DOI: 10.26599/FSHW.2025.9250515

Contents lists available at SciOpen

Food Science and Human Wellness

journal homepage: https://www.sciopen.com/journal/2097-0765

China Food Publishing Co.

Rice protein: Recent advances in composition and protential physiological functions

Bingxiao Liu[a], Zhengxuan Wang[b], Shuangding Lai[a] and Lin Yang[a,*]

[a]*School of Chemistry and Chemical Engineering, Harbin Institute of Technology, Harbin 150001, China*

[b]*Faculty of Food Science and Engineering, Kunming University of Science and Technology, Kunming 650500, China*

ABSTRACT: Rice, a crucial food crop, provides high-quality protein with well-balanced nutrition, consistent with FAO/WTO guidelines. Recent studies have focused on the composition and potential health benefits of rice protein, along with the challenges of applying it in the food industry. Renowned for its hypoallergenic properties, rice protein encompasses albumin, globulin, glutelin, and protein, constituting a rich source of essential amino acids vital for human health. Recent research has found that rice protein has various physiological functions, such as anti-oxidant, anti-inflammatory, DNA protective effect, lipid-lowering effect, anti-hypertensive, anti-diabetic, anti-cancer, etc. Due to its potential role in physiological regulation, rice protein is an ideal source for developing nutritional products and protein-rich ingredients. This review article aims to summarize the latest research progress in these areas. This review article aims to summarize the composition and various physiological functions of rice protein, analyzes the molecular mechanisms of its anti-oxidant, anti-inflammatory, DNA protective effect, and lays a theoretical foundation for the application of functional rice protein.

Keywords: protein component, physiological regulation, health benefits, molecular mechanisms

1. Introduction

Rice (Oryza sativa) is a widely cultivated major cereal crop worldwide, with a global annual production of approximately 740 million tons[1-3]. Rice is a primary staple food in Asian countries, providing nutritional sustenance to over 2 billion people in the region[1, 4]. Rice protein (RP) serves as an essential dietary protein source for the Asian population[5-6]. China, being the largest producer and consumer of rice globally, recorded a rice production of 147 million tons in 2020, accounting for 29% of the global rice production and securing its position as the world's leading rice producer. The consumption of rice in China reached 146.5 million tons, with a self-sufficiency rate of 99.7%. It is noteworthy that while China is a major producer of rice, the focus has been primarily on producing regular milled rice, with a relatively low proportion of rice processing and a significant generation of byproducts such as broken rice and rice bran during the processing[7-9].

***Corresponding author**
ly6617@hit.edu.cn

Received 2 July 2024
Received in revised from 26 October 2024
Accepted 6 January 2025

During rice processing, a significant amount of broken rice is generated. The main component of rice is starch, followed by protein, which accounts for about 8% of the total rice mass[10]. Although the protein content in rice is relatively low, it is still one of the major sources of dietary protein for humans. RP is a high-quality plant protein that serves as a valuable source of nutrition, characterized by its low allergenicity, non-irritating nature, easy digestibility, and absorption[10-11]. Its nutritional value aligns with the balanced nutritional model recommended by FAO/WTO, making it an excellent ingredient for gluten-free products and infant formula[5]. RP has gained significant attention due to its low allergenicity, well-balanced amino acid profile, cholesterol-lowering properties, and high nutritional value[5]. However, due to the low protein content in rice and the complexity of extraction processes, the potential disease-preventive and health-promoting characteristics of RP have not been fully explored and utilized. Current research indicates that RP and its hydrolysates possess various biological activities, including anti-oxidant activity[12-27], anti-inflammatory activity[28-35], DNA protective aciivity[36], lipid-lowering effect[24, 37-50], anti-hypertensive activity[51-52], anti-diabetic activity[52-55] and anticancer effects[52, 56-57], demonstrating significant biological utilization value and vast application potential. This review aims to summarize the potential physiological activities associated with RP and presents a novel approach by integrating both molecular insights and applied nutrition, offering a deeper understanding of its bioactive properties beyond nutritional value. Unlike prior reviews that primarily focus on its protein composition, we emphasize its potential health benefits, specifically its anti-oxidant, anti-inflammatory, and lipid-lowering effects. This comprehensive review not only consolidates existing knowledge but also paves the way for innovative applications in functional foods and nutraceuticals.

2. The composition of RP

RP is composed of four main protagonists: albumin, globulin, glutenin, and prolamin[10-11]. In this ensemble, albumin and globulin play the roles of functional proteins, while glutenin and prolamin take on the responsibilities of storage proteins. According to the Osbourne classification, albumin is the water-soluble member of the RP family, while globulin finds its solubility in dilute salt solutions[58]. Together, albumin and globulin make up only a modest 5% to 10% of rice's total protein content.

Prolamin is the character that dissolves in 50% to 90% ethanol, whereas glutelin, requiring more drastic measures, only dissolves in acid or alkali. These two, glutelin and prolamin, are categorized as the primary storage proteins, with glutelin constituting approximately 80% of the total protein content and prolamin representing about 10%[59-61].

The limited solubility of RP is largely due to its high glutelin content, supplemented by about 10% prolamin. Both glutelin and prolamin are impervious to water, while the water-soluble albumin content in RP remains relatively low. This composition significantly contributes to the overall low solubility of RP in water.

Within the rice endosperm, two main types of protein bodies stand out: Type I protein bodies (PB-I) and Type II protein bodies (PB-II)[38, 62]. PB-I manifests as densely packed spherical particles with a laminated structure, rich in prolamin. PB-II, in contrast, appears as ellipsoidal particles without a layered structure, abundant in glutelin and globulin. PB-II is easily digested and absorbed in the gastrointestinal tract, whereas PB-I resists gastric protease hydrolysis.

The amino acid composition of rice protein and components is shown in Table 1[38, 63-64]. RP is a powerhouse of amino acids, offering all 18 amino acids with a particular emphasis on the eight essential ones[65]. Lysine, often scarce in cereal proteins, is plentiful in RP. Additionally, RP boasts elevated levels of arginine and methionine compared to other plant proteins[66-69].

Table. 1 The essential and non-essential amino acids present in rice protein and composition in g/100 g[38, 63-64].

Amino Acids		Content (g/100 g)				
		Rice Protein	Albumin	Globulin	Glutelin	Prolamin
Essential amino acid	Leucine	7.5–9.0	6.6–8.0	6.6–6.8	7.3–9.3	13.0–15.0
	Valine	5.5–6.4	5.9–7.8	5.4–6.5	6.3–6.9	6.5–7.1
	Phenylalanine	4.9–5.5	3.7–4.6	3.3–4.8	5.4–6.0	5.8–6.7
	Isoleucine	3.7–4.5	3.5–3.8	2.4–4.1	4.3–4.7	4.6–5.2
	Lysine	3.2–3.8	5.1–6.4	1.9–3.7	2.7–4.5	0.3–1.2
	Threonine	2.7–3.2	4.2–5.2	2.5–2.7	2.8–5.1	2.5–2.8
	Histidine	2.1–2.8	2.9–3.4	1.7–2.7	2.6–2.7	1.3–2.1
	Methionine	1.9–2.4	1.9–2.1	3.0–5.4	2.0–3.1	0.5–0.9
	Tryptophan	1.2–1.4	1.5–1.8	1.4–1.5	1.0–1.6	0.5–2.6
Non-essential amino acid	Glutamic acid	17.7–20.5	13.0–18.0	17.0–19.0	19.0–21.0	23.0–33.0
	Aspartic acid	8.2–9.6	10.0–11.0	7.1–14.0	10.0–11.0	8.3–8.7
	Arginine	7.8–10.2	7.9–10.0	7.2–14.0	9.0–11.0	6.1–6.9
	Tyrosine	5.0–6.1	4.4–5.1	5.5–6.3	5.3–5.5	9.2–9.9
	Alanine	4.8–6.0	7.1–8.5	5.6–6.3	5.6–5.9	6.7–7.6
	Serine	4.5–5.2	4.2–5.4	5.5–6.5	4.5–6.2	4.2–6.1
	Glycine	3.8–4.9	6.3–8.4	5.8–6.4	4.3–5.3	3.0–3.7
	Proline	3.4–4.3	4.5–7.1	3.8–7.5	4.9–6.2	5.0–6.7
	Cystine	1.4–2.4	1.9–2.3	3.3–4.0	1.2–1.8	0.0–0.8

The physiological activities of albumin and globulin are noteworthy in RP, while prolamin and glutelin fulfill their roles as storage proteins. Glutelin, which makes up 80% of RP, contains high levels of glutamic acid, aspartic acid, arginine, glycine, and alanine. Its inherent structure dictates its solubility and low surface activity under neutral conditions, resulting in poor solubility in water and other solutions[70].

In summary, RP offers high nutritional value and diverse physiological activities, underscoring its importance as a valuable plant protein source.

3. The potential physiological functions of RP

It has been found that RP and hydrolysates derived and purified from RP have a variety of potential physiological functions, including anti-oxidant activity, anti-inflammatory activity, DNA protective effect, lipid-lowering effect, anti-hypertensive activity, anti-diabetic activity and anti-cancer activity, have been derived and purified from RP. Hydrolysates derived from RP exhibit a wide array of health benefits, including antioxidant, antihypertensive, anticancer, cholesterol-lowering, antidiabetic, and antimicrobial properties. To produce these beneficial hydrolysates and peptides, various processing techniques are employed, with enzymatic hydrolysis of stabilized RP isolate being particularly effective[20]. Next, this paper reviews the physiological functions of RP and hydrolysates from these aspects.

3.1 Anti-oxidant activity

Reactive oxygen species (ROS) are byproducts of respiration and play a critical role in physiological processes[71-72]. However, excessive levels of ROS in the body can cause oxidative damage to cellular macromolecules such as carbohydrates, lipids, proteins, and DNA, leading to diseases like Alzheimer's, cardiovascular conditions, and autoimmune disorders. Normally, the body's antioxidant system regulates ROS levels and prevents oxidative damage[17]. It is important to note that with aging, the antioxidant defense system's capacity diminishes, resulting in a pro-oxidant/antioxidant imbalance and ROS accumulation, ultimately causing bodily harm. Therefore, the intake of exogenous antioxidants can help mitigate ROS damage and reduce the incidence of related diseases.

Antioxidant enzymes are crucial components of the body's antioxidant defense system[18]. Enhancing the expression of antioxidant enzymes through the Nrf2-Keap1 pathway is a significant mechanism by which antioxidant peptides exert their effects[13]. Nuclear factor erythroid 2-related factor 2 (Nrf2) is a key transcription factor in the Nrf2-Keap1 pathway, which regulates the expression of antioxidant enzymes. Under normal conditions, Nrf2 resides in the cytoplasm, bound to Kelch-like ECH-associated protein 1 (Keap1) in an inactive state. When ROS levels increase, Keap1 undergoes modification of its cysteine residues, releasing Nrf2 and allowing its translocation into the nucleus where it becomes activated. This activation leads to the regulation of target gene expression and an increase in the levels of antioxidant enzymes.

This paper reviews the recent research progress on the antioxidant activity of RP, as shown in Table 2. Studies have found that compared to casein, RP significantly promotes the expression of Nrf2 and its target genes in the liver of Wistar rats, increases hepatic glutathione (GSH) content, and reduces hepatic ROS levels[13]. This endogenous antioxidant effect is independent of dietary cholesterol. To further understand the mechanism by which RP activates the endogenous antioxidant defense system, it was discovered that RP effectively reduces the expression of Keap1 in the liver of Wistar rats and activates the Nrf2 signaling pathway[12]. This leads to an increase in the expression of antioxidant enzyme genes and proteins regulated by the antioxidant response element (ARE). Additionally, RP enhances the expression levels of hepatic methionine sulfoxide reductases (Msr), and this effect is not influenced by the age of the experimental animals[19]. In summary, RP possesses endogenous antioxidant capability, and its antioxidant mechanism may involve stimulating the expression of the Msr antioxidant system and activating the Nrf2-Keap1 pathway (Fig.1).

Table. 2 Summary of antioxidant activity of rice protein.

Protential Physiological Functions	Years	Authors	Major findings	References
Antioxidant activity	2009	Zhang et al.	The Neutrase hydrolysate from rice endosperm protein has high antioxidant activity. And the active constituent contains eight amino acids in its sequence (Lys-His-Asn-Arg-Gly-Asp-Glu-Phe).	[21]

Protential Physiological Functions	Years	Authors	Major findings	References
	2010	Zhang et al.	Rice protein hydrolysis digested by various protease were isolated and purified to obtain peptides with antioxidant activity. And the antioxidant peptides were identified to be Phe-Arg-Asp-Glu-His-Lys-Lys and and Lys-His-Asp-Arg-Gly-Asp-Glu-Phe.	[22]
	2012	Yang et al.	RP improved oxidative stress primarily through enzymatic and non-enzymatic antioxidative defense mechanisms, reflected by enhancing the antioxidative status and attenuating the oxidative damage to lipids and proteins.	[23]
	2014	Cai et al.	The antioxidant capability involved in the hypocholesterolemic action exerted by rice protein was independent of dietary cholesterol during adult rats period.	[24]
	2016	Liu et al.	Results suggested that alkali extraction is a vital process to regulate the antioxidant activity of RP through modifying the compositions of amino acids	[25]
	2016	Wang et al.	The present study demonstrated that the in vitro antioxidant responses induced by the hydrolysates and the protein digests of RPs could be affected differently by alkali treatment and α-amylase degradation. The protein digests, in which undigested residues remained, could exhibit more efficacious antioxidant activity compared to the hydrolysates.	[15]
	2016	Li et al.	The present study demonstrates the endogenous antioxidant potential of rice proteins via mechanism through which Nrf2 activation plays an essential role in inducing Phase II antioxidants/detoxification enzymes and preventing ROS generation. This novel antioxidative function of rice protein is independent of dietary cholesterol during in adult rats.	[19]
	2019	Li et al.	To elucidate the influence of methionine, which is an essential sulfur-containing amino acid, on the antioxidant activity of rice protein, methionine was added to RP. Results suggested that the availability of methionine is a critical factor to augment antioxidant ability of RP in the in vitro gastrointestinal tract.	[14]
	2020	Li et al.	Results suggested that the methionine availability might play a key role in inducing and augmenting the endogenous antioxidant response exerted by rice protein, which is independent of age.	[12]
	2020	Li et al.	This study demonstrates that rice protein exerts the endogenous antioxidant capacity in growing and adult rats, which is due to stimulating Msr antioxidant expression and activating Nrf2-ARE pathway. Results suggest that the antioxidant activity induced by rice protein is independent of age.	[13]
	2020	Wang et al.	The endogenous antioxidant response induced by RP is primarily attributed to the methionine availability, in which the stimulation of Msr and GSH antioxidant system via Nrf2-ARE pathway.	[16]
	2021	Chen et al.	Two peptides, Gly-Asp-Met-Asn-Pro and Leu-Leu-Leu-Arg-Trp purified from rice dreg protein hydrolysate exhibite higher antioxidant activities.	[20]
	2022	Ren et al.	Rice protein hydrolysate, SGDWSDIGGR showed good antioxidant activities in the extracellular assay, and it possessed a protective effect against oxidative stress in 2BS cells in a dose-dependent manner. SGDWSDIGGR achieves antioxidant ability by occupying the Nrf2-binding site, activating the Keap1-Nrf2 signaling pathway, and upregulating the expression of antioxidant enzymes.	[17]

Protential Physiological Functions	Years	Authors	Major findings	References
	2022	Lin et al.	The replacement of 10% fishmeal with rice protein meal significantly improves the promotion of digestibility, protein synthesis, antioxidant capacity, and disease resistance of Litopenaeus vannamei.	[26]
	2023	Xie et al.	Drying methods and enzyme type can alter the conformation of protein. Trypsin-derived spray dried RH exhibited higher α-helix contents while neutrase-derived ones had lower α-helix contents. The freeze-dried RH owed higher hydroxyl and DPPH scavenging activity than their spray-dried counterparts, which was related to higher sulfhydryl group and hydrophobic amino acids contents.	[27]
	2023	Chen et al.	Rice protein hydrolysates were further fractionated using ultrafiltration membrane (UF) and classified by molecular weight (MW; MW < 1 kDa, MW 1–10 kDa, and MW > 10 kDa). Peptides with MW < 1 kDa possessed superior antioxidant properties.	[18]

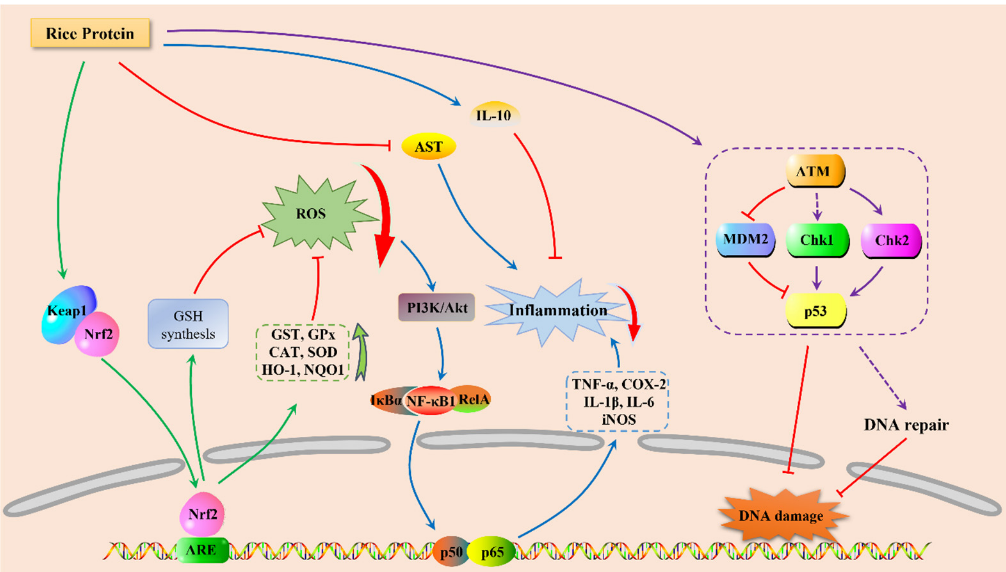

Fig. 1 Molecular mechanisms of rice protein antioxidant, anti-inflammatory, and DNA protective aciivities.

Keap1: Kelch-like ECH-associated protein 1; Nrf2: Nuclear factor erythroid 2-related factor 2; ARE: Antioxidant response element; GSH: Glutathione; ROS: Reactive oxygen species; GST: Glutathione S-transferase; GPx: Glutathione peroxidase; CAT: Catalase; SOD: Superoxide dismutase; HO-1: Heme oxygenase 1; NQO1: NAD (P)H quinone dehydrogenase 1; PI3K/Akt: Phosphoinositide 3-kinase-Akt; NF-κB1: Nuclear factor kappa-light-chain-enhancer of activated B cells; IκBα: Inhibitor of NF-κB α; TNF-α: Tumor necrosis factor-α; COX-2: Cyclooxygenase-2; IL-1β: Interleukin-1 beta; IL-6: Interleukin-6; IL-10: Interleukin-10; iNOS: Inducible nitric oxide sythase; AST: Aspartate transaminase;

Common in vitro assays used to assess the antioxidant activity include 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical-scavenging, reducing power, ferrous ion-chelating, and lipid peroxidation inhibition assays.

The antioxidant potential of RP hydrolysates is attributed to a combination of bioactive compounds, such as soluble peptides, phenolics, α-tocopherol, and γ-oryzanol[18]. This activity is influenced by several factors, including the type of enzyme used for hydrolysis, the degree of hydrolysis, purification methods, and the source or variety of RP. Studies have shown that increasing the degree of hydrolysis enhances DPPH radical scavenging, reducing power, and ferrous chelating activity. Notably, alcalase has demonstrated superior performance compared to flavourzyme and neutrase in producing hydrolysates with higher protein yield and antioxidant activity.

Additionally, the antioxidant efficacy of RP hydrolysates and peptides can be affected by pretreatment methods, such as using different enzymes or sequential hydrolysis followed by purification[17]. The amino acid composition also plays a significant role; hydrophobic amino acids are crucial for free radical scavenging, while polar amino acids are involved in metal ion reduction and chelation. While preliminary research suggests the potential for generating RP-derived hydrolysates with antioxidant properties, further studies are necessary to validate their efficacy in animal models and human subjects[73]. Moreover, the suitability of RP hydrolysates for incorporation into functional food products requires comprehensive examination.

3.2 Anti-inflammatory activity

Inflammation is a contributing factor to the initiation and progression of many diseases, and some food-derived biofunctional proteins show high anti-inflammatory activity[74-75]. This paper reviews the recent research progress on the anti-inflammatory activity of RP, as shown in Table 3. Wang et al. directly demonstrated the anti-inflammatory effect of RP in growing and mature mice through in vivo experiments[30]. The results indicated that, compared with casein, RP decreased the levels of ROS and nitric oxid (NO), as well as the activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the liver of growing and mature mice. Simultaneously, RP increased the expression of interleukin-10 (IL-10) and heme oxygenase-1 (HO-1) in the liver, while decreasing the gene and protein expression of phosphoinositide 3-kinase (PI3K), protein kinase B (Akt), nuclear factor kappa-B-1 (NF-κB1), p65, tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2)[19]. RP was found to increase IκBα expression, leading to a significant decrease in the translocation of p50 and p65 to the nucleus[29]. These results suggest that RP inhibits the activation of the NF-κB pathway in both growing and mature mice, thus playing an anti-inflammatory role (Fig. 1). It is noteworthy that in this study, Wang et al. mentioned that arginine in RP may be a crucial factor for the anti-inflammatory effect of RP by inhibiting the activation of NF-κB[28-29].

Table. 3 Summary of anti-inflammatory activity of rice protein.

Protentional Physiological Functions	Years	Authors	Major findings	References
Anti-inflammatory activity	2019	Wang et al.	The present study demonstrates that RP exerts an anti-inflammatory effect to inhibit ROS-derived inflammation through suppression of the NF-κB pathway in growing and adult rats. Results suggest that the anti-inflammatory capacity of RP is independent of age.	[30]
	2019	Tamura et al.	Peptides derived from trypsin hydrolysis of rice protein REP9 and REP11 significantly inhibited transcription activity of inflammatory and osteoclast-related molecules. Local treatment with the rice peptides, in mice subjected to ligature-induced periodontitis, inhibited inflammatory bone loss. These results suggested that the rice peptides possess a protective effect against periodontitis.	[33]

Protential Physiological Functions	Year s	Authors	Major findings	References
	2020	Wang et al.	The endogenous antioxidant response induced by RP is primarily attributed to the methionine availability, in which the stimulation of Msr and GSH antioxidant system via Nrf2-ARE pathway.	[16]
	2021	Feng et al.	Anti-inflammatory effect of rice protein hydrolysates in LPS-induced RAW264.7 macrophages via NF-κB/MAPKs signaling pathways	[34]
	2022	Qu et al.	Peptides derived from trypsin hydrolysis of rice protein show good immunological activity. Three peptides (DNIQGITKPAIR, IAFKTNPNSMVSHIAGK, and IGVAMDYSASSKR) that demonstrated the highest binding affinity were synthesized, and their in vitro anti-inflammatory activity was investigated.	[31]
	2022	Huang et al.	RP treatment could alleviate the loss of body weight, colon shortening and injury, and the level of disease activity index, repair colonic function, regulate inflammatory factors, and restore oxidative balance in mice. Also, RP treatment could activate the Keap1-Nrf2 signaling pathway, mediate the expression of downstream antioxidant protease, then regulate gut microbiota and adjust short-chain fatty acid levels to alleviate DSS-induced colitis in mice.	[32]
	2022	Kaseda et al.	Rice protein significantly suppresses the inflammatory cytokine response to improve the anti-inflammatory effects of HDL and produces lower atherosclerotic lesion accelerated by the renal mass reduction than casein in a mouse model.	[35]
	2022	Wang et al.	The molecular mechanism responsible for the anti-inflammatory function of RP is the inhibition of NF-κB activation by the downregulation of protein kinase B/phosphoinositide 3 kinase. Further, this study demonstrates that Met availability contributes to the suppression of HNE-induced inflammation through upregulating IL-10 and GST in rats fed RP.	[28]
	2022	Wang et al.	Results showed, under cholesterol-enriched dietary condition, the anti-inflammatory action can be induced by RP and enhanced by methionine in growing and adult rats. And the anti-inflammatory function of RP is dependent on methionine availability and independent of dietary cholesterol.	[29]

Other studies have delved into the anti-inflammatory effects of RP and its hydrolysates[31, 76-77]. For instance, RP hydrolysate demonstrated a reduction in the production of NO and pro-inflammatory cytokines (IL-1β, IL-6, and TNF-α) in lipopolysaccharide (LPS)-induced RAW264.7 macrophages[78]. The hydrolysate also inhibited the phosphorylation of proteins in the NF-κB and mitogen-activated protein kinase (MAPK) signaling pathways, indicating its potential to regulate the inflammatory response by targeting these pathways[79]. Another study by Wang et al. demonstrated that RP hydrolysate lowered the levels of pro-inflammatory cytokines (IL-1β and TNF-α) in the serum of mice with LPS-induced acute lung injury. The hydrolysate additionally suppressed the phosphorylation of proteins in the NF-κB and MAPK signaling pathways, along with reducing the infiltration of inflammatory cells into the lung tissue[32, 79-80]. Overall, these findings suggest that RP and its hydrolysates exhibit potential as anti-inflammatory agents and could be considered in the development of functional foods and nutraceuticals for the prevention and treatment of inflammatory diseases. However, further research is needed to explore their efficacy and safety in human subjects.

3.3 DNA protective effect

DNA damage poses a persistent challenge, frequently occurring in human cells and disrupting critical processes such as replication and transcription[81]. This disruption can lead to genetic mutations and larger-scale genomic abnormalities, contributing to conditions like cancer, aging, and neurodegenerative diseases.

RP exhibits a protective role against DNA damage induced by various factors, including oxidative stress and chemical agents. This protective effect is likely attributed to the presence of bioactive peptides, antioxidants, and other beneficial components in RP.

Oxidative stress, a significant contributor to DNA damage, accelerates aging and predisposes individuals to diseases like cancer. The p53 signaling pathway plays a crucial role in DNA damage response and repair[82]. Strategies involving the activation of endogenous antioxidant mechanisms and the p53 signaling pathway have shown promise in defending against DNA oxidative damage[82-83]. Liang et al. reported that RP can upregulate the expression of key molecules in the liver, such as ataxia-telangiectasia mutated proteins (ATM), checkpoint kinase 2 (Chk2), checkpoint kinase 1 (Chk1), and p53, while downregulating the murine double minute 2 (MDM2) gene and protein expression[36]. This activation of the ATM-p53 signaling pathway initiates DNA repair mechanisms and prevents DNA damage (Fig.1).

Numerous studies have highlighted the DNA-protective effects of RP and its hydrolysates. For instance, RP hydrolysates exhibited significant protection against DNA damage in human liver cells exposed to hydrogen peroxide, attributed to their antioxidant activity. Similarly, in rats exposed to cadmium, RP hydrolysates mitigated oxidative stress and inflammation in liver and kidney tissues, thereby preventing DNA damage[82].

Furthermore, RP hydrolysates demonstrated substantial protection against DNA damage in human colon cells exposed to the genotoxic agent 4-nitroquinoline-1-oxide, linked to the presence of bioactive peptides with antioxidant and anti-inflammatory properties[83].

These findings suggest the potential of RP and its hydrolysates as dietary supplements or functional ingredients for mitigating DNA damage and associated health issues. However, further research is necessary to fully elucidate the mechanisms underlying these protective effects and optimize extraction and purification methods for RP and its bioactive components.

3.4 Lipid-lowering effect

This paper reviews the recent research progress on the lipid-lowering effect of RP, as shown in Table 4. Cholesterol and triglycerides are often widely concerned as indicators of lipid levels.

Table. 4 Summary of lipid-lowering effect of rice protein.

Protential Physiological Functions	Years	Authors	Major findings	References
Lipid-lowering effect	1996	Morita et al.	Rice protein isolates produced by the two different methods lower serum cholesterol concentration in rats compared with casein	[39]

Protential Physiological Functions	Years	Authors	Major findings	References
	1997	Morita et al.	Serum total cholesterol concentrations were lower in rats fed rice protein than in those fed casein. Fecal bile acid plus neutral steroid excretion was significantly higher in rats fed the rice protein diets compared with those fed casein.	[40]
	2007	Yang et al.	RP possessed cholesterol lowering effects in the plasma and liver accompanied with TG-lowering effects in the liver, which may partly be explained by fecal steroid excretion.	[38]
	2009	Yang et al.	Rice proteins effectively regulated hepatic cholesterol output by stimulating of biliary production and inhibiting of hepatic cholesterol secretion. A lower ratio of Met/Gly in rice protein could produce a similar lower rate of hepatic secretion of cholesterol via VLDL into plasma.	[43]
	2011	Zhang et al.	Animals fed the rice protein hydrolysate supplemented diet also had lower final body weight, liver weight, VLDL-C, and liver cholesterol, and higher fecal fat and bile acid excretion than the control.	[44]
	2011	Yang et al.	The hypocholesterolemic response induced by RP-M (methionine-supplemented rice protein) with a higher Met/Gly ratio primarily contributes to the stimulation of hepatic cholesterol for elimination via biliary secretion rather than the inhibition of hepatic cholesterol release via VLDL into circulation.	[45]
	2011	Yang et al.	The digestibility of rice protein affected by extraction method played a major role in the modulation of cholesterol metabolism, and the hypocholesterolemic action induced by rice protein with lower digestibility primarily contributed to the inhibition of cholesterol absorption.	[46]
	2012	Yang et al.	Alkali treatment played a major role in controlling the digestibility and the bile acid binding of rice protein through the modification of amino acid composition. Adding arginine to rice protein enhanced inhibition of digestion and promoted bile acid binding.	[47]
	2012	Yang et al.	The triglyceride-lowering action as well as the potential of anti-adiposity induced by rice protein was attributed to upregulation of lipolysis and downregulation of lipogenesis, and the lower digestibility of rice protein may be the main modulator responsible for the lipidlowering action.	[48]
	2013	Yang et al.	Rice protein stimulated bile acid excretion by increasing cholesterol 7 α-hydroxylase activity and gene expression. Rice protein inhibited liver cholesterol secretion into the bloodstream by reducing acyl-CoA: cholesterol acyltransferase 2 activity and gene expression.	[37]
	2013	Yang et al.	This study elucidated the hypocholesterolemic mechanism exerted by RP in adult rats under cholesterol-enriched dietary condition. RP could induce a cholesterol-lowering effect through modifying cholesterol metabolism-related gene expression and enzyme activity in adult rats.	[42]
	2014	Cai et al.	The hypocholesterolemic effect of rice protein is attributable to inducing antioxidative response and depressing oxidative damage in adult rats fed cholesterol-free/enriched diets.	[24]
	2014	Choi et al.	Cooked rice may prevent HF-induced fat accumulation by regulating lipid metabolism-related gene expression, and it may be a useful carbohydrate source for preventing nonalcoholic fatty liver disease.	[49]
	2019	Higuchi et al.	Rice protein supplementation during the juvenile period may regulate the gut microbiota and thus suppress the development of obesity and related disorders in adulthood in mice.	[41]

RP can significantly reduce serum cholesterol levels by modulating cholesterol metabolism in the liver. Studies have indicated that RP consumption increases the excretion of bile acids and neutral sterols, which are end products of cholesterol metabolism[39-40]. This enhanced excretion reduces the overall cholesterol pool in the body, thereby lowering serum cholesterol levels. RP peptides have been shown to interfere with lipid absorption in the intestine. Specifically, these peptides can disrupt micelle formation, which is essential for the absorption of dietary fats. By preventing micelle formation, RP reduces the amount of lipids absorbed into the bloodstream, thereby lowering lipid levels. Cholesterol levels play a significant role in heart disease risk[84-86]. The hypocholesterolemic effect of RP relies on its amino acid composition and gastrointestinal digestion[38]. Methionine, an essential amino acid for cholesterol metabolism, contributes to this effect. RP aids in the excretion of fecal steroids, leading to reduced cholesterol levels, particularly in plasma and liver triacylglycerols, through bile acid binding.

Studies have shown that RP effectively regulates lipid metabolism and reduces cholesterol levels in the body. It reduces the level of very low density lipoprotein (VLDL) and low density lipoprotein (LDL) in the blood, increases the level of high-density lipoprotein (HDL), enhances cholesterol reversal transport, and effectively reduces the level of cholesterol in the blood. Moreover, RP promotes the secretion of cholesterol and bile acids from the liver into bile, thereby increasing the excretion of cholesterol and bile acids in the feces. RP also inhibits the activity and gene expression of acetyl-CoA: cholesterol acetyltransferase 2 (ACAT2) that regulates cholesterol absorption, thus reducing cholesterol absorption. It significantly promotes the expression of peroxisome proliferator activated receptor alpha (PPARα) and liver X receptor alpha (LXRα), which regulate cholesterol catabolism. Additionally, RP can stimulate the expression of cholesterol 7 alpha-hydroxylase (CYP7A1) and increase bile acid excretion[37, 42, 87].

RP and its hydrolysates demonstrate potential in reducing cholesterol levels in cells and animal models, although confirmation through human trials is necessary. Maintaining cardiovascular health requires consideration of dietary factors and lifestyle choices, including a balanced diet, regular exercise, and avoiding smoking[42]. Among the fractions extracted by α-amylase, the 13 kDa prolamin fraction stands out for its effectiveness[38]. Its enhanced digestibility and promotion of fecal bile acid extraction contribute to its ability to reduce cholesterol levels effectively.

RP also regulates triglyceride metabolism and has functional properties that improve body weight and prevent obesity. RP influences lipid metabolism by regulating the expression of key genes involved in fatty acid oxidation and lipogenesis[41]. It upregulates genes that promote the breakdown of fatty acids and downregulates those that facilitate the synthesis of new lipids. This dual action helps in reducing the lipid content in the body[38]. Studies have shown that RP can inhibit the activity of fatty acid synthase (FAS), glucose-6-phosphate dehydrogenase (G6PD), and malate dehydrogenase (MDH), thereby suppressing lipid synthesis in the body. It also enhances the activities of total lipase and hepatic lipase, accelerating lipid break down and effectively reducing fat accumulation[48]. Recent studies have found that RP regulates triglyceride transport by inhibiting the expression of cluster of differentiation 36 (CD36), microsomal triglyceride transfer protein (MTP), fatty acid transport proteins (FATP), and fatty acid binding protein (FABP), leading to a reduction in triglyceride levels[50].

3.5 Anti-hypertensive activity

Researchers conducted an investigation into the antihypertensive effect of RP hydrolysate (RPH) in spontaneously hypertensive rats (SHRs)[51]. The results revealed that RPH significantly reduced systolic blood pressure and enhanced endothelial function in SHRs. Moreover, RPH led to a decrease in the levels of angiotensin II, aldosterone, and endothelin-1 in plasma, along with a reduction in the expression of angiotensin II type 1 receptor (AT1R) in the aorta of SHRs. Additionally, RPH mitigated oxidative stress by lowering the levels of malondialdehyde (MDA) and enhancing the activity of superoxide dismutase (SOD) in SHRs. The study suggested that RPH exerts antihypertensive effects in SHRs by inhibiting the renin-angiotensin-aldosterone system, improving endothelial function, and mitigating oxidative stress[88].

In summary, these studies underscore the potential of RP and its hydrolysates as natural bioactive components for treating hypertension and cardiovascular disease. However, further research is imperative to ascertain their efficacy and safety in human subjects.

It is crucial to acknowledge that while animal studies have demonstrated promising results regarding the antihypertensive effect of RP hydrolysates, additional research is required to determine the safety and effectiveness of these compounds in humans[89]. Consideration should also be given to the potential for individual variability in response to these treatments, as well as the likelihood of interactions with other medications or health conditions. Therefore, conducting more clinical trials is necessary to comprehensively evaluate the potential of RP hydrolysates as natural treatments for hypertension and cardiovascular disease.

3.6 Anti-diabetic activity

Hyperglycemia, a significant contributor to diabetes mellitus, presents substantial health risks[90-91]. However, studies indicate that RP may offer promise in addressing hyperglycemia. Specifically, alkali-extracted alcalase enzyme-hydrolyzed RP has shown potential in reducing blood pressure by inhibiting the conversion of angiotensin I to angiotensin II. This inhibitory effect is attributed to enzymes like alcalase or protamax present in the protein hydrolysates derived from albumin and glutelin, effectively suppressing angiotensin I converting enzyme activity[92-93]. Notably, the peptide sequence Thr-Gln-Val-Tyr exhibits similar inhibitory properties[94]. Furthermore, enzymatic treatment of rice albumin and globulin has demonstrated stronger inhibitory activity compared to conventional methods for obtaining globulin and prolamin hydrolysates.

Diabetes mellitus, characterized by chronic hyperglycemia due to insufficient insulin secretion or excessive glucagon secretion, represents a significant global health challenge with rising prevalence[93]. Finding effective medications with minimal adverse effects for diabetes treatment remains a crucial focus in medical research[95]. Numerous studies have investigated the potential antidiabetic properties of hydrolysates and peptides derived from RP[55, 96]. Hydrolysates exhibiting α-amylase and α-glucosidase inhibitory activity have been generated from RP using enzymes such as alcalase, neutrase, flavourzyme, and protamax.

The α-amylase and α-glucosidase inhibitory activities of albumin and glutelin hydrolysates produced by alcalase and protamax were comparable to standard anti-diabetic drugs. In another study, α-glucosidase-inhibitory peptides were isolated and identified from fractions of rice albumin hydrolysate produced by alcalase and protamax. Peptides with a molecular weight of less than 3 kDa demonstrated superior α-glucosidase inhibitory activity compared to crude RP digests prepared from RP fractions, with albumin and glutelin peptides exhibiting the highest activity[96-97]. The most active fraction of the hydrolysates contained 39 identified peptides, 37 of which contained peptide sequences known for their antidiabetic activity[98].

However, further research is necessary to confirm the potential antidiabetic effects of RP-derived hydrolysates and peptides in animal models and human subjects.

3.7 Anti-cancer activity

Cancer is a major global health concern with increasing prevalence, particularly in low-income countries[56]. Consequently, the consumption of nutritious foods and natural bioactive ingredients holds promise for reducing cancer risk factors and incidence. Rice-derived hydrolysates and peptides have shown potential anticancer properties[57]. For example, a pentapeptide derived from RP inhibited the growth of various cancer cells, including lung, liver, breast, and colon cancer cells, with a notable 45% inhibition of human prostate cancer at a concentration of 460 μg/mL. Additionally, a glycoprotein isolated from rice (GR), when administered intravenously, resulted in a significant 77% inhibition of lung metastasis in colon cells. Moreover, GR enhanced natural killer (NK) cell cytotoxicity against cancer cells and stimulated murine peritoneal macrophages to produce cytokines, indicating its potential antitumor activity by preventing tumor metastasis and activating immune cells[56].

Rice prolamin was also found to inhibit the viability of murine leukemia L1210 cells and human leukemia Jurkat cells, suggesting an immunomodulatory effect. Oral administration of purified prolamin reduced tumor weight and mitigated leukemia-induced organ weight reduction in mice in a dose-dependent manner without significant toxicity[57]. This suggests that rice prolamin may effectively enhance anti-tumor immunity and inhibit leukemia growth[56].

However, further research is necessary to explore the potential anticancer effects of RP and its hydrolysates in animal models and human subjects.

4. Conclusion

Research studies confirm that RP is rich in nutritional and biological value, showcasing diverse physiological functions, including anti-oxidant, anti-inflammatory, DNA protective effect, anti-hypertensive, anti-diabetic, anti-cancer properties, and a lipid-lowering effect. Although many studies have shown that RP has multiple physiological functions, the various mechanisms of its functions in the body are still not particularly clear. While incorporating RP (RP) and its hydrolysates into nutritious and acceptable food products holds promise for health benefits, challenges like insufficient stabilization of RP extraction methods hinder its broader use as a food ingredient. Addressing these challenges should be a priority in future research to enhance RP's application in food products. Furthermore, comprehensive animal and human studies are essential to establish the confirmed health benefits of RP and its hydrolysates. Future research endeavors should focus on developing healthy RP-enriched food products that meet consumer expectations in terms of acceptability and affordability.

Data availability

No data was used for the research described in the article.

Conflict of interests

The authors declare that there are no conflict of interests.

References

[1] D. Li, M. Yao, Y. Yang et al., Changes of structure and functional properties of rice protein in the fresh edible rice during the seed development, Food Sci Hum Well 12 (2023) 1850-1860. https://dx.doi.org/10.1016/j.fshw.2023.02.049

[2] F. Yang, H. He, Z. Wang et al., Formula optimization and in vitro lipid reducing activity evaluation of nutritious rice bran meal replacement powder, J Food Meas Charact 18 (2024) 1075-1089. https://dx.doi.org/10.1007/s11694-023-02204-z

[3] O. Selamassakul, N. Kaisangsri, C. Sonklin et al., Effects of cluster dextrin encapsulation on the properties and antioxidant stability of fractionated Riceberry protein hydrolysate powder prepared by bromelain, Food Chem 439 (2024) 138161. https://dx.doi.org/10.1016/j.foodchem.2023.138161

[4] F. Xu, J. Chen, W. Wang et al., Polybrominated diphenyl ethers (PBDEs) decreased the protein quality of rice grains by disturbing amino acid metabolism, Environ Pollut 353 (2024) 124162. https://dx.doi.org/10.1016/j.envpol.2024.124162

[5] L. Zheng, Y. San, Y. Xing et al., Rice proteins: A review of their extraction, modification techniques and applications, Int J Biol Macromol 268 (2024) 131705. https://dx.doi.org/10.1016/j.ijbiomac.2024.131705

[6] X. Zhao, R. Gao, C. Cui et al., Structural characteristics, functional properties and *in vitro* digestibility of rice protein prepared from rice wine lees via an alkaline extraction process or carbohydrate-lipid removal process, J Cereal Sci 117 (2024) 103913. https://dx.doi.org/10.1016/j.jcs.2024.103913

[7] X. Huang, B. Xia, Y. Liu et al., Non-covalent interactions between rice protein and three polyphenols and potential application in emulsions, Food Chem X 22 (2024) 101459. https://dx.doi.org/10.1016/j.fochx.2024.101459

[8] Z. Zhang, J. Chen, L. Zheng et al., The potential meat flavoring derived from Maillard reaction products of rice protein isolate hydrolysate-xylose via the regulation of temperature and cysteine, Food Chem X 22 (2024) 101491. https://dx.doi.org/10.1016/j.fochx.2024.101491

[9] D.E. Igartúa, M.C. Dichano, M.N. Morales Huanca et al., Rice proteins-Gum arabic coacervates: Effect of pH and polysaccharide concentration in oil-in-water emulsion stability, Food Res Int 188 (2024) 114399. https://dx.doi.org/10.1016/j.foodres.2024.114399

[10] N. Ghanghas, M. M. T., S. Sharma et al., Classification, composition, extraction, functional modification and application of rice (*Oryza sativa*) seed protein: A comprehensive review, Food Rev Int 38 (2022) 354-383. https://dx.doi.org/10.1080/87559129.2020.1733596

[11] S. Shi, D. Zhao, K. Pan et al., Combination of near-infrared spectroscopy and key wavelength-based screening algorithm for rapid determination of rice protein content, J Food Compos Anal 118 (2023) 105216. https://dx.doi.org/10.1016/j.jfca.2023.105216

[12] H. Li, L. Cai, M. Liang et al., Methionine augments endogenous antioxidant capacity of rice protein through stimulating MSR antioxidant system and activating Nrf2-ARE pathway in growing and adult rats, Eur Food Res Technol 246 (2020) 1051-1063. https://dx.doi.org/10.1007/s00217-020-03464-5

[13] H. Li, M. Liang, Z. Wang et al., Rice Protein Exerts Endogenous Antioxidant Capacity via Methionine Sulfoxide Reductase and the Nrf2 Antioxidant System Independent of Age, J Med Food 23 (2020) 565-574. https://dx.doi.org/10.1089/jmf.2019.4504

[14] H. Li, Z. Wang, M. Liang et al., Methionine augments antioxidant activity of rice protein during gastrointestinal digestion, Int J Mol Sci 20 (2019) 868. https://dx.doi.org/10.3390/ijms20040868

[15] Z. Wang, Y. Liu, H. Li et al., Rice proteins, extracted by alkali and α-amylase, differently affect in vitro antioxidant activity, Food Chem 206 (2016) 137-145. https://dx.doi.org/10.1016/j.foodchem.2016.03.042

[16] Z. Wang, L. Cai, H. Li et al., Rice protein stimulates endogenous antioxidant response attributed to methionine availability in growing rats, J Food Biochem 44 (2020). https://dx.doi.org/10.1111/jfbc.13180

[17] L. Ren, Y. Yang, C. Ma et al., Identification and in silico analysis of novel antioxidant peptides in broken rice protein hydrolysate and its cytoprotective effect against H2O2-induced 2BS cell model, Food Res Int 162 (2022) 112108. https://dx.doi.org/10.1016/j.foodres.2022.112108

[18] H. Chen, F. Dai, C. Chen et al., Effects of molecular weight fraction on antioxidation capacity of rice protein hydrolysates, Sci Rep 13 (2023). https://dx.doi.org/10.1038/s41598-022-14314-7

[19] H. Li, H. He, Z. Wang et al., Rice protein suppresses ROS generation and stimulates antioxidant gene expression via Nrf2 activation in adult rats, Gene 585 (2016) 256-264. https://dx.doi.org/10.1016/j.gene.2016.03.052

[20] M. Chen, P. Ning, Y. Jiao et al., Extraction of antioxidant peptides from rice dreg protein hydrolysate via an angling method, Food Chem 337 (2021) 128069. https://dx.doi.org/10.1016/j.foodchem.2020.128069

[21] J. Zhang, H. Zhang, L. Wang et al., Antioxidant activities of the rice endosperm protein hydrolysate: identification of the active peptide, Eur Food Res Technol 229 (2009) 709-719. https://dx.doi.org/10.1007/s00217-009-1103-3

[22] J. Zhang, H. Zhang, L. Wang et al., Isolation and identification of antioxidative peptides from rice endosperm protein enzymatic hydrolysate by consecutive chromatography and MALDI-TOF/TOF MS/MS, Food Chem 119 (2010) 226-234. https://dx.doi.org/10.1016/j.foodchem.2009.06.015

[23] L. Yang, J. Chen, T. Xu et al., Rice protein improves oxidative stress by regulating glutathione metabolism and attenuating oxidative damage to lipids and proteins in rats, Life Sci 91 (2012) 389-394. https://dx.doi.org/10.1016/j.lfs.2012.08.003

[24] J. Cai, L. Yang, H. He et al., Antioxidant capacity responsible for a hypocholesterolemia is independent of dietary cholesterol in adult rats fed rice protein, Gene 533 (2014) 57-66. https://dx.doi.org/10.1016/j.gene.2013.09.124

[25] Y. Liu, Z. Wang, H. Li et al., *In vitro* antioxidant activity of rice protein affected by alkaline degree and gastrointestinal protease digestion, J Sci Food Agric 96 (2016) 4940-4950. https://dx.doi.org/10.1002/jsfa.7877

[26] H. Lin, S. He, B. Tan et al., Effect of rice protein meal replacement of fish meal on growth, anti-oxidation capacity, and non-specific immunity for juvenile shrimp *Litopenaeus vannamei*, Animals 12 (2022) 3579. https://dx.doi.org/10.3390/ani12243579

[27] H. Xie, L. Zhang, Q. Chen et al., Combined effects of drying methods and limited enzymatic hydrolysis on the physicochemical and antioxidant properties of rice protein hydrolysates, Food Biosci 52 (2023) 102427. https://dx.doi.org/10.1016/j.fbio.2023.102427

[28] Z. Wang, M. Liang, H. Li et al., Rice protein suppresses 4-hydroxy-2-nonenal-induced inflammation owing to methionine availability, Appl Physiol Nutr Metab 47 (2022) 826-838. https://dx.doi.org/10.1139/apnm-2021-0575

[29] Z. Wang, M. Liang, B. Liu et al., Methionine strengthens anti-inflammation of rice protein via depressing NF-κB activation and stimulating Msr expression in rats fed cholesterol-enriched diets, Food Sci Biotechnol 31 (2022) 745-758. https://dx.doi.org/10.1007/s10068-022-01074-3

[30] Z. Wang, M. Liang, H. Li et al., Rice protein exerts anti-inflammatory effect in growing and adult rats via suppressing NF-κB pathway, Int J Mol Sci 20 (2019) 6164. https://dx.doi.org/10.3390/ijms20246164

[31] T. Qu, S. He, C. Ni et al., *In vitro* anti-inflammatory activity of three peptides derived from the byproduct of rice processing, Plant Foods Hum Nutr 77 (2022) 172-180. https://dx.doi.org/10.1007/s11130-022-00963-6

[32] Z. Huang, W. Yang, X. Wang et al., Industrially produced rice protein ameliorates dextran sulfate sodium-induced colitis *via* protecting the intestinal barrier, mitigating oxidative stress, and regulating gut microbiota, J Agric Food Chem 70 (2022) 4952-4965. https://dx.doi.org/10.1021/acs.jafc.2c00585

[33] H. Tamura, T. Maekawa, H. Domon et al., Peptides from rice endosperm protein restrain periodontal bone loss in mouse model of periodontitis, Arch Oral Biol 98 (2019) 132-139. https://dx.doi.org/10.1016/j.archoralbio.2018.11.021

[34] M. Feng, X. Wang, H. Xiong et al., Anti-inflammatory effects of three selenium-enriched brown rice protein hydrolysates in LPS-induced RAW264.7 macrophages *via* NF-κB/MAPKs signaling pathways, J Funct Foods 76 (2021) 104320. https://dx.doi.org/10.1016/j.jff.2020.104320

[35] R. Kaseda, M. Hosojima, S. Kuwahara et al., Rice endosperm protein improves the anti-inflammatory effects of high-density lipoprotein and produces lower atherosclerotic lesion accelerated by the renal mass reduction than casein in a mouse model, J Am Nutr Assoc 41 (2022) 668-678. https://dx.doi.org/10.1080/07315724.2021.1950584

[36] M. Liang, H. Li, Z. Wang et al., Rice protein reduces DNA damage by activating the p53 pathway and stimulating endogenous antioxidant response in growing and adult rats, J Sci Food Agric 99 (2019) 6097-6107. https://dx.doi.org/10.1002/jsfa.9888

[37] L. Yang, J. Chen, T. Xu et al., Hypocholesterolemic effect of rice protein is due to regulating hepatic cholesterol metabolism in adult rats, Gene 512 (2013) 470-476. https://dx.doi.org/10.1016/j.gene.2012.10.042

[38] L. Yang, T. Kumagai, H. Kawamura et al., Effects of rice proteins from two cultivars, Koshihikari and Shunyo, on cholesterol and triglyceride metabolism in growing and adult rats, Biosci Biotech Bioch 71 (2007) 694-703. https://dx.doi.org/10.1271/bbb.60480

[39] T. Morita, A. Oh-Hashi, S. Kasaoka et al., Rice protein isolates produced by the two different methods lower serum cholesterol concentration in rats compared with casein, J Sci Food Agric 71 (1996) 415-424. https://dx.doi.org/10.1002/(SICI)1097-0010(199608)71:4<415:AID-JSFA599>3.0.CO;2-6

[40] T. Morita, A. Oh-hashi, K. Takei et al., Cholesterol-lowering effects of soybean, potato and rice proteins depend on their low methionine contents in rats fed a cholesterol-free purified diet, J Nutr 127 (1997) 470-477. https://dx.doi.org/10.1093/jn/127.3.470

[41] Y. Higuchi, M. Hosojima, H. Kabasawa et al., Rice endosperm protein administration to juvenile mice regulates gut microbiota and suppresses the development of high-fat diet-induced obesity and related disorders in adulthood, Nutrients 11 (2019). https://dx.doi.org/10.3390/nu11122919

[42] L. Yang, G. Han, Q.H. Liu et al., Rice protein exerts a hypocholesterolemic effect through regulating cholesterol metabolism-related gene expression and enzyme activity in adult rats fed a cholesterol-enriched diet, Int J Food Sci Nutr 64 (2013) 836-842. https://dx.doi.org/10.3109/09637486.2013.804038

[43] L. Yang, M. Kadowaki, Effects of rice proteins from two cultivars, Koshihikari and Shunyo, on hepatic cholesterol secretion by isolated perfused livers of rats fed cholesterol-enriched diets, Ann Nutr Metab 54 (2009) 283-290. https://dx.doi.org/10.1159/000230671

[44] H. Zhang, G.E. Bartley, C.R. Mitchell et al., Lower weight gain and hepatic lipid content in hamsters fed high fat diets supplemented with white rice protein, brown rice protein, soy protein, and their hydrolysates, J Agric Food Chem 59 (2011) 10927-10933. https://dx.doi.org/10.1021/jf202721z

[45] L. Yang, M. Kadowaki, Addition of Methionine to Rice Protein Affects Hepatic Cholesterol Output Inducing Hypocholesterolemia in Rats Fed Cholesterol-Free Diets, J Med Food 14 (2011) 445-453. https://dx.doi.org/10.1089/jmf.2010.1405

[46] L. Yang, J. Chen, T. Xu et al., Rice Protein Extracted by Different Methods Affects Cholesterol Metabolism in Rats Due to Its Lower Digestibility, Int J Mol Sci 12 (2011) 7594-7608. https://dx.doi.org/10.3390/ijms12117594

[47] L. Yang, J. Chen, H. Zhang et al., Alkali treatment affects in vitro digestibility and bile acid binding activity of rice protein due to varying its ratio of arginine to lysine, Food Chem 132 (2012) 925-930. https://dx.doi.org/10.1016/j.foodchem.2011.11.068

[48] L. Yang, J.H. Chen, J. Lv et al., Rice protein improves adiposity, body weight and reduces lipids level in rats through modification of triglyceride metabolism, Lipids Health Dis 11 (2012) 24. https://dx.doi.org/10.1186/1476-511X-11-24

[49] W.H. Choi, M.Y. Um, J. Ahn et al., Cooked rice inhibits hepatic fat accumulation by regulating lipid metabolism-related gene expression in mice fed a high-fat diet, J Med Food 17 (2014) 36-42. https://dx.doi.org/https://doi.org/10.1089/jmf.2013.3058

[50] B. Liu, Z. Wang, M. Liang et al., Rice protein reduces triglyceride levels through modulating CD36, MTP, FATP, and FABP expression in growing and adult rats, Foods 13 (2024) 2704. https://dx.doi.org/10.3390/foods13172704

[51] P. Wongsa, K. Yuenyongrattanakorn, W. Pongvachirint et al., Improving anti-hypertensive properties of plant-based alternatives to yogurt fortified with rice protein hydrolysate, Heliyon 8 (2022) e11087. https://dx.doi.org/10.1016/j.heliyon.2022.e11087

[52] M.K.W. Al-Doury, N.S. Hettiarachchy, R. Horax, Rice-endosperm and rice-bran proteins: A review, J Am Oil Chem Soc 95 (2018) 943-956. https://dx.doi.org/10.1002/aocs.12110

[53] S. Budhwar, M. Chakraborty, K. Sethi et al., Antidiabetic properties of rice and wheat bran-A review, J Food Biochem 44 (2020). https://dx.doi.org/10.1111/jfbc.13424

[54] M. Kubota, R. Watanabe, M. Yamaguchi et al., Rice endosperm protein slows progression of fatty liver and diabetic nephropathy in Zucker diabetic fatty rats, Br J Nutr 116 (2016) 1326-1335. https://dx.doi.org/10.1017/S0007114516003512

[55] Y. Ishikawa, T. Hira, D. Inoue et al., Rice protein hydrolysates stimulate GLP-1 secretion, reduce GLP-1 degradation, and lower the glycemic response in rats, Food Funct 6 (2015) 2525-2534. https://dx.doi.org/10.1039/c4fo01054j

[56] B.L. Tan, M.E. Norhaizan, Scientific evidence of rice by-products for cancer prevention: Chemopreventive properties of waste products from rice milling on carcinogenesis *in vitro* and *in vivo*, BioMed Res Int 2017 (2017) 1-18. https://dx.doi.org/10.1155/2017/9017902

[57] B.L. Tan, M.E. Norhaizan, K. Huynh et al., Water extract of brewers'rice induces apoptosis in human colorectal cancer cells via activation of caspase-3 and caspase-8 and downregulates the Wnt/β-catenin downstream signaling pathway in brewers'rice-treated rats with azoxymethane-induced colon carcinogenesis, BMC Complement Altern Med 15 (2015). https://dx.doi.org/10.1186/s12906-015-0730-4

[58] M. Ogawa, T. Kumamaru, H. Satoh et al., Purification of protein body-Ion rice seed and its poiypetide composition, Plant Cell Physiol 28 (1987) 1517-1527. https://dx.doi.org/10.1093/oxfordjournals.pcp.a077446

[59] T. Li, J. Zhou, Q. Wu et al., Modifying functional properties of food amyloid-based nanostructures from rice glutelin, Food Chem 398 (2023) 133798. https://dx.doi.org/10.1016/j.foodchem.2022.133798

[60] T. Zhang, J. Shi, F. Liang et al., Changes in biological activity and gut microbiota of digestion of rice glutelin during storage, J Cereal Sci 104 (2022) 103421. https://dx.doi.org/10.1016/j.jcs.2022.103421

[61] C. Liu, C. Chen, T. Lee et al., Rice protein prolamin promotes anti-leukemia immunity and inhibits leukemia growth in vivo, Food Chem Toxicol 112 (2018) 435-440. https://dx.doi.org/10.1016/j.fct.2017.09.043

[62] K. Tanaka, T. Sugimoto, M. Ogawa et al., Isolation and characterization of two types of protein bodies in the rice endosperm, Agric Biol Chem 44 (1980) 1633-1639. https://dx.doi.org/10.1080/00021369.1980.10864167

[63] L. Amagliani, J. O Regan, A.L. Kelly et al., Composition and protein profile analysis of rice protein ingredients, J Food Compos Anal 59 (2017) 18-26. https://dx.doi.org/10.1016/j.jfca.2016.12.026

[64] L. Amagliani, J. O Regan, A.L. Kelly et al., The composition, extraction, functionality and applications of rice proteins: A review, Trends Food Sci Tech 64 (2017) 1-12. https://dx.doi.org/10.1016/j.tifs.2017.01.008

[65] T. Wang, P. Xu, Z. Chen et al., Alteration of the structure of rice proteins by their interaction with soy protein isolates to design novel protein composites, Food Funct 9 (2018) 4282-4291. https://dx.doi.org/10.1039/c8fo00661j

[66] T. Mu, S. Tan, Y. Xue, The amino acid composition, solubility and emulsifying properties of sweet potato protein, Food Chem 112 (2009) 1002-1005. https://dx.doi.org/10.1016/j.foodchem.2008.07.012

[67] M. Fleddermann, A. Fechner, A. Rößler et al., Nutritional evaluation of rapeseed protein compared to soy protein for quality, plasma amino acids, and nitrogen balance – A randomized cross-over intervention study in humans, Clin Nutr 32 (2013) 519-526. https://dx.doi.org/10.1016/j.clnu.2012.11.005

[68] G.I. Petersen, Y. Liu, H.H. Stein, Coefficient of standardized ileal digestibility of amino acids in corn, soybean meal, corn gluten meal, high-protein distillers dried grains, and field peas fed to weanling pigs, Anim Feed Sci Technol 188 (2014) 145-149. https://dx.doi.org/10.1016/j.anifeedsci.2013.11.002

[69] J.H. Chiang, W. Tay, D.S.M. Ong et al., Physicochemical, textural and structural characteristics of wheat gluten-soy protein composited meat analogues prepared with the mechanical elongation method, Food Struct 28 (2021) 100183. https://dx.doi.org/10.1016/j.foostr.2021.100183

[70] L. Amagliani, J. O Regan, A.L. Kelly et al., Physical and flow properties of rice protein powders, J Food Eng 190 (2016) 1-9. https://dx.doi.org/10.1016/j.jfoodeng.2016.05.022

[71] N.P. Nirmal, S. Medhe, M. Dahal et al., Betalains protect various body organs through antioxidant and anti-inflammatory pathways, Food Sci Hum Well 13 (2024) 1109-1117. https://dx.doi.org/10.26599/FSHW.2022.9250093

[72] Y. Zhou, X. She, Z. Chen et al., Tartary buckwheat (*Fagopyrum tataricum* (L.) Gaertn) protein-derived antioxidant peptides: mechanisms of action and structure-activity relationship in Caco-2 cell models, Food Sci Hum Well 11 (2022) 1580-1590. https://dx.doi.org/10.1016/j.fshw.2022.06.016

[73] X. Qi, Y. Li, J. Li et al., Fibrillation modification to improve the viscosity, emulsifying, and foaming properties of rice protein, Food Res Int 166 (2023) 112609. https://dx.doi.org/10.1016/j.foodres.2023.112609

[74] H. Meng, J. Song, B. Fan et al., Monascus vinegar alleviates high-fat-diet-induced inflammation in rats by regulating the NF-κB and PI3K/AKT/mTOR pathways, Food Sci Hum Well 11 (2022) 943-953. https://dx.doi.org/10.1016/j.fshw.2022.03.024

[75] R. Gao, W. Shu, Y. Shen et al., Peptide fraction from sturgeon muscle by pepsin hydrolysis exerts anti-inflammatory effects in LPS-stimulated RAW264.7 macrophages via MAPK and NF-κB pathways, Food Sci Hum Well 10 (2021) 103-111. https://dx.doi.org/10.1016/j.fshw.2020.04.014

[76] K. Praengam, Y. Sahasakul, P. Kupradinun et al., Brown rice and retrograded brown rice alleviate inflammatory response in dextran sulfate sodium (DSS)-induced colitis mice, Food Funct 8 (2017) 4630-4643. https://dx.doi.org/10.1039/c7fo00305f

[77] M. Ferri, J. Graen-Heedfeld, K. Bretz et al., Peptide fractions obtained from rice by-products by means of an environment-friendly process show *in vitro* health-related bioactivities, PLoS One 12 (2017) e0170954. https://dx.doi.org/10.1371/journal.pone.0170954

[78] F.K. Hartati, S.B. Widjanarko, T.D. Widyaningsih et al., Anti-Inflammatory evaluation of black rice extract inhibits TNF-α, IFN-γ and IL-6 cytokines produced by immunocompetent cells, Food Agric Immunol 28 (2017) 1116-1125. https://dx.doi.org/10.1080/09540105.2017.1332006

[79] D.H. Ngo, Q.T. Tran, Y.S. Kim et al., GABA-enriched rice bran inhibits inflammation in LPS-stimulated macrophages *via* suppression of TLR4-MAPK/NF-κB signaling cascades, J Food Biochem 46 (2022). https://dx.doi.org/10.1111/jfbc.14421

[80] M. Liang, Z. Wang, H. Li et al., l -Arginine prevents 4-hydroxy-2-nonenal accumulation and depresses inflammation via inhibiting NF-κB activation, J Biochem & Molecular Tox 36 (2022). https://dx.doi.org/10.1002/jbt.23087

[81] H. Ou, B. Schumacher, DNA damage responses and p53 in the aging process, Blood 131 (2018) 488-495. https://dx.doi.org/10.1182/blood-2017-07-746396

[82] A.B. Williams, B. Schumacher, p53 in the DNA-damage-repair process, Cold Spring Harb Perspect Med 6 (2016) a026070. https://dx.doi.org/10.1101/cshperspect.a026070

[83] S. Vadivel Gnanasundram, O. Bonczek, L. Wang et al., p53 mRNA metabolism links with the DNA damage response, Genes 12 (2021) 1446. https://dx.doi.org/10.3390/genes12091446

[84] N.J. Stone, J.G. Robinson, A.H. Lichtenstein et al., 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults, Circulation 129 (2014). https://dx.doi.org/10.1161/01.cir.0000437738.63853.7a

[85] M.B. Mortensen, O. Dzaye, H.E. Bøtker et al., Low-density lipoprotein cholesterol is predominantly associated with atherosclerotic cardiovascular disease events in patients with evidence of coronary atherosclerosis: The western denmark heart registry, Circulation 147 (2023) 1053-1063. https://dx.doi.org/10.1161/CIRCULATIONAHA.122.061010

[86] P. Zanoni, S.A. Khetarpal, D.B. Larach et al., Rare variant in scavenger receptor BI raises HDL cholesterol and increases risk of coronary heart disease, Science 351 (2016) 1166-1171. https://dx.doi.org/10.1126/science.aad3517

[87] H. Li, L. Yang, H. Yang et al., Rice protein regulates HDL metabolism-related gene expression and enzyme activity in adult rats, Food Biosci 8 (2014) 1-7. https://dx.doi.org/10.1016/j.fbio.2014.08.001

[88] W.T. Yang, K.S. Lee, Y.J. Hur et al., Spider silk fibroin protein heterologously produced in rice seeds reduce diabetes and hypercholesterolemia in mice, Plants 9 (2020) 1282. https://dx.doi.org/10.3390/plants9101282

[89] X. Xiong, P. Wang, X. Li et al., The effects of red yeast rice dietary supplement on blood pressure, lipid profile, and C-reactive protein in hypertension: A systematic review, Crit Rev Food Sci Nutr 57 (2017) 1831-1851. https://dx.doi.org/10.1080/10408398.2015.1018987

[90] P. Choudhury, S.K. Samanta, S. Bhattacharjee et al., Chemical composite of indigenous whole grain scented joha rice varietal prevents type 2 diabetes in rats through ameliorating insulin sensitization by the IRS-1/AKT/PI3K signalling cascade, Food Funct 13 (2022) 11879-11895. https://dx.doi.org/10.1039/D2FO02373C

[91] O. Wongmekiat, N. Lailerd, A. Kobroob et al., Protective effects of purple rice husk against diabetic nephropathy by modulating PGC-1α/SIRT3/SOD2 signaling and maintaining mitochondrial redox equilibrium in rats, Biomolecules 11 (2021) 1224. https://dx.doi.org/10.3390/biom11081224

[92] J.Y. Yang, M.Y. Kang, S.H. Nam et al., Antidiabetic effects of rice hull smoke extract in alloxan-induced diabetic mice, J Agric Food Chem 60 (2012) 87-94. https://dx.doi.org/10.1021/jf2035077

[93] S. Purwaningsih, J. Santoso, E. Handharyani et al., Artificial rice from *Gracillaria* sp. as functional food to prevent diabetes, IOP Conf Series 414 (2020) 12017. https://dx.doi.org/10.1088/1755-1315/414/1/012017

[94] M. Kubota, R. Watanabe, H. Kabasawa et al., Rice protein ameliorates the progression of diabetic nephropathy in Goto-Kakizaki rats with high-sucrose feeding, Br J Nutr 110 (2013) 1211-1219. https://dx.doi.org/10.1017/S0007114513000354

[95] L. Amagliani, J. O'Regan, C. Schmitt et al., Characterisation of the physicochemical properties of intact and hydrolysed rice protein ingredients, J Cereal Sci 88 (2019) 16-23. https://dx.doi.org/10.1016/j.jcs.2019.04.002

[96] M. Hosojima, H. Shimada, Y. Obi et al., A randomized, double-blind, crossover pilot trial of rice endosperm protein supplementation in maintenance hemodialysis patients, Sci Rep 7 (2017). https://dx.doi.org/10.1038/s41598-017-18340-8

[97] T. Bao, Y. Wang, Y. Li et al., Antioxidant and antidiabetic properties of tartary buckwheat rice flavonoids after *in vitro* digestion, J Zhejiang Univ-Sci B 17 (2016) 941-951. https://dx.doi.org/10.1631/jzus.B1600243

[98] S.I. Chung, T.H. Kim, C.W. Rico et al., Hypoglycemic and antioxidative effects of instant cooked giant embryonic rice in high-fat-fed mice, Cereal Chem J 91 (2014) 50-55. https://dx.doi.org/10.1094/CCHEM-03-13-0044-R