Antioxidant and anti-cancer activities of proanthocyanidins-rich extracts from three varieties of sorghum (Sorghum bicolor) bran

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ABSTRACT
Hepatocellular carcinoma is the fifth most frequently diagnosed cancer in humans. Proanthocyanidins were reported to be an excellent dietary botanical supplement for its antioxidant and anticancer effects. In this study, proanthocyanidins-rich extracts (PREs) were prepared from three varieties (Jinza No. 12, Jinza No. 15 and Jinza No. 18) of sorghum bran. Their proanthocyanidins profiles were characterized. Antioxidant assay showed that PRE samples from Jinza No. 12 and Jinza No. 15 had significantly higher hydroxyl radical, 1-diphenyl-2-picrylhydrazyl radical and oxygen radical-scavenging capacities compared to PRE from Jinza No. 18. Stronger anti-proliferation and inhibition of cell migration in HepG2 cancer cells were also demonstrated among the PRE samples from Jinza No. 12 and Jinza No. 15. Intracellular signaling array analysis demonstrated an up-regulated level of phosphorylated 5’AMP-activated protein kinase α and down-regulated levels of phosphorylated extracellular signal-regulated kinase 1/2 (ERK1/2) and p38.

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1. Introduction
Hepatocellular carcinoma (HCC), as the fifth most common cancer worldwide, has become the third leading cause of cancer-related deaths (Zacharoulis, Hatzitheofilou, Athanasiou, & Zacharoulis, 2005). It is estimated that the incidence of HCC would further increase till 2020 (Siegel, Miller, & Jemal, 2016). Recently, increasing interests among the human population have focused on the use of dietary botanical supplements for prevention and adjuvant therapy of cancer (Martinez, Jacobs, Baron, Marshall, & Byers, 2012). Among the dietary supplements, compounds possessing strong antioxidant activity gained considerable interest. It is known that free radicals induce oxidative stress and cause DNA damage. Persistent oxidative stress leads to chronic inflammation which would further cause the development of cancer (Wang et al., 2010). Several studies have demonstrated a high positive correlation between the free radical-scavenging activity...
and anti-proliferation activity against cancer cells of compounds extracted from various plants (You, Zhao, Liu, & Regenstein, 2011; Sun, Chu, Wu, & Liu, 2002).

Sorghum (*Sorghum bicolor*) is reported to be the fifth most important cereal crop in the world after wheat, rice, corn and barley (Shen, Zhang, Dong, & Chen, 2015). Epidemiological evidences suggest that consumption of sorghum-based food could reduce the risk of certain types of cancer, which may due to the high concentration of proanthocyanidins in it (Awika & Rooney, 2004). Proanthocyanidins are oligomers or polymers of monomeric flavan-3-ols. A flavan-3-ol unit has two aromatic rings (A and B) and a heterocyclic ring C. The monomers are mainly linked through C4 to C8 or sometimes C4 to C6 bonds (Salvadó, Casanova, Fernández-Iglesias, Arola, & Bladé, 2015). It is reported that low-molecular-weight proanthocyanidins, such as catechins, several dimer and trimer proanthocyanidins, always exhibited potential scavenger capacity for superoxide radical, and their antioxidant activity is significantly correlated to the degree of polymerization (DP) (Spranger, Sun, Mateus, de Freitas, & Ricardo-da-Silva, 2008).

Sorghum bran, as a main by-product in Chinese wine industry, is a good source of proanthocyanidins (Hargrove, Greenspan, Hartle, & Dowd, 2011). In the present study, proanthocyanidins-rich extracts (PREs) were prepared from three varieties of sorghum bran, and proanthocyanidins profiles in PRE samples were characterized. Additionally, their antioxidant and anticancer activities towards HepG2 cancer cells in vitro were compared.

### 2. Materials and methods

#### 2.1. Chemicals and reagents

Proanthocyanidins standard (a mixture of oligomeric and polymeric proanthocyanidins, HPLC grade, 95% pure) was purchased from JF-Natural (Tianjin, China). Trolox standard, 1, 1-diphenyl-2-picrylhydrazyl (DPPH), and 2, 2-diazobis (2-aminodinopropane) dihydrochloride were purchased from Sigma Chemical Co. (St. Louis, MO). Williams medium E (WME), hepes, insulin, hydrocortisone, glucagon, fetal bovine serum (FBS), penicillin, streptomycin and gentamicin were purchased from Life Technologies (Grand Island, NY). Other reagents are of analytical or chromatography grade.

#### 2.2. Preparation of PRE from sorghum

Three varieties of sorghum including Jinza No. 12, Jinza No. 15 and Jinza No. 18 were obtained from Shanxi Academy of Agricultural Sciences (Taiyuan, China). The sorghum grains were processed in a mill (Landert-Motoren AG, Buelach, Switzerland) and the sorghum bran fractions were collected. Sorghum bran powder was passed through a 0.25 mm screen, and three PRE samples were extracted, following the method of Wu et al. (2011) with some modifications. Briefly, 25 g of sample was extracted with 250 mL of 70% ethanol (1:10, w/v) for 1.5 h at 70°C. The solution was filtered twice and concentrated to approx. 50 mL. The concentrated extract was loaded onto an AB-8 resin, and then eluted using 30% ethanol. Ethanol fraction was collected and freeze dried, and the resultant PRE samples were stored at room temperature in dry environment.
2.3. Chemical characterization of PRE

The total proanthocyanidins content was measured by the n-butanol/HCl/Fe method (Li et al., 2007). The proanthocyanidins profiles were analyzed according to Wu et al. (2011). The characterization of the three PRE samples was performed on an Agilent 1200 liquid chromatograph (Agilent Technologies, Santa Clara, CA) system. The Silica Luna column (250 × 4.6 mm i.d., 5 μm, Phenomenex Inc., Darmstadt, Germany) was selected. Mobile phase A was dichloromethane/methanol/water/acetic acid (82:14:2:2) and mobile phase B was dichloromethane/methanol/water/acetic acid (10:86:2:2). The injection volume was 10 μL. To identify the extract, both fluorescence detectors (FLD) (λex-280 nm, λem -323 nm) and electrospray ionization tandem mass (ESI-MS/MS) spectrometry were used.

2.4. Hydroxyl radical-scavenging activity assay

The hydroxyl radical-scavenging activity was determined according to a previous method by You et al. (2011) with some modifications. A mix of 600 μL of 1,10-phenanthroline (5.0 mM), 600 μL of FeSO4 (5.0 mM), 600 μL of ethylene-diamine tetra acetic acid (EDTA, 15 mM) and 400 μL of sodium phosphate buffer (0.2 M, pH 7.4) was prepared. Then 600 μL of three PRE samples (As) (or distilled water used as the blank solution, A0) (5–200 μg/mL) and 800 μL of H2O2 (0.01%) (or without H2O2 used as the control solution, Ac) were added, and incubated at 37°C for 60 min. The absorbance was measured at 536 nm on a microplate reader (BioRad, IMAX, Hercules, USA). The Hydroxyl radical-scavenging activity was calculated by the following equation and the IC50 was obtained from the plot of scavenging activity versus concentration of hydrolysate:

\[
\text{Hydroxyl radical scavenging activity (\%) = \left(\frac{A_s - A_0}{A_c - A_0}\right) \times 100.}
\]

2.5. DPPH radical-scavenging activity assay

The DPPH radical-scavenging activity was determined according to a previous method with some modifications (Shi, Yao, Zhu, & Ren, 2016). DPPH (200 μM) was dissolved in 80% methanol. A mix of 1 mL of DPPH solution and 1 mL of samples (As) (5–200 μg/mL) was shaken and permitted to stand at room temperature in the dark for 30 min. A mix of 1 mL of samples and 1 mL of control 80% methanol was used as the control solution (Ac). A mix of 1 mL of DPPH solution and 1 mL of 80% methanol was used as the blank solution (A0). The absorbance of the resulting solution was measured at 525 nm after 10 min on a microplate reader (BioRad, IMAX, Hercules, USA). The DPPH radical-scavenging activity was calculated by the following equation and the IC50 was obtained from the plot of scavenging activity versus concentration of DPPH.

\[
\text{DPPH radical scavenging activity (\%) = \left[1 - \frac{(A_s - A_0)}{A_c}\right] \times 100.}
\]

2.6. Oxygen radical-scavenging capacity (ORAC) assay

The ORAC assay was used to measure the total antioxidant activity of PRE according to the method of Song et al. (2010). Twenty-five microliters of blank, trolox standard or samples (2.5–150 μg/mL) in 50% methanol was added to a 96-well microplate (BioRad, IMAX, Hercules, USA). Two hundred microliters of fluo rescin (0.96 μM dissolved in
working buffer) was then added. After incubation (37°C, 20 min) with intermittent shaking, 20 μL of 2, 20-diazobis (2-aminodinopropane) dihydrochloride (119 mM, dissolved in working buffer) was added. Then decay of fluorescence at 538 nm with excitation at 485 nm was determined (every 2 min for 2.5 h) using a Fluoroskan Ascent FL plate reader (Thermo Lab Systems, Franklin, MA). A standard curve of the areas under the curve for 1.56, 3.13, 6.25, 12.5 and 25 μg/mL Trolox standards minus the area under the curve for the blank was used to obtain quantitative data. The values were expressed as mean mg of Trolox equivalents per mg of PRE.

2.7. Cell culture

HepG2 cells (American Type Culture Collection, ATCC, Rockville, MD) were cultured in WME growth medium, containing 10 mM Hepes, 50 units/mL penicillin, 2 mM L-glutamine, 50 μg/mL streptomycin, 5 μg/mL insulin, 100 μg/mL gentamicin, 0.05 μg/mL hydrocortisone and 5% FBS (Gibco Life Technologies, Grand Island, NY), and maintained at 37°C in 5% CO₂ in an incubator.

2.8. Cell cytotoxicity assay

The cytotoxicity was determined using the method reported by Wang, Chen, Xie, Ju, and Liu (2013). HepG2 cells were seeded into a 96-well plate (4.0 × 10⁵ cells/well) and allowed to adherence for 24 h. PRE samples were added to cell culture at different final concentrations (12.5–150 μg/mL) and incubated for 24 h. Then the medium was removed and cells were stained using 50 μL of Hanks Balanced Salt Solution (HBSS: 1.25% glutaraldehyde and 0.6% methylene blue). After washing with Milli-Q water, 100 μL of elution solution (PBS plus 50% of ethanol and 1% of acetic acid) was added and incubated for 20 min. The absorbance was read at 570 nm on a microplate reader (BioRad, IMAX, Hercules, USA).

2.9. Cell proliferation assay

The anti-proliferation activity was determined using the method reported by You et al. (2011). Cancer cells were seeded into a 96-well plate at a concentration of 2.5 × 10⁵ cells/well. Cell proliferation was measured by the ability of viable cells to reduce 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfenyl)-2H-tetrazolium (MTS) to formazan. After 6 h of incubation, media containing different concentrations (0–150 μg/mL) of PRE samples were added to the cells. Cell proliferation was determined at 96 h from the MTS absorbance (570 nm) reading, and data were expressed as percent of that of the control group.

2.10. Wound-healing assay

Wound-healing assay was conducted as a previous method reported by Wang et al. (2015). In brief, HepG2 cells were seeded into 6-well plate at a concentration of 5×10⁵ cells/wells until confluence with the growth medium. Then a cell-free area was constructed using a pipette tip and cultured with serum-free medium with three PRE samples at a
concentration of their EC$_{50}$ values or control. Healing of the wound was observed after 24 h by a light microscopy (CX-2, Olympus) and analyzed using Image J software (NIH, USA).

### 2.11. Transwell chamber assay

Cell invasiveness was assayed using an extracellular matrix (ECM) invasion assay kit (ECMatrix Cell Invasion Assay (Millipore, Billerica, MA)) according to the manufacturer’s protocols. Assay was terminated after 48 h treatment with three PRE samples at concentration of their EC$_{50}$ values or control.

### 2.12. Intracellular signaling array

HepG2 cells were seeded into a 6-well plate and treated with three samples at the concentration of their EC$_{50}$ values or control for 72 h. Cell lysates were prepared using ice-cold lysis RIPA buffer supplemented with 1% PMSF. Then expression levels of 18 phosphorylated or cleaved signaling molecules were simultaneous detected using a PathScan Intracellular Signaling Array kit (Fluorescent Readout, Cell Signaling Technology, Danvers, MA, USA). The image was obtained by a LiCor Odyssey imaging system (Li-Cor Biosciences, Lincoln Nebraska).

### 2.13. Statistical analysis

The experimental data were expressed as the mean ± SD. All the tests were conducted in triplicate. ANOVA and Tukey’s test were performed using SPSS (Statistics for Social Science) version 17.0 (IBM, New York, USA). Results were considered statistically significant when $p < .05$.

### 3. Results and discussion

#### 3.1. Chemical characterization analysis

The total proanthocyanidins content in PRE samples from three varieties (Jinza No. 12, Jinza No. 15 and Jinza No. 18) of sorghum bran are 52.01%, 54.03% and 52.99%, respectively (Table 1).

As reported (Wu et al., 2011), proanthocyanidins were separated according to their DP. It is shown that oligomers including monomer (P1), dimer (P2), trimer (P3), tetramer (P4), pentamer (P5) and hexamer (P6) were identified (Figure 1).

#### Table 1. The total proanthocyanidins content (%) and proanthocyanidins profiles$^a$ (%) in three PRE samples.

| Sample       | Total proanthocyanidins content (%) | Monomer (P1, %) | Dimer (P2, %) | Trimer (P3, %) | Tetramer (P4, %) | Pentamer (P5, %) | Hexamer (P6, %) | Polymeric proanthocyanidins (PP, %) |
|--------------|-------------------------------------|-----------------|---------------|---------------|-----------------|-----------------|----------------|-----------------------------------|
| Jinza No. 12 | 52.01 ± 1.33a                       | 31.65 ± 0.45a   | 18.98 ± 0.34b | 20.57 ± 0.17q | 9.18 ± 0.21c    | 4.43 ± 0.12c    | 5.06 ± 0.13c   | 10.13 ± 0.45b                      |
| Jinza No. 15 | 54.03 ± 0.89a                       | 26.32 ± 0.77b   | 13.16 ± 0.21c | 21.05 ± 0.22a | 11.84 ± 0.67b   | 7.89 ± 0.33a    | 9.21 ± 0.14a   | 10.52 ± 0.47b                      |
| Jinza No. 18 | 52.99 ± 1.67a                       | 22.03 ± 0.89c   | 25.33 ± 0.88a | 12.78 ± 0.99b | 14.98 ± 0.56a   | 5.07 ± 0.57b    | 6.61 ± 0.68b   | 13.22 ± 0.66a                      |

Note: Data are presented as mean ± SD. Values at the same column that do not share the same lowercase letter are significantly different ($p < .05$). PRE, proanthocyanidins-rich extract.

$^a$Proanthocyanidins profiles were calculated by the peak area measurement.
Figure 1. Normal-phase HPLC-FLD trace of PRE from three varieties of sorghum bran. Labels P1-P6 indicate the degrees of polymerization (DP) of proanthocyanidins in the peaks. Polymeric proanthocyanidins (PP) appear as a single peak at the end of the chromatogram. LU, luminescenceunits. PRE, proanthocyanidins-rich extract.
In agreement with the study of Gu et al. (2002), the method was not able to detect polymeric proanthocyanidins separately; so they were collected as a single peak (PP). The three PRE samples showed significant differences in the distribution of the individual oligomers and polymers. PRE from Jinza No. 12 had a larger relative ratio of the proanthocyanidins oligomers (P1–P6) compared to PRE from Jinza No. 15 and Jinza No. 18. In addition, compared to proanthocyanidins from grape seed which has been demonstrated to have strong antioxidative activity, PRE samples from sorghum bran had higher P1 levels other than P2–P4 levels (Prodanov et al., 2013). Proanthocyanidins chain length affect their effectiveness against oxidative stresses; therefore more detailed information on the relative ratio of the proanthocyanidins oligomers as well as polymers in sorghum bran is needed in predicting its overall effectiveness as antioxidant. However, in this study higher ligomers (DP > 6) were not separated and identified due to the limited scanning range of the mass spectrometer used, and thus further study is needed.

### 3.2. Antioxidant activity

Since there are various methods for assessing antioxidant activity, the present work evaluated the antioxidant activity of PRE samples by determining their scavenger capacity on different types of radicals. Hydroxyl radicals are reactive oxygen species generated in the human body and they can react with much biomolecules, which may lead to physiological disorders (You et al., 2011). In this study, all of the three PRE samples exhibited strong hydroxyl radical-scavenging activity, with the IC50 values (Table 2) of 18.32 μg/mL (Jinza No. 12), 22.31 μg/mL (Jinza No. 15) and 27.28 μg/mL (Jinza No. 18). These results were similar to those of Ling, Xie, and Yang (2005), who reported that oligomeric proanthocyanidins from the seedpod of nelumbo nucifera Gaertn showed antioxidative activity. PRE from Jinza No. 12 presented the lowest IC50 value, indicating the highest hydroxyl radical-scavenging activity. DPPH radical is a useful reagent for evaluation of the free radical-scavenging activity of compounds. Since the DPPH radical is not biologically relevant (Baratto et al., 2003), the DPPH assay was performed as a preliminary study to estimate the direct free radical-scavenging ability of different tested compounds. However, different from the results of hydroxyl radical-scavenging activity, Jinza No. 15 showed the lowest IC50 value (115.77 ± 9.01 μg/mL) for the DPPH method. And there are significant differences among the three samples (p < .05). In addition, three samples showed dose-dependent antioxidant activity in the ORAC assay (Figure 2). PRE from Jinza No. 12 showed the highest ORAC value (70.71 ± 1.86 μM Trolox/mg PRE) when the concentration reached 150 μg/mL, which was consistent with results of hydroxyl

| Samples       | Antioxidative activity (IC50, μg/mL) |
|---------------|-------------------------------------|
|               | Hydroxyl  | DPPH                  |
| Jinza No. 12  | 18.32 ± 1.09c | 122.11 ± 7.88b |
| Jinza No. 15  | 22.31 ± 1.68b | 115.77 ± 9.01b |
| Jinza No. 18  | 27.28 ± 1.73a | 141.23 ± 9.87a |

Note: Values are expressed as the mean ± SD. Values in the same column that do not share the same lowercase letter are significantly different (p < .05). PRE, proanthocyanidins-rich extract; Hydroxyl, The scavenging activity for the hydroxyl radical; DPPH, The scavenging activity for DPPH free radical.
radical-scavenging activity assay. The ORAC method is generally highly regarded due to its use of biologically relevant free radicals and also integration of both degree and time of inhibition (Awika, Rooney, Wu, Prior, & Cisneros-Zevallos, 2003).

3.3. Anti-proliferation activity of PRE samples on hepG2 cancer cells

Human HepG2 human liver cancer cells were widely used for biochemical and nutritional studies as they can retain their morphology and most of their function in culture (You et al., 2011). The anti-proliferation activity and cytotoxic effects of the three PRE samples on HepG2 cells are shown in Figure 3. PRE samples inhibited cell proliferation, Jinza No. 12 and Jinza No. 15 showed significantly higher inhibitory effect than Jinza No. 18 ($p < .05$). The EC$_{50}$ values of the inhibitory effect by different PRE samples are shown in Table 3. The three PRE samples had no cytotoxic effects on HepG2 cells at a concentration from 0 to 150 $\mu$g/mL (Figure 3 and Table 3), which suggested that the anti-proliferation effects were not attributed to cytotoxic effects. Consistent with these results, McDougall, Ross, Ikeji, and Stewart (2008) found that proanthocyanidins derived from lingonberry showed anti-proliferation activity which resulted in its antitumor effects rather than cytoxic effects.

3.4. Inhibitory effects of PRE samples on cell migration

To further investigate the pharmacological activity of the three PRE samples against cancer metastasis, we examined the inhibitory effects on cell migration through wound-
healing assay and transwell chamber assay. Compared with the control group, all of the three samples inhibited the wound closure in HepG2 cells at the concentration of their EC50 values (Figure 4(a)). Quantitative data showed that there is no obvious difference between Jinza No. 12 and Jinza No. 15 (Figure 4(b)). However, the inhibitory effect of Jinza No. 18 was weaker ($p < .05$). The effects of the three PRE samples on cell invasion are shown in Figure 4(c). The invasion of HepG2 cells was inhibited by 30.37%, 29.06% and 27.82% with Jinza No. 12, Jinza No. 15 and Jinza No. 18, respectively. Taken together, these results indicated that all of the three PRE samples have strong inhibitory effects on HepG2 cells’ migration.

### Table 3. Anti-proliferation effects and cytotoxicities of three PRE samples towards HepG2 cells.

| Samples       | Anti-proliferation effects (EC50, μg/mL) | Cytotoxicity effects (CC50, μg/mL) |
|---------------|----------------------------------------|-----------------------------------|
| Jinza No. 12  | 32.23 ± 5.28b                           | >150                              |
| Jinza No. 15  | 31.80 ± 6.45b                           | >150                              |
| Jinza No. 18  | 67.53 ± 11.67a                          | >150                              |

*Note: Values are expressed as the mean ± SD. Values in the same column that do not share the same lowercase letter are significantly different ($p < .05$). PRE, proanthocyanidins-rich extract.*
Figure 4. Inhibition of cell migration by treatment of three PRE samples. For the wound-healing assay, wounds were made when HepG2 cells were 90–100% confluent. Overnight, cells were treated with three PRE samples or control. The closure of wounds was imaged (a) and quantitatively measured (b) at 0 and 24 h. For the transwell chamber assay, HepG2 cells were treated with three PRE samples or control for 48 h. Cells suspended in serum-free medium were seeded on the upper membrane of transwell chamber and incubated for 48 h. Complete growth medium was added on the bottom. Cells on the lower membrane of chambers were counted (c). Data are presented as mean ± SD. Values that do not share the same lowercase letter are significantly different (p < .05).
3.5. Modulations of protein expression and signaling pathways

To get insight into how PRE samples affected the proliferation and migration of HepG2 cancer cells, the protein expression levels of 18 intracellular signaling molecules was examined. Compared with the control group, PRE samples significantly up-regulated the level of 5’AMP-activated protein kinase (AMPK) α (AMPKα), and down-regulated the levels of extracellular signal-regulated kinase 1/2 (ERK1/2) and p38 (Figure 5(a)). AMPK is a serine/threonine protein kinase responsible for cellular energy homeostasis (Chiang et al., 2010). Increasing evidence suggests that it is a potential target for cancer chemotherapy against HCC (Jhaveri, Ju, & Gabrielson, 2013). Chiang et al. demonstrated that activation of the AMPKα pathway (Chiang et al., 2010) is associated with anti-proliferation and autophagy of HepG2 cancer cells. In the present study, expression level of AMPKα was elevated by 2.20, 2.52 and 1.79 times by PRE from Jinza No. 12, Jinza No. 15 and

![Image of Figure 5](image-url)

Figure 5. Modulations of intracellular signaling pathways in HepG2 cells. Cells were treated with three PRE samples or control for 72 h. Total protein was extracted for the analysis. A slide-based antibody array was used for simultaneous detection of 18 signaling molecules when phosphorylated or cleaved using a PathScan Intracellular Signaling Array kit. Image (a) and quantitative data (b) were obtained using a LiCor Odyssey imaging system. Data are presented as mean ± SD. 1, Phosphorylated ERK1/2 (Thr202/Tyr204); 2, Phosphorylated AMPKα (Thr172); 3, Phosphorylated p38(Thr180/Tyr182).
Jinza No. 18, respectively (Figure 5(b)). Protein kinases have recently emerged as a group of molecular targets with the potential to be cancer specific; therefore, molecular targets involved in mitogen-activated protein kinases (MAPK) pathway are recognized as promising targets (Schmitz et al., 2007). Besides, a previous study has reported that inhibition of the MAPK pathway might have the potential to prevent invasion, metastasis and angiogenesis for a wide range of tumors (Vayalil, Mittal, & Katiyar, 2004). ERK1/2 and p38 are important members of MAPks. For ERK1/2, the levels were reduced by 4.33, 5.38 and 2.68 times with PRE from Jinza No. 12, Jinza No. 15 and Jinza No. 18, respectively, compared to the control. And for p38, the levels were reduced by 6.66, 4.65 and 3.61 times with PRE from Jinza No. 12, Jinza No. 15 and Jinza No. 18, respectively, compared to the control (Figure 5(b)). All these results indicated that PRE samples exhibited anticancer effects through activation of the AMPK signaling pathway and inhibition of the MAPK signaling pathway.

4. Conclusion

In summary, we observed different proanthocyanidins profiles in PRE samples from different varieties of sorghum bran. PRE samples from Jinza No. 12 and Jinza No. 15 possessed higher antioxidant effects in vitro. Additionally, PRE samples inhibited HepG2 cancer cells’ proliferation and migration through activation of the AMPKα pathway and inhibition MAPK pathway. These results indicate sorghum bran could be a valuable resource of natural proanthocyanidins extract that exerts antioxidant and HCC prevention effects.

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Disclosure statement

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