Review Article

Bioavailability and Bioactivity of Alkylresorcinols from Different Cereal Products

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Received 13 January 2020; Revised 19 March 2020; Accepted 15 May 2020; Published 30 May 2020

1. Introduction

Polyphenolic compounds from cereal products are an indispensable part of human diet, especially from whole wheat flour, whole rye flour, and whole triticale flour, which have antioxidant properties and potential health benefits, and have attracted extensive attention [1]. Alkylresorcinols (ARs) only exist in wheat and rye bran and are related to preventing and reducing the risks of related chronic diseases such as diabetes, cardiovascular diseases, obesity, and cancer [2–4]. According to a case-control study report, only whole cereal intake dominated by rye consumption may be very important for the prevention of type 2 diabetes, which indicates that ARs have certain effects on the prevention of diabetes [5, 6]. In addition, ARs can also inhibit digestive enzyme activity, reduce oxidative stress, reduce cholesterol absorption, prevent bacterial or fungal infection, reduce cholesterol absorption, and regulate triglyceride metabolism [7–9]. As a phenolic lipid, ARs contain amphiphilic 1, 3-dihydroxybenzene derivatives (Figure 1) with an odd alkyl chain at the 5-th position of the benzene ring, where the length of the saturated alkyl tail varies between 15 and 27 carbons. As shown in Table 1, the homologues are C17:0, C19:0, C21:0, C23:0, and C25:0 [11, 12]. Therefore, C21: C19 can be used to determine whether wheat is a whole wheat or a whole wheat product.

ARs in wheat bran samples were extracted with four different solvents, and ARs in bread were extracted with hot 1-propanol and quantified by gas chromatography-mass spectrometry (GC/MS) [13]. It was found that ARs can be 3, 5-dihydroxybenzoic acid (DHBA) and 3-(3, 5-dihydroxyphenyl)-1-C ionic acid (Population and Health Action Plan) in the hepatic metabolism after being absorbed by the human body. Several studies have reported a positive correlation between whole cereal intake and the presence of ARs in the plasma or its urine metabolites [14–22]. However, the physical and chemical properties of whole cereal foods are also closely related to the ARs content in cereals.

2. The Effect of ARs Content on Whole Cereal Products

The content of ARs in different cereal products is also different. According to the research on different varieties of Italian hard and soft wheat products, the ARs content of whole wheat bread made of hard and soft red wheat is significantly higher than that of other kinds of wheat [13]. The processing of whole wheat flour has a great influence on
ARs. The results showed that the ARs level was significantly reduced when preparing whole wheat bread and rye bread [23]. It is speculated that the decrease of the ARs content may be due to the combined effect of fermentation and baking. The results showed that the baking temperature of bread was 218°C, when the intermediate compound starts sublimation at 196°C–250°C. However, the whole cereal products prepared after whole cereal fermentation showed that the ARs concentration increased slightly, indicating that ARs did not degrade during baking and showed expected stability during cereal preparation, which indicated that fermentation had a significant impact on ARs in whole cereal products [24]. Compared with whole wheat products, crisp bread has the highest ARs content in whole wheat or rye products [25]. Therefore, the ARs content in bread products can be used to distinguish comprehensive and rye products.

It was found that the combined effect of fermentation and germination on rye can effectively enhance the contents of folic acid, total phenol, free phenolic acid, and ARs in whole wheat products, with synergistic effect. Therefore, the nutritional value of whole wheat products can be further enhanced through specific processing. The high content of ARs (0.5–1%) was added to the dough to improve the fermentation performance and increase the volume of rye bread [26]. The result showed that adding ARs could reduce bread quality and bread volume by 26–39% because rye bran contains about 4.3% salt, and it affects the baking of the whole wheat rye bread. Although the ARs content of bread baked with black wheat bran was ten times lower, the size and porosity of the bread were not affected. These results showed that compared with the study, the content of natural ARs in bread was too low, which had no practical influence on the quality of bread [27]. Bread is baked with wheat flour and 20% or 30% fine black bran (not extracted and extracted). The moisture content in the baking test (Table 2) is the optimum amount of each flour mixture.

### 3. Bioactivity of ARs in Different Cereal Products

ARs have a variety of physiological and biological activities, such as bactericidal, antioxidant, affecting membrane phospholipid activity and enzyme activity, and inhibiting tumors. The role of ARs in the body is closely related to its absorption and metabolism. The small intestine can partially absorb or metabolize ARs. The concentration of ARs in the plasma was 1.47–124 µg/L. The biological activity of ARs is related to its alkyl chain length, mainly because the longer the alkyl chain, the better the fat solubility.

#### 3.1. Antibacterial Activity of ARs in Different Cereal Products

ARs with high concentration have been proved to have antibacterial and antifungal activities and the ability to kill mollusks. This is mainly because alkylresorcinol inhibits phenol oxidase in mollusks. ARs had a strong and persistent effect on Gram-positive bacteria, but they have little effect on Gram-negative bacteria [28]. C15:0 has an inhibitory effect on the bread mold Aspergillus parasitic bacteria in the
United States and *Penicillium chrysogenum*, but only at high concentration (10 mg/ml agar medium) [29]. Carol has an obvious effect on malaria parasites. The side chain was found to be important for the anti-allergic effect [30]. Antibacterial activity of ARs in more detail can be seen in [28]. In addition, ARs also play an important role in protecting wheat seedlings from fungal infection [29].

### 3.2. Antioxidant Properties of ARs in Different Cereal Products.

The free radical mechanism is considered to be one of the mechanisms of oxidative aging. Some in vitro experiments have shown that 5-alkylresorcinol has antioxidant activity, which is mainly due to the two indirect positions of hydroxyl groups on the benzene ring which can scavenge free radicals and generate protons. When studying the oxidation resistance of 5-alkylresorcinol on biofilms, 5-alkylresorcinol exhibits strong oxidation resistance, and the alkyl chain may play an important role in this process. 5-Alkylresorcinol exhibits strong oxidation resistance on membranes, mainly because it can be inserted into membranes and bind to adjacent phospholipids in the form of hydrogen bonds [31], thereby interfering with the structure of these membranes, affecting its performance, and resisting oxidation. To some extent, this theory can be used to explain the relationship between antioxidant performance and the alkyl chain length of 5-alkylresorcinol. The longer the alkyl chain is, the stronger the antioxidant activity is.

Most of the cereal foods that people need in daily life need to undergo production and processing. Processing affects the flavor and nutritional value of cereal products. This process may affect the active substance content and bioavailability in whole grain foods [32]. Research by Ross et al. [33] showed that ARs can be extracted from baked bread. Ross et al. [14] studied the combined effects of fermentation and germination on rye and found that the combination of these two processing methods can very effectively enhance the content of folic acid, total phenol, free phenolic acids, and ARs in whole wheat products. Therefore, the nutritional value of whole wheat products can be further enhanced through specific processing. Ross et al. [34] measured the ARs content of yeast, dough, and bread at different stages of wheat and rye whole flour through research, and the research showed that the ARs content decreased significantly during fermentation and baking. At the same time, Weipert and ElBaya reported that when flour is made into bread, the amount of ARs decreases significantly [35, 36]. Ross et al. [37] found that natural whole wheat increased its ARs content to a certain extent during fermentation. Winata, and Lorenz [38] compared alkylresorcinol, fatty acids, and antioxidant activities of wheat processed by traditional and modern plants and found that whole grains showed higher ARs content and resistance to the corresponding crushed products oxidative activity, a reduction in total ARs content was observed after pulverization, and the lowest amount was detected in the semolina-like portion. Yu et al. [39] reported the effects of different peeling levels on wheat flour ARs. Studies have shown that peeling treatment has a significant effect on nutrients in wheat nutrition powder, and the ARs content gradually decreases with increasing peeling time.

### 3.3. Anticancer Properties of ARs in Different Cereal Products.

Wheat bran plays an important role in preventing the occurrence and development of colon cancer. There is evidence that eating wheat bran can reduce the risk of colon cancer. Most of the animal and human tests have shown the relationship between wheat bran and reduction in the risk of colon cancer [10, 40, 41]. The main component of wheat bran oil, 5-alkylresorcinol, has a strong inhibitory effect on the proliferation of colon cancer cells [42], but the relevant mechanism has not been fully elucidated.

ARs can reduce the induction of some indirectly induced substances. Compared with anthocyanin, ARs can effectively inhibit the induction rate and frequency of inducers in the lymphocyte culture. The induction effect of ARs on reducing four standard inducers was found through the Ames test, and it was found that its effect is very significant [43]. In the sister chromosome hybridization test, ARs can significantly reduce the frequency of chromosome exchange. Further research shows that ARs can accelerate the death rate of damaged cells with genotoxicity and inhibit the formation of cancer cells. Later, the anticancer effect of ARs is attributed to the ability to increase apoptosis of cells damaged by genetic toxins [44]. Chain length seems to be very important for the cytotoxicity of cancer cells in vitro95 and inhibition of the formation of cancer, while shorter chain lengths (C15:0 and C17:0) may not be the most effective [45], further confirming that oxidative damaged DNA has strong induction and carcinogenic effects. Studies have shown that ARs inhibit oxidative damage caused by hydrogen peroxide to colon cancer cells. By adding 5-alkylphloroglucinol directly related to colon cancer, reproductive toxicity of cancer cell excreta is also reduced. It can be proved that 5-alkylisophenol is a natural DNA polymer, which can be used as an inhibitor.

### 3.4. Inhibition of ARs on Enzymes in Different Cereal Products.

Sileshi et al. [46] proposed that ARs and related compounds may have inhibitory effects on certain metabolic enzymes. C15:0 can inhibit the key enzyme GPDH of triacylglycerol synthesis, and the inhibitory effect is related to the alkyl chain length [47]. The metabolized alkylresorcinol can inhibit the action of phosphorylase and activate the synthesis

| Flour mixture | Water amount (mL) |
|---------------|------------------|
| Wheat +       |                  |
| 30% nonextracted rye bran | 141 |
| 30% finely milled nonextracted rye bran | 143 |
| 30% extracted rye bran | 142 |
| 30% finely milled extracted rye bran | 144 |
| Wheat +       |                  |
| 20% nonextracted rye bran | 138 |
| 20% finely milled nonextracted rye bran | 141 |
| 20% extracted rye bran | 138 |
| 20% finely milled extracted rye bran | 141 |

**Table 2:** Water amount added to different flour mixtures.
of glycen [48]. For example, 5-pentadecylresorcinol can inhibit glycerol 3-phosphate glycerol dehydrogenase activity. In a study, mice were fed with high concentrations of purified rye ARs (0.1%−0.4%). It was found that the level of VE in the liver was increased and hepatic cholesterol was reduced by 47% relative to the control group when the mice were fed with 0.4% of ARs [34]. The reduction in liver cholesterol is 47% [34]. The decrease of liver cholesterol may be due to the fact that ARs can interfere with lipid absorption or liver sterol synthesis, but its mechanism of action requires further research to clarify.

ARs are natural alpha-glycosidase inhibitors in whole grain foods. Wheat bran ARs can reduce fasting blood glucose in obese mice, induced by high-fat and high-sugar diets, increase glucose tolerance and insulin sensitivity in mice, increase fecal cholesterol excretion in mice, and reduce cholesterol concentrations in the blood [47].

Maria et al. [49] studied the effect of phenolic lipids extracted from whole wheat on the activity of acetylcholinesterase. The experimental results show that phenolic lipids can inhibit the activity of acetylcholinesterase, and the effect of phenolic lipids and the structural characteristics of its hydrophilic part and the alkyl chain length is related.

4. Conclusion

The combined effect of fermentation and germination on rye can effectively enhance the contents of folic acid, total phenol, free phenolic acid, and ARs in whole wheat products, with synergistic effect. The nutritional value of whole wheat products can be further enhanced through specific processing. High content of ARs (0.5−1%) was added to the dough to improve the fermentation performance and increase the volume of rye bread. ARs have a variety of physiological and biological activities, such as bactericidal, antioxidant, affecting membrane phospholipids’ activity and enzyme activity, and inhibiting tumors. The role of ARs in the body is closely related to its absorption and metabolism. The small intestine can partially absorb or metabolize ARs. There is also a certain concentration of ARs in the plasma. The biological activity of ARs is related to its alkyl chain length, mainly because the longer the alkyl chain, the better the fat solubility.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

The authors would like to acknowledge the National Key Research and Development Program (no. 2018YFD0401000) and the Province Key Laboratory of Cereal Resource Transformation and Utilization, Henan University of Technology (PL2018007).

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