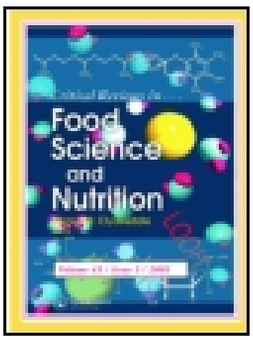

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Proanthocyanidins in cereals and pseudocereals

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ABSTRACT

Proanthocyanidins (PAs) are a class of oligomeric flavonoids found in a variety of plant foods. Intake of PAs in human diet has been associated with a reduced occurrence of various chronic disorders. Cereal and pseudocereal grains are staple food items. Grain genotypes containing PAs can be developed as functional foods to efficiently improve human health. This review summarises the occurrence of PAs in diverse grains, including rice, wheat, barley, sorghum, millets, buckwheat, and some forage grasses. Great diversity in PA structure and composition has been recorded. The biological activities of the grain PAs, such as antioxidant, antiinflammatory, anticancer, and antidiabetic capacities, are also reviewed. The bioavailability and metabolism of grain PAs in human digestive tract are discussed. Future research directions are suggested on how to improve our understandings of the chemistry of PAs in cereals and pseudocereals and of the biological properties for human health applications.

KEYWORDS

Rice; wheat; sorghum; buckwheat; condensed tannin; human health; polyphenol

Introduction

Proanthocyanidins (PAs), commonly known as condensed tannins, are a group of polyphenols that naturally occur in a wide range of plants (e.g., tea, cocoa, grape seed, berries, and cereals) (Gu et al. 2004). PAs are structurally diverse due to the different hydroxylation patterns of the basic flavan-3-ol units and the linkages between the units (Hellström et al. 2009; Fraser et al. 2016) (Figure 1A). The common basic units are (epi)gallocatechins, (epi)catechins, and (epi)afzelechins, resulting in the formation of prodelphinidin, procyanidin, and propelargonidin structures, respectively (Hellström et al. 2009). More than just one unit are commonly found in naturally-occurring PAs. The units are commonly linked through B-type bonds (C4→C6 or C4→C8 linkage), while an additional linkage (C2→O5 or C2→O7) contributes to the formation of A-type bonds (Hellström et al. 2009; Schofield et al. 2001).

There has been increasing research interest in PAs from different plant food sources due to the attractive nutritional properties (Aron & Kennedy, 2008). PAs from diverse plant sources showed a variety of biological activities such as antioxidant, free radical scavenging, anticarcinogen, cardiopreventive, antimicrobial, antiviral, and neuroprotective capacities (Aron & Kennedy, 2008). A systematic and comparative study showed that PAs have the highest *in vitro* antioxidant activity among a range of different polyphenols (over 100 types) (Cai et al. 2006). Therefore, it is encouraged to increase the intake of plant foods rich in PAs to a certain extent to reduce the occurrence of chronic disorders and to improve the health conditions of humans.

Cereals and pseudocereals are staple foods for human nutrition. Developing grain genotypes containing PAs for human consumption can be an efficient and feasible strategy to improve human health. Common cereals are maize (*Zea mays*), rice (*Oryza sativa*), wheat (*Triticum* spp.), barley (*Hordeum vulgare*), and sorghum (*Sorghum bicolor*), millets, oats (*Avena sativa*), rye (*Secale cereale*), and so on. Common pseudocereals are buckwheat (*Fagopyrum* spp.), quinoa (*Chenopodium quinoa*), amaranth (*Amaranthus* spp.), and others. So far, only some genotypes of rice, wheat, barley, sorghum, millets, buckwheat, and forage grasses [perennial ryegrass (*Lolium perenne*) and tall fescue (*Festuca arundinacea*)] have been found to contain PAs (Fraser et al. 2016) (Table 1). Apart from the potential health effects of PAs as described in the last paragraph, the presence of PAs may also impact on the food quality. For example, discoloration of barley dough is positively correlated with the amount of catechin (Quinde-Axtell and Baik, 2006). PAs contribute to the astringent taste and decreased digestion of sorghum food/beverage products (Bvochora et al. 1999). Therefore, understanding the occurrence of PAs in cereals and pseudocereals and their biological activities contributes to the development of functional grains to improve human health/combat medical disorders. However, the information on grain PAs is rather scattered, and a systematic review is needed to support the current exploits. This also fits in the large picture of exploring the health benefits of plant polyphenols for human nutrition in response to the rising "healthy" food markets.

This review summarises the current knowledge of the chemical composition and biological activities of PAs in different cereals and pseudocereals. Other aspects considered in this review include the impact of food processing on PA composition, factors affecting the PA quantification, roles of other components in the biological activities of PA-containing grain samples, and digestion and metabolism of PAs in human digestive tract.

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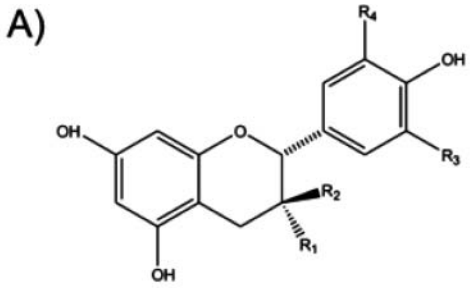

R1	R2	R3	R4	Monomers
H	OH	H	H	Afzelechin (A)
OH	H	H	H	Epiafzelechin (EA)
H	OH	OH	H	Catechin (C)
OH	H	OH	H	Epicatechin (EC)
H	OH	OH	OH	Gallocatechin (GC)
OH	H	OH	OH	Epigallocatechin (EGC)

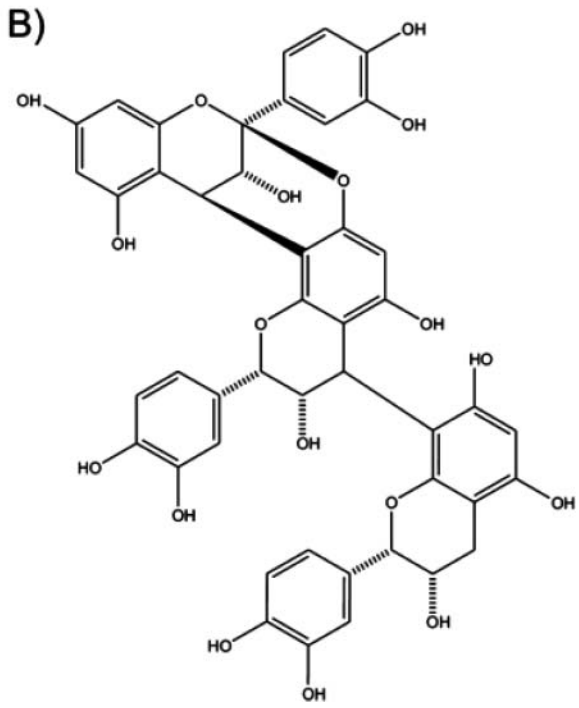

Figure 1A. A, variations in flavan-3-ol structures as monomer units; B, a procyanidin trimer containing B-type and A-type bonds (Fraser et al. 2016).

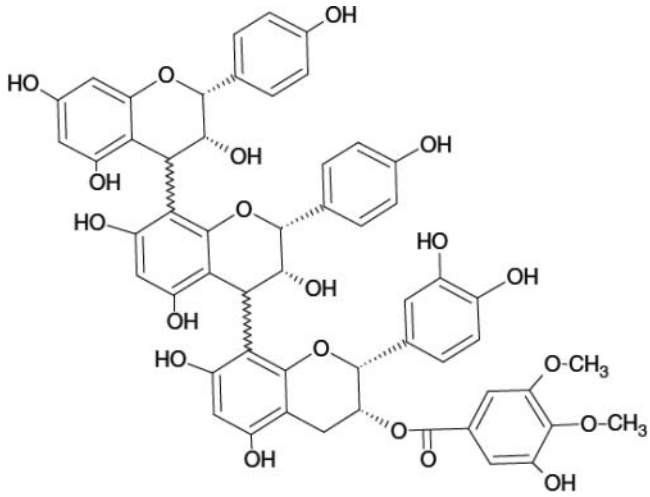

Figure 1B. Trimeric galloylated propelargonidin, epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate from buckwheat (Ölschläger et al. 2008). All the figures are reprinted with permission from the publishers.

PAs in diverse cereals and pseudocereals

Rice (Oryza sativa)

The occurrence of PAs in rice has been the mostly studied among various grains (Table 1). PAs have been mostly detected in red rice, or black rice but not in white coloured grain (Gunaratne et al. 2013; Jiamyangyuen et al. 2017). Great diversity in PA concentration of rice grains has been recorded (Gunaratne et al. 2013; Shao et al. 2015). For example, the PA concentration of rice brans (8 genotypes) varied from 12–25 mg/g (Gunaratne et al. 2013). The effects of developing kernels, growing environment, and storage conditions on PA concentration in rice have been studied (Jiamyangyuen et al. 2017; Zhou et al. 2014; Shao et al. 2015). Ripening process greatly affected the PA content in rice (Jiamyangyuen et al. 2017). PA concentration of a red rice genotype reached a maximum [58 mg CE (catechin equivalent)/100 g] at the milk grain stage before decreasing to 4 mg CE/100 g at the fully ripe stage. In contrast, PA concentration of a black rice genotype reached a maximum (29 mg CE/100 g) at the mature stage before decreasing to 19 mg CE/100 g at the fully ripe stage (Jiamyangyuen et al. 2017). Analysis of 14 rice genotypes grown in 2 very different locations in China (Hainan and Hangzhou) showed that the PA concentrations in the grains were equally affected by genotype and environment (Shao et al. 2015). PA concentration in rice could also be affected by the time and temperature of post-harvest storage (Zhou et al. 2014). It was not affected by a storage of 6 months at 4°C, but decreased (e.g., from 53 to 45 mg CE/100 g) at 37°C. Therefore, manipulating the harvesting time, growing locations, and post-harvest storage conditions may maximize the PA content and minimize the PA loss in rice.

Diversity of PA composition in rice has been recorded (Chen et al. 2012; Gunaratne et al. 2013). The PAs in rice were mostly of B-type bonds (Shao et al. 2015). Shao et al. (2015) reported that the catechin was the most abundant PA in the extract of whole grain rice. Chen et al. (2012) fractionated a rice bran extract (1 genotype) to obtain a PA-rich fraction. The concentrations of PAs with DP (degree of polymerization) of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10–14, and > 14 in the fraction reached the maximum values of 2.8, 6.4, 13.5, 16.8, 15.6, 17.3, 19.3, 16.4, 20.8, 98.2, and 93.8 mg/g, respectively. The diversity in the composition of individual PAs in whole grain rice remains to be better characterized.

Wheat (Triticum aestivum)

There have been only a few studies on the PA composition in wheat (Table 1). Vanillin-HCl staining qualitatively revealed the presence of PAs in red wheat bran (Matus-Cádiz et al. 2008). McCallum and Walker (1990) analysed the PA composition in wheat bran and showed the presence of prodelphinidin and some procyanidin units (oligomeric PAs), propelargonidin units (dimeric PAs), procyanidin B3, and prodelphinidin B3. Dinelli et al. (2011) showed that PAs in wheat were not present

Table 1. Composition of PAs in diverse cereals and pseudocereals.

Grain type	No./form	Extraction method	Quantification method	Concentration	Composition	Reference
Rice	3/bran	Ethanol (70%) extract of rice bran	DMAC assay, normal phase HPLC-fluorescence detection	67 mg procyanidin B2 equiv./g extract for red rice bran and o for purple rice bran	Red rice bran extract was fractionated on Sephadex LH-20 column. Two fractions containing more PAs were analyzed for the composition. The concentrations (mg/g) of PAs with DP of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10–14, and >14 were 2.8 and 0.1, 6.4 and 3.0, 1.7 and 13.5, 0.8 and 16.8, 0.9 and 15.6, 1.5 and 17.3, 1.9 and 19.3, 2.8 and 16.4, 2.1 and 20.8, 4.7 and 98.2, and 2.7 and 93.8, respectively	Chen et al. 2012
Rice	3/bran, whole	Methanol extract of both bran and whole grain flour	Vanillin assay	0.22–3.06 for bran and 0.03–0.45 for whole rice [CE mg/g (db)]		Parvathy et al. 2014
Rice	2 a/whole	Methanol/acetone/water/acetic acid of whole grain flour	Vanillin assay	7.8 to 7, and 50 to 45 at 37°C, 6 months, at 4°C, the contents hardly changed (mg CE per 100 g)		Zhou et al. 2014
Rice	14 b/whole	Methanol (80%) extraction of defatted whole flour	Vanillin assay, LC-MS/MS	1.69–4.61, average values of 3 and 3.6 for rice grown at different locations, respectively (mg of CE/g)	B-type PAs including catechin (most abundant), dimer, trimer, tetramer, and pentamer	Shao et al. 2015
Rice	5/bran	Ethanol (70%) extract of bran	DMAC assay	0–22 mg procyanidin A2 equiv./g		Boue et al. 2016
Rice	2 c/whole	Methanol: HCl (1N) (85:15)	Vanillin assay	2.5–58 for red rice, 19–29 for black rice [mg CE/100 g (db)]		Jiamyangyuen et al. 2017
Rice	8/bran, refined, whole	Methanol (80%)	Vanillin assay, reversed phase-HPLC-MS	12–25 mg/g (bran), 1.1–2.3 mg/g (brown rice)	Dimers, trimers	Gunaratne et al. 2013
Wheat (*T. aestivum*)	1/bran	Aqueous acetone with 0.1% of ascorbic acid (bran)	Acid degradation, chromatography, UV		Prodelphinidin and some procyanidin units (oligomeric PAs), propelargonidin units (dimeric PAs), procyanidin B3, and prodelphinidin B3	McCallum & Walker, 1990
Wheat (*T. aestivum*)	22/whole	Ethanol (80%) for free polyphenols, alkaline and acid hydrolysis and ethyl acetate extraction for bound polyphenols	HPLC-ESI-TOF-MS		PAs were not found in free polyphenols. PAs in bound form were procyanidin B3 and related isomers	Dinelli et al. 2011
Barley	11/whole, refined	Acetone (75%) for whole flour extraction	Reversed phase HPLC-UV, HPLC-MS/MS	2–937 μg CE/g	Catechin (2–86), prodelphinidin B3 (0–288), procyanidin (0–255), trimeric 1 (0–141), trimeric 2 (0–100), trimeric 3 (0–95), procyanidin C2 (0–160)	Quinde-Axtell and Baik 2006
Barley	16/whole	Acetone (60%)	Reversed phase HPLC-UV	325–527 mg/g (wb)	G, gallocatechin; C, catechin, mg/g (wb), catechin (14–41), GC prodelphinidin B3 (59–106), CC procyanidin B3 (63–126), GGC prodelphinidin C2 (40–105), GCC (65–104), CGC (33–62), CCC procyanidin C2 (31–81)	Holtekjølen et al. 2006

(*Continued on next page*)

Table 1. (*Continued*)

Grain type	No./form	Extraction method	Quantification method	Concentration	Composition	Reference
Barley	1/flour	Acetone:methanol: water at 2:2:1 for extractable PAs in flour, and unextractable PAs were released by the residue after depolymerization with acid-hydrolysis	Normal phase HPLC-fluorescence detection for extractable PAs and reversed phase HPLC-UV for unextractable PAs after depolymerization with acid-hydrolysis	Total, 25.5 mg/100 g (wb), moisture content 9%; 8.7 for unextractable PAs; 16.8 for extractable PAs	Prodelphinidin, procyanidin-type PAs with A-type linkages. For extractable PAs, contents of P1, P2, P3, P4–6, P7–10, and P>10 were 1.3, 4.7, 5.5, 5.3, 0, and 0 mg/100 g (wb), respectively; for unextractable PAs, the average DP was 5.2	Hellström et al. 2009
Barley	14/whole	Acetone 80%	Normal phase HPLC-fluorescence detection-MS, near-infrared (NIR) spectroscopy	293–653 μg/g	HPLC method, catechin/epicatechin (11–87), procyanidin dimer (48–98), prodelphinidin dimer I (15.5–37.6), prodelphinidin dimer II (49.3–96.7), procyanidin trimer (36.7–167), prodelphinidin trimer I (monogalloylated) (54.2–105.3), prodelphinidin trimer II (digalloylated) (23.8–63.7), procyanidin tetramer (7.3–18.9), prodelphinidin tetramer (digalloylated) (14.6–36.3), procyanidin pentamer (4.5–22.7) (unit: μg/g)	Verardo et al. 2015
Sorghum	1/whole	Acetone (70%) with ultrasound	MALDI-TOF MS		Heteropolyflavan-3-ols (tetramers, pentamers, hexamers, heptamers, octamers, nonamers), glucosylated heteropolyflavans (trimer + 2/3 glucose, tetramer + 3/4 glucose, pentamer + 4/5 glucose, hexamer + 5/6 glucose, heptamer + 6/7 glucose)	Krueger et al. 2003
Sorghum	381/whole		Near-infrared spectroscopy (NIRS)	0–78.51 mg CE/g		Rhodes et al. 2014
Sorghum	2/whole	n.a.	Vanillin-HCl method, HPLC-MS/MS	1.1 and 4.5 g CE/100 g (db)	Procyanidins of DP from 2 to 6, and 12	Adetunji et al. 2015
Diverse millets	7/whole	Crude extract	Vanillin-HCl method	Finger millet (110 and 311), foxtail (40), little (20), pearl, proso, and kodo millets contained little PAs (μmol of CE/g of defatted meal)		Chandrasekara & Shahidi, 2010
Finger millet	11/whole grain, hull	Acetone (70%) extract of whole grain and hull	Vanillin assay	10–115 for whole grain and 0–20 for hull (μmol CE/g dry matter)		Kumari et al. 2017
2 forage grasses d	2/leaf, grain	Methanol (80%) with 0.1% acetic acid	LC-MS/MS		The PAs were trans-flavan-3-ols of afzelechin and catechin, which are mostly linked by B-type bonds. A small amount of A-type bonds was also present	Fraser et al. 2016
Common buckwheat	1/hull	Buckwheat hull ethanol extract	Vanillin-HCl assay to qualitative identification		The presence of propelargonidin and procyanidin-type PAs in buckwheat hull was confirmed	Watanabe et al. 1997
Common buckwheat	1/grits	Acetone:methanol: water at 2:2:1 for extractable PAs, and unextractable PAs were released from residue after depolymerization with acid-hydrolysis	Normal phase HPLC-fluorescence detection for extractable PAs and reversed phase HPLC-UV for unextractable PAs after depolymerization with acid-hydrolysis	Total, 118; 22.2 for unextractable PAs; 95.4 for extractable PAs [mg/100 g (wb)]	Propelargonidin, procyanidin-type PAs with B-type linkage were found. For extractable PAs, concentrations of P1, P2, P3, P4–6, P7–10, and P > 10 were 13, 34, 41, 27, 7.6, and 0 mg/100 g (wb), respectively; for unextractable PAs, the average DP was 4.3	Hellström et al. 2009

Common buckwheat	8/whole	Methanol (80%) extraction with ultrasound, which was further fractionated on Sephadex LH-20 column	RP-HPLC-MS/MS, enzyme hydrolysis	15.4–40.6 mg/100 g, db	Catechin (0.6–6.6), epicatechin (2.3–11), epicatechingallate (0.4–2.2), epicatehin-3-*O*-dimethylgallate (0.1–1.1), procyanidin B2 (0.3–1.3), procyanidin B5 (0.4–1.1), epiafzelechin-(4–6)-epicatechin (0.3–0.9), epiafzelechin-(4–8)-epicatechin-*p*-OH-benzoate (0–0.9), epiafzelechin-(4–8)-epicatechin-methylgallate (0.1–0.3), epiafzelechin-(4–8)-epicatechin-(3,4-dimethyl)-gallate (1.7–5.7), epicatechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (0.1–0.6), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin (0–0.4), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (0.8–3.4) (unit: mg/100 g, db)	Ölschläger et al. 2008
Common buckwheat	1/whole	Phenolics were extracted in ethanol solution (80%) under an ultrasound bath	RP-HPLC–ESI-TOF-MS		Catechin, epicatechin, procyanidin B2-3-*O*-gallate, epiafzelchin-epiafzelchin-epicatechin, epicatechin-gallate, (epi)afzelchin-(epi)catechin isomer A, (epi)afzelchin-(epi)catechin isomer B, epiafzelchin-epicatechin-*O*-methyl gallate, (epi)afzelchin-(epi) catechin isomer C, (epi)afzelchin-(epi)catechin isomer D, (–)-epicatechin-3-(3''-*O*-methyl) gallate, procyanidin B2 dimethyl gallate, epiafzelchin-epicatechin-*O*-di methylgallate, epicatechin-*O*-3,4-dimethylgallate	Verardo et al. 2010
Common buckwheat	4/whole, commercial flour	Free phenolics were extracted by water and ethanol solution. Bound phenolics were extracted by alkaline solution	LC–ESI-Q-TOF-MS		Catechin, epicatechin, epicatechin-*O*-3,4-dimethylgallate, (–)-epicatechin-3-(3''-*O*-methyl)-gallate, (epi)afzelchin–(epi)-catechin, epiafzelchin–epicatechin-*O*-methylgallate, epiafzelchin–epicatechin-*O*-dimethylgallate, procyanidin B2-dimethylgallate, epiafzelchin–epiafzelchin–epicatechin	Inglett et al. 2011
A wild buckwheat species e	1/whole	Methanol (80%) extraction with ultrasound, which was further fractionated on Sephadex LH-20 column	RP-HPLC-MS/MS, enzyme hydrolysis	113.9 mg/100 g, db	Catechin (0.9), epicatechin (22.6), epicatechingallate (3.9), epicatehin-3-*O*-dimethylgallate (10.8), procyanidin B2 (1.6), procyanidin B5 (2.5), epiafzelechin-(4–6)-epicatechin (3.0), epiafzelechin-(4–8)-epicatechin-*p*-OH-benzoate (0.7), epiafzelechin-(4–8)-epicatechin-methylgallate (0.6), epiafzelechin-(4–8)-epicatechin-(3,4-dimethyl)-gallate (16.7), epicatechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (1.6), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin (0.5), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (10.6) (unit: mg/100 g, db)	Ölschläger et al. 2008
A buckwheat hybrid f	33/whole	Methanol (80%) extraction with ultrasound, which was further fractionated on Sephadex LH-20 column	RP-HPLC-MS/MS, enzyme hydrolysis	23.4–219.7 mg/100 g, db	Catechin (0.2–9.5), epicatechin (2.6–78.9), epicatechingallate (1.1–32.2), epicatehin-3-*O*-dimethylgallate (0.1–10.7), procyanidin B2 (0.5–12.6), procyanidin B5 (0.4–6.5), epiafzelechin-(4–6)-epicatechin (0.3–4.0), epiafzelechin-(4–8)-epicatechin-*p*-OH-benzoate (0.2–14.7), epiafzelechin-(4–8)-epicatechin-methylgallate (0.05–3.9), epiafzelechin-(4–8)-epicatechin-(3,4-dimethyl)-gallate (1–12.9), epicatechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (0.2–2.7), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin (0.1–11.4), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (0.1–6.2) (unit: mg/100 g, db)	Ölschläger et al. 2008
Tartary buckwheat g	1/ flower, stem, leaf, root	Acetone (70%) with acetic acid (0.5%), extracts of flower, stem, leaf, root	DMAC assay	0.8–2.5 μg/g		Bai et al. 2014

No., number of genotypes analysed in the study; form, the form (e.g., whole grain, bran, refined, hull, grits, milling fraction) of the grain used in the study; db, dry basis; wb, wet basis; a, samples stored at different temperatures (4 to 37°C) up to 6 months; b, samples grown in 2 different locations; c, at 5 stages of ripening; d, foxtail millet (*Setaria italica*), proso millet (*Panicum miliacium*), 2 finger millet (*Elusine coracana*) varieties (Ravi and local), kodo millet (*Paspalum crobiculatum*), little millet (*Panicum sumatrense*), and pearl millet (*Pennisetum glaucum*); d, tall fescue (*Festuca arundinacea*) and perennial ryegrass (*Lolium perenne*); e, *Fagopyrum homotropicum*; f, *F. esculentum* × *F. homotropicum* hydrid; g, *F. tataricum*; h, CE, catechin equivalent, unit is in the ( ); matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS)

in the free form. Procyanidin B3 and the isomers were found in the bound form. Therefore, the composition and concentration of PAs in wheat species (*Triticum* spp.) remain to be better studied.

Barley (Hordeum vulgare)

Genetic diversity of PA concentration in barley has been observed (Holtekjølen et al. 2006; Quinde-Axtell and Baik, 2006; Verardo et al. 2015). For example, PA concentrations in barley (14 genotypes) ranged from 293–653 μg/g (Verardo et al. 2015). There is also a great diversity of PA composition in barley (Verardo et al. 2015; Holtekjølen et al. 2006; Quinde-Axtell and Baik, 2006). For example, HPLC (high-performance liquid chromatography) analysis revealed the presence of catechin/epicatechin (11–87 μg/g), procyanidin dimer (48–98 μg/g), prodelphinidin dimer I (15.5–37.6 μg/g), prodelphinidin dimer II (49.3–96.7 μg/g), procyanidin trimer (36.7–167 μg/g), prodelphinidin trimer I (monogalloylated) (54.2– 105.3 μg/g), prodelphinidin trimer II (digalloylated) (23.8–63.7 μg/g), procyanidin tetramer (7.3–18.9 μg/g), prodelphinidin tetramer (digalloylated) (14.6–36.3 μg/g), and procyanidin pentamer (4.5–22.7 μg/g) in barley (14 genotypes) (Verardo et al. 2015) (Figure 2A). Waxy barley samples (4 genotypes) appeared to contain more PAs (293–442 μg/g) than non-waxy samples (10 genotypes) (567–653 μg/g) (Verardo et al. 2015). Another study employing 16 genotypes showed that the PA concentration had no apparent correlation with the barley phenotype (hulled or hull-less, two-rowed or six-rowed, genotypes varying in amylose contents) (Holtekjølen et al. 2006). Therefore, PA concentration in barley in relation to waxy genes remains to be better studied by assessing more genotypes.

Sorghum (Sorghum bicolor)

Great genetic diversity of PA concentration in sorghum (381 genotypes) has been recorded (0–78.51 mg CE /g) (Rhodes et al. 2014). The main PAs in sorghum included heteropolyflavan-3-ols (tetramers, pentamers, hexamers, heptamers, octamers, nonamers), glucosylated heteropolyflavans (trimer + 2or 3 glucosyl units, tetramer + 3 or 4 glucosyl units, pentamer + 4 or 5 glucosyl units, hexamer + 5 or 6 glucosyl units, heptamer + 6 or 7 glucosyl units) (Krueger et al. 2003; Adetunji et al. 2015). A comparative study showed that sorghum (tannin-type) contained the highest amount of PAs among a range of food and beverage products (Gu et al. 2004). Compared with the PAs in grape seed, sorghum PAs tend to be more polymerised (Girard et al. 2016) (Figure 2B). Overall, the results of sorghum PAs from the recent reports in general agreed with the results published before 2003 as summarised by Awika and Rooney (2004).

Millets

Millet is a generic term to describe a range of small-seeded grasses in the Poaceae family. Chandrasekara & Shahidi (2010) analysed the PA concentrations in foxtail (*Setaria italica*) (40 μmol of CE/g of defatted meal), proso (*Panicum miliacium*) (0), two finger millet (*Elusine coracana*) varieties (110 and 311 μmol of CE/g of defatted meal), kodo (*Paspalum scrobiculatum*) (0), little millet (*Panicum sumatrense*) (20 μmol of CE/g of defatted meal), and pearl millet (*Pennisetum glaucum*) (0). Kumari et al. (2017) recorded the genetic diversity of PA concentration in 11 finger millet genotypes [10–115 μmol CE/g whole grain (db, dry basis)]. The structure and composition of PAs in the millets remain to be studied.

Other grass species

PAs were detected in the seeds of tall fescue (*Festuca arundinacea*) and perennial ryegrass (*Lolium perenne*) (forage species) by LC-MS/MS (liquid chromatography–tandem mass spectrometry) based techniques (Fraser et al. 2016). The PAs are based on trans-flavan-3-ols of afzelechin and catechin, which are mostly linked by B-type bonds with a small amount of A-type bonds. The monomers included afzelechin, catechin, and gallocatechin. The dimers were afzelechin-(4–8)-afzelechin, afzelechin-(4–6)-afzelechin, catechin-(4–8)-afzelechin, afzelechin-(4–8)-catechin, afzelechin-(4–6)-catechin, catechin-(4–8)-catechin, and catechin-(4–6)-catechin. The trimers were afzelechin-afzelechin-afzelechin, catechin-afzelechin-afzelechin, afzelechin-afzelechin-catechin, catechin-catechin-afzelechin, and catechin-catechin-catechin (Fraser et al. 2016). The presence of PAs in the forage species improves animal health and production.

Buckwheat (Fagopyrum spp.)

Buckwheat (*Fagopyrum* spp.) is the only pseudocereal that has been reported to contain PAs so far (Table 1). Genetic diversity in PA concentration of diverse buckwheat species has been reported (Ölschläger et al. 2008). The PA concentrations in common buckwheat (*F. esculentum*) (8 genotypes) ranged from 15.4–40.6 mg/100 g (db), whereas that of a hydrid (*F. esculentum* × *F. homotropicum*) (33 genotypes) varied from 23.4–219.7 mg/100 g (db) (Ölschläger et al. 2008). Diversity in the PA composition of buckwheat has been studied (Ölschläger et al. 2008). The identified PAs in common buckwheat (8 genotypes) included catechin (0.6–6.6 mg/100 g, db), epicatechin (2.3–11 mg/100 g, db), epicatechingallate (0.4–2.2 mg/100 g, db), epicatehin-3-*O*-dimethylgallate (0.1–1.1 mg/100 g, db), procyanidin B2 (0.3–1.3 mg/100 g, db), procyanidin B5 (0.4–1.1 mg/100 g, db), epiafzelechin-(4–6)-epicatechin (0.3–0.9 mg/100 g, db), epiafzelechin-(4–8)-epicatechin-*p*-OH-benzoate (0–0.9 mg/100 g, db), epiafzelechin-(4–8)-epicatechin-methylgallate (0.1–0.3 mg/100 g, db), epiafzelechin-(4–8)-epicatechin-(3,4-dimethyl)-gallate (1.7–5.7 mg/100 g, db), epicatechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (0.1–0.6 mg/100 g, db), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin (0–0.4 mg/100 g, db), epiafzelechin-(4–8)-epiafzelechin-(4–8)-epicatechin-*O*-(3,4-dimethyl)-gallate (0.8–3.4 mg/100 g, db) (Ölschläger et al. 2008) (Figure 1B). It appeared that the majority of PAs (> 70%) in buckwheat are extractable (Verardo et al. 2010). The unextractable PAs can be released by acid/alkaline-hydrolysis (Hellström et al. 2009; Inglett et al. 2011). The PAs appeared to be in the bound or free forms depending on the PA type (Inglett et al. 2011). For example, epiafzelchin–epicatechin-*O*-dimethylgallate was only found in free form (extracted by water and ethanol

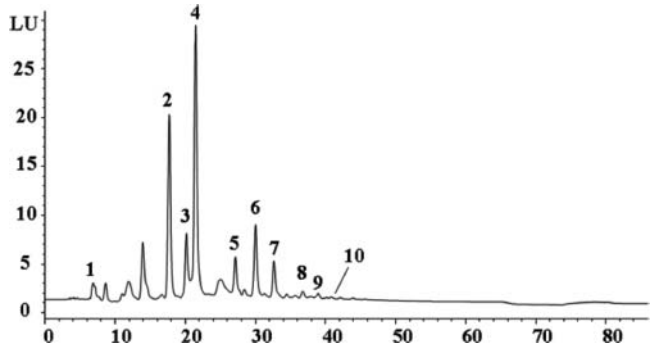

Figure 2A. Normal phase HPLC-fluorescence detection of PAs from barley; the numbers (1 to 10) on the peaks represent catechin/epicatechin, procyanidin dimer, prodelphinidin dimer I, prodelphinidin dimer II, procyanidin trimer, prodelphinidin trimer I (monogalloylated), prodelphinidin trimer II (digalloylated), procyanidin tetramer, prodelphinidin tetramer (digalloylated), and procyanidin pentamer, respectively (Verardo et al. 2015).

solution) in buckwheat (Inglett et al. 2011). The occurrence of certain types of PAs also depended on the genotype of buckwheat (Inglett et al. 2011). The hull of common buckwheat, which is commonly treated as a waste product, can also be a source of PAs, though quantification studies remain to be conducted (Watanabe et al. 1997).

Impact of food processing on PA composition

Cereals/pseudocereals are processed for food formulation and production. The impact of some food processing techniques on the PA composition in sorghum, barley, and common buckwheat based products has been studied (Bvochora et al. 1999; Verardo, Arráez-Román, et al. 2011; Verardo, Gómez-Caravaca, Messia, et al. 2011; Verardo, Gómez-Caravaca, 'Marconi et al. 2011; Adetunji et al. 2015; Gómez-Caravaca et al. 2015). Sorghum was fermented to produce "Mahewu" (a traditional non-alcoholic beverage in Southern Africa) (Bvochora et al. 1999). The microbial population was found to be lactic acid bacteria, yeasts, and aerobic mesophilic bacteria. The fermentation (84 h) decreased the contents of soluble PAs to different extents of 50 to 60%, depending on the sorghum genotype. The reduced PA concentration in the beverage may make the beverage more palatable by reducing the astringency (Bvochora et al. 1999). Another report studied the effect of dilute NaOH (0.4%) steeping on the PA composition and starch liquefaction of sorghum rich in PAs (Adetunji et al. 2015). The alkaline steeping greatly reduced the α-amylase inhibition by up to 80% and starch liquefaction time, while increasing the free amino nitrogen content. Increasing steeping time and NaOH concentration increased the molecular size of PAs. Large PAs appeared to be too bulky to interact efficiently with α-amylase. The reduced α-amylase inhibition suggested better sorghum utilization for bioethanol production (Adetunji et al. 2015).

Air classification technology has been used to produce barley flour fractions rich in bioactive components including PAs (Gómez-Caravaca et al. 2015; Verardo, Gómez-Caravaca, Marconi, et al. 2011). The fractions from air classification had a much higher concentration of free PAs (e.g., by 57% to 73%) compared to the whole flours (Verardo, Gómez-Caravaca, Marconi, et al. 2011). Apart from PAs, the fractions also had much higher concentrations of other bioactive components such as

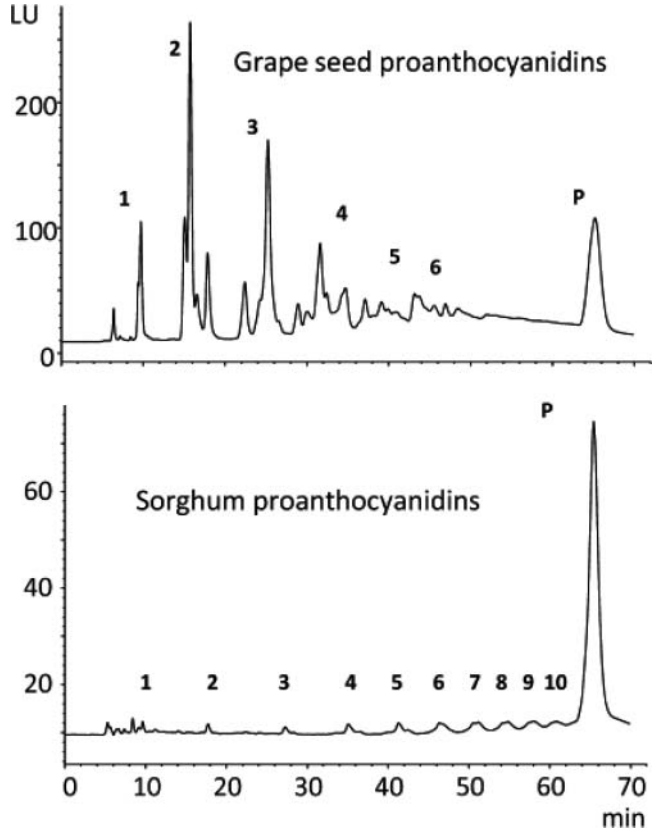

Figure 2B. Normal phase HPLC-fluorescence detection of PAs from grape seed and sorghum; numbers above the peaks denote DP of PAs, and P indicates DP > 10 (Girard et al. 2016).

other types of polyphenols, β-glucans, and alkylresorcinols (Gómez-Caravaca et al. 2015). The fraction has been incorporated in spaghetti formulation (Verardo, Gómez-Caravaca, Messia, et al. 2011). The barley fraction-enriched spaghetti had a high concentration of PAs (e.g., 555 μg tannic acid equivalent/g db in uncooked sample), whereas no PAs were detected in commercial semolina spaghetti. Cooking greatly reduced the PA content in the spaghetti (e.g., from 555 to 299 tannic acid equivalent/g db). Adding vital gluten increased the cooking quality of the spaghetti enriched with the barley fraction (Verardo, Gómez-Caravaca, Messia, et al. 2011). Verardo, Arráez-Román, et al. (2011) also studied the impact of thermal processing on the PAs in buckwheat based gluten free spaghetti. Processing raw flour to cooked spaghetti drastically reduced the contents of total free and bound polyphenols by ~75% and ~81%, respectively. Cooking alone caused a loss of 50% of total polyphenol content. The content of PAs was also much reduced by the processing steps. For example, the concentration of (epi) afzelchin-(epi) catechin-*O*-dimethyl gallate was reduced from 47 (whole buckwheat flour) to 10 (cooked spaghetti) mg (+)-catechin/kg (db) (Verardo, Arráez-Román, et al. 2011). Therefore, non-thermal processing methods such as high pressure treatment may be employed to test if they may better retain the PAs (and polyphenols and other bioactive components in general) in the final products.

Increasing intake of polyphenols and PAs is positively linked with the reduced occurrence of chronic diseases and medical disorders (Campbell & Campbell, 2005). Therefore, suitable processing methods should be employed to better retain PAs in

food products. Non-thermal processing may better retain the PA concentration in cereal and pseudocereal products, which should be better studied. On the other hand, foods rich in PAs may be astringent/bitter, negatively affecting the sensory quality and commercial potential (Bvochora et al. 1999). Textural and rheological properties of cereal/pseudocereal food products may as well be affected by the presence of PAs (Zhu, 2015). Therefore, suitable food processing and formulation techniques should be employed to address this apparent contradiction of food quality.

Extraction and quantification methods affect proanthocyanidin composition

One notable observation from the literature survey is that different studies tend to employ different extraction and quantification methods for PAs in cereals and pseudocereals (Table 1). Different experimental conditions and expression of results (e.g., dry basis *vs* wet basis) may be used in different studies even the same type of quantification method was employed (Table 1). For example, methanol/ethanol/acetone/combinations aqueous solutions (70 or 80%) with/without acid (e.g., 0.1% acetic acid) were used for PA extraction in different studies. Ultrasound assisted extraction was employed in some studies (Ölschläger et al. 2008). Most of the reports only studied the extractable PAs in the cereals and pseudocereals (Hellström et al. 2009). The PA concentration in the samples has been quantified by vanillin assay, DMAC (4-dimethylaminocinnamaldehyde) assay, near-infrared spectroscopy (NIRS), and HPLC-fluorescence/UV detection. Procyanidin A2, procyanidin B2 or catachin were used as the standards in different studies. The variations in the above mentioned factors contribute to difficulty/impossibility to directly compare the results (e.g., PA concentration) of different studies (Deshpande et al. 1986; Schofield et al. 2001; Prior et al. 2010). Such a discrepancy in methodology reflects the fact that standardization of the method for PA quantification in cereals and pseudocereals should be seriously considered through multi-laboratory collaboration (Prior et al. 2010). Especially, DMAC assay should be compared with vanillin assay for PA quantification in cereals and pseudocereals. Different types of grains share similarity as well as differences in the chemical composition and the structure (e.g., dietary fibre composition). There is also a large diversity in the PA types and composition among different grains (Table 1). Such differences may as well contribute to the complexity and difficulty of PA analysis in cereals and pseudocereals (Deshpande et al. 1986; Schofield et al. 2001). It was suggested that more than one type of assays for PA quantification may be conducted to reflect different aspects of the PA composition in the samples (Schofield et al. 2001). The results should be expressed in the same manner using the same standard, so that those of different studies can be compared directly.

Spectrophotometry based methods (e.g., DMAC assay) tend to be economic and easy to conducted. However, compared to spectrophotometry based method, HPLC based methods possess a much higher specificity and can quantify the composition and concentration of individual PAs (Hellström et al. 2009). Reversed-phase HPLC appeared to be not an efficient method to resolve individual PAs, whereas normal-phase HPLC can separate individual PAs from each other (Figure 2A) (Verardo et al. 2015; Gunaratne et al. 2013). The reversed-phase HPLC-MS approach can

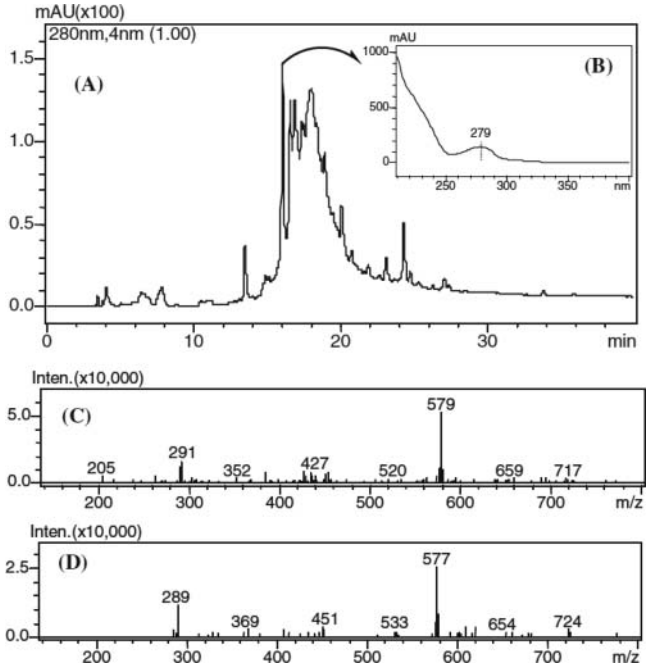

Figure 2C. (A), reversed-phase HPLC-UV detection of PAs from rice; (B), UV spectrum with the λ_{max} of 279 nm; (C) and (D), APCI (atmospheric pressure chemical ionization)-MS spectra (C for positive mode and D for negative mode) (Gunaratne et al., 2013). All the figures are reprinted with permission from the publishers.

effectively identify the existence of PAs in the sample (Gunaratne et al. 2013) (Figure 2C). Krueger et al. (2003) showed that matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) can qualitatively identify the individual PAs from sorghum. Overall, some of the PAs summarized in Table 1 are only tentatively identified, which remain to be structurally illustrated by other techniques such as NMR (nuclear magnetic resonance) spectroscopy. Furthermore, there appears to be a lack of consistency in the nomenclatures of the PAs among different studies, which needs to be standardised to avoid any unnecessary confusion.

Potential health effects of PAs in cereals and pseudocereals

Various extracts of cereals and pseudocereals rich in PAs have shown different health effects *in vitro*, including antioxidation, antiinflammation, antidiabetes, anticancer and glycemic regulation (Table 2). Only one *in vivo* study on the health effects of grain PAs has been reported (Mohanlal et al. 2013). Therefore, *in vivo* and clinical studies are needed in future to confirm the results from the *in vitro* studies.

Antioxidation

Extracts of rice samples have been tested for *in vitro* antioxidant and free radical scavenging activities by ABTS [2,2'-azinobis(3-ethylbenzothiazoline-6-sulphonic acid)], DPPH (2,2-diphenyl-1-picrylhydrazyl), ORAC (oxygen radical absorbance capacity), and FRAP (ferric reducing ability of plasma) assays (Chen et al. 2012; Shao et al. 2015; Kim et al. 2014) (Table 2). PA concentrations in the extracts of rice samples were positively correlated with the antioxidant activities, suggesting PAs

Table 2. Biological activities of PA-containing extracts from rice and sorghum.

Bioactivity	Grain type	Experiment	Major findings	Reference
Antioxidation	Rice	Ethanol extracts (70%) of brans of purple, red and brown rice varieties were tested by DPPH and ORAC assays	Red rice extract containing PAs showed the highest DPPH value, whereas purple rice extract without PAs showed the highest ORAC value	Chen et al. 2012
Antioxidation	Rice	Methanol (80%) extracts of defatted whole grains (14 genotypes grown in 2 different locations) were used. ABTS and DPPH assays were employed to study the antioxidant properties	PA contents of rice samples were highly and positively correlated with the antioxidant activities	Shao et al. 2015
Antioxidation	Rice	Whole flour (9 genotypes) was extracted with a methanol/water/chloroform mixture. ABTS, DPPH, and FRAP assays were employed to study the antioxidant properties	PA contents of rice samples were highly and positively correlated with the antioxidant activities	Kim et al. 2014
Antiinflammation	Rice	Methanol extracts of defatted bran and whole flour of a rice variety containing PAs were used (5 mg/kg bodyweight) to study antiinflammatory effect *in vivo* (rat model)	The bran extract showed the highest inhibition of inflammation (83%), whereas the extracts of the whole rice and the other rice varieties containing little PAs showed much lower inhibition (16–66%)	Mohanlal et al. 2013
Antiinflammation	Rice	Whole grain red rice flour was extracted with 50% ethanol solution to obtain the polar fraction before *n*-butanol extraction to get the non-polar fraction. Effect of the fractions on raw 264.7 macrophages treated by lipopolysaccharide (LPS) was studied	Polar but not the non-polar fraction inhibited the production of tumor necrosis factor-α, interleukin-6, and nitric oxide in the cells, while reducing the expression of inflammation enzymes. The NF-κB, AP-1, and MAPKs pathways were suppressed as well. The antiinflammatory effect was mostly due to the presence of PAs in the polar fraction	Limtrakul et al. 2016
Antiinflammation	Sorghum	Ethanol extracts of sorghum genotypes with contrasting polyphenol composition were added to mouse macrophage cell line RAW 264.7	Cells treated with PA-containing samples produced more cytokines (TNF-α and IL-6) than those without PA	Rhodes & Kresovich, 2016
Antidiabetes	Rice	Brans of 5 rice genotypes (brown, red, purple) differing in polyphenol composition were employed. Inhibitory effect of ethanol extracts of rice brans on amylases was studied. The effect on stimulating glucose uptake in 3T3-L1 adipocytes was also studied	The extracts of all the brans inhibited α-glucosidase activity, whereas only those of red rice containing PAs inhibited α-amylase activity. While the extracts of red and purple brans increased the basal glucose uptake in the adipocytes by 2 to 3 folds, the presence of PAs appeared to be not a determinant. The extracts increased the expression of genes encoding insulin-signalling pathway proteins, and GLUT4 and GLUT1 mRNA	Boue et al. 2016
Glycaemic regulation	Sorghum	Bran extracts (50% methanol) were tested for inhibitory effect on α-amylase activity	Extract rich in PAs better inhibited the α-amylase activity than that containing no PAs. The effect was attributed to the PAs as adding bovine serum albumin greatly reduced the inhibition	Hargrove et al. 2011
Anticancer	Rice	Ethanol extracts (70%) of brans of purple, red and brown rice varieties were tested on a range of different cancer cells	Brown rice extract showed no effect on the cancer cells. Purple rice sample showed minor impact on the cells. Red rice sample exhibited strong anticancer activities against cervical, leukemia, and stomach cancer cells. The former two samples contained no PAs, whereas red rice sample contained much PAs. Fractionation of the red rice extract confirmed the role of PAs in anticancer capacity	Chen et al. 2012
Anticancer	Rice	PA-rich fraction of whole grain red rice was obtained by extraction and fractionation through chromatography. The fraction was tested for the anti-breast cancer property (MDA-MB-231 human breast cancer cells)	The fraction reduced the expression of proteins associated with extracellular matrix degradation. The fraction reduced the activity of collagenase and metalloproteinase-9, while suppressing the expression of intercellular interleukin-6 and adhesion molecule-1. Overall, the fraction rich in PAs mediated the cancer cell invasion	Pintha et al. 2015
Anticancer	Sorghum	Bran extracts (50% methanol) were tested for inhibitory effect on aromatase, a molecular target for treating breast cancer	Extract rich in PAs better inhibited the aromatase activity than that containing no PAs. The effect was attributed to the PAs as adding bovine serum albumin greatly reduced the inhibition	Hargrove et al. 2011

ABTS, DPPH, ORAC, and FRAP represent 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid), 2,2-diphenyl-1-picrylhydrazyl, oxygen radical absorbance capacity, and ferric reducing ability of plasma assays, respectively

as the major antioxidants in the rice grains (Shao et al. 2015; Kim et al. 2014). Indeed, a systematic study showed that PAs possess the highest *in vitro* antioxidant activity among over 100 polyphenols from diverse medicinal/food plants (Cai et al. 2006). Chen et al. (2012) showed that a purple rice extract rich in anthocyanins but without PAs showed a higher ORAC value than that of red rice containing PAs. Therefore, other types of polyphenols also contribute to the antioxidant activities of rice grains. A major concern is related to the significance of the antioxidant activities from the chemical assays (e.g., ABTS method) in relation to health effects *in vivo* (Wang & Zhu, 2017). Assays to measure the cellular antioxidant activities, which appears to be more related to the real situation *in vivo*, may be employed to partially address this issue (Meng et al. 2017).

Antiinflammation

The antiinflammatory effect of rice and sorghum extracts rich in PAs has been studied *in vitro* and *in vivo* (Table 2). A comparative study showed that the sorghum extract containing PAs more enhanced the production of cytokines (TNF-α and IL-6) in mouse macrophage cell line RAW 264.7 than the extract without PAs (Rhodes & Kresovich, 2016). Another comparative study fractionated a rice extract into polar and non-polar fractions (Limtrakul et al. 2016). Only the polar fraction containing PAs inhibited the

formation of tumor necrosis factor-α, interleukin-6, and nitric oxide in the cells, while reducing the expression of inflammation-related enzymes. Therefore, the antiinflammatory effect of the extracts could be due to the PAs. The *in vitro* antiinflammatory effect of PA-containing extracts of grains has been further confirmed *in vivo* (Mohanlal et al. 2013). The PA-containing extract from rice bran showed higher antiinflammatory effect than those with little/nil PAs in rat model (Mohanlal et al. 2013).

Antidiabetes and glycemic regulation

The antidiabetic effect of rice bran extracts with or without PAs has been studied (Boue et al. 2016). α-Glucosidase activity was inhibited by all the extracts, and that of α-amylase was inhibited only by PA-containing samples. This is consistent with the results of Hargrove et al. (2011) who showed that PA may bind with α-amylase for complexation and precipitation. In adipocytes, both the PA-containing and PA-free extracts increased the basal glucose uptake up to 3 times. Therefore, PAs are not the only polyphenols with antidiabetic effect (Boue et al. 2016).

Anticancer

The *in vitro* anticancer property of sorghum and rice extracts containing PAs has been studied on a range of different cancer cells (Table 2). A comparative study showed that the extract of rice mostly containing PAs showed strong anticancer effect against cervical, leukemia, and stomach cancer cells (Chen et al. 2012). The activity of aromatase, a possible molecular target for the anticancer property, was much inhibited by the sorghum extract containing PAs (Hargrove et al. 2011). Fractionation of the extract was conducted to produce PA-rich fraction, which showed even stronger effect against cancer cell invasion (Pintha et al. 2015). This confirms the role of PAs in anticancer function.

Other potential health effects

Aron and Kennedy (2008) reviewed the biological activity of flavan-3-ols from a range of botanical sources (tea, grape seed, cranberry, cocoa, apple, pine, blueberry, and others). The flavan-3-ols showed various health effects such as antioxidant, free radical scavenging, anticarcinogen, cardiopreventive, antimicrobial, anti-viral, and neuro-protective capacities. Though PAs of cereals and pseudocereals may be structurally different from those of the other sources to certain extents, it may be expected that they also possess these biological activities due to a degree of structural similarity, which remain to be studied. It should also be stressed that PAs have antinutritive and health detriment effects (Aron & Kennedy, 2008). PAs can bind to proteins and carbohydrates, reducing the food digestion. They also affects the utilization of minerals and vitamins. The potential health detriment effects include procarcinogens, prooxidants, mutagens, hemorrhage inducers, and hepatotoxins (Aron & Kennedy, 2008). These detriment effects appear to be dependent on type, quantity, and existence of other dietary components. Therefore, the PAs of cereals and pseudocereals should be tested for these possible detriment effects to determine the dosages that may cause health issues. This is especially urgent because cereals and pseudocereals are staple foods and the possible intake of the PAs by humans may be high.

PAs can be functional ingredients in food formulation. Perumalla and Hettiarachchy (2011) reviewed the applications of green tea and grape seed extracts rich in PAs for food safety and quality. For example, the PA-containing extracts showed inhibitory activities against lipid oxidation and antimicrobial properties against food borne pathogens (e.g., *Escherichia coli* O157: H7). Therefore, PAs of cereals and pseudocereals may be used for food safety and quality applications. In particular, by-products of the crops such as leaves and hulls containing PAs may be exploited for the purposes and value-added applications.

Role of other bioactive components in cereals and pseudocereals

The above mentioned studies on the health effects of PA-containing grains employed extracts rather than pure PAs (Table 2). Cereals and pseudocereals in whole grain form contain many other polyphenols and bioactives such as phenolic acids, anthocyanins, and phytosterols (Liu, 2007). They also possess diverse biological activities, some of which are similar to those of PAs (Chen et al. 2012; Boue et al. 2016; Hargrove et al. 2011). For example, though PA-containing extract of sorghum showed inhibitory effects on aromatase and α-amylase, those containing no PAs but other flavonoids (e.g., anthocyanins) also exhibited similar inhibitory effects (Hargrove et al. 2011). Chen et al. (2012) showed that purple rice extract rich in anthocyanins showed a higher ORAC value than red rice extract rich in PAs. Boue et al. (2016) showed that both red (with PAs) and purple (without PAs) rice extracts increased the basal glucose uptake in the adipocytes to similar extents. Indeed, various studies showed the health effects of non-PA polyphenols. For example, ferulic acid, a major phenolic acid in cereal/pseudocereal brans, possesses a range of biological activities against disorders such as cancer and cardiovascular diseases (Mancuso & Santangelo, 2014). A range of plant materials rich in polyphenols showed antidiabetic effect (Wang and Zhu, 2016). These bio-functions are rather similar to those of PAs (Aron & Kennedy, 2008). Furthermore, synergistic interactions in health promoting effects may occur between PAs and other bioactives in food systems and humans (Wang & Zhu, 2017; Perumalla & Hettiarachchy, 2011). Epidemiological studies showed that health effects of plant foods tend to be associated with multiple food components rather than a single factor (Campbell & Campbell, 2005). Nevertheless, pure PAs or fractions highly enriched with PAs should be employed to distinguish the bioactivities from those of other components in the extracts. The interactions of PAs with other food components such as starch and non-starch polysaccharides should be studied as well for potential health effects (Zhu, 2015 and 2017).

Bioavailability and metabolism of cereal and pseudocereal PAs

The bioavailability and metabolism of PAs in grain matrix is fundamentally critical for the current research activities of developing cereal/pseudocereal genotypes rich in PAs. A diet with sorghum bran rich in PAs was fed to female Sprague-

Dawley rats up to 50 days, and the metabolites were analysed by HPLC-MS/MS (Gu et al. 2007). The bran incorporation increased the urinary excretion and serum concentrations of 3'-*O*-methylcatechin (up to 9.5 nmol/day) and catechin (up to 2.2 nmol/day) in a dose-dependent manner. Major phenolic acids in the serum included 3-methoxy-4-hydroxybenzoic acid, 4-hydroxyphenylacetic acid, and 3,4-dihydroxybenzoic acid. 3-Hydroxyphenylacetic acid, 3-methoxy-4-hydroxyphenylacetic acid, and 3-hydroxyphenylpropionic acid were predominant in the urine, which increased in concentrations with increasing level of the bran in the diet. The level of hippuric acid excretion ranged from 2.2 to 16.2 μmol/day, which reached a maximum with 10% of sorghum bran in the diet. PAs degraded mostly in the cecum and colon of the rats. Sorghum catechin and procyanidins were bioavailable, and phenolic acids from bacterial fermentation were the dominant metabolites. Procyanidin depolymerisation was not recorded (Gu et al. 2007). So far, there has been no other studies on the bioavailability and metabolism of PAs from other cereals and pseudocereals. Ou and Gu (2014) recently reviewed the absorption and metabolism of proanthocyanidins from different sources (e.g., grape) in human digestive tract. Overall, the bioavailability of PAs is much affected by the size (DP). The absorption rate of PA dimers is only up to 10% of that of epicatechin, whereas trimers and tetramers have even lower rates. When absorbed, they undergo metabolism in the liver and intestine as revealed in rat model systems. PAs with DP of > 4 showed no absorption due to the large size. PAs undergo little depolymerisation in the gastrointestinal part. Therefore, the majority of PAs reaches the large intestine for fermentation, where they are microbially degraded into phenolic acids and phenylvalerolactones. The metabolites may contribute to the health effects by affecting the gut microbiota composition and through further absorption and metabolism (Ou & Gu, 2014). Therefore, most of the PAs of cereals and pseudocereals tend to reach the colon for fermentation due to the chemical composition as described in the section 2. How the microbial metabolites of PAs from cereals may affect human health remain to be better studied. Cereals and pseudocereals can also be rich in non-PA components such as starch, non-starch polysaccharides, and proteins. They may interact with PAs in food systems and during human digestion, affecting the bioavailability and metabolism (Zhu, 2015 and 2017). So far, little is known about the food matrix effect on the PA metabolism in human digestive tract.

Conclusions and future research directions

Great genetic diversity in PA concentration and composition in different cereals and pseudocereals (rice, wheat, barley, sorghum, millets, and buckwheat) has been recorded. PAs structurally vary with DP from 1 to over 10 (e.g., procyanidin and prodelphinidin based PAs) among different grains. The composition of PAs appears to be species-dependent. The bonds of the PAs are mostly B-type, while a low level of A-type bonds exists in some cereals such as tall fescue and perennial ryegrass. To archive the maximum of PA concentration in the grains, strategies may include selecting the correct genotypes, breeding, agricultural practice (e.g., growing environment, fertilizer type), post-harvest storage conditions, and cooking/processing methods. It should be noted that the methods for PA quantification may greatly affect the results. Apart from the quantification method (e.g., DMAC assay *vs* vanillin assay), factors affecting PA concentrations include extraction procedures (e.g., solvent type and composition), sample status (e.g., flour particle size), and choice of standards. Genotypes of other cereals and pseudocereals (e.g., maize, oats, rye) containing PAs remain to be developed through genetic means. In particular, grains with endosperm (instead of bran layer) rich in PAs can be as well developed. Other parts of the crop such as leaves and husks containing PAs would also be sources of PAs as a functional ingredient. Some of the PA components in the cereals and pseudocereals, tentatively identified so far, remain to be better identified by various techniques such as NMR spectroscopy.

Extracts of rice and sorghum rich in PAs showed a range of biological activities, including antioxidant, antiinflammatory, antidiabetic, and anticancer capacities. However, most of the studies were *in vitro*, and *in vivo* and clinical studies are needed to confirm the claimed health effects. Non-PA components in the extracts should also play roles in the health effects. Possible negative health effects of PAs from the grains remain to be studied. In human digestive tract, only a small amount of PAs with low DP (< 4) can be absorbed at very low levels. The majority of the PAs enters into the colon for microbial fermentation and further metabolism. The absorption of PAs in humans can be manipulated by food processing techniques such as hydrolysis, though the roles of absorbed and fermented PAs on human health is not clearly defined yet. The influence of PAs from cereals and pseudocereals on the composition of gut microbiota and related health effects should be better studied, which is fundamental to the exploitation of PA-rich grains as functional foods.

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