Journal of Food Science and Technology (Iran)

Homepage:www.fsct.modares.ir

Scientific Research

The Role of NLRP3 Inflammasome in Cardiovascular Disease Progression: Integrating Food Science and Technology for Therapeutic Advancements

Zena Zmat Ghilan[1], Noorhan Khalid Shafeeq[1]

1-Department of Chemistry/ College of Education, for pure Science (Ibn-Al-Haitham) University of Baghdad. Iraq.Iraq. Ai-Adhamiyah, Antar Square

ARTICLE INFO

Article History:

Received: 2025/5/14
Accepted: 2025/6/3

Keywords:

Cardiovascular Disease,

Inflammasome,

NLRP3,

Therapeutic Advancements

DOI: 10.22034/FSCT.22.164.62.

*Corresponding Author E-Mail:

noorhan.k.s@ihcoedu.uobaghdad.edu.iq

ABSTRACT

The NLRP3 inflammasome has emerged as a pivotal player in the progression of cardiovascular diseases, acting as a critical mediator of inflammation and immune responses. This multi-protein complex is activated in response to various stress signals, leading to the production of pro-inflammatory cytokines such as IL-1β and IL-18, which are implicated in the pathogenesis of atherosclerosis, myocardial infarction, and heart failure. Recent studies have highlighted the potential of targeting the NLRP3 inflammasome as a therapeutic strategy to mitigate cardiovascular disease progression. Integrating food science and technology offers promising avenues for developing novel interventions. Nutraceuticals and functional foods rich in anti-inflammatory compounds, such as omega-3 fatty acids, polyphenols, and flavonoids, have shown efficacy in modulating inflammasome activity. Advances in food processing and biotechnology can enhance the bioavailability and efficacy of these compounds, providing a complementary approach to conventional pharmacotherapy. Furthermore, understanding the interactions between dietary components and genetic predispositions may enable personalized nutrition strategies to prevent or treat cardiovascular diseases. As research continues to unravel the complexities of the NLRP3 inflammasome and its role in cardiovascular health, interdisciplinary collaborations between food scientists, technologists, and medical researchers are crucial for translating these findings into practical therapeutic advancements.

1-Introduction

In recent years, advances in medical research have brought to light the intricate interplay between inflammation and cardiovascular diseases (CVD), a leading cause of morbidity and mortality worldwide. Central to this discussion is the NLRP3 inflammasome, a complex that acts as a critical sensor of cellular stress and inflammation [1-3]. Its activation has been implicated in various pathophysiological processes, including atherogenesis, myocardial infarction, and hypertension. Understanding the role of the NLRP3 inflammasome in these conditions opens up innovative avenues for therapeutic intervention, particularly in the realm of food science and technology [4]. Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality worldwide. Characterized by conditions such as coronary artery disease, heart failure, and stroke, CVD presents a significant public health challenge [5]. Various risk factors, including hypertension, diabetes, obesity, and hyperlipidemia, contribute to the pathogenesis of cardiovascular disorders. Recent research has shifted focus to the role of inflammation in mediating cardiovascular events, thereby highlighting the NLRP3 inflammasome as a critical player in the progression of CVD [6].

Understanding the NLRP3 Inflammasome the NLRP3 inflammasome, a multiprotein complex, serves as a critical component of the innate immune system. It is activated in response to a variety of cellular stressors, including pathogens, metabolic changes, and environmental toxins. Upon activation, NLRP3 promotes the maturation and secretion of pro inflammatory cytokines such as IL 1β and IL 18, which play pivotal roles in modulating inflammatory responses [7]. NLRP3 Inflammasome in Cardiovascular Disease Progression Emerging evidence indicates that the NLRP3 inflammasome contributes significantly to cardiovascular disease progression through various mechanisms. The activation of NLRP3 has been associated with endothelial dysfunction, atherosclerosis, ischemia reperfusion injury, and heart failure [8].

Integrating Food Science and Technology in Therapeutic Advancements The interconnection between diet, inflammation, and cardiovascular health is well documented. Foods rich in antioxidants, polyphenols, and omega 3 fatty acids have demonstrated anti-inflammatory effects that can modulate the NLRP3 inflammasome's activity [9]. Various studies suggest that diets rich in fruits, vegetables, whole grains, and healthy fats can attenuate NLRP3 activation. For instance, components such as flavonoids found in berries, curcumin in turmeric, and resveratrol in grapes exhibit potential NLRP3 inhibitory effects [10]. Innovations in food processing, fortification, and delivery methods may help increase public consumption of these health promoting substances. Moreover, novel nutraceutical formulations targeting NLRP3 inhibition could become pivotal in CVD prevention strategies [11].

In this study, the current status of integrating food science and technology into the NLRP3 Inflammasome for the progression of cardiovascular diseases was reviewed.

2- NLRP3 Inflammasome

The NLRP3 inflammasome is a crucial component of the innate immune system that plays a pivotal role in inflammation and host defense against pathogens. inflammasomes

are multi protein complexes formed in response to harmful stimuli [5-7]. They serve to activate caspase 1, which, in turn, processes pro inflammatory cytokines, such as interleukin 1β (IL 1β) and interleukin 18 (IL 18). Among the numerous types of inflammasomes, the NLRP3 (NOD like receptor family, pyrin domain containing 3) inflammasome is the most studied. It is known for its ability to detect a wide range of stimuli, including microbial pathogens and environmental irritants. Inflammasome The NLRP3 inflammasome consists of three central components: NLRP3 protein: A cytoplasmic sensor that contains a C terminal leucine rich repeat domain (LRR), a central NACHT (NOD, LRR, and CARD domain) domain, and an N terminal pyrin domain (PYD). ASC (apoptosis associated speck like protein containing a CARD): An adaptor protein with both a PYD and a CARD that links NLRP3 to pro caspase 1. Pro caspase 1: An inactive form of the cysteine protease that, once activated, cleaves pro IL 1β and pro IL 18 to their active forms. Upon assembly, the NLRP3 inflammasome forms a large speck like structure that facilitates caspase 1 activation [7-9].

2-1. Activation Mechanisms

The activation of the NLRP3 inflammasome occurs in two distinct steps:

2-1-1 Priming Phase

In the first step, known as priming, signals such as pathogen associated molecular patterns (PAMPs) or damage associated molecular patterns (DAMPs) lead to upregulation of NLRP3 and pro IL 1β synthesis through TLR (Toll like receptor) signaling pathways. During this phase, NF κB is activated, stimulating the transcription of NLRP3 and related genes [12].

2-1-2 Activation Phase

The second step involves NLRP3 activation upon sensing a wide range of danger signals. These signals include: K+ efflux: Diminished potassium levels within the cytosol trigger oligomerization of NLRP3 [13].

2-1-3 Mitochondrial dysfunction

Mitochondrial damage leads to the release of reactive oxygen species (ROS), which can serve as secondary signals for NLRP3 activation. Lysosomal destabilization: Release of lysosomal contents and cathepsins can activate NLRP3 as well. Upon activation, NLRP3 undergoes a conformational change, recruiting ASC and pro caspase 1 to form the inflammasome complex, culminating in the cleavage of caspase 1 and subsequent maturation of IL 1β and IL 18 [14].

2-2 Functions of the NLRP3 Inflammasome

The principal function of the NLRP3 inflammasome is the regulation of a robust inflammatory response. It impacts various physiological processes, such as: Cytokine release [The maturation of pro inflammatory cytokines IL 1β and IL 18 leads to the recruitment of immune cells like monocytes and neutrophils to sites of infection or tissue damage], Pyro ptosis [NLRP3 activation can also induce a form of programmed cell death known as pyro ptosis, which is characterized by cell swelling, membrane rupture, and release of intracellular content, further amplifying inflammation], Antimicrobial response [By promoting inflammation and recruiting immune cells, the NLRP3 inflammasome helps to clear pathogens and orchestrate effective immune responses] [14-16].

3-NLRP3 Inflammasome and Cardiovascular Disease

Activation of the NLRP3 inflammasome is appreciably implicated in numerous cardiovascular diseases (CVDs). The dynamics of NLRP3 activation additionally fluctuate among acute and continual damage. Acute damage is related to a speedy and strong boom withinside the NLRP3 inflammasome [17]. In those situations, the healing window for focused on the inflammasome is narrower (i.e., hours to days) relying on the character of the damage. Conversely, in continual situations including atherosclerosis, hypertension, diabetes, obesity, coronary heart failure (HF), in which low-grade basal activation of the NLRP3 inflammasome contributes to disorder progression, inhibition of the NLRP3 inflammasome at extraordinary levels can also additionally lessen the worsening of continual disorder, with the healing window being appreciably broader (i.e., days to months to years). This impact may additionally fluctuate in acute as opposed to continual situations. In acute situations, inhibition of NLRP3 inflammasome interest can also additionally cause the salvage of feasible tissue and feature many useful effects, however its effectiveness additionally relies upon on the character of the damage and the timing of the intervention [18]. In continual situations, inhibition of the NLRP3 inflammasome can modify the volume of degenerative disorder progression. Its efficacy may additionally rely upon the interest of the NLRP3 inflammasome in comparison to the continual nature of the disorder, the harm already done, and the cap potential of the remedy to enhance and modify the route of situations which might be probable to development and/or recur over time [11, 16,17]. We offer right here a top-level view of the cap potential function of NLRP3 in cardiovascular diseases, which includes atherosclerosis, ischemic coronary heart disorder, diabetic cardiomyopathy, hypertensive cardiomyopathy, dilated cardiomyopathy, drug-precipitated cardiotoxicity, myocarditis, cardiac sarcoidosis, pericarditis, and venous thromboembolism [18].

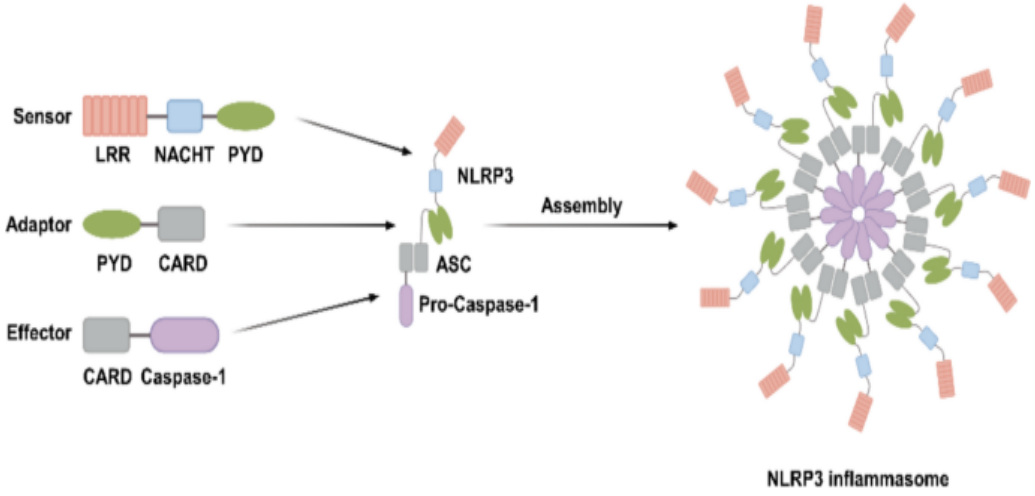

Fig. 1 The Structure and Assembly of the NLRP3 Infammasome [7].

3.1 Atherosclerosis

Atherosclerosis is a chronic inflammatory illness and a diagnosed motive of numerous cardiovascular illnesses [19]. Macrophage infiltration of the vascular wall is an indicator of atherosclerosis [20]. In macrophages, ldl cholesterol and calcium phosphate crystals result in lysosomal instability, which triggers the release of cathepsin B, ultimately activating the NLRP3 inflammasome with the secretion of IL-1β [21,22]. The significance of the NLRP3 inflammasome has been highlighted in several animal models of atherosclerosis. Attenuation of atherosclerosis emerge as validated in low-density lipoprotein receptor (Ldlr) knockout mice transplanted with bone marrow from Nlrp3, Asc, and Il-1β mice [23]. This proof makes the NLRP3 inflammasome a promising healing goal for atherosclerosis.

3.2 Ischemic heart ailment

Inhibition of NLRP3 and extraordinary inflammasome components in animal fashions of ischemic coronary heart harm has verified useful effects in terms of lowering infarct length and improving cardiac characteristic [21,22]. Activation of NLRP3 after ischemia is a time-based mechanism [23]. DAMPs and signaling molecules released from ischemia-damaged cells strongly stimulate the inflammatory reaction thru manner of means of recruiting distinctly activated inflammatory cells to the web website online of damage. This feed-beforehand mechanism exacerbates the initial ischemic damage [24]. In experimental models of reperfusion and non-reperfusion AMI, top activation of the NLRP3 inflammasome takes area 1 and 3 days after ischemia, respectively [25]. NLRP3 inflammasome spots can be detected in leukocytes, endothelial cells, fibroblasts, and cardiomyocytes after AMI [23]. however, as soon as the recovery section starts, ASC clusters are drastically localized in fibroblasts and cardiomyocytes [27], suggesting that the reaction to inflammatory activation is molecular kind-particular. Leukocytes, fibroblasts, and endothelial cells reply at the complete thru way of means of generating IL-1β. In cardiomyocytes, NLRP3 activation consequences in caspase-1 activation and culminates in pyro ptosis molecular loss of life [28]. After ischemia-reperfusion in mice, genetic or pharmacological inhibition of the NLRP3 inflammasome reduces infarct duration and preserves cardiac feature. that is summarized in research with mice lacking caspase-1 or ASC (reviewed beneath) [25].

3.3 Dilated Cardiomyopathy

a few strains of prove recommend that a provocative element is critical in the pathogenesis of expanded cardiomyopathy. Circulating stages of the NLRP3 inflammasome show up to be clinically related with cardiac paintings, NT-proBNP degrees, and combination readmission prices at 6 months [29]. At dissection, pyroptotic cell passing has been illustrated to be altogether increased in the hearts of patients with accelerated cardiomyopathy [30].

3.4 Hypertensive heart sickness

Hypertensive cardiac harm promotes myocardial hypertrophy and fibrosis, most important to left ventricular transforming and the improvement of coronary heart failure (HF). Cardiac NLRP3 and IL-1β upregulation have been diagnosed in distinctive hypertensive mouse models: transverse aortic constriction, a stress overload model of myocardial fibrosis and transforming, and an angiotensin II injection

version of hypertension [31]. In every model, inhibition or deletion of NLRP3 progressed cardiac transforming, and reduced contamination and fibrosis [32,33]. but, the mechanisms of inflammasome activation withinside the absence of ischemic damage and molecular demise have now not been in reality elucidated. A contemporary observe suggests that, in response to strain overload, cardiac NLRP3 priming and activation are mediated thru Ca2+/calmodulin-mounted protein kinase II δ (CaMKIIδ) [31].

3.5. Cardiac damage related to cancer therapy

a few beneficial modalities applied to deal with special types of cancer (i.e., radiotherapy and chemotherapy) are related with the development of cardiomyopathy in both creatures and people. Mice infused with doxorubicin create cleared out ventricular growth, diminished cardiac paintings, and elevated cardiac fibrosis [34]. The faded cardiac work is paralleled with the aid of extended cardiomyocyte expression of NLRP3, caspase-1, IL-1β, and IL-18, and plenteous pyro ptosis [35]. blocking NLRP3 via pharmacological restraint or satisfactory erasure diminishes cardiac brokenness and myocardial damage due to pyro ptosis [33,35]. Given the beneficial impacts of IL-1β and IL-18 bar in radiation-brought about cardiomyopathy, a coordinate affiliation of the NLRP3 inflammasome inside the start and movement of radiation-prompted cardiac damage has been proposed [36].

3.6 Metabolic problems and diabetic cardiomyopathy

in the placing of cardiometabolic disarranges, IL-1β and IL-18 are key cross between of the pernicious impacts of weight and maturing [37]. fats tissue efficiently contributes to a systemic proinflammatory kingdom, which is characterized by extended plasma ranges of proinflammatory cytokines [38]. Upregulation of the NLRP3 inflammasome has been unique in fats tissue of hefty sufferers and creatures [37-39]. In creature models of maturing and corpulence, restraint of NLRP3 turned into associated with progressed metabolic profiles [40]. decided metabolic anomalies may lead to diabetic cardiomyopathy [41], wherein cardiac NLRP3 particularly contributes to organ brokenness [42]. Cardiomyocyte dying seems to be the primary step in beginning the auxiliary transforming that ends in diabetic cardiomyopathy [38]. Glucotoxicity and lip toxicity are robust triggers for the NLRP3 inflammasome [43]. mainly, in a few mobile sorts, tall glucose ranges provoke ROS technology and resulting actuation of atomic figure kappa light chain enhancer of enacted B cells (NF-κB) and TXNIP, eventually performing as preparing and fortifying indicators for infection [44].

3.7 Pericarditis

Acute pericarditis is characterized through an extreme inflammatory reaction because of acute harm of mesothelial cells withinside the pericardium [42]. The key position of NLRP3 in pericarditis has been showed in numerous preclinical and medical studies [43]. Furthermore, the efficacy of colchicine, an anti-inflammatory agent with NLRP3 inflammasome inhibitory activity (reviewed below), withinside the remedy of acute pericarditis similarly helps an immediate position for NLRP3 on this condition [45]. A current examines verified the presence of inflammatory components (NLRP3, ASC, and caspase-1) in pericardial samples from sufferers with persistent pericarditis experiencing acute flare-ups [46]. Consistent

findings have been acquired in a unique mouse version wherein pericarditis changed into prompted through intrapericardial injection of zymosan [47]. In this version, inhibition of infection or IL-1α/β reduces pericardial effusion and thickening [48]. These observations are constant with the medical efficacy of rilonacept, which inhibits each IL-1α and IL-1β, in sufferers with recurrent pericarditis [49]. In the segment III RHAPSODY trial, rilonacept monotherapy changed into related to a 96% discount in relapse as compared with placebo [50]. Similar blessings have been visible withinside the smaller AIRTRIP trial with anakinra, a recombinant IL-1 receptor antagonist, in sufferers with colchicine-resistant recurrent pericarditis [51]. IL-1 blockers are presently taken into consideration the same old of take care of the remedy of recurrent pericarditis in sufferers who've failed preliminary therapy. The capability position of interleukin-1 blockade in acute pericarditis is below investigation [52].

3.8 Myocarditis

The nearness of the NLRP3 inflammasome has been illustrated in endomyocardial biopsies of patients with excessive myocarditis [51]. sickness with coxsackievirus B3 (CVB3), one of the main common infections causing myocarditis, is associated with increased NLRP3 enactment and expanded expression of ASC, caspase 1, and IL-1β watched interior 7 days of contamination in mice [52]. Restraint of caspase 1 or IL-1β progresses cardiac paintings and reduces myocardial chemical emission [53]. Of be aware, in check CVB3-precipitated myocarditis, inflammasome actuation and resulting pyro ptosis show up to be intervened by means of cathepsin B [54]. a specific form of myocarditis, cardiac sarcoidosis, is characterized by using the association of giant cell granulomas inside the coronary heart, which dynamically result in heart unhappiness and arrhythmias [55]. As of late, strong expression of the NLRP3 inflammasome and its items in granulomas has been depicted [54]. A medical trial with anakinra in cardiac sarcoidosis is as of now underway [56].

3-9 Venous thromboembolism

Venous thromboembolism (VTE), counting profound vein thrombosis and pneumonic embolism, is the third using motive of cardiovascular mortality round the arena [57]. In growth, post-thrombotic disease (PTS), a inveterate fiery circumstance that complicates VTE, money owed for crucial horribleness and affects 20–40% of patients after VTE [55]. The begin and proliferation of venous thrombosis may be a multifactorial put together including a complicated grouping of activities in which inflammation straightforwardly enacts the coagulation framework and endothelium, in addition to the enlistment of leukocytes and platelets, which form totals and compound thrombosis [58]. a few traces of show advocate that the NLRP3 inflammasome is included within the path of those events [59]. Blood stream confinement and hypoxia taking after check venous thrombosis had been seemed to actuate NLRP3, caspase 1, and IL-1β [60]. In mice, hereditary cancellation of the NLRP3 inflammasome and pharmacological restraint of caspase 1 or IL-1β altogether improve venous thrombosis [61].

4. Food and NLRP3 Inflammasome

The NLRP3 inflammasome is an integral part of the innate immune response and plays a significant role in the regulation of

inflammation and metabolism [62]. Recent studies have highlighted the critical interactions between dietary components and the NLRP3 inflammasome, pointing to the profound effects that food can have on immune responses and overall health. Understanding this relationship is essential to developing dietary strategies for managing inflammation-related diseases [63]. The NLRP3 inflammasome is a multiprotein complex that plays a key role in the activation of inflammatory responses. It consists of three main components: 1. NLRP3 Protein: A pattern recognition receptor (PRR) that detects danger signals in the form of pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs) [64]. A signaling molecule that facilitates the formation of the inflammasome complex. An enzyme that, once activated, cleaves pro-inflammatory cytokines such as pro-IL-1β and pro-IL-18 into their active forms [65]. Priming involves the upregulation of NLRP3 and pro-IL-1β expression in response to various signals, including microbial components or cytokines. Following this, activation takes place in response to triggers such as cellular stress, ATP release, or reactive oxygen species (ROS), leading to the formation of the inflammasome and the subsequent release of active cytokines that promote inflammation. The Role of Food in NLRP3 Inflammasome Activation Nutrients and NLRP3 Inflammasome The composition of our diet has significant implications for the activity of the NLRP3 inflammasome [66]. Several nutrients and dietary components have been identified to either promote or inhibit inflammasome activation: 1. Omega-3 Fatty Acids: Found in fish and flaxseed, omega-3 fatty acids are known for their anti-inflammatory properties. They can inhibit NLRP3 inflammasome activation, which may help mitigate chronic inflammation. 2. Polyphenols: Present in fruits, vegetables, and teas, polyphenols have antioxidant properties that reduce oxidative stress. Studies have shown that certain polyphenols, such as resveratrol, can inhibit NLRP3 inflammasome activation by modulating signaling pathways. 3. High-Fat Diets: Diets rich in saturated fats can promote NLRP3 activation. Research suggests that saturated fatty acids may induce endoplasmic reticulum (ER) stress and mitochondrial dysfunction, leading to the activation of the NLRP3 inflammasome. 4. Fiber: A diet high in soluble fiber can modify gut microbiota, influencing the production of short-chain fatty acids (SCFAs), which have been shown to inhibit NLRP3 activation, fostering an anti-inflammatory environment. Food Additives and Inflammasome Some studies have suggested that artificial sweeteners may modulate the gut microbiome, potentially leading to NLRP3 inflammasome activation and systemic inflammation. Certain preservatives, like sodium nitrite, and flavor enhancers, such as monosodium glutamate (MSG), have been associated with inflammatory responses that may activate the NLRP3 inflammasome. Implications for Disease Management Understanding the relationship between food and NLRP3 inflammasome activation can have significant implications for managing various diseases, Metabolic Disorders Chronic inflammation, mediated by the NLRP3 inflammasome, is closely linked to obesity, type 2 diabetes, and cardiovascular diseases. A diet rich in anti-inflammatory foods, such as fruits, vegetables, and fatty fish, can help mitigate the risk of these conditions by suppressing NLRP3 activation [67]. Autoimmune Diseases Many autoimmune

diseases, including rheumatoid arthritis and inflammatory bowel diseases, involve chronic inflammation driven by the NLRP3 inflammasome. Dietary interventions aimed at reducing NLRP3 activation may provide complementary therapeutic strategies alongside conventional treatments. Cancer Emerging evidence suggests that chronic inflammation mediated by the NLRP3 inflammasome may play a role in cancer progression. Specific dietary patterns that reduce inflammation could, therefore, contribute to cancer prevention strategies. The NLRP3 inflammasome serves as a crucial bridge between diet and inflammation, highlighting how our food choices can significantly impact immune responses and disease susceptibility. A deeper understanding of this relationship offers valuable opportunities for dietary interventions aimed at promoting health and preventing inflammation-related diseases. As ongoing research continues to unveil the complexities of diet and the inflammasome, it will become increasingly important for healthcare professionals to consider nutritional strategies as a part of comprehensive patient care [68].

5- food compounds for treating NLRP3

5.1. Polyphenols

Polyphenols are secondary metabolites produced through plant metabolic pathways, primarily derived from phenylalanine or shikimic acid. Over 8,000 polyphenols have been identified, typically existing in conjugated forms with sugars, organic acids, amines, lipids, or other phenols. These compounds are classified into several groups based on their phenolic ring structures and connecting elements, with the major classes including phenolic acids, flavonoids, stilbenes, and lignans [68]. Polyphenols have attracted substantial interest due to their antioxidant and anti-inflammatory properties, which contribute to the prevention and mitigation of cancer, chronic inflammation, diabetes, aging, and infections [69]. Notably, many polyphenols exert anti-inflammatory effects through inhibition of the NLRP3 inflammasome [68]. Among phenolic acids, compounds such as Sinopic acid, ferulic acid, and chlorogenic acid exhibit pronounced anti-inflammatory activity. Sinopic acid, found in vegetables, spices, cereals, and fruits, has demonstrated NLRP3 inflammasome inhibition in murine colitis models, reducing NLRP3, ASC, IL-1β, and caspase-1 expression dose-dependently [71,73]. Ferulic acid, present in grains, seeds, and turmeric, ameliorated NLRP3 and caspase-1 expression and decreased IL-1β levels in a methotrexate-induced nephrotoxicity rat model [58]. Similarly, chlorogenic acid—abundant in coffee, fruits, and vegetables—downregulated NLRP3 components and IL-1β production in colitis models and LPS-stimulated macrophages [75,76].

Certain cinnamaldehyde derivatives, notably cinnamaldehyde and 2-methoxycinnamaldehyde, have effectively suppressed NLRP3 and pro-IL-1β expression, whereas related compounds such as cinnamic acid and cinnamyl alcohol were ineffective, underscoring the significance of the propenal moiety [74–77]. Flavones like apigenin, is orientin, chrysin, and luteolin have also demonstrated NLRP3 modulation. Apigenin, abundant in parsley, onions, and tea, reduced NLRP3 expression and ROS levels in models of NAFLD and endothelial inflammation [78,79]. Is orientin suppressed NLRP3 activation in hyperuricemia models

by inhibiting xanthine oxidase and inflammatory cytokine release [80]. Chrysin and luteolin, administered in models of hyperuricemia and spinal cord ischemia-reperfusion injury, respectively, attenuated NLRP3, IL-1β, and IL-18 expression [81,82]. Flavanones such as hesperidin methyl chalcone and naringin have similarly reduced NLRP3 activation. Hesperidin methyl chalcone, derived from citrus fruits, lowered NLRP3 and associated cytokine expression in gout arthritis models [83]. Naringin reduced inflammasome markers in DSS-induced colitis in mice in a dose-dependent manner [84]. While isolating individual contributions of polyphenols in complex mixtures remains challenging due to potential synergistic or antagonistic interactions [85], food-derived polyphenolic combinations have demonstrated notable anti-inflammasome activity. For instance, the fermented non-digestible fraction (FNDF) of corn and bean snacks inhibited NLRP3 assembly, caspase-1 activity, and IL-1β production in THP-1 and Caco-2 cells [86]. Similarly, green tea polyphenols, particularly epigallocatechin-3-gallate (EGCG), suppressed NLRP3, ASC, caspase-1, and IL-1β expression in murine models of liver injury in a dose-dependent manner [87,88].

5.2. Organosulfur Compounds

Organosulfur compounds (OSCs) are bioactive molecules present in various dietary sources, with Allium (e.g., garlic, onion) and Brassica (e.g., broccoli, cabbage, cauliflower) genera serving as primary contributors [89]. These compounds—including isothiocyanates, indoles, allyl sulfur compounds, and sulfones—exhibit diverse biological activities, notably antioxidant, anticancer, antimicrobial, and anti-inflammatory effects [90]. Among their anti-inflammatory mechanisms, suppression of NLRP3 inflammasome activation has been demonstrated for several OSCs. Allicin, a prominent sulfur compound in garlic, has been shown to mitigate acrylamide-induced liver inflammation in Sprague-Dawley rats and Kupffer cells. Both in vitro (1 mM acrylamide; 3.75–15 μM allicin) and in vivo (30 mg/kg/day acrylamide; 25 or 50 mg/kg allicin, equivalent to 2–4 mg/kg HED) studies revealed reductions in NLRP3 inflammasome components, ROS production, and endoplasmic reticulum stress markers [91]. Similarly, benzyl isothiocyanate, derived from cruciferous vegetables, attenuated NLRP3 activation in diet-induced non-alcoholic steatohepatitis (NASH). Administration in vitro (2.5–5 μM) and in vivo (1 g/kg/day; 80 mg/kg/day HED) decreased NLRP3, caspase-1 p20, IL-1β, and cathepsin β expression in serum and liver [92]. Conversely, sulforaphane, an allyl sulfur compound abundant in broccoli, increased expression of NLRP3, caspase-1 p20, and IL-1β in cerulean-induced acute and recurrent pancreatitis models at doses of 5 mg/day (0–4 mg/kg HED) [93]. Lastly, methyl sulfonyl methane, another OSC found in Allium vegetables, demonstrated NLRP3 inhibition in human and mouse macrophages at concentrations of 0.3–1% [94]. This suppression occurred via inhibition of NF-κB signaling and pro-IL-1β expression, leading to reduced IL-1β production and mitochondrial ROS generation.

5.3. Terpenes and Terpenoids

Terpenes are volatile hydrocarbon compounds derived from isoprene units and are key constituents of plant essential oils. These molecules exhibit a broad spectrum of bioactivities, including antitumor, anti-inflammatory, antibacterial, antiviral,

antimalarial, and cardiovascular effects [95]. Notably, inhibition of the NLRP3 inflammasome has emerged as a common anti-inflammatory mechanism among various terpenes. Carno sic acid, a diterpenoid from Rosmarinus and Salvia species, reduced dextran sulfate sodium (DSS)-induced colitis in BALB/c mice when administered at 50 or 100 mg/kg (4–8 mg/kg HED) for 10 days. This effect correlated with modulation of caspase activity, inflammatory cytokines, and ROS in colonic tissues, showing comparable efficacy to 5-aminosalicylic acid [96]. Similarly, geranylgeraniol, a diterpenoid found in plant oils such as flax, sunflower, and olive, suppressed NLRP3 gene expression and reduced cell death in vitro following 50 μM treatment after statin or mevalonate exposure in Dao mice models [97]. Conversely, kaurenoic acid, a diterpenoid present in Xylo Pia aethiopica and other herbal sources, dose-dependently induced NLRP3 activation (10–90 μM), increasing nitric oxide and IL-1β production in BALB/c mice \[98]. Beyond dietary sources, several terpenoids—including α-bisabol, aucuba, abscisic acid, triptolide, triptolide, ammo shin, cannabidiol, tanshinone IIA sulfonate, paclitaxel, phorbol myristate acetate, andrographolide, oridonin, glycocalyx A, and thuvinsenone F—have demonstrated significant NLRP3 inhibitory activity. These compounds suppressed IL-6, IL-1β, IL-18, caspase-1, and ROS production [99]. Additionally, triterpenoids like celastrol and sesquiterpenoids from Ainsliaea yumminess have also been shown to modulate NLRP3 inflammasome activation [100].

5.4. Fatty Acids

Current evidence indicates that saturated fatty acids (SFAs) generally promote NLRP3 inflammasome activation, whereas monounsaturated (MUFAs) and polyunsaturated fatty acids (PUFAs) tend to inhibit it, though these conclusions remain under scrutiny [101]. The literature on fatty acids and NLRP3 inflammasome can be broadly divided into two categories: SFAs and unsaturated fatty acids (UFAs) [102]. Mechanistic studies have shown that palmitate impairs AMP-activated protein kinase (AMPK) in LPS-primed macrophages, leading to increased mitochondrial reactive oxygen species (ROS) production, NLRP3 activation, and release of caspase-1, IL-1β, and IL-18. Robblee et al. demonstrated that palmitic and stearic acids activate IRE-sensitive stress pathways due to the accumulation of saturated phosphatidylcholine, which correlates with NLRP3 activation in primary LPS-stimulated dendritic cells [103]. Gianfrancesco et al. further reported that saturated phosphatidylcholine reduces membrane fluidity, impairing Na^+/K^+-ATPase function and enhancing potassium influx, a known NLRP3 activator. However, certain SFAs exhibit anti-inflammatory effects. Virgin coconut oil (VCO), rich in medium-chain saturated fatty acids (C6–C12), has been shown to reduce IL-1β, caspase-1, and NLRP3 gene expression in amyloid-β-induced models and high-fat diet scenarios [104]. Lauric acid, the predominant component of VCO (55%), likely contributes to these effects through its conversion to monolaurin, which modulates immune responses [105].

Research has predominantly focused on the anti-inflammatory properties of PUFAs, particularly ω-3 fatty acids (DHA and EPA) from fish oil. These fatty acids consistently reduce NLRP3 expression and inflammatory

cytokines (IL-1β, IL-18) in obese mice, DSS-induced colitis models, LPS-treated Kupffer cells, and other systems [102,103]. Dong et al. found that angelica oil attenuates LPS-induced neuroinflammation via modulation of the P2X7R/NLRP3 axis [101], while Miao et al. highlighted PUFA-mediated inhibition of ROS production, NLRP3/ASC/caspase-1 signaling, modulation of gut microbiota, and short-chain fatty acid levels [105]. More recently, Qingyao et al. proposed that DHA suppresses NLRP3 activation via PI3K/Akt-mediated inhibition of TXNIP in adipocyte precursors [104]. ω-3 PUFAs may also exert effects through GPR120 and GPR40, which inhibit NLRP3 inflammasome assembly [103]. Comparative analyses have emphasized the superior anti-inflammatory efficacy of ω-3 over ω-6 PUFAs. Schuster et al. demonstrated that across macrophages, monocytes, and hepatocytes, ω-3 PUFAs more effectively inhibited ATP-induced NLRP3 activation than ω-6 PUFAs [106].

5.5. Carotenoids

Recently, two carotenoids have been connected to the in vivo regulation of NLRP3 activation. Zeaxanthin Di palmitate, a lipid soluble antioxidant recognized for its presence in various beneficial natural products (e.g., Lycium barbarum), has demonstrated its ability to alleviate ethanol related liver damage by triggering the AMPK3 pathway leading to FoxO3a and N3NPLAPL in ethanol treated mice. The AMPK pathway FoxO3a to mitophagy and NPL3R3A to 7 receptors on the hepatocyte membrane [107]. Given that NLRP3 is associated with nearly all liver infections, this compound or foods containing it could offer advantageous or preventative effects against multiple human diseases. Conversely, astaxanthin, which seems to be lacking in standard Western diets but plentiful in fish (23% NPL via a regulated circuit, tweak 3%), is utilized. Gut microbiota in mice indicates that supplementation (0.04% w/w) enhances stimulation and metabolic balance for routine weight loss [108].

5.6. Proteins and Amino Acid Derivatives

Proteins, peptides, and amino acids are involved in the repression of the stimulatory pathway. Two short peptides, RDP2 (rice deduced peptide 2, AAAAGAMPK NH2, 785.97 Da) and RDP3 (rice deduced peptide 3, AAAAMAGPK NH2, 785.97 Da), were linked for consideration. The RDP2 peptide [109]. was examined in hypouricemic rats that entered intraperitoneal injections formerly a day for 7 days and distributed into 7 groups control, marker, allopurinol (Allo, 10 mg/ kg, 0.8 mg/ kg HED), benzbromarone (0.10, 0.8, and 1 μg/ kg; Benz. 0.8 and 8 μg/ kg HED). The RDP2 groups effectively lowered serum uric acid situations by dwindling renal aggravation. Specifically, serum IL 1β, the product of which is told by the NLRP3 inflammasome, showed a significant drop in hypouricemic treated with the RDP2 peptide, while the expression of NLRP3, ASC, and caspase 1 was set up to be lower in the feathers. A hypouricemic rodent model was employed to explore the goods of RDP2 and RDP3. The mice were separated into colorful groups control, sham, allopurinol, benzbromarone, and RDP3. Hyperuricemia was convinced by intraperitoneal injection of uric acid. latterly, for a duration of 7 days, the groups entered intraperitoneal administrations of the standard specific's allopurinol (10 mg/ kg,

0.8 mg/ kg HED) or benzbromarone (8 mg/ kg, 0.6 mg/ kg HED) [110]. On the other hand, the RDP3 groups were administered varying boluses of RDP3 via intraperitoneal injections (100 μg/ kg, 500 μg/ kg, and 1 mg/ kg; 8 μg/ kg, 40 μg/ kg, and 0.08 mg/ kg). compliances indicated that the serum uric acid situations in the RDP3 group were generally lower compared to other treatments. also, Western spot analysis was performed to assess NLRP3 inflammasome expression in the feathers of mice, revealing that the NLRP3 inflammasome was more current in feathers treated with allopurinol than in those treated with RDP3. Again, the expression of the NLRP3 inflammasome was specially lowered in the RDP3 treated feathers. The trials validated that TMOP effectively reduced hyperuricemia in a cure dependent manner, regulating uric acid metabolism in diet convinced hyperuricemia rats. TMOP administration hindered the activation of the NLRP3 inflammasome complex, and the positive goods of TMOP were further examined through intestinal microbiota transplantation. Proteins, peptides, and amino acids feel to play a part in gumming the seditious pathway. The two nippy peptides, RDP2 and RDP3 (rice deduced peptides 2 and 3 AAAAGAMPK NH2, 785.97 Da, and AAAAMAGPK NH2, 785.97 Da, independently), were uprooted from water shell and estimated for their antimicrobial parcels. The RDP2 peptide was administered intraperitoneally to hyperuricemia mice over 7 days, divided into 7 groups control, tradition, allopurinol (Allo, 10 mg/ kg, 0.8 mg/ kg HED), benzbromarone (benzbromarone, 0.8 and 8 μg/ kg HED) [111]. RDP2 administrations verified that serum uric acid situations were lowered through reduced renal excitation. specially, serum IL 1β situations, which are contingent on NLRP3 activation, were significantly lower in hyperuricemia mice treated with RDP2 peptide, with dropped expressions of NLRP3, ASC, and caspase 1 in the feathers. A hyperuricemia mouse model was drafted to probe RDP3 peptide mechanisms and characteristics through beast trials, dividing mice into control, allopurinol, benzbromarone, and RDP3 groups. Mice were convinced with hyperuricemia by intraperitoneal uric acid injections. later, for a week, the groups entered known medicines via intraperitoneal injection allopurinol (10 mg/ kg, 0.8 mg/ kg HED) or benzbromarone (8 mg/ kg, 0.6 mg/ kg HED). In discrepancy, the RDP3 groups were treated with varying boluses of RDP3 (100 μg/ kg, 500 μg/ kg, and 1 mg/ kg; 8 μg/ kg, 40 μg/ kg, and 0.08 mg/ kg). The findings indicated a significant reduction of serum uric acid attention within the RDP3 groups [112].

5.7. Saponins and Sterols

Ginseng is regarded as an exceptionally prized factory and is considerably employed in salutary supplements and herbal drugs due to its nonsupervisory impacts on the endocrine system, the nervous system, metabolism, and multitudinous physiological conditioning [113]. The energy of ginseng is largely credited to its primary active ingredients, ginsenosides, a collection of triterpene saponins featuring a steroidal frame. Research has demonstrated that 25 OCH3 PPD (20(S), 25 methoxy dammarane 3β, 12β, 20 triol), a panaxoside sourced from Panax Ginseng, mitigates liver injury by promoting apoptosis in hepatic stellate cells [114]. Given the connection between inflammation and liver fibrosis, a study delved the impact of 25 OCH3 PPD (administered at boluses of 5 mg/ kg, 10 mg/ kg, or 20 mg/ kg over five weeks, amounting

to 0.4, 0.8, or 1.6 mg/ kg) on liver fibrosis and inflammation in cases of thioacetamide convinced liver fibrosis (TAA convinced fibrosis) [115]. The results vindicated that 25 OCH3 PPD possesses hepatoprotective parcels against liver fibrosis and diminishes inflammation by modulating NLRP3 inflammasome exertion via the P2X7 receptor. Wang et al [116] examined the influence of saponins deduced from Panax Noto ginseng in enhancing NAFLD by inhibiting seditious activation. The saponin excerpt, in discrepancy to conventional red ginseng, contained notable situations of RH1 (10.34 x) and RG2 (7.1 x) ginsenosides, which are likely crucial rudiments that emphasize ginseng's medicinal capability. In this trial, mice were subordinated to a high fat diet for sixteen weeks to induce NAFLD, followed by treatment with saponin excerpt (50 or 100 mg/ kg) for nine weeks to estimate its goods. It was particularly observed that RH1 and RG2 ginsenosides deliveranti inflammatory benefits and suppress NLRP3 inflammasome activation through improvement of mitophagy, reduction of mtROS product, and inhibition of NLRP3 inflammasome exertion. The emulsion ginsenoside K (CK) stands out as a distinctive emulsion, the terminal metabolite of ginsenoside panaxadiol. CK appears to contribute to the stimulation of insulin stashing, and its defensive effect against diabetic nephropathy has shown to be intermediated via the inhibition of oxidative stress, the NLRP3 inflammasome, and the NF κB/ p38 pathway. colorful studies have affirmed the neuroprotective and antidiabetic parcels of CK, illustrating its capacity to address memory poverties and cognitive decline linked with diabetes. In particular, a review concerning CK's goods on memory and cognitive dysfunction was conducted in diabetic db/ db mice treated with 10 mg/ kg CK for 12 weeks. The findings verified that CK enhanced insulin perceptivity, lowered cognitive decline, lowered oxidative stress, soothed seditious responses in the hippocampus, and inhibited NLRP3 activation. Specifically, CK lessens the product of seditious cytokines and intercessors through the repression of the NLRP3 inflammasome pathway. Magnesium isoglycyrrhizinate, the magnesium swab of the 18α stereoisomer of glycyrrhizic acid uprooted from the rhizome of the Glycyrrhiza glabra factory, operates as a hepatoprotective agent in immunomodulatory andante inflammatory liver conditions. The impacts of magnesium isoglycyrrhizinate on metabolic pattern functions have been delved in fructose fed rats [117]. Rats were given a 100 ml result of water containing 10 fructose for six weeks, after which boluses of 10, 20, and 40 mg/ kg (0.8, 1.6, and 3.2 mg/ kg HED) of magnesium isoglycyrrhizinate were administered intraperitoneally (4 mg/ kg) or pioglitazone (for intragastric administration) for eleven weeks. substantiation substantiated that magnesium isoglycyrrhizinate inhibits NF κB/ NLRP3 activation, therefore dwindling the vulnerable seditious response, hepatic lipid metabolism complaint, and accumulation under conditions of inordinate fructose [118]. A phytosterol uprooted from the factory Moringa oleifera, β sitosterol.

5.8. Polysaccharides

Polysaccharides deduced from colorful origins (fungi, shops, algae) have demonstrated Ananta inflammatory part by modulating the NLRP3 seditious pathway. still, a thorough disquisition of the mechanisms by which polysaccharides influence NLRP3 activation still needs to be

conducted [119]. specially, numerous polysaccharides intertwined in the seditious modulation of NLRP3 appear from traditional Chinese drug, but they can also be set up in salutary shops. For case, the primary bioactive emulsion of Trametes oriental is, employed for lung complaint treatment, is a polysaccharide made up of galactose, glucose, mannose, and arabinose in the molar rate of 5.795.773.451.20, which consists of 6 active factors importing 3000 MW. NLRP3 inflammation and the reduction of seditious cytokines, similar as TNF α, IL1β, and IL6, can be detected through assessing the expression range of proteins in lung towel associated with the NLRP3 seditious pathway [120]. Liang et al. set up that theanti inflammatory effect of polysaccharides uprooted from Dendrobium officinale (DOPS) significantly altered the repression of mRNA expression for NLRP3, ASC, caspase 1, IL1β, and IL 18 mRNA both in vivo and in acute ulcerative stimulated DSS cells and a colitis inspired LNCM model in laboratory mice, potentially through a reduction in β arrestin1 expression (which can clearly regulate NLRP3) [121]. Current examinations by Lee et al. discovered CYP 1, a recently linked Manno glucan from Chinese potato able of dwindling the expression of several crucial genes involved in seditious colorectal signaling pathways (including NF κB and NLRP3) in DDS convinced colitis mice [122]. Polysaccharides from Ganoderma lucidum (GLPS), uprooted from a Chinese medicinal mushroom, have been shown to specially inhibit hepatic seditious factors by suppressing NLRP3 in liver apkins. specially, mice with acute liver injury treated with GLPS endured a significant reduction in NLRP3, ASC, and caspase 1 protein expression [123]. Armilla Riella tabescens (AT), a notable medicinal mushroom belonging to the Tracheomalacia family, is noted for its high polysaccharide content, comprising 86.52 (mannose, arabinose, and fucose in a molar rate of 1.61.02.7). AT exhibits strong antioxidant andante inflammatory parcels, presumably attributed to its inhibition of the TXNIP/ NLRP3 seditious pathway in the liver of T2D mice [124]. Among factory deduced polysaccharides, low methoxy pectin (LMP) has been verified to play a significant part in autoimmune diabetes by suppressing the expression of NLRP3 and related proteins in the cecum (NLRP3, adhered caspase 1 p20, IL 1β and IL 18). This NLRP3 inhibition may be due to the upregulation of short chain adipose acids (SCFAs) by the gut microbiota, which is inspired by LMP supplementation. also, LMP functions as a histone deacetylase (HDAC) asset of the NLRP3 inflammasome [125]. likewise, Wu et al. observed that LMP supplementation also inhibits NLRP3 activation in the pancreas; still, a detailed mechanistic disquisition of how LMP modulates NLRP3 inflammasome activation in the pancreas remains to be conducted [126]. lately, Castro Alves et al. assessed then on digestible carbohydrates (NDCs) from chayote fruits, specially pectic homogalacturonan and largely fanned rhamnogalacturonan II, along with hemicelluloses like glucomannan, xyloglucan, and glucurono (arabino) Xylan THP 1 in humans [127]. The findings verified that NDCs widely inhibit NLRP3 activation through relations between NDCs and colorful pattern recognition receptors, which could be vital for regulating the early signals necessary for activation [128].

5.9. Vitamins and Derivatives

Wallert et al [128] have considerably examined the significance of lipophilic

salutary E and its derivations, which are especially rich in nuts and oilseeds, in driving and responding to oxidative stress. Different forms of salutary E or their long- chain metabolites have the eventuality to impact ROS generation, NF- κB priming, or NLRP3 activation. Recent exploration has revealed that these goods can be reversed in specific high- fat- diet and alloxan- convinced diabetic murine models, especially concerning γ- tocopherol supplementation, either in its natural form or within complex excerpts (e.g., Rosa Mosqueta oil painting consists of roughly 74 g/ 100 g of α-tocopherol, while roasted rosehip oil painting has about 359 g/ 100 g of γ- tocopherol) [129]. also, vitamin D and its derivations have been delved, both collectively and in combination with probiotics and micronutrients as salutary supplements, for their part in regulating inflammation that hinders the original processes necessary for NLRP3 (and NLRP1) activation within vulnerable cells, placental explants, and among pregnant women passing natural or medically convinced preeclampsia [130]. This has counteraccusations for the development of proliferative diabetic retinopathy, diabetic corneal mending and reinnervation, nonalcoholic adipose liver complaint, and acute renal injury.

5.10. Probiotics, Symbiotics, and Their main additives

Lactic acid bacteria (LAB) are widely recognized for their application as dietary supplements, primarily due to their beneficial regulatory effects on gastrointestinal health, immunomodulatory functions, and host metabolism. The efficacy of these probiotics is intricately dependent on both the bacterial species and the specific cell lines utilized in experimental models. Recent investigations have focused on elucidating the anti-inflammatory properties of LAB and their key metabolites—such as butyrate (administered at 200 mg/kg, equivalent to a human dose of 16.3 mg/kg)—through the suppression of inflammasome activation. Several bacterial strains have been evaluated in this context, including Lactobacillus piracies KW3110 (1×10^6 cells/mL), Bifidobacterium infants (2×10^8 CFU/mL) administered in combination with the prebiotic Xylo oligosaccharide (XOS; 230 mg/kg, human equivalent dose 18.7 mg/kg), Enterococcus faecium NCIMB 10415 (1×10^7 CFU/mL), and heat-treated cells of Enterococcus faecalis (17 mg/kg, HED 1.4 mg/kg). These probiotic formulations have been evaluated in a variety of both in vitro and in vivo disease models, including dextran sulfate sodium (DSS)-induced ulcerative colitis [131], high-fat diet (HFD)-induced type 2 diabetes (T2D) [132], cerulean-induced acute pancreatitis [133], and colitis-associated colorectal carcinoma [134], as well as in studies involving porcine dendritic cells [135]. Furthermore, the beneficial effects of directly modulating the NLRP3 inflammasome have been demonstrated by the downregulation of pro-inflammatory cytokines and the concomitant upregulation of anti-inflammatory mediators. Similar immunomodulatory outcomes have been observed in animal feed trials and cell culture studies, where probiotics such as Lactobacillus rhamnoses GR-1 (1×10^5 CFU) and Lactobacillus johnsonii L531 (3×10^5 to 2×10^7 CFU) were employed to mitigate inflammation caused by bacterial pathogens. Specifically, these probiotics were effective in alleviating inflammatory responses triggered by Escherichia coli in porcine mammary epithelial cells, MAC-T cells, and a murine mastitis model, as well as by

Salmonella typhimurium in IPEC-J2 intestinal epithelial cells [135]. The application of these probiotics resulted in a reduction of bacterial adherence to host cells and diminished pathogen-induced alterations in cellular architecture. This, in turn, curtailed the production of reactive oxygen species (ROS) and subsequent activation of the host immune response. Attenuation of NLRP3 activity was associated with a downregulation of interleukins, tumor necrosis factor-alpha (TNF-α), and chemokine Cxcl2 expression. Simultaneously, the expression of the autophagic receptor SQSTM1/p62 was reduced, thereby preserving the integrity of tight junctions and limiting tissue damage [136].

6- Future Perspectives and conclusion

Future investigations may enhance our comprehension of the molecular and cellular dynamics of the NLRP3 inflammasome. Such insights could unveil novel pharmacological targets for addressing cardiovascular diseases. Given the NLRP3 inflammasome's connection to inflammation and heart-related ailments, there exists potential for the creation of advanced medications that directly aim at NLRP3. These medications may encompass either chemical or biological entities. By leveraging the principles of food science and technology, dietary supplements or particular nutritional formulations could be crafted to mitigate NLRP3 inflammasome stimulation, aiding in the prevention or management of cardiovascular illnesses. Upcoming studies might involve interdisciplinary partnerships that merge medical knowledge, food science, technology, and engineering acumen. These alliances could lead to groundbreaking progress in treating and preventing cardiovascular conditions. Innovations in modeling and simulation approaches could empower researchers to better discern the varying impacts of foods and supplements on the NLRP3 inflammasome and cardiovascular health. The specific pathways linking the NLRP3 inflammasome to cardiovascular disease remain inadequately delineated, and this ambiguity could pose obstacles to the formulation of effective therapies. Individual reactions to treatments and dietary interventions may differ, complicating the establishment of a uniform, efficacious strategy. Merging scientific principles with practical applications across these two disciplines may encounter difficulties, particularly in fostering collaboration between experts from both arenas. Assessing and gauging the efficacy of novel treatments and dietary interventions is intricate, particularly within clinical environments, necessitating meticulously structured clinical trials. The formulation of new therapies and nutritional compounds may also grapple with ethical and regulatory hurdles, potentially delaying research advancements. By capitalizing on available opportunities and surmounting the outlined challenges, a promising horizon for the treatment and prevention of cardiovascular ailments can be envisioned.

7- Reference

[1] Toldo, S., Mezzaroma, E., Buckley, L. F., Potere, N., Di Nisio, M., Biondi-Zoccai, G., ... & Abbate, A. (2022). Targeting the NLRP3 inflammasome in cardiovascular diseases. *Pharmacology & therapeutics*, *236*, 108053.

[2] Liu, D., Zeng, X., Li, X., Mehta, J. L., & Wang, X. (2018). Role of NLRP3 inflammasome in the pathogenesis of cardiovascular diseases. *Basic research in cardiology*, *113*, 1-14.

[3] Tong, Y., Wang, Z., Cai, L., Lin, L., Liu, J., & Cheng, J. (2020). NLRP3 inflammasome and its central role in the cardiovascular diseases. *Oxidative medicine and cellular longevity*, *2020*(1), 4293206.
[4] Pellegrini, C., Martelli, A., Antonioli, L., Fornai, M., Blandizzi, C., & Calderone, V. (2021). NLRP3 inflammasome in cardiovascular diseases: pathophysiological and pharmacological implications. *Medicinal Research Reviews*, *41*(4), 1890-1926.
[5] Toldo, S., & Abbate, A. (2024). The role of the NLRP3 inflammasome and pyroptosis in cardiovascular diseases. *Nature Reviews Cardiology*, *21*(4), 219-237.
[6] An, N., Gao, Y., Si, Z., Zhang, H., Wang, L., Tian, C., ... & Xing, Y. (2019). Regulatory mechanisms of the NLRP3 inflammasome, a novel immune-inflammatory marker in cardiovascular diseases. *Frontiers in immunology*, *10*, 1592.
[7] Zhou, H., Wang, L., Lv, W., & Yu, H. (2024). The NLRP3 inflammasome in allergic diseases: mechanisms and therapeutic implications. *Clinical and Experimental Medicine*, *24*(1), 231.
[8] Zheng, Y., Xu, L., Dong, N., & Li, F. (2022). NLRP3 inflammasome: The rising star in cardiovascular diseases. *Frontiers in Cardiovascular Medicine*, *9*, 927061.
[9] Mo, B., Ding, Y., & Ji, Q. (2025). NLRP3 inflammasome in cardiovascular diseases: an update. *Frontiers in Immunology*, *16*, 1550226.
[10] Takahashi, M. (2022). NLRP3 inflammasome as a key driver of vascular disease. *Cardiovascular research*, *118*(2), 372-385.
[11] Pavillard, L. E., Marín-Aguilar, F., Bullon, P., & Cordero, M. D. (2018). Cardiovascular diseases, NLRP3 inflammasome, and western dietary patterns. *Pharmacological research*, *131*, 44-50.
[12] Spano, M., Di Matteo, G., Ingallina, C., Ambroselli, D., Carradori, S., Gallorini, M., ... & Mannina, L. (2022). Modulatory properties of food and nutraceutical components targeting NLRP3 inflammasome activation. *Nutrients*, *14*(3), 490.
[13] Granato, D. (2022). Functional foods to counterbalance low-grade inflammation and oxidative stress in cardiovascular diseases: a multilayered strategy combining food and health sciences. *Current Opinion in Food Science*, *47*, 100894.
[14] Eussen, S. R., Feenstra, T. L., Toxopeus, I. B., Hoekstra, J., Klungel, O. H., Verhagen, H., ... & Rompelberg, C. J. (2011). Costs and health effects of adding functional foods containing phytosterols/-stanols to statin therapy in the prevention of cardiovascular disease. *European journal of pharmacology*, *668*, S91-S100.
[15] Lin, X., Bo, H., Gu, J., Yi, X., Zhang, P., Liu, R., ... & Lin, C. H. (2022). Astaxanthin, a carotenoid antioxidant, pretreatment alleviates cognitive deficits in aircraft noised mice by attenuating inflammatory and oxidative damage to the gut, heart and hippocampus. *Biomedicine & Pharmacotherapy*, *148*, 112777.
[16] Donia, T., & Khamis, A. (2021). Management of oxidative stress and inflammation in cardiovascular diseases: mechanisms and challenges. *Environmental Science and Pollution Research*, *28*(26), 34121-34153.
[17] Toldo, S., & Abbate, A. (2018). The NLRP3 inflammasome in acute myocardial infarction. *Nature Reviews Cardiology*, *15*(4), 203-214.
[18] Toldo, S., Mezzaroma, E., Mauro, A. G., Salloum, F., Van Tassell, B. W., & Abbate, A. (2015). The inflammasome in myocardial injury and cardiac remodeling. *Antioxidants & redox signaling*, *22*(13), 1146-1161.
[19] Abbate, A., Toldo, S., Marchetti, C., Kron, J., Van Tassell, B. W., & Dinarello, C. A. (2020). Interleukin-1 and the inflammasome as therapeutic targets in cardiovascular disease. *Circulation research*, *126*(9), 1260-1280.
[20] Toldo, S., Mauro, A. G., Cutter, Z., & Abbate, A. (2018). Inflammasome, pyroptosis, and cytokines in myocardial ischemia-reperfusion injury. *American Journal of Physiology-Heart and Circulatory Physiology*, *315*(6), H1553-H1568.
[21] Mezzaroma, E., Abbate, A., & Toldo, S. (2021). NLRP3 inflammasome inhibitors in cardiovascular diseases. *Molecules*, *26*(4), 976.
[22] Moore, K. J., Sheedy, F. J., & Fisher, E. A. (2013). Macrophages in atherosclerosis: a dynamic balance. *Nature Reviews Immunology*, *13*(10), 709-721.
[23] Pazár, B., Ea, H. K., Narayan, S., Kolly, L., Bagnoud, N., Chobaz, V., ... & Busso, N. (2011). Basic calcium phosphate crystals induce monocyte/macrophage IL-1β secretion through the NLRP3 inflammasome in vitro. *The Journal of Immunology*, *186*(4), 2495-2502.
[24] Duewell, P., Kono, H., Rayner, K. J., Sirois, C. M., Vladimer, G., Bauernfeind, F. G., ... & Latz, E. (2010). NLRP3 inflammasomes are required for atherogenesis and activated by cholesterol crystals. *Nature*, *464*(7293), 1357-1361.
[25] Sun, Q., Fan, J., Billiar, T. R., & Scott, M. J. (2017). Inflammasome and autophagy regulation: a two-way street. *Molecular Medicine*, *23*, 188-195.
[26] Liu, Y., Lian, K., Zhang, L., Wang, R., Yi, F., Gao, C., ... & Tao, L. (2014). TXNIP mediates NLRP3 inflammasome activation in cardiac microvascular endothelial cells as a novel mechanism in myocardial ischemia/reperfusion injury. *Basic research in cardiology*, *109*, 1-14.

[27] Kawaguchi, M., Takahashi, M., Hata, T., Kashima, Y., Usui, F., Morimoto, H., ... & Ikeda, U. (2011). Inflammasome activation of cardiac fibroblasts is essential for myocardial ischemia/reperfusion injury. *Circulation*, *123*(6), 594-604.
[28] Toldo, S., Marchetti, C., Mauro, A. G., Chojnacki, J., Mezzaroma, E., Carbone, S., ... & Abbate, A. (2016). Inhibition of the NLRP3 inflammasome limits the inflammatory injury following myocardial ischemia–reperfusion in the mouse. *International Journal of Cardiology*, *209*, 215-220.
[29] Westman, P. C., Lipinski, M. J., Luger, D., Waksman, R., Bonow, R. O., Wu, E., & Epstein, S. E. (2016). Inflammation as a driver of adverse left ventricular remodeling after acute myocardial infarction. *Journal of the American College of Cardiology*, *67*(17), 2050-2060.
[30] Seropian, I. M., Toldo, S., Van Tassell, B. W., & Abbate, A. (2014). Anti-inflammatory strategies for ventricular remodeling following ST-segment elevation acute myocardial infarction. *Journal of the American College of Cardiology*, *63*(16), 1593-1603.
[31] Zeng, C., Duan, F., Hu, J., Luo, B., Huang, B., Lou, X., ... & Tan, H. (2020). NLRP3 inflammasome-mediated pyroptosis contributes to the pathogenesis of non-ischemic dilated cardiomyopathy. *Redox biology*, *34*, 101523.
[32] Gan, W., Ren, J., Li, T., Lv, S., Li, C., Liu, Z., & Yang, M. (2018). The SGK1 inhibitor EMD638683, prevents Angiotensin II–induced cardiac inflammation and fibrosis by blocking NLRP3 inflammasome activation. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, *1864*(1), 1-10.
[33] Lian, D., Lai, J., Wu, Y., Wang, L., Chen, Y., Zhang, Y., ... & Chen, Y. (2018). Cathepsin B-mediated NLRP3 inflammasome formation and activation in angiotensin II-induced hypertensive mice: role of macrophage digestion dysfunction. *Cellular Physiology and Biochemistry*, *50*(4), 1585-1600.
[34] Suetomi, T., Willeford, A., Brand, C. S., Cho, Y., Ross, R. S., Miyamoto, S., & Brown, J. H. (2018). Inflammation and NLRP3 inflammasome activation initiated in response to pressure overload by Ca2+/calmodulin-dependent protein kinase II δ signaling in cardiomyocytes are essential for adverse cardiac remodeling. *Circulation*, *138*(22), 2530-2544.
[35] Renu, K., Abilash, V. G., PB, T. P., & Arunachalam, S. (2018). Molecular mechanism of doxorubicin-induced cardiomyopathy–An update. *European journal of pharmacology*, *818*, 241-253.
[36] Singla, D. K., Johnson, T. A., & Tavakoli Dargani, Z. (2019). Exosome treatment enhances anti-inflammatory M2 macrophages and reduces inflammation-induced pyroptosis in doxorubicin-induced cardiomyopathy. *Cells*, *8*(10), 1224.
[37] Singla, D. K., Johnson, T. A., & Tavakoli Dargani, Z. (2019). Exosome treatment enhances anti-inflammatory M2 macrophages and reduces inflammation-induced pyroptosis in doxorubicin-induced cardiomyopathy. *Cells*, *8*(10), 1224.
[38] Cai, J., Lu, S., Yao, Z., Deng, Y. P., Zhang, L. D., Yu, J. W., ... & Jiang, G. J. (2014). Glibenclamide attenuates myocardial injury by lipopolysaccharides in streptozotocin-induced diabetic mice. *Cardiovascular diabetology*, *13*, 1-11.
[39] Ralston, J. C., Lyons, C. L., Kennedy, E. B., Kirwan, A. M., & Roche, H. M. (2017). Fatty acids and NLRP3 inflammasome–mediated inflammation in metabolic tissues. *Annual review of nutrition*, *37*(1), 77-102.
[40] Feng, H., Gu, J., Gou, F., Huang, W., Gao, C., Chen, G., ... & Xu, Y. (2016). High glucose and lipopolysaccharide prime NLRP3 inflammasome via ROS/TXNIP pathway in mesangial cells. *Journal of Diabetes Research*, *2016*(1), 6973175.
[41] Chen, W., Zhao, M., Zhao, S., Lu, Q., Ni, L., Zou, C., ... & Qiu, Q. (2017). Activation of the TXNIP/NLRP3 inflammasome pathway contributes to inflammation in diabetic retinopathy: a novel inhibitory effect of minocycline. *Inflammation Research*, *66*, 157-166.
[42] Mauro, A. G., Bonaventura, A., Vecchié, A., Mezzaroma, E., Carbone, S., Narayan, P., ... & Toldo, S. (2021). The role of NLRP3 inflammasome in pericarditis: potential for therapeutic approaches. *Basic to Translational Science*, *6*(2), 137-150.
[43] Klein, A. L., Imazio, M., Cremer, P., Brucato, A., Abbate, A., Fang, F., ... & Paolini, J. F. (2021). Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. *New England Journal of Medicine*, *384*(1), 31-41.
[44] Brucato, A., Imazio, M., Gattorno, M., Lazaros, G., Maestroni, S., Carraro, M., ... & Martini, A. (2016). Effect of anakinra on recurrent pericarditis among patients with colchicine resistance and corticosteroid dependence: the AIRTRIP randomized clinical trial. *Jama*, *316*(18), 1906-1912.
[45] Wang, Y., Gao, B., & Xiong, S. (2014). Involvement of NLRP3 inflammasome in CVB3-induced viral myocarditis. *American Journal of Physiology-Heart and Circulatory Physiology*, *307*(10), H1438-H1447.
[46] Wang, Y., Jia, L., Shen, J., Wang, Y., Fu, Z., Su, S. A., ... & Xiang, M. (2018). Cathepsin B aggravates coxsackievirus B3-induced myocarditis

through activating the inflammasome and promoting pyroptosis. *PLoS pathogens*, *14*(1), e1006872.
[47] Kron, J., Mauro, A. G., Bonaventura, A., Toldo, S., Salloum, F. N., Ellenbogen, K. A., & Abbate, A. (2019). Inflammasome formation in granulomas in cardiac sarcoidosis. *Circulation: Arrhythmia and Electrophysiology*, *12*(9), e007582.
[48] Gupta, N., Sahu, A., Prabhakar, A., Chatterjee, T., Tyagi, T., Kumari, B., ... & Ashraf, M. Z. (2017). Activation of NLRP3 inflammasome complex potentiates venous thrombosis in response to hypoxia. *Proceedings of the National Academy of Sciences*, *114*(18), 4763-4768.
[49] Yadav, V., Chi, L., Zhao, R., Tourdot, B. E., Yalavarthi, S., Jacobs, B. N., ... & Kanthi, Y. (2019). ENTPD-1 disrupts inflammasome IL-1β–driven venous thrombosis. *The Journal of clinical investigation*, *129*(7), 2872-2877.
[50] Campos, J., Ponomaryov, T., De Prendergast, A., Whitworth, K., Smith, C. W., Khan, A. O., ... & Brill, A. (2021). Neutrophil extracellular traps and inflammasomes cooperatively promote venous thrombosis in mice. *Blood advances*, *5*(9), 2319-2324.
[51] Rabinovich, A., Cohen, J. M., Cushman, M., Kahn, S. R., Anderson, D. R., Chagnon, I., ... & Yeo, E. (2015). Association between inflammation biomarkers, anatomic extent of deep venous thrombosis, and venous symptoms after deep venous thrombosis. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *3*(4), 347-353.
[52] Wu, C., Lu, W., Zhang, Y., Zhang, G., Shi, X., Hisada, Y., ... & Li, Z. (2019). Inflammasome activation triggers blood clotting and host death through pyroptosis. *Immunity*, *50*(6), 1401-1411.
[53] Roumen-Klappe, E. M., Janssen, M. C. H., Van Rossum, J., Holewijn, S., Van Bokhoven, M. M. J. A., Kaasjager, K., ... & Den Heijer, M. (2009). Inflammation in deep vein thrombosis and the development of post-thrombotic syndrome: a prospective study. *Journal of Thrombosis and Haemostasis*, *7*(4), 582-587.
[54] Jara-Palomares, L., Solier-Lopez, A., Elias-Hernandez, T., Asensio-Cruz, M. I., Blasco-Esquivias, I., Sanchez-Lopez, V., ... & Otero-Candelera, R. (2018). D-dimer and high-sensitivity C-reactive protein levels to predict venous thromboembolism recurrence after discontinuation of anticoagulation for cancer-associated thrombosis. *British journal of cancer*, *119*(8), 915-921.
[55] Kunutsor, S. K., Seidu, S., Blom, A. W., Khunti, K., & Laukkanen, J. A. (2017). Serum C-reactive protein increases the risk of venous thromboembolism: a prospective study and meta-analysis of published prospective evidence. *European Journal of Epidemiology*, *32*, 657-667.
[56] Zheng, M., Williams, E. P., Malireddi, R. S., Karki, R., Banoth, B., Burton, A., ... & Kanneganti, T. D. (2020). Impaired NLRP3 inflammasome activation/pyroptosis leads to robust inflammatory cell death via caspase-8/RIPK3 during coronavirus infection. *Journal of Biological Chemistry*, *295*(41), 14040-14052.
[57] Gupta, N., Sahu, A., Prabhakar, A., Chatterjee, T., Tyagi, T., Kumari, B., ... & Ashraf, M. Z. (2017). Activation of NLRP3 inflammasome complex potentiates venous thrombosis in response to hypoxia. *Proceedings of the National Academy of Sciences*, *114*(18), 4763-4768.
[58] Colling, M. E., Tourdot, B. E., & Kanthi, Y. (2021). Inflammation, infection and venous thromboembolism. *Circulation research*, *128*(12), 2017-2036.
[59] Pellegrini, C., Martelli, A., Antonioli, L., Fornai, M., Blandizzi, C., & Calderone, V. (2021). NLRP3 inflammasome in cardiovascular diseases: pathophysiological and pharmacological implications. *Medicinal Research Reviews*, *41*(4), 1890-1926.
[60] Hotamisligil, G. S. (2017). Inflammation, metaflammation and immunometabolic disorders. *Nature*, *542*(7640), 177-185.
[61] Alvarenga, L., Cardozo, L. F., Borges, N. A., Lindholm, B., Stenvinkel, P., Shiels, P. G., ... & Mafra, D. (2020). Can nutritional interventions modulate the activation of the NLRP3 inflammasome in chronic kidney disease?. *Food Research International*, *136*, 109306.
[62] DROBNY, E. C., ABRAMSON, E. C., & BAUMANN, G. (1984). Insulin receptors in acute infection: a study of factors conferring insulin resistance. *The Journal of Clinical Endocrinology & Metabolism*, *58*(4), 710-716.
[63] Calder, P. C., Ahluwalia, N., Brouns, F., Buetler, T., Clement, K., Cunningham, K., ... & Winklhofer-Roob, B. M. (2011). Dietary factors and low-grade inflammation in relation to overweight and obesity. *British journal of nutrition*, *106*(S3), S1-S78.
[64] Lumeng, C. N., & Saltiel, A. R. (2011). Inflammatory links between obesity and metabolic disease. *The Journal of clinical investigation*, *121*(6), 2111-2117.
[65] Barbaresko, J., Koch, M., Schulze, M. B., & Nöthlings, U. (2013). Dietary pattern analysis and biomarkers of low-grade inflammation: a systematic literature review. *Nutrition reviews*, *71*(8), 511-527.
[66] Schroder, K., & Tschopp, J. (2010). The inflammasomes. *cell*, *140*(6), 821-832.
[67] Tack, C. J., Stienstra, R., Joosten, L. A., & Netea, M. G. (2012). Inflammation links excess fat to insulin resistance: the role of the interleukin-1 family. *Immunological reviews*, *249*(1), 239-252.

[68] Pandey, K. B., & Rizvi, S. I. (2009). Plant polyphenols as dietary antioxidants in human health and disease. *Oxidative medicine and cellular longevity*, *2*(5), 270-278.
[69] Li, A. N., Li, S., Zhang, Y. J., Xu, X. R., Chen, Y. M., & Li, H. B. (2014). Resources and biological activities of natural polyphenols. *Nutrients*, *6*(12), 6020-6047.
[70] Tsao, R. (2010). Chemistry and biochemistry of dietary polyphenols. *Nutrients*, *2*(12), 1231-1246.
[71] Zhang, H., & Tsao, R. (2016). Dietary polyphenols, oxidative stress and antioxidant and anti-inflammatory effects. *Current Opinion in Food Science*, *8*, 33-42.
[72] Chen, C. (2016). Sinapic acid and its derivatives as medicine in oxidative stress-induced diseases and aging. *Oxidative medicine and cellular longevity*, *2016*(1), 3571614.
[73] Rosazza, J. P. N., Huang, Z., Dostal, L., Volm, T., & Rousseau, B. (1995). Biocatalytic transformations of ferulic acid: an abundant aromatic natural product. *Journal of industrial microbiology and biotechnology*, *15*(6), 457-471.
[74] Santana-Gálvez, J., Cisneros-Zevallos, L., & Jacobo-Velázquez, D. A. (2017). Chlorogenic acid: Recent advances on its dual role as a food additive and a nutraceutical against metabolic syndrome. *Molecules*, *22*(3), 358.
[75] Ho, S. C., Chang, Y. H., & Chang, K. S. (2018). Structural moieties required for cinnamaldehyde-related compounds to inhibit canonical IL-1β secretion. *Molecules*, *23*(12), 3241.
[76] Liu, P., Wang, J., Wen, W., Pan, T., Chen, H., Fu, Y., ... & Xu, S. (2020). Cinnamaldehyde suppresses NLRP3 derived IL-1β via activating succinate/HIF-1 in rheumatoid arthritis rats. *International Immunopharmacology*, *84*, 106570.
[77] Zeng, J., Zhang, D., Wan, X., Bai, Y., Yuan, C., Wang, T., ... & Liu, C. (2020). Chlorogenic acid suppresses miR-155 and ameliorates ulcerative colitis through the NF-κB/NLRP3 inflammasome pathway. *Molecular Nutrition & Food Research*, *64*(23), 2000452.
[78] Lv, Y., Gao, X., Luo, Y., Fan, W., Shen, T., Ding, C., ... & Yan, L. (2019). Apigenin ameliorates HFD-induced NAFLD through regulation of the XO/NLRP3 pathways. *The Journal of nutritional biochemistry*, *71*, 110-121.
[79] Yamagata, K., Hashiguchi, K., Yamamoto, H., & Tagami, M. (2019). Dietary apigenin reduces induction of LOX-1 and NLRP3 expression, leukocyte adhesion, and acetylated low-density lipoprotein uptake in human endothelial cells exposed to trimethylamine-N-oxide. *Journal of cardiovascular pharmacology*, *74*(6), 558-565.
[80] An, M. F., Wang, M. Y., Shen, C., Sun, Z. R., Zhao, Y. L., Wang, X. J., & Sheng, J. (2021). Isoorientin exerts a urate-lowering effect through inhibition of xanthine oxidase and regulation of the TLR4-NLRP3 inflammasome signaling pathway. *Journal of natural medicines*, *75*, 129-141.
[81] Chang, Y. H., Chiang, Y. F., Chen, H. Y., Huang, Y. J., Wang, K. L., Hong, Y. H., ... & Hsia, S. M. (2021). Anti-inflammatory and anti-hyperuricemic effects of chrysin on a high fructose corn syrup-induced hyperuricemia rat model via the amelioration of urate transporters and inhibition of NLRP3 inflammasome signaling pathway. *Antioxidants*, *10*(4), 564.
[82] Fu, J., Sun, H., Zhang, Y., Xu, W., Wang, C., Fang, Y., & Zhao, J. (2018). Neuroprotective effects of luteolin against spinal cord ischemia–reperfusion injury by attenuation of oxidative stress, inflammation, and apoptosis. *Journal of Medicinal Food*, *21*(1), 13-20.
[83] Cao, H., Liu, J., Shen, P., Cai, J., Han, Y., Zhu, K., ... & Cao, Y. (2018). Protective effect of naringin on DSS-induced ulcerative colitis in mice. *Journal of agricultural and food chemistry*, *66*(50), 13133-13140.
[84] Ruiz-Miyazawa, K. W., Pinho-Ribeiro, F. A., Borghi, S. M., Staurengo-Ferrari, L., Fattori, V., Amaral, F. A., ... & Verri Jr, W. A. (2018). Hesperidin methylchalcone suppresses experimental gout arthritis in mice by inhibiting NF-κB activation. *Journal of agricultural and food chemistry*, *66*(25), 6269-6280.
[85] Wang, S., Meckling, K. A., Marcone, M. F., Kakuda, Y., & Tsao, R. (2011). Synergistic, additive, and antagonistic effects of food mixtures on total antioxidant capacities. *Journal of agricultural and food chemistry*, *59*(3), 960-968.
[86] Luzardo-Ocampo, I., Loarca-Piña, G., & de Mejia, E. G. (2020). Gallic and butyric acids modulated NLRP3 inflammasome markers in a co-culture model of intestinal inflammation. *Food and chemical toxicology*, *146*, 111835.
[87] Wang, D., Gao, Q., Wang, T., Kan, Z., Li, X., Hu, L., ... & Granato, D. (2020). Green tea polyphenols and epigallocatechin-3-gallate protect against perfluorodecanoic acid induced liver damage and inflammation in mice by inhibiting NLRP3 inflammasome activation. *Food Research International*, *127*, 108628.
[88] Wang, D., Zhang, M., Wang, T., Cai, M., Qian, F., Sun, Y., & Wang, Y. (2019). Green tea polyphenols prevent lipopolysaccharide-induced inflammatory liver injury in mice by inhibiting NLRP3 inflammasome activation. *Food & function*, *10*(7), 3898-3908.

[89] Ruhee, R. T., Roberts, L. A., Ma, S., & Suzuki, K. (2020). Organosulfur compounds: A review of their anti-inflammatory effects in human health. *Frontiers in nutrition*, *7*, 64.
[90] Putnik, P., Gabrić, D., Roohinejad, S., Barba, F. J., Granato, D., Mallikarjunan, K., ... & Kovačević, D. B. (2019). An overview of organosulfur compounds from Allium spp.: From processing and preservation to evaluation of their bioavailability, antimicrobial, and anti-inflammatory properties. *Food chemistry*, *276*, 680-691.
[91] Dong, Z., Shang, H., Chen, Y. Q., Pan, L. L., Bhatia, M., & Sun, J. (2016). Sulforaphane protects pancreatic acinar cell injury by modulating Nrf2-mediated oxidative stress and NLRP3 inflammatory pathway. *Oxidative medicine and cellular longevity*, *2016*(1), 7864150.
[92] Ahn, H., Kim, J., Lee, M. J., Kim, Y. J., Cho, Y. W., & Lee, G. S. (2015). Methylsulfonylmethane inhibits NLRP3 inflammasome activation. *Cytokine*, *71*(2), 223-231.
[93] Chen, H. W., Yen, C. C., Kuo, L. L., Lo, C. W., Huang, C. S., Chen, C. C., & Lii, C. K. (2020). Benzyl isothiocyanate ameliorates high-fat/cholesterol/cholic acid diet-induced nonalcoholic steatohepatitis through inhibiting cholesterol crystal-activated NLRP3 inflammasome in Kupffer cells. *Toxicology and Applied Pharmacology*, *393*, 114941.
[94] Nan, B., Yang, C., Li, L., Ye, H., Yan, H., Wang, M., & Yuan, Y. (2021). Allicin alleviated acrylamide-induced NLRP3 inflammasome activation via oxidative stress and endoplasmic reticulum stress in Kupffer cells and SD rats liver. *Food and Chemical Toxicology*, *148*, 111937.
[95] Yang, W., Chen, X., Li, Y., Guo, S., Wang, Z., & Yu, X. (2020). Advances in pharmacological activities of terpenoids. *Natural Product Communications*, *15*(3), 1934578X20903555.
[96] Yang, N., Xia, Z., Shao, N., Li, B., Xue, L., Peng, Y., ... & Yang, Y. (2017). Carnosic acid prevents dextran sulfate sodium-induced acute colitis associated with the regulation of the Keap1/Nrf2 pathway. *Scientific Reports*, *7*(1), 11036.
[97] Marcuzzi, A., Piscianz, E., Zweyer, M., Bortul, R., Loganes, C., Girardelli, M., ... & Celeghini, C. (2016). Geranylgeraniol and neurological impairment: Involvement of apoptosis and mitochondrial morphology. *International journal of molecular sciences*, *17*(3), 365.
[98] Miranda, M. M., Panis, C., da Silva, S. S., Macri, J. A., Kawakami, N. Y., Hayashida, T. H., ... & Pavanelli, W. R. (2015). Kaurenoic Acid Possesses Leishmanicidal Activity by Triggering a NLRP12/IL-1β/cNOS/NO Pathway. *Mediators of inflammation*, *2015*(1), 392918.
[99] Yang, X., Wu, F., Li, L., Lynch, E. C., Xie, L., Zhao, Y., ... & Chen, G. (2021). Celastrol alleviates metabolic disturbance in high-fat diet-induced obese mice through increasing energy expenditure by ameliorating metabolic inflammation. *Phytotherapy research*, *35*(1), 297-310.
[100] Li, J., Li, X., Wang, X., Zhong, X., Ji, L., Guo, Z., ... & Shang, X. (2019). Sesquiterpenoids and their anti-inflammatory activity: Evaluation of Ainsliaea yunnanensis. *Molecules*, *24*(9), 1701.
[101] Ralston, J. C., Lyons, C. L., Kennedy, E. B., Kirwan, A. M., & Roche, H. M. (2017). Fatty acids and NLRP3 inflammasome–mediated inflammation in metabolic tissues. *Annual review of nutrition*, *37*(1), 77-102.
[102] Wen, H., Gris, D., Lei, Y., Jha, S., Zhang, L., Huang, M. T. H., ... & Ting, J. P. (2011). Fatty acid–induced NLRP3-ASC inflammasome activation interferes with insulin signaling. *Nature immunology*, *12*(5), 408-415.
[103] Robblee, M. M., Kim, C. C., Abate, J. P., Valdearcos, M., Sandlund, K. L., Shenoy, M. K., ... & Koliwad, S. K. (2016). Saturated fatty acids engage an IRE1α-dependent pathway to activate the NLRP3 inflammasome in myeloid cells. *Cell reports*, *14*(11), 2611-2623.
[104] Gianfrancesco, M. A., Dehairs, J., L'homme, L., Herinckx, G., Esser, N., Jansen, O., ... & Legrand-Poels, S. (2019). Saturated fatty acids induce NLRP3 activation in human macrophages through K+ efflux resulting from phospholipid saturation and Na, K-ATPase disruption. *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids*, *1864*(7), 1017-1030.
[105] Witcher, K. J., Novick, R. P., & Schlievert, P. M. (1996). Modulation of immune cell proliferation by glycerol monolaurate. *Clinical Diagnostic Laboratory Immunology*, *3*(1), 10-13.
[106] Mirzaei, F., Khazaei, M., Komaki, A., Amiri, I., & Jalili, C. (2018). Virgin coconut oil (VCO) by normalizing NLRP3 inflammasome showed potential neuroprotective effects in Amyloid-β induced toxicity and high-fat diet fed rat. *Food and Chemical Toxicology*, *118*, 68-83.
[107] Gao, H., Lv, Y., Liu, Y., Li, J., Wang, X., Zhou, Z., ... & Xiao, J. (2019). Wolfberry-derived zeaxanthin dipalmitate attenuates ethanol-induced hepatic damage. *Molecular Nutrition & Food Research*, *63*(11), 1801339.
[108] Wu, L., Lyu, Y., Srinivasagan, R., Wu, J., Ojo, B., Tang, M., ... & Lin, D. (2020). Astaxanthin-shifted gut microbiota is associated with inflammation and metabolic homeostasis in mice. *The Journal of Nutrition*, *150*(10), 2687-2698.
[109] Liu, N., Meng, B., Zeng, L., Yin, S., Hu, Y., Li, S., ... & Yang, X. (2020). Discovery of a novel rice-

derived peptide with significant anti-gout potency. *Food & Function*, *11*(12), 10542-10553.
[110] Liu, N., Wang, Y., Zeng, L., Yin, S., Hu, Y., Li, S., ... & Yang, X. (2020). RDP3, a novel antigout peptide derived from water extract of rice. *Journal of Agricultural and Food Chemistry*, *68*(27), 7143-7151.
[111] Han, J., Wang, X., Tang, S., Lu, C., Wan, H., Zhou, J., ... & Su, X. (2020). Protective effects of tuna meat oligopeptides (TMOP) supplementation on hyperuricemia and associated renal inflammation mediated by gut microbiota. *The FASEB Journal*, *34*(4), 5061-5076.
[112] Bitzer, Z. T., Wopperer, A. L., Chrisfield, B. J., Tao, L., Cooper, T. K., Vanamala, J., ... & Lambert, J. D. (2017). Soy protein concentrate mitigates markers of colonic inflammation and loss of gut barrier function in vitro and in vivo. *The Journal of nutritional biochemistry*, *40*, 201-208.
[113] Huang, Y. C., Lin, C. Y., Huang, S. F., Lin, H. C., Chang, W. L., & Chang, T. C. (2010). Effect and mechanism of ginsenosides CK and Rg1 on stimulation of glucose uptake in 3T3-L1 adipocytes. *Journal of agricultural and food chemistry*, *58*(10), 6039-6047.
[114] Wu, Y. L., Wan, Y., Jin, X. J., OuYang, B. Q., Bai, T., Zhao, Y. Q., & Nan, J. X. (2011). 25-OCH3-PPD induces the apoptosis of activated t-HSC/Cl-6 cells via c-FLIP-mediated NF-κB activation. *Chemico-Biological Interactions*, *194*(2-3), 106-112.
[115] Han, X., Song, J., Lian, L. H., Yao, Y. L., Shao, D. Y., Fan, Y., ... & Nan, J. X. (2018). Ginsenoside 25-OCH3-PPD promotes activity of LXRs to ameliorate P2X7R-mediated NLRP3 inflammasome in the development of hepatic fibrosis. *Journal of Agricultural and Food Chemistry*, *66*(27), 7023-7035.
[116] Wang, F., Park, J. S., Ma, Y., Ma, H., Lee, Y. J., Lee, G. R., ... & Roh, Y. S. (2021). Ginseng saponin enriched in Rh1 and Rg2 ameliorates nonalcoholic fatty liver disease by inhibiting inflammasome activation. *Nutrients*, *13*(3), 856.
[117] Han, G. C., Ko, S. K., Sung, J. H., & Chung, S. H. (2007). Compound K enhances insulin secretion with beneficial metabolic effects in db/db mice. *Journal of Agricultural and Food Chemistry*, *55*(26), 10641-10648.
[118] Li, C. W., Deng, M. Z., Gao, Z. J., Dang, Y. Y., Zheng, G. D., Yang, X. J., ... & Wu, X. L. (2020). Effects of compound K, a metabolite of ginsenosides, on memory and cognitive dysfunction in db/db mice involve the inhibition of ER stress and the NLRP3 inflammasome pathway. *Food & Function*, *11*(5), 4416-4427.
[119] Zhao, X. J., Yang, Y. Z., Zheng, Y. J., Wang, S. C., Gu, H. M., Pan, Y., ... & Kong, L. D. (2018). Dataset on assessment of magnesium isoglycyrrhizinate injection for dairy diet and body weight in fructose-induced metabolic syndrome of rats. *Data in brief*, *18*, 69.
[120] Zheng, Y., Fan, J., Chen, H. W., & Liu, E. Q. (2019). Trametes orientalis polysaccharide alleviates PM 2.5-induced lung injury in mice through its antioxidant and anti-inflammatory activities. *Food & function*, *10*(12), 8005-8015.
[121] Liang, J., Chen, S., Chen, J., Lin, J., Xiong, Q., Yang, Y., ... & Lai, X. (2018). Therapeutic roles of polysaccharides from Dendrobium Officinaleon colitis and its underlying mechanisms. *Carbohydrate Polymers*, *185*, 159-168.
[122] Li, P., Xiao, N., Zeng, L., Xiao, J., Huang, J., Xu, Y., ... & Du, B. (2020). Structural characteristics of a mannoglucan isolated from Chinese yam and its treatment effects against gut microbiota dysbiosis and DSS-induced colitis in mice. *Carbohydrate Polymers*, *250*, 116958.
[123] Chen, Y. S., Chen, Q. Z., Wang, Z. J., & Hua, C. (2019). Anti-inflammatory and hepatoprotective effects of Ganoderma lucidum polysaccharides against carbon tetrachloride-induced liver injury in Kunming mice. *Pharmacology*, *103*(3-4), 143-150.
[124] Yang, R., Li, Y., Cai, J., Ji, J., Wang, Y., Zhang, W., ... & Chen, Y. (2020). Polysaccharides from Armillariella tabescens mycelia ameliorate insulin resistance in type 2 diabetic mice. *Food & Function*, *11*(11), 9675-9685.
[125] Wu, C., Pan, L. L., Niu, W., Fang, X., Liang, W., Li, J., ... & Sun, J. (2019). Modulation of gut microbiota by low methoxyl pectin attenuates type 1 diabetes in non-obese diabetic mice. *Frontiers in immunology*, *10*, 1733.
[126] Castro-Alves, V. C., Shiga, T. M., & do Nascimento, J. R. O. (2019). Polysaccharides from chayote enhance lipid efflux and regulate NLRP3 inflammasome priming in macrophage-like THP-1 cells exposed to cholesterol crystals. *International Journal of Biological Macromolecules*, *127*, 502-510.
[127] Liu, Y., Wu, X., Wang, Y., Jin, W., & Guo, Y. (2020). The immunoenhancement effects of starfish Asterias rollestoni polysaccharides in macrophages and cyclophosphamide-induced immunosuppression mouse models. *Food & Function*, *11*(12), 10700-10708.
[128] Wallert, M., Börmel, L., & Lorkowski, S. (2021). Inflammatory diseases and vitamin E—what do we know and where do we go?. Molecular Nutrition & Food Research, 65(1), 2000097.
[129] Tapia, G., Silva, D., Romero, N., Pettinelli, P., Dossi, C. G., De Miguel, M., & González-Mañán, D. (2018). Role of dietary α-and γ-tocopherol from Rosa mosqueta oil in the prevention of alterations

induced by high-fat diet in a murine model. *Nutrition*, *53*, 1-8.
[130] Tapia, G., Silva, D., Romero, N., Pettinelli, P., Dossi, C. G., De Miguel, M., & González-Mañán, D. (2018). Role of dietary α-and γ-tocopherol from Rosa mosqueta oil in the prevention of alterations induced by high-fat diet in a murine model. *Nutrition*, *53*, 1-8.
[131] Sheng, K., He, S., Sun, M., Zhang, G., Kong, X., Wang, J., & Wang, Y. (2020). Synbiotic supplementation containing Bifidobacterium infantis and xylooligosaccharides alleviates dextran sulfate sodium-induced ulcerative colitis. *Food & Function*, *11*(5), 3964-3974.
[132] Suzuki, H., Yamazaki, T., Ohshio, K., Sugamata, M., Yoshikawa, M., Kanauchi, O., & Morita, Y. (2020). A specific strain of lactic acid bacteria, lactobacillus paracasei, inhibits inflammasome activation in vitro and prevents inflammation-related disorders. *The Journal of Immunology*, *205*(3), 811-821.
[133] Pan, X., Fang, X., Wang, F., Li, H., Niu, W., Liang, W., ... & Sun, J. (2019). Butyrate ameliorates caerulein-induced acute pancreatitis and associated intestinal injury by tissue-specific mechanisms. *British journal of pharmacology*, *176*(23), 4446-4461.
[134] Chung, I. C., OuYang, C. N., Yuan, S. N., Lin, H. C., Huang, K. Y., Wu, P. S., ... & Chen, L. C. (2019). Pretreatment with a heat-killed probiotic modulates the NLRP3 inflammasome and attenuates colitis-associated colorectal cancer in mice. *Nutrients*, *11*(3), 516.
[135] Loss, H., Aschenbach, J. R., Ebner, F., Tedin, K., & Lodemann, U. (2018). Effects of a pathogenic ETEC strain and a probiotic Enterococcus faecium strain on the inflammasome response in porcine dendritic cells. *Veterinary immunology and immunopathology*, *203*, 78-87.
[136] Zou, Y. J., Xu, J. J., Wang, X., Zhu, Y. H., Wu, Q., & Wang, J. F. (2020). Lactobacillus johnsonii l531 ameliorates Escherichia coli-induced cell damage via inhibiting NLRP3 inflammasome activity and promoting ATG5/ATG16L1-mediated autophagy in porcine mammary epithelial cells. *Veterinary Sciences*, *7*(3), 112.