733.
177. Tani S, Kawauchi K, Atsumi W, Matsuo R, Ashida T, Imatake K, Suzuki Y, Yagi T, Takahashi A, Matsumoto N, Okumura Y. Association among daily fish intake, white blood cell count, and healthy lifestyle behaviors in an apparently healthy Japanese population: implication for the anti-atherosclerotic effect of fish consumption. Heart Vessels. 2021;36:924–33. https://doi.org/10.1007/s00380-020-01769-9.
178. Tani S, Matsuo R, Atsumi W, Kawauchi K, Ashida T, Yagi T, Imatake K, Suzuki Y, Takahashi A, Matsumoto N, Okumura Y. Higher frequency of fish intake may be associated with a lower neutrophil/lymphocyte ratio: anti-atherosclerotic effects of fish consumption. Ann Nutr Metab. 2021;77:146–53. https://doi.org/10.1159/000515915.
179. Acosta-Estrada BA, Reyes A, Rosell CM, Rodrigo D, Ibarra-Herrera CC. Benefits and challenges in the incorporation of insects in food products. Front Nutr. 2021;8: 687712. https://doi.org/10.3389/fnut.2021.687712.
180. Stull VJ, Finer E, Bergmans RS, Febvre HP, Longhurst C, Manter DK, Patz JA, Weir TL. Impact of edible cricket consumption on gut microbiota in healthy adults, a double-blind, randomized crossover trial. Sci Rep. 2018;8:10762. https://doi.org/10.1038/s41598-018-29032-2.
181. Khatibi N, Shahvazi S, Nadjarzadeh A, Samadi M, Zare F, Salehi-Abargouei A. Empirically derived dietary patterns and serum inflammatory markers in Iranian female teachers: a cross-sectional study. Nutr Diet. 2019;76:462–71. https://doi.org/10.1111/1747-0080.12463.
182. Jiang Y, Wu SH, Shu XO, Xiang YB, Ji BT, Milne GL, Cai Q, Zhang X, Gao YT, Zheng W, Yang G. Cruciferous vegetable intake is inversely correlated with circulating levels of proinflammatory markers in women. J Acad Nutr Diet. 2014;114:700-8.e2. https://doi.org/10.1016/j.jand.2013.12.019.
183. Navarro SL, Schwarz Y, Song X, Wang CY, Chen C, Trudo SP, Kristal AR, Kratz M, Eaton DL, Lampe JW. Cruciferous vegetables have variable effects on biomarkers of systemic inflammation in a randomized controlled trial in healthy young adults. J Nutr. 2014;144:1850–7. https://doi.org/10.3945/jn.114.197434.
184. Jiang R, Jacobs DR Jr, Mayer-Davis E, Szklo M, Herrington D, Jenny NS, Kronmal R, Barr RG. Nut and seed consumption and inflammatory markers in the multi-ethnic study of atherosclerosis. Am J Epidemiol. 2006;163:222–31. https://doi.org/10.1093/aje/kwj033.
185. Yu Z, Malik VS, Keum N, Hu FB, Giovannucci EL, Stampfer MJ, Willett WC, Fuchs CS, Bao Y. Associations between nut consumption and inflammatory biomarkers. Am J Clin Nutr. 2016;104:722–8. https://doi.org/10.3945/ajcn.116.134205.
186. Ren GY, Chen CY, Chen GC, Chen WG, Pan A, Pan CW, Zhang YH, Qin LQ, Chen LH. Effect of flaxseed intervention on inflammatory marker C-reactive protein: a systematic review and meta-analysis of randomized controlled trials. Nutrients. 2016;8:136. https://doi.org/10.3390/nu8030136.

187 Moreira Alves RD, Boroni Moreira AP, Macedo VS, Bressan J, de Cássia Gonçalves Alfenas R, Mattes R, Brunoro Costa NM. High-oleic peanuts: new perspective to attenuate glucose homeostasis disruption and inflammation related obesity. Obesity (Silver Spring). 2014;22:1981–8. https://doi.org/10.1002/oby.20825.

188. Liu JF, Liu YH, Chen CM, Chang WH, Chen CY. The effect of almonds on inflammation and oxidative stress in Chinese patients with type 2 diabetes mellitus: a randomized crossover controlled feeding trial. Eur J Nutr. 2013;52:927–35. https://doi.org/10.1007/s00394-012-0400-y.

189. Rajaram S, Connell KM, Sabaté J. Effect of almond-enriched high-monounsaturated fat diet on selected markers of inflammation: a randomised, controlled, crossover study. Br J Nutr. 2010;103:907–12. https://doi.org/10.1017/S0007114509992480.

190. Madan J, Desai S, Moitra P, Salis S, Agashe S, Battalwar R, Mehta A, Kamble R, Kalita S, Phatak AG, Udipi SA, Vaidya RA, Vaidya AB. Effect of almond consumption on metabolic risk factors-glucose metabolism, hyperinsulinemia, selected markers of inflammation: a randomized controlled trial in adolescents and young adults. Front Nutr. 2021;8: 668622. https://doi.org/10.3389/fnut.2021.668622.

191. Fitó M, Cladellas M, de la Torre R, Martí J, Muñoz D, Schröder H, Alcántara M, Pujadas-Bastardes M, Marrugat J, López-Sabater MC, Bruguera J, Covas MI, SOLOS Investigators. Anti-inflammatory effect of virgin olive oil in stable coronary disease patients: a randomized, crossover, controlled trial. Eur J Clin Nutr. 2008;62:570–4. https://doi.org/10.1038/sj.ejcn.1602724.

192. Bogani P, Galli C, Villa M, Visioli F. Postprandial anti-inflammatory and antioxidant effects of extra virgin olive oil. Atherosclerosis. 2007;190:181–6. https://doi.org/10.1016/j.atherosclerosis.2006.01.011.

193. Qi L, van Dam RM, Liu S, Franz M, Mantzoros C, Hu FB. Whole-grain, bran, and cereal fiber intakes and markers of systemic inflammation in diabetic women. Diabetes Care. 2006;29:207–11. https://doi.org/10.2337/diacare.29.02.06.dc05-1903.

194. Vitaglione P, Mennella I, Ferracane R, Rivellese AA, Giacco R, Ercolini D, Gibbons SM, La Storia A, Gilbert JA, Jonnalagadda S, Thielecke F, Gallo MA, Scalfi L, Fogliano V. Whole-grain wheat consumption reduces inflammation in a randomized controlled trial on overweight and obese subjects with unhealthy dietary and lifestyle behaviors: role of polyphenols bound to cereal dietary fiber. Am J Clin Nutr. 2015;101:251–61. https://doi.org/10.3945/ajcn.114.088120.

195. Hoevenaars FPM, Esser D, Schutte S, Priebe MG, Vonk RJ, van den Brink WJ, van der Kamp JW, Stroeve JHM, Afman LA, Wopereis S. Whole grain wheat consumption affects postprandial inflammatory response in a randomized controlled trial in overweight and obese adults with mild hypercholesterolemia in the Graandioos Study. J Nutr. 2019;149:2133–44. https://doi.org/10.1093/jn/nxz177.

196. Wu SH, Shu XO, Chow WH, Xiang YB, Zhang X, Li HL, Cai Q, Ji BT, Cai H, Rothman N, Gao YT, Zheng W, Yang G. Soy food intake and circulating levels of inflammatory markers in Chinese women. J Acad Nutr Diet. 2012;112(996–1004):1004.e1-4. https://doi.org/10.1016/j.jand.2012.04.001.

197. Saraf-Bank S, Esmaillzadeh A, Faghihimani E, Azadbakht L. Effect of non-soy legume consumption on inflammation and serum adiponectin levels among first-degree relatives of patients with diabetes: a randomized, crossover study. Nutrition. 2015;31:459–65. https://doi.org/10.1016/j.nut.2014.09.015.

198. Hermsdorff HH, Zulet MÁ, Abete I, Martínez JA. A legume-based hypocaloric diet reduces proinflammatory status and improves metabolic features in overweight/obese subjects. Eur J Nutr. 2011;50:61–9. https://doi.org/10.1007/s00394-010-0115-x.

199. Noronha NY, Pinhel MAS, Nicoletti CF, Quinhoneiro DCG, Pinhanelli VC, Oliveira BAP, Cortes-Oliveira C, Delfino HBP, Wolf LS, Frantz FG, Marchini JS, Nonino CB. Green tea supplementation improves oxidative stress biomarkers and modulates IL-6 circulating levels in obese women. Nutr Hosp. 2019;36:583–8. https://doi.org/10.20960/nh.2159.

200. Bogdanski P, Suliburska J, Szulinska M, Stepien M, Pupek-Musialik D, Jablecka A. Green tea extract reduces blood pressure, inflammatory biomarkers, and oxidative stress and improves parameters associated with insulin resistance in obese, hypertensive patients. Nutr Res. 2012;32:421–7. https://doi.org/10.1016/j.nutres.2012.05.007.

201. Kempf K, Herder C, Erlund I, Kolb H, Martin S, Carstensen M, Koenig W, Sundvall J, Bidel S, Kuha S, Tuomilehto J. Effects of coffee consumption on subclinical inflammation and other risk factors for type 2 diabetes: a clinical trial. Am J Clin Nutr. 2010;91:950–7. https://doi.org/10.3945/ajcn.2009.28548.

202. Lopez-Garcia E, van Dam RM, Qi L, Hu FB. Coffee consumption and markers of inflammation and endothelial dysfunction in healthy and diabetic women. Am J Clin Nutr. 2006;84:888–93. https://doi.org/10.1093/ajcn/84.4.888.

203. Loftfield E, Shiels MS, Graubard BI, Katki HA, Chaturvedi AK, Trabert B, Pinto LA, Kemp TJ, Shebl FM, Mayne ST, Wentzensen N, Purdue MP, Hildesheim A, Sinha R, Freedman ND. Associations of coffee drinking with systemic immune and inflammatory markers. Cancer Epidemiol Biomarkers Prev. 2015;24:1052–60. https://doi.org/10.1158/1055-9965.EPI-15-0038-T.

204. Zampelas A, Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C. Associations between coffee consumption and inflammatory markers in healthy persons: the ATTICA study. Am J Clin Nutr. 2004;80:862–7. https://doi.org/10.1093/ajcn/80.4.862.

205. di Giuseppe R, Di Castelnuovo A, Centritto F, Zito F, De Curtis A, Costanzo S, Vohnout B, Sieri S, Krogh V, Donati MB, de Gaetano G, Iacoviello L. Regular consumption of dark chocolate is associated with low serum concentrations of C-reactive protein in a healthy Italian population. J Nutr. 2008;138:1939–45. https://doi.org/10.1093/jn/138.10.1939.

206. Jafarirad S, Ayoobi N, Karandish M, Jalali MT, Haghighizadeh MH, Jahanshahi A. Dark chocolate effect on serum adiponectin, biochemical and inflammatory parameters in diabetic patients: a randomized clinical trial. Int J Prev Med. 2018;9:86. https://doi.org/10.4103/ijpvm.IJPVM_339_17.

207. Kuebler U, Arpagaus A, Meister RE, von Känel R, Huber S, Ehlert U, Wirtz PH. Dark chocolate attenuates intracellular pro-inflammatory reactivity to acute psychosocial stress in men: a randomized controlled trial. Brain Behav Immun. 2016;57:200–8. https://doi.org/10.1016/j.bbi.2016.04.006.

208. Hamed MS, Gambert S, Bliden KP, Bailon O, Singla A, Antonino MJ, Hamed F, Tantry US, Gurbel PA. Dark chocolate effect on platelet activity, C-reactive protein and lipid profile: a pilot study. South Med J. 2008;101:1203–8. https://doi.org/10.1097/SMJ.0b013e31818859eb.

209. Kunnumakkara AB, Sailo BL, Banik K, Harsha C, Prasad S, Gupta SC, Bharti AC, Aggarwal BB. Chronic diseases, inflammation, and spices: how are they linked? J Transl Med. 2018;16:14. https://doi.org/10.1186/s12967-018-1381-2.

210. Jiang TA. Health benefits of culinary herbs and spices. J AOAC Int. 2019;102:395–411. https://doi.org/10.5740/jaoacint.18-0418.

211. Hadi V, Kheirouri S, Alizadeh M, Khabbazi A, Hosseini H. Effects of Nigella sativa oil extract on inflammatory cytokine response and oxidative stress status in patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled clinical trial. Avicenna J Phytomed. 2016;6:34–43.

212. Amizadeh S, Rashtchizadeh N, Khabbazi A, Ghorbanihaghjo A, Ebrahimi AA, Vatankhah AM, Malek Mahdavi A, Taghizadeh M. Effect of Nigella sativa oil extracts on inflammatory and oxidative stress markers in Behcet's disease: a randomized,

double-blind, placebo-controlled clinical trial. Avicenna J Phytomed. 2020;10:181–9.
213. Mahdavi R, Namazi N, Alizadeh M, Farajnia S. Nigella sativa oil with a calorie-restricted diet can improve biomarkers of systemic inflammation in obese women: a randomized double-blind, placebo-controlled clinical trial. J Clin Lipidol. 2016;10:1203–11. https://doi.org/10.1016/j.jacl.2015.11.019.
214. Kazemi S, Yaghooblou F, Siassi F, Rahimi Foroushani A, Ghavipour M, Koohdani F, Sotoudeh G. Cardamom supplementation improves inflammatory and oxidative stress biomarkers in hyperlipidemic, overweight, and obese pre-diabetic women: a randomized double-blind clinical trial. J Sci Food Agric. 2017;97:5296–301. https://doi.org/10.1002/jsfa.8414.
215. Davari M, Hashemi R, Mirmiran P, Hedayati M, Sahranavard S, Bahreini S, Tavakoly R, Talaei B. Effects of cinnamon supplementation on expression of systemic inflammation factors, NF-kB and Sirtuin-1 (SIRT1) in type 2 diabetes: a randomized, double blind, and controlled clinical trial. Nutr J. 2020;19:1. https://doi.org/10.1186/s12937-019-0518-3.
216. Azimi P, Ghiasvand R, Feizi A, Hariri M, Abbasi B. Effects of cinnamon, cardamom, saffron, and ginger consumption on markers of glycemic control, lipid profile, oxidative stress, and inflammation in type 2 diabetes patients. Rev Diabet Stud. 2014;11:258–66. https://doi.org/10.1900/RDS.2014.11.258.
217. Mashhadi NS, Ghiasvand R, Askari G, Feizi A, Hariri M, Darvishi L, Barani A, Taghiyar M, Shiranian A, Hajishafiee M. Influence of ginger and cinnamon intake on inflammation and muscle soreness endued by exercise in Iranian female athletes. Int J Prev Med. 2013;4:S11–5.
218. Askari F, Rashidkhani B, Hekmatdoost A. Cinnamon may have therapeutic benefits on lipid profile, liver enzymes, insulin resistance, and high-sensitivity C-reactive protein in nonalcoholic fatty liver disease patients. Nutr Res. 2014;34:143–8. https://doi.org/10.1016/j.nutres.2013.11.005.
219. Shishehbor F, Rezaeyan Safar M, Rajaei E, Haghighizadeh MH. Cinnamon consumption improves clinical symptoms and inflammatory markers in women with rheumatoid arthritis. J Am Coll Nutr. 2018:1–6. https://doi.org/10.1080/07315724.2018.1460733.
220. Zareie A, Sahebkar A, Khorvash F, Bagherniya M, Hasanzadeh A, Askari G. Effect of cinnamon on migraine attacks and inflammatory markers: a randomized double-blind placebo-controlled trial. Phytother Res. 2020;34:2945–52. https://doi.org/10.1002/ptr.6721.
221. Mammen RR, Natinga Mulakal J, Mohanan R, Maliakel B, Illathu MK. Clove bud polyphenols alleviate alterations in inflammation and oxidative stress markers associated with binge drinking: a randomized double-blinded placebo-controlled crossover study. J Med Food. 2018;21:1188–96. https://doi.org/10.1089/jmf.2017.4177.
222. Morovati A, Pourghassem Gargari B, Sarbakhsh P, Azari H, Lotfi-Dizaji L. The effect of cumin supplementation on metabolic profiles in patients with metabolic syndrome: a randomized, triple blind, placebo-controlled clinical trial. Phytother Res. 2019;33:1182–90. https://doi.org/10.1002/ptr.6313.
223. Xu C, Mathews AE, Rodrigues C, Eudy BJ, Rowe CA, O'Donoughue A, Percival SS. Aged garlic extract supplementation modifies inflammation and immunity of adults with obesity: a randomized, double-blind, placebo-controlled clinical trial. Clin Nutr ESPEN. 2018;24:148–55. https://doi.org/10.1016/j.clnesp.2017.11.010.
224. Zare E, Alirezaei A, Bakhtiyari M, Mansouri A. Evaluating the effect of garlic extract on serum inflammatory markers of peritoneal dialysis patients: a randomized double-blind clinical trial study. BMC Nephrol. 2019;20:26. https://doi.org/10.1186/s12882-019-1204-6.
225. van Doorn MB, Espirito Santo SM, Meijer P, Kamerling IM, Schoemaker RC, Dirsch V, Vollmar A, Haffner T, Gebhardt R, Cohen AF, Princen HM, Burggraaf J. Effect of garlic powder on C-reactive protein and plasma lipids in overweight and smoking subjects. Am J Clin Nutr. 2006;84:1324–9. https://doi.org/10.1093/ajcn/84.6.1324.
226. Asgharpour M, Khavandegar A, Balaei P, Enayati N, Mardi P, Alirezaei A, Bakhtiyari M. Efficacy of oral administration of Allium sativum powder "garlic extract" on lipid profile, inflammation, and cardiovascular indices among hemodialysis patients. Evid Based Complement Alternat Med. 2021;2021:6667453. https://doi.org/10.1155/2021/6667453.
227. Soleimani D, Parisa Moosavian S, Zolfaghari H, Paknahad Z. Effect of garlic powder supplementation on blood pressure and hs-C-reactive protein among nonalcoholic fatty liver disease patients: a randomized, double-blind, placebo-controlled trial. Food Sci Nutr. 2021;9:3556–62. https://doi.org/10.1002/fsn3.2307.
228. Mahluji S, Ostadrahimi A, Mobasseri M, Ebrahimzade Attari V, Payahoo L. Anti-inflammatory effects of zingiber officinale in type 2 diabetic patients. Adv Pharm Bull. 2013;3:273–6. https://doi.org/10.5681/apb.2013.044.
229. Zare Javid A, Bazyar H, Gholinezhad H, Rahimlou M, Rashidi H, Salehi P, Haghighi-Zadeh MH. The effects of ginger supplementation on inflammatory, antioxidant, and periodontal parameters in type 2 diabetes mellitus patients with chronic periodontitis under non-surgical periodontal therapy. A double-blind, placebo-controlled trial. Diabetes Metab Syndr Obes. 2019;12:1751–61. https://doi.org/10.2147/DMSO.S214333.
230. Daneshi-Maskooni M, Keshavarz SA, Qorbani M, Mansouri S, Alavian SM, Badri-Fariman M, Jazayeri-Tehrani SA, Sotoudeh G. Green cardamom increases Sirtuin-1 and reduces inflammation in overweight or obese patients with non-alcoholic fatty liver disease: a double-blind randomized placebo-controlled clinical trial. Nutr Metab (Lond). 2018;15:63. https://doi.org/10.1186/s12986-018-0297-4.
231. Cheshmeh S, Ghayyem M, Khamooshi F, Heidarzadeh-Esfahani N, Rahmani N, Hojati N, Mosaieby E, Moradi S, Pasdar Y. Green cardamom plus low-calorie diet can decrease the expression of inflammatory genes among obese women with polycystic ovary syndrome: a double-blind randomized clinical trial. Eat Weight Disord. 2021:1–10. https://doi.org/10.1007/s40519-021-01223-3.
232. Jafari S, Sattari R, Ghavamzadeh S. Evaluation the effect of 50 and 100 mg doses of Cuminum cyminum essential oil on glycemic indices, insulin resistance and serum inflammatory factors on patients with diabetes type II: a double-blind randomized placebo-controlled clinical trial. J Tradit Complement Med. 2016;7:332–8. https://doi.org/10.1016/j.jtcme.2016.08.004.
233. Heidari-Beni M, Moravejolahkami AR, Gorgian P, Askari G, Tarrahi MJ, Bahreini-Esfahani N. Herbal formulation "turmeric extract, black pepper, and ginger" versus Naproxen for chronic knee osteoarthritis: a randomized, double-blind, controlled clinical trial. Phytother Res. 2020;34:2067–73. https://doi.org/10.1002/ptr.6671.
234. Kim KA, Yim JE. The effect of onion peel extract on inflammatory mediators in korean overweight and obese women. Clin Nutr Res. 2016;5:261–9. https://doi.org/10.7762/cnr.2016.5.4.261.
235. Panahi Y, Sahebkar A, Parvin S, Saadat A. A randomized controlled trial on the anti-inflammatory effects of curcumin in patients with chronic sulphur mustard-induced cutaneous complications. Ann Clin Biochem. 2012;49:580–8. https://doi.org/10.1258/acb.2012.012040.
236. Jarhahzadeh M, Alavinejad P, Farsi F, Husain D, Rezazadeh A. The effect of turmeric on lipid profile, malondialdehyde, liver echogenicity and enzymes among patients with nonalcoholic fatty liver disease: a randomized double blind clinical trial.

Diabetol Metab Syndr. 2021;13:112. https://doi.org/10.1186/s13098-021-00731-7.
237. Salehi M, Mashhadi NS, Esfahani PS, Feizi A, Hadi A, Askari G. The effects of curcumin supplementation on muscle damage, oxidative stress, and inflammatory markers in healthy females with moderate physical activity: a randomized, double-blind, placebo-controlled clinical trial. Int J Prev Med. 2021;12:94. https://doi.org/10.4103/ijpvm.IJPVM_138_20.
238. Saraf-Bank S, Ahmadi A, Paknahad Z, Maracy M, Nourian M. Effects of curcumin supplementation on markers of inflammation and oxidative stress among healthy overweight and obese girl adolescents: a randomized placebo-controlled clinical trial. Phytother Res. 2019;33:2015–22. https://doi.org/10.1002/ptr.6370.
239. Saadati S, Sadeghi A, Mansour A, Yari Z, Poustchi H, Hedayati M, Hatami B, Hekmatdoost A. Curcumin and inflammation in non-alcoholic fatty liver disease: a randomized, placebo controlled clinical trial. BMC Gastroenterol. 2019;19:133. https://doi.org/10.1186/s12876-019-1055-4.
240. Saier MH Jr, Mansour NM. Probiotics and prebiotics in human health. J Mol Microbiol Biotechnol. 2005;10:22–5. https://doi.org/10.1159/000090345.
241. Tabrizi R, Ostadmohammadi V, Lankarani KB, Akbari M, Akbari H, Vakili S, Shokrpour M, Kolahdooz F, Rouhi V, Asemi Z. The effects of probiotic and synbiotic supplementation on inflammatory markers among patients with diabetes: a systematic review and meta-analysis of randomized controlled trials. Eur J Pharmacol. 2019;852:254–64. https://doi.org/10.1016/j.ejphar.2019.04.003.
242. Zhang XF, Guan XX, Tang YJ, Sun JF, Wang XK, Wang WD, Fan JM. Clinical effects and gut microbiota changes of using probiotics, prebiotics or synbiotics in inflammatory bowel disease: a systematic review and meta-analysis. Eur J Nutr. 2021;60:2855–75. https://doi.org/10.1007/s00394-021-02503-5.
243. Vinolo MA, Rodrigues HG, Hatanaka E, Sato FT, Sampaio SC, Curi R. Suppressive effect of short-chain fatty acids on production of proinflammatory mediators by neutrophils. J Nutr Biochem. 2011;22:849–55. https://doi.org/10.1016/j.jnutbio.2010.07.009.
244. Compare D, Rocco A, Coccoli P, Angrisani D, Sgamato C, Iovine B, Salvatore U, Nardone G. Lactobacillus casei DG and its postbiotic reduce the inflammatory mucosal response: an ex-vivo organ culture model of post-infectious irritable bowel syndrome. BMC Gastroenterol. 2017;17:53. https://doi.org/10.1186/s12876-017-0605-x.
245. Eichelmann F, Schwingshackl L, Fedirko V, Aleksandrova K. Effect of plant-based diets on obesity-related inflammatory profiles: a systematic review and meta-analysis of intervention trials. Obes Rev. 2016;17:1067–79. https://doi.org/10.1111/obr.12439.
246. Jaceldo-Siegl K, Haddad E, Knutsen S, Fan J, Lloren J, Bellinger D, Fraser GE. Lower C-reactive protein and IL-6 associated with vegetarian diets are mediated by BMI. Nutr Metab Cardiovasc Dis. 2018;28:787–94. https://doi.org/10.1016/j.numecd.2018.03.003.
247. Craddock JC, Neale EP, Peoples GE, Probst YC. Vegetarian-based dietary patterns and their relation with inflammatory and immune biomarkers: a systematic review and meta-analysis. Adv Nutr. 2019;10:433–51. https://doi.org/10.1093/advances/nmy103.
248. Lankinen M, Uusitupa M, Schwab U. Nordic diet and inflammation-a review of observational and intervention studies. Nutrients. 2019;11:1369. https://doi.org/10.3390/nu11061369.
249. Ulven SM, Holven KB, Rundblad A, Myhrstad MCW, Leder L, Dahlman I, Mello VD, Schwab U, Carlberg C, Pihlajamäki J, Hermansen K, Dragsted LO, Gunnarsdottir I, Cloetens L, Åkesson B, Rosqvist F, Hukkanen J, Herzig KH, Savolainen MJ, Risérus U, Thorsdottir I, Poutanen KS, Arner P, Uusitupa M, Kolehmainen M. An isocaloric nordic diet modulates RELA and TNFRSF1A gene expression in peripheral blood mononuclear cells in individuals with metabolic syndrome-a SYSDIET sub-study. Nutrients. 2019;11:2932. https://doi.org/10.3390/nu11122932.
250. Calvo-Malvar Mdel M, Leis R, Benítez-Estévez AJ, Sánchez-Castro J, Gude F. A randomised, family-focused dietary intervention to evaluate the Atlantic diet: the GALIAT study protocol. BMC Public Health. 2016;16:820. https://doi.org/10.1186/s12889-016-3441-y.
251. Guallar-Castillón P, Oliveira A, Lopes C, López-García E, Rodríguez-Artalejo F. The Southern European Atlantic Diet is associated with lower concentrations of markers of coronary risk. Atherosclerosis. 2013;226:502–9. https://doi.org/10.1016/j.atherosclerosis.2012.11.035.
252. Konishi K. Associations between healthy Japanese dietary patterns and depression in Japanese women. Public Health Nutr. 2021;24:1753–65. https://doi.org/10.1017/S1368980020001548.
253. Pan MH, Chiou YS, Tsai ML, Ho CT. Anti-inflammatory activity of traditional Chinese medicinal herbs. J Tradit Complement Med. 2011;1:8–24. https://doi.org/10.1016/s2225-4110(16)30052-9.
254. Santiago-Torres M, Tinker LF, Allison MA, Breymeyer KL, Garcia L, Kroenke CH, Lampe JW, Shikany JM, Van Horn L, Neuhouser ML. Development and use of a traditional Mexican diet score in relation to systemic inflammation and insulin resistance among women of Mexican descent. J Nutr. 2015;145:2732–40. https://doi.org/10.3945/jn.115.213538.
255. Valerino-Perea S, Lara-Castor L, Armstrong MEG, Papadaki A. Definition of the traditional Mexican diet and its role in health: a systematic review. Nutrients. 2019;11:2803. https://doi.org/10.3390/nu11112803.
256. Whalen KA, McCullough ML, Flanders WD, Hartman TJ, Judd S, Bostick RM. Paleolithic and Mediterranean diet pattern scores are inversely associated with biomarkers of inflammation and oxidative balance in adults. J Nutr. 2016;146:1217–26. https://doi.org/10.3945/jn.115.224048.
257. Saneei P, Hashemipour M, Kelishadi R, Esmaillzadeh A. The Dietary Approaches to Stop Hypertension (DASH) diet affects inflammation in childhood metabolic syndrome: a randomized cross-over clinical trial. Ann Nutr Metab. 2014;64:20–7. https://doi.org/10.1159/000358341.
258. Sakhaei R, Shahvazi S, Mozaffari-Khosravi H, Samadi M, Khatibi N, Nadjarzadeh A, Zare F, Salehi-Abargouei A. The Dietary Approaches to Stop Hypertension (DASH)-style diet and an alternative mediterranean diet are differently associated with serum inflammatory markers in female adults. Food Nutr Bull. 2018;39:361–76. https://doi.org/10.1177/0379572118783950.
259. Juraschek SP, Kovell LC, Appel LJ, Miller ER 3rd, Sacks FM, Chang AR, Christenson RH, Rebuck H, Mukamal KJ. Effects of diet and sodium reduction on cardiac injury, strain, and inflammation: the DASH-Sodium trial. J Am Coll Cardiol. 2021;77:2625–34. https://doi.org/10.1016/j.jacc.2021.03.320.
260. Urpi-Sarda M, Casas R, Chiva-Blanch G, Romero-Mamani ES, Valderas-Martínez P, Arranz S, Andres-Lacueva C, Llorach R, Medina-Remón A, Lamuela-Raventos RM, Estruch R. Virgin olive oil and nuts as key foods of the Mediterranean diet effects on inflammatory biomakers related to atherosclerosis. Pharmacol Res. 2012;65:577–83. https://doi.org/10.1016/j.phrs.2012.03.006.
261. Estruch R. Anti-inflammatory effects of the Mediterranean diet: the experience of the PREDIMED study. Proc Nutr Soc. 2010;69:333–40. https://doi.org/10.1017/S0029665110001539.
262. Urpi-Sarda M, Casas R, Chiva-Blanch G, Romero-Mamani ES, Valderas-Martínez P, Salas-Salvadó J, Covas MI, Toledo E, Andres-Lacueva C, Llorach R, García-Arellano A, Bulló M, Ruiz-Gutierrez V, Lamuela-Raventos RM, Estruch R. The Mediterranean diet pattern and its main components are associated with lower plasma concentrations of tumor necrosis factor receptor 60 in patients at high risk for cardiovascular disease. J Nutr. 2012;142:1019–25. https://doi.org/10.3945/jn.111.148726.

263. Urpi-Sarda M, Casas R, Sacanella E, Corella D, Andrés-Lacueva C, Llorach R, Garrabou G, Cardellach F, Sala-Vila A, Ros E, Ruiz-Canela M, Fitó M, Salas-Salvadó J, Estruch R. The 3-year effect of the mediterranean diet intervention on inflammatory biomarkers related to cardiovascular disease. Biomedicines. 2021;9:862. https://doi.org/10.3390/biomedicines9080862.
264. Christ A, Lauterbach M, Latz E. Western diet and the immune system: an inflammatory connection. Immunity. 2019;51:794–811. https://doi.org/10.1016/j.immuni.2019.09.020.
265. Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, Hu FB. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr. 2004;80:1029–35. https://doi.org/10.1093/ajcn/80.4.1029.
266. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns and markers of systemic inflammation among Iranian women. J Nutr. 2007;137:992–8. https://doi.org/10.1093/jn/137.4.992.
267 Lopes AEDSC, Araújo LF, Levy RB, Barreto SM, Giatti L. Association between consumption of ultra-processed foods and serum C-reactive protein levels: cross-sectional results from the ELSA-Brasil study. Sao Paulo Med J. 2019;137:169–76. https://doi.org/10.1590/1516-3180.2018.0363070219.
268. Martins GMDS, França AKTDC, Viola PCAF, Carvalho CA, Marques KDS, Santos AMD, Batalha MA, Alves JDA, Ribeiro CCC. Intake of ultra-processed foods is associated with inflammatory markers in Brazilian adolescents. Public Health Nutr. 2021:1–9. https://doi.org/10.1017/S1368980021004523.
269. Bärebring L, Winkvist A, Gjertsson I, Lindqvist HM. Poor dietary quality is associated with increased inflammation in Swedish patients with rheumatoid arthritis. Nutrients. 2018;10:1535. https://doi.org/10.3390/nu10101535.
270. Chaix A, Manoogian ENC, Melkani GC, Panda S. Time-restricted eating to prevent and manage chronic metabolic diseases. Annu Rev Nutr. 2019;39:291–315. https://doi.org/10.1146/annurev-nutr-082018-124320.
271. Zhu S, Cui L, Zhang X, Shu R, VanEvery H, Tucker KL, Wu S, Gao X. Habitually skipping breakfast is associated with chronic inflammation: a cross-sectional study. Public Health Nutr. 2021;24:2936–43. https://doi.org/10.1017/S1368980020001214.
272. Nas A, Mirza N, Hägele F, Kahlhöfer J, Keller J, Rising R, Kufer TA, Bosy-Westphal A. Impact of breakfast skipping compared with dinner skipping on regulation of energy balance and metabolic risk. Am J Clin Nutr. 2017;105:1351–61. https://doi.org/10.3945/ajcn.116.151332.
273. Zouhal H, Bagheri R, Ashtary-Larky D, Wong A, Triki R, Hackney AC, Laher I, Abderrahman AB. Effects of Ramadan intermittent fasting on inflammatory and biochemical biomarkers in males with obesity. Physiol Behav. 2020;225: 113090. https://doi.org/10.1016/j.physbeh.2020.113090.
274. Liu B, Hutchison AT, Thompson CH, Lange K, Heilbronn LK. Markers of adipose tissue inflammation are transiently elevated during intermittent fasting in women who are overweight or obese. Obes Res Clin Pract. 2019;13:408–15. https://doi.org/10.1016/j.orcp.2019.07.001.
275. Rothschild J, Hoddy KK, Jambazian P, Varady KA. Time-restricted feeding and risk of metabolic disease: a review of human and animal studies. Nutr Rev. 2014;72:308–18. https://doi.org/10.1111/nure.12104.
276. Moro T, Tinsley G, Longo G, Grigoletto D, Bianco A, Ferraris C, Guglielmetti M, Veneto A, Tagliabue A, Marcolin G, Paoli A. Time-restricted eating effects on performance, immune function, and body composition in elite cyclists: a randomized controlled trial. J Int Soc Sports Nutr. 2020;17:65. https://doi.org/10.1186/s12970-020-00396-z.
277. Razavi R, Parvaresh A, Abbasi B, Yaghoobloo K, Hassanzadeh A, Mohammadifard N, Clark CCT, Morteza SS. The alternate-day fasting diet is a more effective approach than a calorie restriction diet on weight loss and hs-CRP levels. Int J Vitam Nutr Res. 2021;91:242–50. https://doi.org/10.1024/0300-9831/a000623.
278. Stekovic S, Hofer SJ, Tripolt N, Aon MA, Royer P, Pein L, Stadler JT, Pendl T, Prietl B, Url J, Schroeder S, Tadic J, Eisenberg T, Magnes C, Stumpe M, Zuegner E, Bordag N, Riedl R, Schmidt A, Kolesnik E, Verheyen N, Springer A, Madl T, Sinner F, de Cabo R, Kroemer G, Obermayer-Pietsch B, Dengjel J, Sourij H, Pieber TR, Madeo F. Alternate day fasting improves physiological and molecular markers of aging in healthy, non-obese humans. Cell Metab. 2019;30:462-476.e6. https://doi.org/10.1016/j.cmet.2019.07.016.
279. Kinsey AW, Ormsbee MJ. The health impact of nighttime eating: old and new perspectives. Nutrients. 2015;7:2648–62. https://doi.org/10.3390/nu7042648.
280. Martínez-Lozano N, Tvarijonaviciute A, Ríos R, Barón I, Scheer FAJL, Garaulet M. Late eating is associated with obesity, inflammatory markers and circadian-related disturbances in school-aged children. Nutrients. 2020;12:2881. https://doi.org/10.3390/nu12092881.
281. Curti ML, Jacob P, Borges MC, Rogero MM, Ferreira SR. Studies of gene variants related to inflammation, oxidative stress, dyslipidemia, and obesity: implications for a nutrigenetic approach. J Obes. 2011;2011: 497401. https://doi.org/10.1155/2011/497401.
282. Ramos-Lopez O, Milagro FI, Riezu-Boj JI, Martinez JA. Epigenetic signatures underlying inflammation: an interplay of nutrition, physical activity, metabolic diseases, and environmental factors for personalized nutrition. Inflamm Res. 2021;70:29–49. https://doi.org/10.1007/s00011-020-01425-y.
283. Aranaz P, Ramos-Lopez O, Cuevas-Sierra A, Martinez JA, Milagro FI, Riezu-Boj JI. A predictive regression model of the obesity-related inflammatory status based on gut microbiota composition. Int J Obes (Lond). 2021;45:2261–8. https://doi.org/10.1038/s41366-021-00904-4.
284. Saklatvala J, Dean J, Clark A. Control of the expression of inflammatory response genes. Biochem Soc Symp. 2003;70:95–106. https://doi.org/10.1042/bss0700095.
285. Fitzpatrick M, Young SP. Metabolomics–a novel window into inflammatory disease. Swiss Med Wkly. 2013;143: w13743. https://doi.org/10.4414/smw.2013.13743.
286. Palmnäs M, Brunius C, Shi L, Rostgaard-Hansen A, Torres NE, González-Domínguez R, Zamora-Ros R, Ye YL, Halkjær J, Tjønneland A, Riccardi G, Giacco R, Costabile G, Vetrani C, Nielsen J, Andres-Lacueva C, Landberg R. Perspective: metabotyping-a potential personalized nutrition strategy for precision prevention of cardiometabolic disease. Adv Nutr. 2020;11:524–32. https://doi.org/10.1093/advances/nmz121.
287. Ramos-Lopez O, Milton-Laskibar I, Martínez JA, Collaborators: Rodrigo San-Cristobal and Maria P. Portillo. Precision nutrition based on phenotypical traits and the (epi)genotype: nutrigenetic and nutrigenomic approaches for obesity care. Curr Opin Clin Nutr Metab Care. 2021;24:315–25. https://doi.org/10.1097/MCO.0000000000000754.