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Review

Antioxidant properties of diverse cereal grains: A review on *in vitro* and *in vivo* studies

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ABSTRACT

Cereal grains and products have gained popularity in contributing to healthy eating behavior because of their antioxidant properties associated with protection against chronic diseases. In this review, notable studies on the *in vitro* and *in vivo* antioxidant activity of commonly consumed cereal grains are summarized. Cereals contain phytochemicals or certain minor components with antioxidant properties. The antioxidant potential of cereals depends on their bioaccessibility, absorption in the gastrointestinal and their bioavailability utilization *in vivo*. The *in vitro* gastrointestinal digestion and fermentation of cereals increased their antioxidant potentials which are significantly correlated with their total phenolic contents. Most studies performed *in vivo* have been concerned with the antioxidant properties of colored rice, wheat bran and rye products. There are inadequate *in vitro* and *in vivo* studies on antioxidative potentials of fermented versus unfermented cereals. Therefore, further studies are necessary to maximize possible health benefits of cereal antioxidative phytochemicals.

Contents

Abbreviations: ABTS, 2,2-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid); AOP, antioxidant potential; CAA, cellular antioxidant activity; CAT, catalase; CUPRA, copper reduction assay; DPPH, 2,2,-diphenyl-1-picrylhydrazyl; FOs, feruloyl oligosaccharides; FRAP, ferric reducing ability of plasma; GAE, gallic acid equivalent; GPx, glutathione peroxidase; GSH, reduced glutathione; GSSG, oxidized glutathione; HAT, hydrogen atom transfer; LDL, low density lipoprotein; LOX, lipoxygenase; NSP, nonstarch polysaccharides; ORAC, oxygen radical absorbance capacity; POX, peroxidase; ROS, reactive oxygen species; SOD, superoxide dismutase; TAC, total anthocyanin contents; TBARS, thiobarbituric acid reactive substances; TE, trolox equivalents; TEAC, trolox equivalent antioxidant capacity; TOSC, total oxyradical scavenging capacity; TP, total phenolics; TPC, total phenolic content; TRAP, total peroxyl radical trapping antioxidant parameter; WEAX, water extractable arabinoxylans.

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1. Introduction

Epidemiological and experimental studies have suggested that diet plays a crucial role in the prevention of chronic diseases such as heart disease, cancer, diabetes, and Alzheimer's disease (Temple, 2000; Willet, 1994). Consumption of cereal grains has gained popularity with whole grain products being regarded as "healthy foods" because of their potential protection against life-style and diet related disorders such as obesity, diabetes (Fardet, Edmond, & Remesy, 2008; Liu et al., 2000; Meyer et al., 2000), cardiovascular diseases (Fardet et al., 2008; Kelly, Summerbell, Brynes, Whittaker, & Frost, 2007) and cancers (Fardet et al., 2008; Schatzkin et al., 2007). This effect is thought to be partly due to their phytochemicals that combat oxidative stress. Overproduction of oxidants can cause oxidative damage to large biomolecules such as lipids, DNA and proteins resulting in increased risk for cancer, cardiovascular and other diseases (Ames, Shigenaga, & Gold, 1993; Temple, 2000; Wagner, Hu, & Ames, 1992). Dietary antioxidants may reduce such oxidative damages to biomolecules through several mechanisms (Duthie, Ma, Ross, & Collins, 1996; Fraga et al., 1991).

The importance and health benefits of regular cereal grain consumption in the prevention of chronic diseases are a focus for many research laboratories. Current research data suggest that whole-grains contain more antioxidant phytochemicals than was previously reported (Lui, 2007). The aim of this review is to critically discuss research data pertaining to the antioxidant activities of cereal grains produced by *in vitro* and *in vivo* studies. Such information has been summarized here for a better understanding of antioxidant properties of commonly consumed cereal grains (wheat, corn, rice, barley, sorghum, rye, oats and millet).

1.1. Antioxidants in cereal grains

Cereal grains have a long history as major sources of staple foods worldwide. Whole grain cereals are good sources of phenolic compounds which include derivatives of benzoic and cinnamic acids, anthocyanidins, quinines, flavonols, chalcones, flavones, flavanones, and amino phenolic compounds (Bellido & Beta, 2009; Hosseinian, Li, & Beta, 2008; Jang & Xu, 2009; Lloyd, Siebenmorgen, & Beers, 2000; Shahidi & Naczk, 1995; Thompson, 1994). Grains contain tocotrienols and tocopherols (Thompson, 1994), and oryzanols (Lloyd et al., 2000). This wide range of phytochemicals has been recognized to support overall health through their antioxidant potential. The protective function of antioxidants in the body is through balanced oxidative stress free radicals. Cereal grain antioxidants are thought to act as direct free radical scavengers, cofactors of antioxidant enzymes or as indirect antioxidants (Fardet et al., 2008). Free radical compounds result from normal metabolic activities as well as from the diet and environment. Excess amounts of these reactive substances can cause oxidative damage to biomolecules such as lipids, protein and DNA (Temple, 2000) resulting in an increased risk of chronic disease and contribution to general inflammatory response and tissue damage (Slavin, 2003; Young & Woodside, 2001).

Reactive oxygen species (ROS) including superoxide anion, hydrogen peroxide, peroxyl radical, hydroxyl radical, singlet oxygen and peroxynitrite are produced during cellular metabolic processes (Sánchez-Moreno, 2002). Several studies suggested a strong association between elevated levels of these molecules and the pathogenesis of several chronic diseases through the process of oxidative stress (Leavy, 2014; Nogueira & Hay, 2013; Sugamura & Keaney, 2011). ROS are involved in a variety of physiological and pathological processes, including cell signaling transduction, cell proliferation, differentiation, apoptosis, as well as ischemia–reperfusion, inflammation and many neurodegenerative disorders (Ames, Shigenaga, & Hagen, 1993; Bland, 1995). The process of ROS generation/production occurs when there is an imbalance between pro-oxidants and antioxidants leading to oxidative stress (Qingming et al., 2010). The process of oxidation in cells is regulated by antioxidants, which delay or prevent cellular damage. Antioxidant protection is normally achieved through a balance between pro-oxidants and endogenous and/or dietary antioxidants (Hancock, Desikan, & Neill, 2001; Sobha & Andallu, 2013).

The dietary antioxidants (minerals, trace elements, vitamins, carotenoids, polyphenols, alkylresorcinols, betaine, choline, sulfur amino acids, phytic acids, lignans and avenanthramides) of whole grain cereals are primarily located in the bran and germ fractions (Fardet, 2010). Different antioxidant mechanisms have been attributed to cereal grain phytochemicals. These include prevention of oxidation of polyunsaturated lipids (vitamin E), reduction of the concentration of plasma homocysteine (vitamin B9, betaine, choline), acting as cofactor of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase and thioredoxine (Zn, Fe, Se, Cu, Mn), or stabilization and delocalization of unpaired electrons (vitamin E, polyphenols, alkylresorcinols). Phenolic acids (ρ-coumaric acid, ferulic, syringic, sinapic and vanillic) are also believed to chelate transition metals as well as activate or repress particular genes, while sulfur-containing amino acids (cysteine and methionine) contribute to the synthesis of a major endogenous antioxidant glutathione (Čukelj, Novotni, and Curic, 2010; Fardet et al., 2008). Whole cereal grain antioxidants are water and fat soluble, providing protection through the entire digestive tract (Slavin, 2003).

2. *In vitro* cereal grain antioxidant activity

The antioxidant capacity of different cereals is evaluated based on two chemical antioxidant assays, namely the electron transfer (ET) and hydrogen atom transfer (HAT) methods. The ET method is characterized by change in color during the reduction of oxidants. HAT involves competition between the antioxidant and substrate (probe) for free radicals (Huang, Ou, & Prior, 2005). Examples of ET assays include trolox equivalent antioxidant capacity (TEAC), the ferric reducing ability of plasma (FRAP) assay, copper reduction assay (CUPRAC), and 2,2,-diphenyl-1-picrylhydrazyl (DPPH) assay. The HAT assay includes the crocin bleaching assay, oxygen radical absorbance capacity (ORAC) and total peroxyl radical trapping antioxidant parameter (TRAP) (Huang et al., 2005).

Most methods are based mainly on solvent extraction and quencher procedures which may largely underestimate total antioxidant capacity of cereals. However, both solvent extraction and quencher procedures are performed prior to digestion. In this section, antioxidants released by solvent extraction methods, quencher procedure, enzymatic digestive extraction and solid-state fermentation extraction will be described.

2.1. Wheat

Yu, Nanguet, and Beta (2013) investigated the antioxidant properties of refined and whole wheat flour and their resultant bread. Their data showed that whole wheat flour and bread were superior to refined flour and bread in regard to their *in vitro* antioxidant properties. Žilić, Serpen, Akillioğlu, Janković, and Gökmen (2012) studied the distribution of phenolic compounds and yellow pigments in wheat grains and their relation to the total antioxidant capacity of bran and debranned flour. The color intensity of yellow pigments, the activity of lipoxygenase (LOX) and peroxidase (POX) enzymes were also measured. Their results showed that bran fraction contains significantly higher concentrations of phenolic acids, flavonoids and yellow pigments. The LOX activity was concentrated in endosperm and embryo, while the POX activity was mostly concentrated in the bran fraction. Therefore, their results suggest that the

bran fraction of wheat would potentially provide natural antioxidants. Liu, Qiu, and Beta (2010) used the DPPH assay to investigate antioxidant activities of various colored wheat grains and their phenolic compounds. The results showed that Charcoal purple wheat had the highest antioxidant activity (up to 6899 μmol/100 g) followed by red Fife wheat and yellow Luteus wheat; while white AC vista wheat had the lowest antioxidant activity. The antioxidant activity was positively correlated to phenolic contents in these grains. The major phenolic composition identified in wheat grains consisted of phenolic acids, flavonoids, and anthocyanins. Ferulic acid was reported as the most dominant phenolic acid (74–87 mg/100 g). Vanillic, ρ-coumaric, and sinapic acids were found in moderate levels (about 2 mg/100 g), whereas caffeic acid was present in the least amount (<1 mg/100 g). Purple wheat, compared with colored wheat grains, was distinguished by higher contents of vanillic acid (>2.58 mg/100 g) and ferulic acid (>81.38 mg/100 g). The flavonoids ranged from 21.59–102.95 mg/100 g in purple wheat, 13.44 mg/100 g and 10.72 mg/100 g for yellow and red wheats respectively, and 9.6 mg/100 g for white wheat. Anthocyanin contents were only present in purple wheats ranging from 2.5 to 23.5 mg/100 g. Verma, Hucl, and Chibbar (2008) measured the free, bound, and total phenolic contents and antioxidant activities in the bran of 51 wheat cultivars belonging to eight Western Canadian spring wheat market classes grown in a replicated trials at Saskatoon, Saskatchewan, Canada. The free phenolic content ranged from 854.1 ± 265.1 to 1754.9 ± 240.3 μg/g of bran gallic acid equivalent (GAE). Saponification followed by a liquid–liquid solvent extraction released bound phenols ranged from 2304.9 ± 438.0 to 5386.1 ± 927.5 μg/g of bran GAE, contributing 66–82% of the total wheat bran phenolic content. Total phenolic acids ranged from 3406.4 ± 32.3 to 6702.7 ± 19.6 μg/g of bran GAE, with an average of 5197.2 ± 804.9 μg/g of bran GAE. Antioxidant activity was determined as % discolouration = (1 − [(absorbance of sample at 30 min)/(absorbance of control at time 0)]) and ranged from 11.86 ± 2.59 to 20.12 ± 0.51%, while the overall average was 15.6 ± 2.2%. Based on varietal means, antioxidant activity correlated with free, bound and total phenolic contents (TPC; $r = 0.8$, $P < 0.05$).

Anson, Havenaar, Bast, and Haenen (2010) investigated the antioxidant and anti-inflammatory capacity of bioaccessible compounds from wheat fractions after gastrointestinal digestion. In their study, the bioaccessible compounds from aleurone, bran and flour were obtained from a dynamic *in vitro* model of the upper gastrointestinal tract. They found that bioaccessible compounds from aleurone had the highest antioxidant capacity and provided a prolonged anti-inflammatory effect as compared to bran and flour. Bhanja, Kumari, and Banerjee (2009) investigated the TPC and antioxidant potential of ethanolic extract of non-fermented and fermented wheat grains with two filamentous fungi (*Aspergillus oryzae* and *Aspergillus awamori* nakazawa). They found that the total phenolic content and antioxidant property of wheat (54% ethanol extraction) was drastically increased when fermented with *A. oryzae* and *A. awamori* nakazawa. Moore et al. (2007) evaluated the potential of solid-state yeast fermentation for their ability to improve the extractable antioxidant properties of wheat. The results demonstrated that solid state yeast treatment significantly increased releasable antioxidant properties ranging from 28% to 65%, 0% to 20%, 23% to 19%, 0% to 25%, 50% to 100% and 3% to 333% for scavenging capacity against ORAC, ABTS, DPPH TPC, and phenolic acids, respectively.

2.2. Rice

Shao, Xu, Sun, Bao, and Beta (2014a, 2014b) investigated total phenolic contents, antioxidant capacity by using DPPH and ORAC assays, and phenolic acids in fractions of white (unpolished), red, and black rice after flowering and maturity, as well as the distribution of phenolic acids and anthocyanins in endosperm, embryo, and bran of white, red, and black rice. Their study showed that the total phenolic contents (TPC) of white rice (14.6–33.4 mg/100 g) and red rice (66.8–422.2 mg/100 g) were higher at 1-week development than at late stage, and black rice (56.5–82.0 mg/100 g) had a higher antioxidant activity at maturity (Shao et al., 2014a, 2014b). Shao et al. (2014a, 2014b) also demonstrated that rice bran had a higher TPC (7.35 mg GAE/g average) and contributed to 60%, 86% and 84% of phenolics in white, red and black rice whole grain, respectively. The average TPC of the embryo and endosperm were 2.79 and 0.11 mg GAE/g accounting for 17% and 23%, 4% and 10% and 7% and 9% in white, red and black rice, respectively. The antioxidant capacity followed a similar trend to TPC. Deng et al. (2012) used spectrophotometric methods to investigate the antioxidant properties and lipophilic and hydrophilic phenolic contents in 24 cereal grains from China. Their results showed that cereals have diverse antioxidant capacities. The phenolic compounds gallic acid, kaempferol, quercetin, galangin and cyanidin 3-glucoside were widely found in the cereals tested. The pigmented cereals, such as black rice, red rice, and purple rice had the highest antioxidant capacities and total phenolic contents among tested cereals.

Qiu, Liu, and Beta (2009, 2010) used DPPH and ORAC assays to evaluate antioxidant properties of wild rice. In both studies, their results showed that wild rice had a higher antioxidant activity than white rice (control), most likely due to their high phenolic acid contents. Zhang, Zhang, Zhang, and Liu (2010) determined the phytochemical profiles and antioxidant activity of rice bran samples from 12 diverse varieties of black rice. Their data showed that there are significant differences in phytochemical content and antioxidant activity among the different black rice varieties. Black rice bran has a higher content of phenolics, flavonoids, and anthocyanins as well as higher antioxidant activity compared to white rice. The phenolic, flavonoids and anthocyanins of black rice bran are mainly present in the free form.

Bhanja, Rout, Banerjee, and Bhattacharyya (2008) investigated a self-designed new bioreactor (NB) for the improvement of phenolics and antioxidant activity in rice koji and compared the results with solid-state fermentation (SSF). Rice fermented in the NB resulted in a higher yield of phenolics and DPPH compared to the SSF and control. This might be due to higher titre values of β-glucosidase (62.7%) and α-amylase (40.7%) in the extraction media of NB compared to SSF.

2.3. Other cereal grains

Kljak and Grbeša (2015) evaluated the relationship between carotenoid content and antioxidant activity in six Croatian commercial high-yield corn hybrids using TEAC, ABTS and thiobarbituric acid reactive substances (TBARS) systems. Their data showed that the corn hybrids varied in carotenoid content and antioxidant activity. Antioxidant activity in both assays increased linearly with total carotenoid content. Ndolo and Beta (2013) investigated carotenoid antioxidant activity using DPPH scavenging activity on aleurone, endosperm and germ fractions of barley (purple and regular), yellow corn, oats and wheat (purple and regular). The data suggested that antioxidant activity of carotenoids from the germ fraction showed higher scavenging activity compared to aleurone and endosperm. Malunga and Beta (2015) analyzed the antioxidant capacity of water-extractable nonstarch polysaccharides (NSP) and feruloylated arabinoxylans (WEAX) from commercial barley, wheat and wheat fractions (germ, bran, and aleurone) using DPPH, ABTS and ORAC assays. Their data showed that NSP and WEAX exhibited antioxidant activity. The results demonstrated that arabinoxylan content, TPC, xylose and

degree of substitution influenced the NSP and WEAX antioxidant capacity. Gamel and Abdel-Aal (2012) investigated phenolic acid composition and antioxidant capacity against DPPH and ABTS radicals, and inhibition of oxidation of human low density lipoprotein (LDL) cholesterol of selected Canadian and Egyptian barley whole grain flours and four pearling fractions. The data showed significant variations among barley wholegrain flour and pearling/milling fractions in terms of phenolic acid composition and antioxidant capacity.

Bhanja Dey and Kuhad (2014) evaluated the antioxidant potential of various filamentous fungi-fermented products derived from different whole grain cereals (wheat, brown rice, oats and maize). The fermented products showed a high efficiency for the improvement of water soluble TPC and antioxidant properties including ABTS and DPPH. Fermented wheat showed a 14-fold improvement in TPC, and 6.6 and 5-fold enhancement of DPPH and ABTS respectively. This study demonstrates that fermented wheat can be a powerful source of natural antioxidants. Gong, Jin, Wu, and Zhang (2013) compared the *in vitro* procedure of antioxidant extraction with the Quencher method and water as an extracting solvent. Total antioxidant capacity values of cereal grains obtained using an *in vitro* procedure were 1.8–10.3 times higher than the Quencher procedure and 3.5–10.5 times higher than the water extract. This indicates that the *in vitro* gastrointestinal digestion procedure is more useful in the screening of grains, and assessing for their health benefits compared to the Quencher procedure and water extraction. Prajapati, Patel, Parekh, and Subhash (2013) evaluated the total phenol content, flavonoids, flavonol and antioxidant activity of five cereals (wheat, pearl millet, rice, maize and sorghum) by *in vitro* digestion and chemical extraction along with the effect of cooking. Their results showed higher values of total phenolics, flavonoids, flavonols as well as increase in antioxidant activity measured by the FRAP method in *in vitro* digesta (enzymatic extract) of cereals compared to their chemical extracts. Cooking of cereal also resulted in increased total antioxidant capacity and enhanced phenolics, flavonoid and flavonol content. Based on this study, antioxidant components like phenolic compounds, flavonoids and flavonols of selected cereals were affected by *in vitro* digestion. Pazanatto, Malta, Pastore, and Netto (2013) evaluated the effect of different process-defatting, protein concentration, thermal treatment, hydrolysis with Alcalase and *in vitro* digestion on the antioxidant capacity of amaranth seeds. The combination of protein concentration and hydrolysis with Alcalase led to a product with high antioxidant activity as evaluated by DPPH and ORAC. After *in vitro* digestion, protein concentrate and its hydrolysate showed similar antioxidant capacity. Cai et al. (2012, 2014) evaluated the potential of solid-state fermentation for the improvement of TPC and antioxidant potential of oat. They found that fermentation increased TPC and the antioxidant activity. Đorđević, Šiler-Marinković, and Dimitrijević-Branković (2010) evaluated the influence of fermentation by *Lactobacillus rhamnosus* and *Saccharomyces cerevisiae* on antioxidant activities and total phenolic content of 4 cereals (buckwheat, wheat germ, barley and rye) and compared them to their unfermented counterparts. Total phenolic content increased significantly and antioxidant activities were enhanced through fermentation by lactic acid bacteria and yeast.

2.4. Intracellular antioxidant cereal grains

Masisi et al. (2015) investigated antioxidant potential of carotenoids from aleurone, germ, and endosperm of barley, corn, and wheat. The antioxidant properties using DPPH, ABTS and ORAC assays revealed significantly higher antioxidant activity in the germ than in the aleurone and endosperm fractions. 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide (MTT) assay, and 2,2′azobis (2-amidinopropane)dihydrochloride (AAPH)-induced cell loss was effectively reduced by pre-incubating Caco-2, HT-29, and FHs 74 Int cells with carotenoid extracts. The data showed that carotenoids of germ, aleurone, and endosperm fractions improve biochemical and intracellular antioxidant activity. Hirawan, Diehl-Jones, and Beta (2011) investigated the properties of whole purple wheat, unpolished red rice and partially polished red rice infant cereals. ORAC, TPC, total anthocyanin contents (TAC) and cellular antioxidant activity (CAA) were measured. Home- and laboratory-made unpolished red rice had higher TPC and peroxyl radical scavenging activities than purple wheat infant cereals; the latter had higher TAC. Pigmented infant cereals were found to have higher TPC, TAC and ORAC than commercial ones. Anthocyanins were identified in whole purple wheat but not in unpolished red rice. Purple wheat infant cereal had higher CAA than unpolished rice. Whole purple wheat infant cereals showed higher antioxidant activities than the commercial infant cereals. Stein, Borowicki, Scharlau, and Glei (2010) investigated the effects of fermented wheat aleurone on the expression of genes involved in stress response, toxicity, activity of drug-metabolizing enzymes and anti-genotoxic potential. They also investigated the protection against H_2O_2-induced DNA damage in HT29 cells. The data showed that fermented aleurone significantly induced mRNA expression in *CAT*, *GSTP1* and *SLUT2B1* (HT29) and *GSTP1* (epithelial stripe). The enzyme activity of GST (HT29) and CAT (HT29, epithelial stripes) were also increased. DNA damage induced by H_2O_2 was significantly reduced by the fermented aleurone.

3. *In vivo* cereal grain antioxidant activity

Although *in vitro* experiments indicate great antioxidant abilities of the whole grain cereals, it is questionable if the methods underestimate physiological antioxidant capacity. Several studies have been done in order to evaluate the bioactivity of cereal grain phytochemicals, mostly on animals and human.

3.1. Animal studies

Qingming et al. (2010) evaluated the antioxidant activity of malt extract from barley *in vivo* (male Kunming mice). Scavenging effects on the hydroxyl and superoxide radicals, and protection against reactive oxygen species induced lipid, protein and DNA damage were evaluated. The Kunming mice were induced with D-galactose to evaluate the ability of malt extract to behave as an antioxidant. The extract exhibited high antioxidant activities in both *in vitro* and *in vivo*, evidenced by its ability to scavenge hydroxyl- and superoxide-radicals, high reducing power, and protection against macromolecular (lipid, protein and DNA) oxidation damage. Malt extract prevented the decrease of antioxidant enzyme activities, decreased liver and brain malondialdehyde levels and carbonyl contents and improved total antioxidant capacity in D-galactose-treated mice. Wang, Sun, Cao, and Wang (2010) investigated the protective effect of wheat feruloyl oligosaccharides (FOs) against oxidative stress in rat plasma. The oxidative markers (oxidized glutathione and malondialdehyde) and the activity of antioxidant enzymes (superoxide dismutase, catalase, and glutathione peroxidase) in the plasma of rats fed a standard diet supplemented with 1% FOs were evaluated. The anti-radical capacity of rat plasma after ingestion of 0.5 mg FOs was measured using AAPH as the free radical inducer. The results suggested that FOs enhanced plasma antioxidant enzyme activity and lowered oxidized glutathione and malondialdehyde levels for the group supplemented with FOs compared to the control. Moreover, the plasma of rats after ingestion of FOs were resistant to AAPH-induced hemolysis than was the control group.

Zhang, Cao, Agellon, and Zhai (2009) studied the effect of replacing white rice and processed wheat starch with wild rice

Table 1
In vivo antioxidant activity of cereal grains.

Cereal grains	Potential bioactive compounds	Observed biological activity	Animal model	References
Millet	Phenolics	Scavenged hydroxyl-and superoxide-radicals, high reducing power, and protect against macromolecular (lipid, protein and DNA oxidation damage.	D-galactose-induced mouse aging model	Qingming et al. (2010)
	Phenolics, tannins and phytates	Improvement in the enzymatic (glutathione, Vitamin E and C) and non enzymatic antioxidants (SOD, CAT, GPx, glutathione reductase).	Alloxan-induced diabetic rats	Hegde et al. (2005)
Oats	Avenanthramides and Phenolics	Absorbed oats phenolic did not change the resistance of hamster LDL particles against CA^{2+}-induced oxidation until ascorbic acid was introduced.	BioF1B hamster	Chen et al. (2004)
		Serum SOD and reduced glutathione hormones increased by 8.4% and 17.9% respectively; malondialdehyde decreased by 28%; TC, TAG, and LDL cholesterol were lowered by 11.1%, 28.1%, 15.1% respectively	Healthy human	Liu et al. (2011)
		Increased antioxidant capacity.	Healthy old adults	Chen et al. (2007)
Black rice	Anthocyanin	Prevented development of fructose-induced insulin resistant; lowered plasma TBARS concentration and blood oxidized glutathione	Fructose-fed rats	Guo et al. (2007)
		Increased SOD and CAT activities by 161.1% and 73.4% respectively	C57BL/6 mice	Chiang et al. (2006)
		Decreased aortic 8-OhdG and serum and aortic malondialdehyde	Rabbits	Ling et al. (2002)
		Enhanced plasma TAC, reduced plasma levels of vascular cell adhesion molecule-1, soluble CD40 ligand and high sensitive C-reactive protein	CHD human	Wang et al. (2007)
Brown rice		Plasma GPx activity increased by 15%	Over weight Korean women	Kim et al. (2008)
Wild rice		Increased SOD and reduced malondialdehyde concentration, in serum and liver	Male sprague–dawley rats	Zhang et al. (2009)
Wild rice	Phenolics	Increased SOD and CAT activities	LDL-receptor-deficient mice	Surendrian et al. (2013)
Rice bran	Polyphenol	Improved GSSG, GSSG/GSH ratio, catalase activity and lipid oxidative damage	Healthy mice	Álvarez et al. (2006)
Rye	Ferulic acid	Improved oxidation resistance of LDL	Healthy human	Söderholm et al. (2012)
		Significant reduction in mtDNA 8-OhdG levels in liver, kidney and pancreas	Streptozotocin-induced diabetes rats	Hsieh et al. (2005)
		Increased urine ferulic acid but did not change measurable antioxidative effect on the subject's LDL	Healthy human	Harder et al. (2004)
Wheat (Bran germ and flour)	Phenolics	Decreased transit time and Increased TBARS	Obese rat	Kim, Son, and Lee (2012)
		Consumption of aleurone-rich products provided substantial amounts of micronutrients and phytochemicals which may function as antioxidant	Overweight human	Price et al. (2012)
		Improved GSSG, GSSG/GSH ratio, catalase activity and lipid oxidative damage	Healthy mice	Álvarez et al. (2006)
		Increased SOD and reduced malondialdehyde concentration, in serum and liver	Male sprague–dawley rats	Zhang et al. (2009)
		WGF produced metabolic change	Rats	Fardet et al. (2007)
		Enhanced antioxidant status	Healthy human	Price et al. (2008)

as the chief source of dietary carbohydrates in rats fed a high fat diet/cholesterol diet. The rats fed wild rice were found to suppress the build-up of oxidative stress by improving antioxidant capacity, increasing superoxide dismutase (SOD) activities and reducing malondialdehyde concentrations, both in serum and liver tissue of the rats. Another study on the potential cardiovascular benefits of wild rice in male and female LDL-receptor-deficient (LDL-r-KO) mice showed that a wild rice diet has protective roles in improving the plasma lipids profile in LDL-r-KO mice (Surendrian et al., 2013). Guo et al. (2007) evaluated the effect of an anthocyanin-rich extract from black rice on hyperlipidemia and insulin resistance in fructose-fed rats. Dietary supplementation with the anthocyanin-rich extract (5 g/kg of high-fructose) prevented the development of fructose-induced insulin resistance. In addition, rats supplemented by the extract exhibited lower oxidative stress than the fructose-fed control animals, as indicated by the lower concentrations of plasma TBARS and blood oxidized GSH. Fardet et al. (2007) investigated the metabolic responses of 2 groups of rats fed 2 diets (whole-grain wheat flour, WGF and refined wheat flour, RF) for 2 weeks each in a crossover design. Their metabolic approach showed that consumption of WGF produced metabolic changes, some of which may protect the organism against oxidative stress. Álvarez, Alvarado, Matheiu, Jiménez, and De la Fuente (2006) fed healthy mice for 5 weeks with a cereal fraction (wheat germ, buckwheat flour, rice bran and wheat middlings) to investigate supplementation effect. The results showed that all cereal fractions caused improvement of the leukocyte parameters including chemotaxis capacity, microbicidal activity, lymphoproliferative response to mitogens, interleukin-2 (IL-2) and tumor necrosis factor (TNF) release, as well as oxidized glutathione (GSSG), GSSG/reduced glutathione (GSH) ratio, CAT activity and lipid oxidative damage. The observation was similar among the cereal fractions. These effects may be due to the antioxidant activity of polyphenols naturally present in cereals.

A study on black rice by Chiang et al. (2006) showed that black rice extract significantly increased superoxide dismutase and catalase activities by 161.6% and 73.4%, respectively. Hsieh et al. (2005) evaluated the effect of oxidative damage to DNA by feeding rice bran oil to streptozotocin-induced diabetes rats. They measured the levels of 8-hydroxy-2′-deoxyguanosine (8-OhdG) oxidative

DNA damage in various tissues of rats with streptozotocin-induced diabetes. There were significant reductions in mtDNA 8-OhdG levels in the liver, kidney, and pancreas of rats treated with rice bran oil as compared to those in diabetic rats without intervention. Another study using rabbits showed that a black rice diet significantly decreased aortic 8-OhdG and serum and aortic malondialdehyde, hence indicating decreased oxidative stress (Ling, Wang, & Ma, 2002). In a study conducted by Hegde, Rajasekaran, and Chandra (2005) alloxan-induced diabetic rats were fed a diet supplemented with 55% (w/w) finger millet and kodo millet. Blood glucose, cholesterol, enzymatic and nonenzymatic antioxidants, lipid peroxides in plasma, and glycation of tail tendon collagen were measured. Feeding diabetic rats diet supplemented with millet restored the levels of enzymatic (GSH, vitamin E and C) and nonenzymatic antioxidants (SOD, CAT, GPx and glutathione reductase) and lipid peroxide which were reduced by their diabetic condition. Blood sugar and total cholesterol were lowered in rats fed diets formulated with millet. Another confirmation for postulating that the beneficial effects could involve mechanisms related to free-radical scavenging activity is the inhibition of glycation of rat-tail tendon collagen in the millet-fed diabetic rats. Chen et al. (2004) examined the bioavailability of avenanthramides and phenolics from oats using BioF1B hamsters. Absorbed oats phenolics did not change the resistance of hamster LDL particles against Cu^{2+}-induced oxidation until ascorbic acid was introduced to the assay mixture.

3.2. Human studies

The effects of a diet high in wheat aleurone on plasma antioxidants status, markers of inflammation and endothelial function, were studied by Price et al. (2012). Seventy-nine healthy, older, overweight participants incorporated either aleurone-rich cereal products (27 g aleurone/d), or control products balanced for fiber and macronutrients, into their habitual diets for 4 weeks. Fasting blood were collected at baseline and on day 29. The results showed that, compared to the control, consumption of aleurone-rich products provided substantial amounts of micronutrients and phytochemicals which may function as antioxidant. However, no changes were found in other markers of inflammation, antioxidant status or endothelial function. Söderholm, Alfthan, Tikkanen, and Adlercreutz (2012) evaluated the effect of none versus high intake of rye bread on the oxidation resistance of LDL in healthy humans while otherwise on habitual diet. Their data showed that intake of rye in 4-weeks improved significantly resistance of LDL. However, they were unable to identify rye-originating substances in LDL responsible for the enhancement. The antioxidant ability of capsules containing oats avenanthramides was evaluated in 120 healthy individuals (60 women and 60 men). The materials were randomly assigned to 4 groups, which consumed 4 basal corn oil capsules (placebo), 4 capsules containing 1.56 mg of oat avenanthramides-enriched extract (OAEs) and 8 capsules containing 3.12 mg of OAEs or without treatment (control) for 1 month. Plasma lipid peroxides and antioxidant status were measured. For the 8 capsules group, the level of serum SOD and reduced glutathione hormones were significantly increased by 8.4% and 17.9%, respectively ($P < 0.05$) and malondialdehyde level significantly decreased by 28.1%. The total cholesterol, triglyceride, and low density lipoprotein cholesterol levels were lowered by 11.1%, 28.1% and 15.1%, respectively ($P < 0.05$), while the high density lipoprotein cholesterol level was increased by 13.2%. Oat extracts containing avenanthramides possess a high antioxidative activity in humans (Liu et al., 2011). A study on the bioavailability and bioactivity of avenanthramides in six healthy older adults showed an increased antioxidant capacity after consuming skimmed milk containing avenanthramides (Chen, Milbury, Collins, & Blumberg, 2007). A study by Wang et al. (2007) investigated the influence of black rice pigment fraction (BRF) supplementation in sixty patients with coronary heart diseases (CHD) for 6 months. After 6 months of intervention, compared to white rice pigment fraction supplementation, BRF supplementation greatly enhanced plasma total antioxidant capacity. The physiological consequences of using white rice or mixed rice were evaluated in overweight Korean women. The data showed that plasma GPx activity increased by 15% when subjects consumed brown and/or black rice for 6 week (Kim, Kim, Lee, Kim, & Lee, 2008).

Price, Welch, Lee-Manion, Bradbury, and Strain (2008) evaluated total phenolics (TP) and antioxidant potential (AOP) in plasma and urine of humans following consumption of a single meal of unprocessed wheat bran or a refined cereal (ground white rice). Their data showed that wheat bran phenolics are relatively well absorbed and may enhance antioxidant status. The potential antioxidative effect of rye bran intervention was investigated by measuring LDL susceptibility to copper oxidation *ex vivo*. Rye bran intervention had no influence on lag time or propagation rate of the LDL oxidation *ex vivo* (Harder, Tetens, Let, & Meyer, 2004). Table 1 summarizes the findings on i*n vivo* antioxidant activity of cereal grains.

4. Conclusion

Cereal grains remain a staple component of diets worldwide. They provide significant levels of bioactive phytochemicals including folates, phenolic acids, carotenoids, betaine, choline, sulfur amino acids, phytic acid, lignins, avenanthramides and alkylresorcinols. These phytochemicals are unevenly distributed between the various tissues and cell types of the grains. *In vitro* and *in vivo* studies have shown that cereal grain phytochemicals may improve antioxidant capacity, and thus have the potential to mitigate oxidative stress hence delaying the onset of some chronic diseases. However, there are inadequate studies in humans in which real, complex cereal foods are used. The beneficial health effects are associated with the additive and/or synergistic action of these phytochemicals as have been supported by results from studies on the activity of single or combination of a number of antioxidants. However, the antioxidant capacity of cereal grains have probably been underestimated, since most methods are based on the solvent extraction and quencher procedures which are both performed before digestion. The antioxidant potential of cereals depends on their bioaccessibility, absorption in the gastrointestinal tract and their bioavailability *in vivo*. The antioxidant potential of cereals may be improved *in vitro* by the action of fermentation and *in vitro* gastrointestinal digestion of cereals which significantly correlated with their total phenolic contents. Thus fermentation and *in vitro* gastrointestinal digestion offers a tool to further increase the bioactive potential of cereals. Further studies are necessary on fermented and *in vitro* gastrointestinal digesta of other cereal antioxidative phytochemicals. Most studies performed *in vivo* have been concerned with the antioxidant properties of colored rice, wheat bran and rye products. However, there are inadequate *in vivo* studies on other cereal grains and antioxidant potential of fermented versus unfermented cereals. *In vivo* studies are therefore needed to further explore the antioxidant potential of other cereal grains and fermented versus unfermented cereals so as to maximize possible beneficial health effects of cereal phytochemicals.

Polyphenols (mainly ferulic and phenolic acid) are the main contributors in these antioxidant properties of cereal grains in both *in vitro* and *in vivo* studies. Correlations between antioxidant activities and other types of components remain to be investigated.

Few clinical studies on the antioxidant potential of cereals in animals and humans have been carried out. The mechanisms, however, are not fully established. Therefore, more information on the

mechanisms involved is necessary in order to provide strong, convincing arguments about their health benefits and new health claims in the future. Few studies deal with cereal grain consumption on the induction/repression of genes coding for antioxidants compounds. Therefore, further studies are necessary to explore this new area of research using the most recent comprehensive analysis of genomic and transcriptomic techniques. Moreover, cereal grain consumption can be investigated through metabolomics which will allow further investigation on how complex antioxidant-rich cereal grains can modify metabolism and elucidate metabolic pathways affected by cereal grains antioxidants. Such findings will provide novel information on the health benefits of cereal grains and the development of healthy functional cereal grains products.

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