Mini-review

PREDOMINANT RICE PHYTOCHEMICALS AND THEIR DISEASE-PREVENTIVE EFFECTS

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The imbalance between the generated free radicals and the endogenous antioxidant systems causes oxidative stress implicated in the development of several chronic diseases and cancers. Epidemiological evidence has shown that the risks of certain diseases are comparatively lower in the rice-consuming regions, which might be ascribed to the presence of several bioactive phytochemicals in rice, including (poly)phenolic compounds, γ-oryzanols, tocopherols, and tocotrienols. Therefore, this paper reviews recent findings about the predominant phytochemicals in rice based on their contents, chemical structures, absorption, metabolism, and antioxidant activities. This paper also summarizes the health-promoting effects of phytochemicals in rice, thus presenting evidence for rice being developed as a rich source of antioxidants and improving our comprehension of the practicality of this staple food. Further research is warranted to explore the synergistic interaction of individual phytochemicals in rice with consideration of the underlying mechanism of the health-beneficial functions.

Key Words: rice, phytochemicals, ferulic acid, γ-oryzanol, tocopherol, antioxidant

1. INTRODUCTION

Phytochemicals are usually regarded as plant-produced non-nutritive compounds with beneficial functions for humans by virtue of various biological properties, such as anti-oxidant, anti-proliferative, and anti-cancer effects(1). Whole grains have been identified as rich sources of various phytochemicals, including phenolic compounds, phytosterols, vitamin E derivatives, carotenoids, lignans, β-glucan, and inulin(2). Epidemiological studies have also suggested that the dietary intake of whole grains or whole grain-based products is beneficial to lower the incidence of certain chronic diseases, such as cardiovascular disease, coronary heart disease, and cancers(3–5). For example, a meta-analysis of 19 prospective cohort studies reported a daily intake of 28 grams of whole grains with respective 9%, 14%, and 3% reduced the risk of total, cardiovascular and cancer mortality(3). Another dose-response analysis of 45 prospective studies reported that the daily ingestion of three servings of whole grains (approximately 90 grams) could lower 19%, 22%, 15%, and 17% risk of coronary heart disease, cardiovascular disease, total cancer, and all causes of mortality, respectively(5). A 2020 meta-analysis of 35 studies reported an inverse association between whole grains consumption and digestive tract cancer occurrences(5).

Rice serves as the primary crop in addition to maize and wheat, not only feeding more than half of the world’s population, but also representing a kind of cultural identity(6). According to the cultivated species, rice could be generally classified into Oryza sativa and Oryza glaberrima, the former of which is widely cultivated in the Asian, American, and
European areas and the latter dominates the African regions\(^7\). Depending on the milling degrees, rice is categorized into brown rice and white rice. Brown rice is made up of a 6-7% bran layer, 2-3% embryo, and 90% endosperm\(^6\). Among these three parts, the bran layer and embryo are rich sources of biologically-active compounds\(^6\). Therefore, even though the removal of the bran layer and embryo renders white rice a superior palatability and flavor, its bioactive value is decreased at the expense of milling.

2. PHYTOCHEMICAL PROFILE OF RICE

Brown rice and its extract are rich sources of biologically-active compounds, which are positively correlated to the promotion of human health. The content of these bioactive phytochemicals in brown rice varies depending on the rice variety, solvent type, and extraction conditions. For instance, the total amount of rice phytosterol esters (\(\gamma\)-oryzanols) in organic brown rice (65.6 ± 2.7 mg/100 g) was slightly higher than that detected in a conventional sample (60.2 ± 1.8 mg/100 g)\(^9\). In addition, isopropanol extracts of 10 varieties of brown rice possessed the highest phenolic contents (203.8-293.5 mg gallic acid equivalent (GAE)/kg), followed by methanol extracts (130.2-201.8 mg GAE/kg) and ethanol extracts (130.5-196.3 mg GAE/kg)\(^10\). It was recently found that the extracted amounts of total phenolics in the low ethanol concentrations (40-60 % (v/v) aqueous ethanol) was higher than that in the high concentrations (80-100% (v/v) aqueous ethanol)\(^11\). Generally, the main bioactive phytochemicals extracted from rice could be categorized as phenolic compounds, \(\gamma\)-oryzanols, and vitamin E derivatives.

1. Phenolics

Phenolic compounds, having at least one aromatic ring with one or more hydroxyl groups, are some of the major plant-derived secondary metabolites\(^1\). Conventionally, phenolic acids and flavonoids are the most common phenolics in rice, existing in the forms of free, soluble-conjugated, and bound\(^2\). Phenolic acids could be further subdivided into \(p\)-hydroxybenzoic acid and \(p\)-hydroxycinnamic acid derivatives. Among them, \(trans\)-ferulic acid (FA) is the most abundant \(p\)-hydroxycinnamic acid analogue, accounting for 16.1-37.5 mg/100g in brown rice\(^6,12\). After oral-administration, the free form of FA can be absorbed in the small intestine, while a few portions of the bound-form FA are released from the conjugation through hydrolysis by enzymes in the small intestine and the majority being released via interaction with microflora in the colon\(^13\). The most common metabolites of FA in the liver is sulfoglucuronide, followed by glucuronide and the unmodified one\(^14\).

As a phenolic-based acid, FA is thought to be effective as a free radical scavenger. For example, FA alleviated the oxidative damages caused by hydroxyl and peroxyl radicals in neuronal cell lines along with recovering the conformational changes of biomarkers in the synaptoosomal membrane\(^15\). FA also exhibits cytoprotective effects through modulating the endogenous signaling pathways. In a model of lymphocytes, Ma et al.\(^16\) corroborated that 0.1 \(\mu\)M of FA reduced the oxidative stress caused by \(\gamma\)-ray irradiation via mediation of the extracellular signal-regulated kinase (ERK)/NF-E2-related factor (Nrf2)/heme oxygenase-1 (HO-1) pathway. Besides, FA can help to relieve cognition impairment in diabetic rats, possibly through the suppression of the protein tyrosine phosphatase 1B and insulin signaling pathway\(^17\). These findings validated the widely-receivable idea that FA is one of the predominant bioactive antioxidants in brown rice.

2. \(\gamma\)-Oryzanols

\(\gamma\)-Oryzanols (ORYs), the most abundant group of compounds in brown rice (26.2 to 62.7 mg/100 g), are the \(trans\)-ferulic acid esters of several triterpene alcohols and phytosteroles\(^18\). To date, at least ten varieties of phytosteryl ferulates have been identified, among which campesterol, cycloartenyl, 24-methylenecycloartenyl, and sitosteryl ferulates contribute 80% of the total ORYs\(^18,19\). As expected from their chemical structures, ORYs have been considered as potential antioxidants. Upon collision with free radicals, the hydroxy group on the phenolic ring could donate the hydrogen atom for scavenging the formed phenoxy radical would be stabilized by the unsaturated side chain in the FA moiety of the ORY\(^20\). Besides, the \(\alpha,\beta\)-unsaturated carbonyl moiety of ORY might mimic the electrophiles in the body, inducing electrophile counterattack responses which occur in the cytoprotection system\(^21\). For example, in the human embryonic kidney cellular model of hydrogen peroxide-induced injury, ORY effectively reduced the production of reactive oxygen and nitrogen species together with the positive induction of the Nrf2-dependent pathway\(^22\).

Due to the fact that oxidative stress plays a pertinent role in the development of chronic diseases, several studies have also suggested the modulating effects of ORY on facilitating the glucose metabolism and anti-obesity. For instance, in mice supplemented with a high-fat diet, the intake of ORY or FA markedly decreased the plasma glucose index, possibly through the elevation of the insulin contents and restored enzymes activities\(^23\). ORY and FA up-regulated the activities of several lipogenic and
antioxidative enzymes with the acceleration of the lipid metabolism in the animal model\textsuperscript{23}. On the other hand, ORYs have also shown biologically-active properties as phytosterols. For example, ORY has been found to facilitate the metabolism of cholesterol along with changes in the concentrations of the plasma high-density lipoprotein cholesterol\textsuperscript{25}. Moreover, ORY presented a suppressed tendency on the gene expression of lipogenesis-related enzymes, which in turn decreased the final conversion of the triglycerides\textsuperscript{26}. These results indicated that ORYs are expected to be a hybrid phytochemical with the antioxidant FA and phytosterols.

(3) Vitamin E

Vitamin E is a collective term for a group of fat-soluble antioxidants, including tocopherols (Ts) and tocotrienols (T3s), designated according to the saturation of a phytol side chain, both of which are naturally present in each of the α-, β-, γ-, or δ-form\textsuperscript{27}. Upon digestion, similar to the other dietary fats, all forms of the vitamin E family are absorbed from the gastrointestinal tract and subsequently transported into the liver. The α-tocopherol transfer protein (α-TTP) prefers transporting α-T for distribution in the human body, while other forms are considered as xenobiotics, metabolized into their sulfate and glucuronide conjugates\textsuperscript{27}. In brown rice, the average contents of vitamin E are approximately 6.0 mg/100g, among which γ-T3 and α-T are large proportions (27–63% and 10–30% of total vitamin E amounts, respectively)\textsuperscript{22}.

It has been proposed that the antioxidant capability is one of the most significant biological properties of vitamin E. In homogeneous solutions, Ts and T3s presented similar abilities in scavenging peroxyl radicals\textsuperscript{28}, whereas, in heterogeneous oxidation systems, such as liposomal membranes\textsuperscript{29} and rat liver microsomes\textsuperscript{30}, the antioxidative efficacies of the T3s are higher than those of the Ts, possibly due to their difference in permeating into the bio-membranes. Generally, T3s with fewer methyl groups more readily incorporate into cells to interact with oxidants or electrophiles than the corresponding Ts\textsuperscript{12, 28}. Moreover, the vitamin E varieties have also shown modulatory effects on the gene and enzyme expressions, which are linked to exhibiting cytoprotective effects. In a recent study, 100 μM of α-T enhanced the expression levels of the antioxidative genes (superoxide dismutase 2 and catalase) and cell cycle regulation gene (apoptosis tumor protein 53) with a decrease in the expression of the apoptosis-related cysteine protease, all of which benefit the developmental competence of rabbit oocytes\textsuperscript{31}. Furthermore, α-T and γ-T equally attenuated the mitochondrial ROS production, whereas the latter exhibited a superiority in improving the mitochondrial function and repression of apoptosis-related proteins to prevent Alzheimer’s disease\textsuperscript{32}.

3. CONCLUSION

This review summarized several predominant phytochemicals in brown rice with attractive biological properties. These bioactive compounds endow rice with health-beneficial potentials. Therefore, rice is acceptable as a feasible source of such potential food components to modulate and/or prevent chronic diseases caused by a redox imbalance. On the contrary, the present knowledge of identifying the effective compounds and determining their synergistic interaction in rice extract remains limited. To resolve this challenging issue, future efforts will be associated with not only comparing the modulating effects of the rice varieties and their individual components, but also evaluating the efficacy of the combination of rice phytochemicals on the endogenous defense system.

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