Phenolic Fraction from Peanut (Arachis hypogaea L.) By-product: Innovative Extraction Techniques and New Encapsulation Trends for Its Valorization

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Abstract
Peanut skin is a by-product rich in bioactive compounds with high nutritional and pharmaceutical values. The phenolic fraction, rich in proanthocyanidins/procyanidins, is a relevant class of bioactive compounds, which has been increasingly applied as functional ingredients for food and pharmaceutical applications and is mostly recovered from peanut skins through low-pressure extraction methods. Therefore, the use of green high-pressure extractions is an interesting alternative to value this peanut by-product. This review addresses the benefits of the phenolic fraction recovered from peanut skin, with a focus on proanthocyanin/procyanidin compounds, and discusses the improvement of their activity, bioavailability, and protection, by methods such as encapsulation. Different applications for the proanthocyanidins, in the food and pharmaceutical industries, are also explored. Additionally, high-pressure green extraction methods, combined with micro/nanoencapsulation, using wall material derived from peanut industrial processing, may represent a promising biorefinery strategy to improve the bioavailability of proanthocyanidins recovered from underutilized peanut skins.

Keywords Procyanidins · Peanut skins · Green extractions · Bioavailability · Encapsulation

Introduction
Food industries are redesigning their production chains to address the emerging consumer demand for high-nutritional foods, products with enhanced functional and physical properties, and enriched with health-promoting constituents (Galanakis, 2021). With population growth, emphasis is directed towards the reprocessing of agro-industrial by-products (Sorita et al., 2022). Among them, peanut meal (derived from oil production), skins, and shells are the main by-products of peanut processing, which are mostly used for animal feed (Sorita et al., 2020). Particularly, peanut skins are valuable by-products from peanut processing operations, with more than one million tons produced worldwide every year and presenting considerably high contents of proanthocyanidins and their isomers (Xu et al., 2022).

Peanut (Arachis hypogaea L.) is an important oilseed cultivated and appreciated worldwide. The processing of peanut oilseeds provides various popular peanut goods, generating large amounts of by-products (Sorita et al., 2022). Among them, peanut meal (derived from oil production), skins, and shells are the main by-products of peanut processing, which are mostly used for animal feed (Sorita et al., 2020). Particularly, peanut skins are valuable by-products from peanut processing operations, with more than one million tons produced worldwide every year and presenting considerably high contents of proanthocyanidins and their isomers (Xu et al., 2022).

The phenolic-rich fraction recovered from peanut skins is becoming increasingly popular due to the growing demand for functional foods, beyond the interest from pharmaceutical industries. The use of the peanut-phenolic fraction (rich in procyandins) in food and pharmaceutical formulations can promote several health benefits, such as antioxidant (Constanza et al., 2012), anti-cancer (Liu et al., 2020), cardioprotective (Rauf et al., 2019), anti-diabetic and anti-obesity (Unusan, 2020), antimicrobial (Camargo et al., 2017b), neuroprotective (Singh et al., 2017), antiviral (Makau et al., 2018), and anti-asthmatic (Kandhare et al., 2013).
In connection to that, this review evaluates possible uses for the phenolic-rich fraction from peanut skin, mainly composed by proanthocyanidins/procyanidins components, in food and pharmaceutical formulations, adding value to this underestimated by-product. For this purpose, a fast search at SCOPUS Database (up to June, 2022) shows that 2538 studies are relate to peanut and its by-products (“peanut”) AND (“by-products” OR “waste” OR “residue”). Refining the search, 86 works were founded related to peanut skin and phenolic compounds (“phenolic” AND “peanut skin”), showing the growing interest from the scientific community about phenolic compounds from food by-products, particularly peanut skin. Specifically, in the last 10 years (2012–2021), 61 works were published (71% of total studies), and 5 studies were published up to June 2022. The criteria used for article selection were within the title, abstract, and keywords. The USA, with 27 works, was the first in publication ranking, followed by Brazil (22 studies) and Argentina (9 studies). Additionally, among the 86 studies, 62 are related to agricultural and biological sciences; 32 to chemistry; 19 to biochemistry, genetic, and molecular biology; and 15 are related to chemical engineering, showing the multidisciplinary enrolled in this subject, rising the application possibilities.

To identify alternative sources of phenolic compounds and the efficient methods for their recovery is of utmost scientific and industrial interest. Then, within the viable sources of this relevant fraction, peanut skin emerges with high potential due to the relevant content of these components that can promote several health benefits. Because the recovery of phenolics from peanut skin can be achieved by several methods, this review provides an update about the extraction techniques, focusing on green methods with non-toxic solvents, such as supercritical fluid extractions (SFE), pressurized liquid extraction (PLE), subcritical water extraction (SFE), ultrasound-assisted extraction, and microwave-assisted extractions (MAE) and its combination, in a biorefinery concept.

Although some phenolic characteristics, such as fast delivery and degradation, combined with low solubility and bioavailability, may restrict its direct use in pharmaceutical and food formulations (Xu et al., 2022), nevertheless, encapsulation processes are exciting alternatives to overcome the restrictions for its applications, and these options are also compiled in this review. Association of sustainable extraction methods (for selective extractions), health benefit characteristics, and encapsulation strategies can be an interesting way to value food by-products, allowing further applications of the recovered fractions in food and pharmaceutical products.

Therefore, the present review provides the connection of two strategies for the valorization of peanut by-product, the innovative and sustainable extraction methods and green encapsulation procedures. This approach can stimulate the circular economy, integrating the industry 4.0 design by means of developing green process and products.

### Peanut: Increase in By-product Generation

The world population growth connected to the increasing use of oilseed commodities as input for biofuel production had led to higher demand for oil production, affecting consequently the oil prices (Shokoohi & Saghaian, 2022). For that reason, the oilseed production and market are growing fast, and the 5 main world producers of peanut in 2021 are shown in Fig. 1 (USDA, 2022).

China, India, Nigeria, the USA, and Sudan, the main peanut producers in 2021, were responsible for 69% of the world production, where China contributed most, with 36% of world production (18.2 K MT). India and Nigeria were the second and third highest peanut producers, being responsible for 14% (6.8 K MT) and 8% (4.22 K MT), respectively, followed by the USA and Sudan (6 and 5% of world production), providing 2.9 and 2.3 K MT, respectively.

The projection for 2022, related to peanut meal, destined for industrial uses, and oil consumption, indicates near historic levels, reaching the peanut production in the USA, while the Brazilian production is estimated to increase by 60% of the production compared to 2018/2019. Still for 2022, it is projected a peanut production rise in 17% related to whole seed, oils, and food uses (USDA, 2022).

Considering that most peanut-based products do not contain the red skin layer, the amount of this by-product is increasing. Besides, taking into account the circular economy context, the transformation of agro-industrial residues (like peanut skin), as sources of valuable products, contributes to sustainable industrial processes, and can be of relevance to contribute to peanut industrial processing. Then, because peanut skin represents about 3% of the peanut weight (Lorenzo et al., 2018; Sorita et al., 2020), and the world peanut production in 2021 was 50.22 K MT (USDA, 2022), it is estimated that approximately 1.50 K MT of peanut skin were generated in 2021. Also, considering the representative amount of phenolic compounds from peanut skin, this by-product can be considered an emerging and promising feedstock for the recovery of bioactive ingredients.

Therefore, with the increase in peanut skin generation, worldwide studies (mainly from the USA, Brazil, and Argentina, as reported in the “Introduction” section) have been focusing on the extraction of the phenolic-rich fraction from this valuable by-product, rising food and pharmaceutical applications, as substitute of synthetic additives, as discussed in the next sections.
Phenolic Compounds in Peanut By-products

Peanut skin contains several compounds (mainly phenolic components) with diverse potential biological activities. In nature, the phenolic compounds from plants (generally concentrated at the skins or peels) are responsible for color, taste, and flavor attributes, indicating the plant maturity. These compounds have two main functions: (i) protect against insects, pathogens, and herbivorous animals, and (ii) attract insects for flower pollination.

Phenolic compounds can be classified in four subgroups (categories): phenolic acids, flavonoids (including flavonols, flavones, flavanols, anthocyanidins, and isoflavones), tannins, and stilbenes (An et al., 2021; Neuenfeldt et al., 2022; Singh et al., 2017). Figure 2 illustrates the phenolic compounds identified in peanut by-products.

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Phenolic acids are a minor phenolic group from peanut skins, mainly composed by coumaric, caffeic, and ferulic acids, and this class of components are represented by the phenolic compounds with one carboxylic acid group. Protocatechuic, ferulic, caffeic, and p-coumaric are the main compounds identified and quantified in peanut skin. Chlorogenic acids (and their monomers, quinic acid) can also be found in peanut skin, although rarely, but their presence can be associated to peanut cultivars and industrial processing (Dean, 2020; Lan et al., 2020; Ma et al., 2013; Sarnoski et al., 2012a).

Stilbenes, also identified from peanut skin, are extensively recovered from numerous food by-products due to their valuable biological activities. Resveratrol is the main stilbene from peanut skin, among other derivatives such as isopentadienylresveratrol, piceatannol, piceid, and some prenylated resveratrol analogs. The resveratrol content varies with peanut cultivar and processing; for instance, Spanish skins (15.04 μg g⁻¹) have higher content than Runner and Virginia types (4.30 and 3.66 μg g⁻¹, respectively) (Francisco & Resurreccion, 2009).

Flavonoid components (monomeric and condensed) are the main fraction of phenolic compounds from peanut skin, such as catechin, epicatechin, epigallocatechin, catechin gallate, epicatechin gallate, epigallocatechin gallate, quercetin, and proanthocyanidins and a complex series of procyanidins oligomers, which have been already identified and quantified from this by-product. Then, because procyanidin (A-type procyanidin dimer, trimers, and tetramers) can achieve a remarkable value of 85.7% of the total phenolic components from peanut skin (Xu et al., 2022), the present study focuses on the flavonoid group (specifically, in proanthocyanidins/procyanidins oligomers), which is presented in terms structures and the biological activities associated.

Fig. 1 The five most peanut producers worldwide in the 2021 year. Source: USDA (2022)
PHENOLIC COMPOUNDS IDENTIFIED IN PEANUT SKIN

**PHENOLIC ACIDS**
- Ellagic acid
- p-coumaric acid
- Caffeic acid
- Chlorogenic acid
- Gallic acid
- Protocatechuic acid

**STILBENES**
- Resveratrol
- Piceatannol
- Piceid

**FLAVONOLS**
- Epicatechin
- Quercetin
- Apigenin
- Isoquercetin
- Kaempferol
- Epigallocatechin gallate
- Isorhamnetin
- Fisetin
- Chrysins
- Biochanin A

*Fig. 2* Phenolic groups identified in peanut skin
Proanthocyanidins and Its Structures

Proanthocyanidins are high molecular weight polyphenolic compounds, which, for peanut skin, are originated from the polymerization of flav-3-ol by saturated linkage between two carbon molecules (C–C), and occasionally by C–O–C bonds, as shown in Fig. 3.

In Fig. 3(I), a general molecular structure of common monomeric anthocyanins (subclasses), such as procyanidins, prodelphinidins, propelargonidins, proisetinidins, prorobinetinidins, and proguibourtinidins, is shown (Xie & Dixon, 2005). These subgroups are obtained from depolymerization and/or decomposition at high temperature in acid medium. The most common subgroups from proanthocyanidins are the procyanidins, oligomers of (epi)catechin units, and their galloyl derivatives (Bansode et al., 2014), widely present in peanut skin.

The proanthocyanidin molecular structures, considering linkage types, are presented at Fig. 3(II, III), which show A-type (C₄–C₈ and C₂–O₇) and B-type (C₄–C₈ and C₄–C₆) proanthocyanidins, respectively. The linkage of monomeric units (Fig. 3(I)) occurs mostly between C₄ from the “upper” monomeric unit and C₈ or C₆ from the “lower” monomeric unit (B-type, Fig. 3(III)), called B-type because the linkage is based on the lower unit, the B-ring. The most common B-type proanthocyanidin dimers are found in nature, frequently from plant tissues, the B₁, B₂, B₃, and B₄, which are related to C₄–C₈ bonding (Fig. 3(IV)). Types B₅, B₆, B₇, and B₈ are less frequent and related to C₄–C₆ bonds. Sometimes, an extra ether group is found between C₂ and O₅ or O₇, and the structure is called A-type due to linkage based on A-ring; more specifically, the C-ring of the “upper” monomeric unit is linked with the A-ring of the “lower” monomeric unit (Fig. 3(II)) (Neto et al., 2020; Rauf et al., 2019), with A₁ and A₂ as the most common A-type proanthocyanidins (Fig. 3(IV)). The synthesis of proanthocyanidins from the chemical, biochemical, and molecular genetic perspectives is presented in detail by Xie and Dixon (2005).

The structure, the monomeric composition, the degree of polymerization, and the specific linkages of the proanthocyanidins affect their bioactivities (Dong et al., 2013). For instance, according to Andersen-Civil et al. (2021), the bioavailability, stability, and activity of polyphenolic compounds, such as proanthocyanidins, may be correlated with the amount of hydroxyl groups, mean polymerization, and/or bond type and position between the monomers. Besides, Vazquez-Flores et al. (2018) suggested that proanthocyanidins with low degree of polymerization are more apt to inhibit digestive enzymes, such as intestinal lipase, amylase, and proteases, due to their capacity to bind with specific cavities from the enzymes, better than polymer or oligomer molecules.

Proanthocyanidins/Procyanidins from Peanut By-products

Proanthocyanidins/procyanidins derived from plant and food by-products emerged as functional ingredients, attracting attention from the food industry and health organizations due to their well-being beneficial properties, such as the protective effect against diabetic retinopathy (Sun et al., 2016), complementary and alternative strategy to prevent

Fig. 3 (I) General molecular structure of common monomeric anthocyanins, (II) molecular linkage structure for A-type proanthocyanidins (C₄–C₈ and C₂–O₇), (III) molecular linkage structure for B-type proanthocyanidins (C₄–C₈ and C₄–C₆), and (IV) procyanidins A₁, A₂, B₁, B₂, B₃, and B₄ types. Source: Adapted from Neto et al. (2020), Xie and Dixon (2005) and He et al. (2008)
skin cancer by attenuating the adverse UV radiation effects (Katiyar et al., 2017), and also atherosclerosis prevention, cardiovascular protection, and reduction of total cholesterol from blood plasm (Blade et al., 2010). Besides that, proanthocyanidins are related to maintaining vascular elasticity and normal blood pressure (Odai et al., 2019), among other health-promoting characteristics.

The linkage types from A- and B-proanthocyanidins affect their activities; for instance, A-type (peanut skin) has higher trypsin inhibitor activity and higher affinity for α-casein (useful for wall material attributes, facilitating encapsulation) and strongly inhibits α-amylase, compared to B-type (Le Bourvellec & Renard, 2018). Besides, A-type proanthocyanidins help prevent recurrent urinary tract infections, a property not observed from B-type proanthocyanidins (Liu et al., 2012). A comprehensive approach of the benefits of A- and B-type proanthocyanidins is discussed below.

Recently, several researchers have shown that peanut skins are excellent sources of phenolic compounds, particularly proanthocyanidins/procyanidins, present in high concentration (~86%) (Xu et al., 2022) with innumerable biological activities (Appeldoorn et al., 2009; Bodoira et al., 2019; Munekata et al., 2016; Oldoni et al., 2016). Then, Table 1 summarizes the scientific works related to the recovery of proanthocyanidins from peanut skin by-products, with results detected.

It is important to point that the content of proanthocyanidins from peanut skin by-products varies with the source, as well as the recovery and quantification procedures (Table 1 data). Besides, the proanthocyanidin content can be affected by several factors, such as (i) peanut cultivation, for instance, specie or variety, climate, and soil conditions; (ii) peanut processing, like mechanical peeling and roasting; and (iii) extraction conditions.

Chukwumah et al. (2012) compared the total proanthocyanidin content (in cyanidin chloride equivalent (CCE)) of twenty-seven cultivars from different regions, with results ranging from 0.101 to 1.030 mg CCE g⁻¹ of peanut skins, where the lower value was from Valencia variety while the higher content was from Runner variety. Yu et al. (2006) showed that peanut processing (oilseed roasting) affected the procyanidin content from the skin, compared with non-roasted peanut skin. For instance, the content of trimer and tetramer proanthocyanidins reduced with temperature increase, from 0.221 and 0.296 mg g⁻¹ (non-roasted skin) to 0.157 and 0.204 mg g⁻¹ (roasted skin), respectively. Otherwise, the dimers’ content increases, from 0.111 (non-roasted skin) to 0.143 mg g⁻¹ (roasted skin), due to degradation of larger proanthocyanidins into lower ones (dimers).

Most studies for the recovery of proanthocyanidins from peanut skins apply conventional extraction methods (maceration and Soxhlet extraction), which are generally highly time- and solvent-consuming. Mostly, these methods have low selectivity, resulting in less pure extracts, with residual solvent, that compromises its use for food industries (Belwal et al., 2020). In addition, the long extraction time that is normally required can cause proanthocyanidin degradation, reducing their antioxidant and antimicrobial properties (Bodoira et al., 2017).

Usually, conventional extraction of proanthocyanidins from peanut skin requires two steps: lipid extraction by nonpolar solvents that act as a barrier for proanthocyanidins extraction, followed by polar solvent extraction, from defatted peanut skin, to obtain the polyphenol fraction (e.g., proanthocyanidins) (Tamkutė et al., 2020).

Larrauri et al. (2016) recovered proanthocyanidins from peanut skin by conventional three-step extraction: (1) lipid extraction by Soxhlet with n-hexane for 6 h, followed by (2) polyphenol extraction by maceration with ethanol/water (70:30 v/v) at room temperature for 24 h, and (3) purification with ethyl acetate in a column (Sephadex LH-20) eluted with ethanol. Fractions (2) and (3) were analyzed by HPLC–ESI–MS/MS, detecting phenolic acids (quinic, gallic, and cuminic acids), flavonoids (catechin, epicatechin, quercetin, isoquercetin, genistein, isorhamnetin, apigenin, chrysin, procyanidins, and proanthocyanidins), and stilbenes (resveratrol). The main proanthocyanidins from fraction (3) were as follows: procyanidin dimer A-type (31.49%), proanthocyanidin dimer (24.33%), and procyanidin dimer B-type (14.15%). Using four-step extraction, Munekata et al. (2016) recovered proanthocyanidins from peanut skin by (1) stirring maceration (ethanol/water 80:20 v/v) at 60 °C for 50 min, (2) 15-min sonication, (3) centrifugation (6000 rpm for 15 min), and (4) filtration.

The number of extraction steps, process conditions, recovery efficiency, and quality of the recovered fractions can be modified by the extraction method and solvent used. Alternative high-pressure methods and environmentally friendly solvents may contribute to green processes, stimulating the sustainable development (Benvenutti et al., 2021).

**Innovative Extraction of Proanthocyanidins/Procyanidins**

Recently, with the increasing demand of natural products, additives, or bioactive extracts for foods, cosmetics, and pharmaceutical applications, the extraction specialists have focused on improving the processes efficiency, reducing extraction time, number of operations, energy consumption, and amount of solvent, which reduce environmental impact, economical costs, and generated waste, but simultaneously keeping attention on the extract’s quality (Chemat et al., 2019).
| Study objective                                                                 | Conventional extraction method | Extraction conditions | Quantification/identification | Highlight results                                                                 | Reference          |
|--------------------------------------------------------------------------------|--------------------------------|-----------------------|-------------------------------|-----------------------------------------------------------------------------------|--------------------|
| Develop a simple method for preparing sufficient amount of A-type dimers from peanut skins and persimmon pulp | Soxhlet extraction            | 3 followed extractions with 20% (v/v) of methanol followed by filtration and lyophilization | HPLC–MS                      | A-type proanthocyanidin content: 378.3 mg kg⁻¹ dry peanut skins (88.72% of purity) | Dong et al. (2013) |
| Inhibitory activity of proanthocyanidins from peanut skin on inflammatory cytokine production and melanin synthesis in cultured cell lines | Maceration followed by ultrasound, filtration, and evaporation | Maceration: acetone/water (70:30 v/v) for 24 h Ultrasound: 30 min | UPLC-DAD-EIS-MS | 11 proanthocyanidins were identified Peanut skin extracts decreased melanogenesis in cultured human melanoma | Tatsuno et al. (2012) |
| Determine the effects of processing on phenolic composition of peanut skin and identify/quantify peanut skin procyanidins | Maceration with stirring followed by centrifugation | Ethanol/water (8:92 v/v) | LC–MS                        | Procyanidin dimer, trimers, and tetramers content were 0.111, 0.221, and 0.296 mg g⁻¹ of non-roasted peanut skin and 0.143, 0.157, and 0.204 mg g⁻¹ of roasted peanut skin | Yu et al. (2006) |
| Isolation of A-type (from peanut skins) and B-type (from grape seeds) dimers by combining normal phase (NP), reversed phase (RP), and HPLC chromatography | Soxhlet extraction followed sonication | Soxhlet: methanol/water (20:80 v/v) Ultrasound: water/ethyl acetate (50:50 v/v) for 10–15 min at room temperature followed by lyophilization | NF-RF-HPLC-NMR | Yields increased 20–400 times for A-type dimers and 10 times for B-type dimers compared to other methods | Appeldoorn et al. (2009) |
| Provide scientifically valuable information of proanthocyanidins for better utilization of peanut skin | Maceration followed by ultrasound, filtration, and evaporation | Maceration: acetone/water (70:30 v/v) for 24 h Ultrasound: 30 min | UPLC-DAD-EIS-MS | A type proanthocyanidin trimer was identified, isolated, and purified This compound presented strong antioxidant activity and inhibition on sucrase | Zhang et al. (2013) |
| Evaluate the antioxidant activity of crude extract and fractions of peanut skin, and isolate proanthocyanidins by bioassay-guided fractionation technique | Extraction with water acidifier followed by filtration, evaporation and lyophilization | 23 g of peanut skins Solvents: acetone/water (60:40), acidified to pH 1.5 with 0.1 mol/L HCl, in a thermostatic bath at 70 °C for 30 min | Quantification: HPLC Identification: NMR | The authors isolated proanthocyanidins A₁ and A₂ type Proanthocyanidins A₁ proved to be more active than A₂ related to antioxidant activity | Oldoni et al. (2016) |
Table 1 (continued)

| Study objective                                                                 | Conventional extraction method | Extraction conditions                                                                 | Quantification/identification       | Highlight results                                                                 | Reference            |
|--------------------------------------------------------------------------------|--------------------------------|--------------------------------------------------------------------------------------|------------------------------------|----------------------------------------------------------------------------------|----------------------|
| Peanut skins and dry-blanched peanuts as sources of phenolic compounds and evaluate their antimicrobial effect | Maceration with stirring followed by centrifugation | Mass of skin: 2.5 g  
Time of extraction: 20 min  
Acetone/water (70:30 v/v)  
Temperature: 30 °C  
Liquid/solid ratio of 1:5 (w/v) | HPLC–DAD–ESI–MS               | Phenolic acids content: 175.3 μg g⁻¹, proanthocyanidins: 4959 μg g⁻¹ and monomeric flavonoids 791.3 μg g⁻¹ of dry biomass  
Extracts inhibited the growth of gram-positive and gram-negative bacteria | Camargo et al. (2017a)         |
| Compare proanthocyanidin composition of single solvent and multistep extraction procedures of peanut skins by HPLC–UV-vis absorbance | Ultrasound                      | Mass of skins: 1 g  
Solvents: acetone, ethanol, methanol, or boiling water (99.7 °C) for 15 min followed by filtration  
Solid/liquid ratio of 1:10 | HPLC–MS–UV–vis absorbance     | A-type proanthocyanidins was identified  
Multistep extraction procedure is an effective means of concentrating procyanidins | Sarnoski et al. (2012a)        |
| Compare flavan-3-ol composition and antioxidant capacity of roasted skin obtained by peanut, hazelnut, and almonds | Sharking water bath followed by evaporation | Solvent: acetone/water (80:20 v/v)  
Solid/liquid ratio of 1:10 (w/v)  
Temperature: 50 °C  
Time of extraction: 30 min | HPLC–DAD–fluorescence and HPLC–DAD/ESI–MS | Peanut presented both A- and B-type proanthocyanidins (A forms were predominant) with higher antioxidant capacity compared to almond | Monagas et al. (2009) |
| Chemical composition and antioxidant activities of extracts and purified fractions obtained from the peanut skins separated by blanching and roasting processes | Maceration followed by evaporation | Solvent: ethanol/water (70:30 v/v)  
Room temperature at 24 h | HPLC–ESI–MS/MS               | The major component of factionary extracts was procyanidin dimer type A (31.49%), proanthocyanidin dimer (24.33%), and procyanidin dimer type B (14.15%) | Larrauri et al. (2016) |
| Isolate proanthocyanidins from peanut skin extracts and evaluate their activity against hyaluronidase | Boiling water                   | Solvent: distilled water  
Time of extraction 2 h | HPLC and 13C NMR         | Proanthocyanidin A2 and proanthocyanidin A4 were identified with substantial activity against hyaluronidase | Lou et al. (2001) |
| Compare profiles of proanthocyanidins extracted from peanut skins and cranberry | Ultrasound followed by centrifugation, evaporation and freeze dried | Solvent: acetone/water/acetic acid (70:28:2, v/v/v)  
5 min of extraction | HPLC and MALD-TOF MS   | Peanut skins and cranberries have similar proanthocyanidins composition; they contain both A-type and B-type proanthocyanidins, with the A-type being predominant | Ye and Neilson (2016) |
Table 1 (continued)

| Study objective                                                                 | Conventional extraction method | Extraction conditions                                                                 | Quantification/identification | Highlight results                                                                                                                                                                                                 | Reference                  |
|---------------------------------------------------------------------------------|--------------------------------|--------------------------------------------------------------------------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Produce a dried extract from the peanut skin using the spray-drying technology and evaluate the processing conditions | Ultrasound followed by centrifugation, filtration, and evaporation | Solvent: ethanol/water (80:20 v/v)  
Temperature of 60 °C for 15 min  
Centrifugation at 6000 rpm for 15 min | HPLC–DAD-UV | Encapsulated procyanidins presented remarkable antioxidant activity, bacteriostatic activity against Gram-positive bacteria (*S. aureus* and *L. monocytogenes*), and bactericidal activity against *S. aureus*  | Calomeni et al. (2017)      |
| Evaluate the phenolic profile and antioxidant activity in vitro of peanut skin extract and their effect on characteristics of sheep patties during storage | Maceration followed by sonication, centrifugation, and filtration | Mass of skin: 30 g  
Solvent: ethanol/water (80:20 v/v)  
Temperature of 60 °C; and 50 min of extraction; then the mixture was sonicated for 15 min at room temperature | HPLC–ESI–MS | The major group of phenolic compounds in peanut skin was the proanthocyanidins  
Lipid and protein oxidation in sheep patties was effectively inhibited by the extracts | Munekata et al. (2016)       |
| Determine the antioxidant activity and anti-inflammatory properties of peanut skin extracts | Maceration with stirring followed by filtration and freeze-dryer | Solvent: acetone/water (50:50 v/v) or ethanol/water (90:10 v/v) | HPLC–MS | Procyanidins were present in acetone extracts in the range 0.4 to 31.9 mg g⁻¹ of skin and 0.2 to 13.2 mg g⁻¹ of skin in ethanol extracts  
The extracts presented antioxidant and anti-inflammatory effects | Lewis et al. (2013)          |
| Produce spray-dried powders from peanut skin extracts with high antioxidant activity and procyanidin content that could be used as value-added food ingredients | Stirring followed by filtration and evaporation | Solvent: ethanol/water (70:30 v/v)  
Solid–liquid ratio: 1.5 w/v  
Time of stirring: 20 min | HPLC–ESI–MS | Spray-drying increased the proportion of flavan-3-ols and degree of polymerization 2 procyanidins in the extracts  
The power presented higher antioxidant capacity and total phenolics and increased solubility compared to milled skins | Constanza et al. (2012)      |
| Define the structure elucidation of four new naturally occurring A-type procyanidins from peanut skins, also develop an analytical protocol for accurately defining the chemical structure of the A-type procyanidins | Percolation | 1st extraction: 30% MeOH  
2nd extraction: 70% acetone  
1st and 2nd extracts were combined and portioned three times | Reversed-phase HPLC combined with ¹³C NMR | Four new A-type procyanidins of tri- and tetrameric structures were identified, also tetramers presented anti-inflammatory cytokines | Dudek et al. (2017)          |
Green extractions, besides reducing energy consumption, also allow the use of generally recognized as safe (GRAS) solvents and are applied for renewable natural products or underused by-products from industrial processes (Chemat et al., 2019; Moro et al., 2021; Wang et al., 2022). High-pressure methods such as supercritical fluid extraction (SFE) and pressurized liquid extraction (PLE) are within the promising techniques for the recovery of proanthocyanidins from peanut skin because they are fast processes with low solvent consumption, generally green solvents, such carbon dioxide, ethanol, water, or their mixtures (Mazzutti et al., 2017; Rifna et al., 2021).

High-pressure methods and other alternative techniques (like MAE and ultrasound) are established procedures, with well-known properties and advantages. Ameer et al. (2017) presented a comprehensive review about these green methods for polyphenol extraction, comparing efficiencies, applications, and characteristics. Also, several works proposed sequential high-pressure extractions to value different biomasses, such as peanut (Sorita et al., 2020), cacao (Mazzutti et al., 2018), and tamarind (Martins et al., 2020) by-products.

Porto and Natolino (2017) applied SFE with CO2, combined with ethanol or water as co-solvents, to recover proanthocyanidins from grape seeds. The process optimization consisted of following a Box-Behnken design to study the effects of pressure, co-solvent amount, and CO2 flow rate on polyphenol and proanthocyanidins extraction. The best condition (80 bar, CO2 flow rate of 6 kg h−1 and 20% (v/v) of ethanol as co-solvent) provided more than 10 mg g−1 of dry biomass of monomeric proanthocyanidins and above 8 mg g−1 of dry biomass of oligomeric proanthocyanidins.

PLE, a promising green method, was recently used by Rossi et al. (2020) to obtain proanthocyanidins from peanut skin at 7 MPa, 220 °C, and 7 g min−1 of ethanol/water (60:40 v/v) as solvent. The recovered extract had 24 compounds identified by HPLC–ESI–MS/MS, represented by procyanidin dimers (about 75%), monomeric flavonoids (4.31%), and proanthocyanidin dimmers (about 5%). The extract quality suggests the high-pressure PLE method as an alternative to value industrial peanut skin.

Other non-conventional promising techniques, such as MAE (Chen et al., 2016), sub-critical water extraction (SWE) (Bodoira et al., 2017), and ionic liquid extraction (Liu et al., 2012), have also been applied for the recovery of proanthocyanidins from different feedstocks. Table 2 shows different raw materials used as source of proanthocyanidins, recovered by green extraction techniques. Table 2 data also list the solvents used, extraction parameters, content of recovered proanthocyanidins, and suggested applications.

Chen et al. (2020a) used MAE and conventional maceration with ethanol/water (94:6 v/v) to recover proanthocyanidins from grape seeds. Higher content of proanthocyanidins,
Table 2 Recovery of proanthocyanidins and oligomers from different feedstocks

| Feedstock                  | “Green” recovery            | Solvent                        | Parameters of extractions                                  | Proanthocyanidins content                  | Application                                                                 | Reference                  |
|----------------------------|------------------------------|--------------------------------|------------------------------------------------------------|-------------------------------------------|--------------------------------------------------------------------------------|-----------------------------|
| Peanut skin                | Pressurized liquid extraction| Ethanol/water (60:40 v/v)      | 7 MPa; 220 °C; flow rate of 7 g min⁻¹                     | Proanthocyanidin dimer ~75% (w/w)         | Functional ingredients for foods                                                 | Rossi et al. (2020)        |
| Peanut skin                | Supercritical fluid extraction| CO₂ with ethanol as co-solvent (0.15 mL min⁻¹) | 10 MPa, 343 K, and 0.15 mL min⁻¹ for 30 min              | Proanthocyanidin content: 0.352 mg g⁻¹   | Unspecified                                                                    | Putra et al. (2021)        |
| Grape seeds                | Supercritical fluid extraction| CO₂ + 20% (w/w) of ethanol     | 80 bar; 6 kg of CO₂ h⁻¹ and 200 min of extraction         | Monomeric > 10 mg g⁻¹ of dry biomass     | Production of dietary supplements, functional food, and antioxidant additives for food and cosmetic products | Porto and Natolino (2017)   |
| Cinnamomum cortex          | Microwave-assisted simultaneous distillation | Water                          | Liquid–solid ratio of 18.0 mL g⁻¹, microwave irradiation power of 374 W for 58 min | 1.60 ± 0.07% (w/w)                        | Food additive                                                              | Chen et al. (2016)         |
| Peanut skins               | Sub-critical water extraction | Ethanol/water (60.5:39, 5 v/v) | 7 MPa; 220 °C; flow rate of 7 g min⁻¹; 105 min of extraction | Unquantified                             | Food applications                                                            | Bodoira et al. (2017)      |
| Cinnamomum cortex          | Ionic liquid-based microwave-assisted simultaneous extraction | 1-butyl-3-methylimidazolium bromide ionic liquid (0.5 M) | 20.0 g mass of sample 230 W microwave irradiation power; 15 min of extraction; and 10 mL g⁻¹ of liquid:solid ratio | 1.24 ± 0.04% (w/w)                        | Spice; perfumery, flavoring, and pharmaceutical industries                     | Liu et al. (2012)          |
| Cinnamomum japonicum Sieb. leaves | Solvent-free microwave-assisted distillation followed by homogenate extraction | Distillation: water Microwave: 71% ethanol volume fraction | Microwave extraction: 540 W of microwave power and a 40-min irradiation time Homogenate extraction: 16 mL g⁻¹ liquid–solid ratio and 4-min homogenate time | 71.97 ± 2.71 mg g⁻¹ dry leaves | Foods, perfumery, and Chinese traditional medicine industries                 | Zhao et al. (2020)         |
| Pinus pinaster (Maritime pine) | Microwave-assisted extraction | Ethanol/water (80:20 v/v)      | Solid-liquid rate: 1:10; 100 W; 3 min of extraction | 37.1 mg g⁻¹ dry biomass                  | Unspecified                                                                    | Chupin et al. (2015)       |
| Maritime pine (Pinus pinaster Ait.) | Supercritical fluid extraction | CO₂/ethanol (70:30 v/v) | CO₂/ethanol (70:30 v/v) | 25.1 kPa; 303 K; flow rate 7.610⁴ kg s⁻¹ and 210 min of extraction | 19.8% (w/w) | Food and pharmaceutical applications | Seabra et al. (2012)       |
in terms of catechin equivalent (CE), was provided by MAE at 170 °C for 55 min (56.37 mg CE g⁻¹ dry peanut skin) compared to maceration (9.70 mg CE g⁻¹ dry peanut skin). This behavior is justified by microwaves that increase solvent penetration into the solid material, improving the extraction yield.

The use of high-pressure green methods to obtain proanthocyanidins from different sources is still very limited, particularly from peanut skin. Some proanthocyanidins sources, listed at Table 2, are lingonberry pomace, peanut skin, and cranberry pomace, which provided the highest proanthocyanidins content by PLE recovery. For instance, Kitrytė et al. (2020) and Tamkutė et al. (2020) used SWE at 10.3 MPa and 130 °C to recover proanthocyanidins from cranberry (806.44 mg g⁻¹ of biomass) and from lingonberry pomace (289.59 mg g⁻¹ of biomass), respectively. Rossi et al. (2020) used ethanol/ water (60:40 v/v) at 7 MPa and 220 °C to recover proanthocyanidins from peanut skin, reaching yield of 75% and 0.05% (w/w) for procyanidin and proanthocyanidin dimers, respectively. These results show that high-pressure methods are sustainable for proanthocyanidin recovery.

### Food and Pharmaceutical Uses of Proanthocyanidin/Procyanidin-Rich Extracts from Peanut Skin

Considering the numerous health benefits from proanthocyanidins (the “Proanthocyanidins/Procyanidins from Peanut By-products” section), useful for food and pharmaceutical formulations, it is relevant to develop green strategies that can be industrially used for their successful recovery and quality application. Therefore, it is relevant to know the properties of these components in order to provide successful applications. Table 3 summarizes studies related to food and pharmaceutical uses of proanthocyanidins from peanut by-products, listing applications, bioactivities associated, and most relevant results.

#### Pharmaceutical Applications
Proanthocyanidins show potential benefits for different pharmaceutical applications (Table 3). Tatsuno et al. (2012) show that proanthocyanidin extracts from peanut skin, obtained by water maceration, have beneficial effects on human skins. The use of 200 µg mL⁻¹ of extract decreased melanogenesis in cultured human melanoma (HMV-II co-stimulated with phorbol-12-myristate-13-acetate), reducing production of inflammatory cytokines (at 100 µg mL⁻¹), tumor necrosis factor-α, and interleukin-6, in cultured human monocytic THP-1 cell. Proanthocyanidin dimers and trimers had stronger inhibitory activity, related to melanogenesis and inflammatory cytokine production, than the monomer or the tetrarmers. These promising results inspire the use of SWE or PLE with
Table 3  Food and pharmaceutical applications of proanthocyanidin extracts recovered from peanut skin

| Application | Activity evaluated                                                                 | Relevant results                                                                                                                                                                                                 | Reference               |
|------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Pharmaceutical | Inflammatory and anti-melanogenic activity                                             | Peanut skin extracts showed suppressive activities against melanogenesis (in cultured human melanoma HMV-II co-stimulated with phorbol-12-myristate-13-acetate) and cytokine production (in cultured human monocytic THP-1 cells) | Tatsuno et al. (2012)   |
| Reduction of dermatological conditions (inflammation and melanogenesis) | Proanthocyanidin extracted from peanut skin by-product inhibited degranulation of RBL-2H3 (basophilic leukemia cells) in rat, mainly by inhibition of signal transduction leading to secretion | Tomochika et al. (2011)                                                                                                                                         |                         |
| Reduction of proliferation of liver cancer cells and hepatocellular carcinogenesis | Peanut skin proanthocyanidin B2 appears to bind to the catalytically active kinase domain and regulatory pleckstrin homology domain to lock the protein in a closed conformation, thus suppressing tumor cell proliferation and metabolism | Liu et al. (2020)                                                                                                                                             |                         |
| Inhibition of alpha-glucosidase and lipase activity | The crude and fractionated extracts (composed mainly by proanthocyanidin) showed inhibition of alpha-glucosidase and lipase activities, reducing the absorption of glucose and triacylglycerols | Camargo et al. (2017b)                                                                                                                                           |                         |
| Cytotoxicity, cytoprotection (antioxidant) | Peanut proanthocyanidin extract did not present cytotoxicity on normal epithelial cells, rat ileum cells, monkey kidney cells, or human peripheral blood mononuclear cells at concentrations with antioxidant effects, also reduced the reactive oxygen species and superoxide dismutase activity in IEC-18 cells against menadione-induced oxidative stress | Rossi et al. (2020)                                                                                                                                            |                         |
| Cytotoxicity and genotoxicity of the extracts | Peanut skin extracts rich in proanthocyanidin have low cytotoxicity and genotoxicity, but the treatments with extracts at 2000 mg kg\(^{-1}\) revealed (highest concentrations evaluated) some toxicity on blood marrow cells of mice | Candela et al. (2020)                                                                                                                                         |                         |
| Antioxidant and membrane effects (availability) of dimer and trimer procyanidins | Absorption of trimers from the gut was extremely limited; otherwise, monomers and dimers can be readily detected in the plasma pool within 2 h after the consumption | Verstraeten et al. (2005)                                                                                                                                    |                         |
| Proanthocyanidin bioavailability and reduction of plasm triglyceride | Rats upon extracts’ supplementation showed reduced plasm triglyceride, also increasing plasma VLDL-C levels significantly | Bansode et al. (2014)                                                                                                                                         |                         |
| Antiviral in vitro activities against H1N1 influenza | Notably, the extract exhibited a potent activity against a clinical isolate of the 2009 H1N1 pandemic, which had reduced sensitivity to oseltamivir. Moreover, a combination of peanut skin extract with the anti-influenza drugs, oseltamivir and amantadine, synergistically increased their antiviral activity | Makau et al. (2018)                                                                                                                                         |                         |
| Food | Cooking loss, microbial growth, aroma acceptability, and texture | The added extracts did not cause color change (indicated by CIE, L\(^*\), a\(^*\), and b\(^*\) values), sensory aroma. Also, the extracts had no effect on the on the cooking loss and not affected the microbial growth | O’Keefe and Wang (2006)                                                                                                                                       |                         |
| In vitro antioxidant activity and the effect of peanut skin extract (rich in proanthocyanidin) on characteristics of sheep patties during storage | The addition of peanut skin extracts reduces the microbial growth and caused reduction on the loss of redness and sensory properties over time. In addition, it was effective in the inhibition of lipid and protein oxidation in sheep patties | Munekata et al. (2016)                                                                                                                                       |                         |
| Application                                                                 | Activity evaluated                                                                 | Relevant results                                                                                                                                                  | Reference          |
|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| Lipid oxidation and antimicrobial agent in raw ground beef                 | Peanut skin extracts (rich in proanthocyanidins) inhibited the oxidation of meat pigments, preserving the fresh redness of treated meat, also present complete inhibition of *Bacillus subtilis*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Streptococcus faecalis*, and *Escherichia coli* (at concentration of 0.4% w/w) | Yu et al. (2010)                                                                                                                                                |
| Composition, polyphenols, antioxidant properties, and sensory quality      | Insoluble fiber was increased by up to 52%; total phenolic content (30%) and antioxidant capacities also increased as evidenced by increases of epicatechin and procyanidin dimers A and B. In addition, sensory evaluation results demonstrated that peanut skin-fortified cookies were well accepted by the consumers | Camargo et al. (2014)                                                                                                                                     |
| Effect of gamma radiation on the antioxidant activity in soybean oil       | Antioxidant activity of the peanut skins was higher than synthetic antioxidant (BHT). In addition, gamma radiation did not affect the peanut skin extracts' antioxidative properties when added to soybean oil | Camargo et al. (2012)                                                                                                                                       |
| Antimicrobial activity                                                     | The proanthocyanidins from peanut skin extracts extended the lag phase growth of the 3 yeasts studied (1–10 mg mL⁻¹); yeast growth was totally inhibited for 120 h in apple juice | Sarnoski et al. (2012b)                                                                                                                                     |
| Antioxidant activity and quality characteristics of the yoghurt fortified  | Fortification of yoghurt with peanut skin extracts increased the apparent viscosity, antioxidant activity, total phenolic, acetaldehyde, and diacetyl contents when compared to control. The syneresis effect of fortified yoghurt was reduced, and the final product gained highest acceptability by the consumers at 50 mg L⁻¹ | Hamed et al. (2021)                                                                                                                                       |
| with peanut skin extracts during cold storage                              |                                                                                                                                                               |                      |
| Lettuce sanitizers                                                        | Peanut skin extracts combined with benzethonium chloride (10% w/w) showed good washing effect regardless of pathogenic bacteria type, 3.06 and 2.83 log reductions, for *L. monocytogenes* and *E. coli* populations inoculated on romaine lettuce leaves, respectively, compared to washing control (water alone) | Lee et al. (2021)   |
| Antioxidant                                                               | Addition of the peanut skin extract increased the antioxidant capacity of the product, measured by in vitro assays (DPPH)                                         | Dean et al. (2016)   |
| Inhibition effect on the retrogradation properties of maize starch         | Peanut skin proanthocyanidins showed the most substantial inhibition effect on starch retrogradation, which might be attributed to its structural features (determined by DSC, XRD, and SEM analyses), suggesting that peanut proanthocyanidins could be a new type of inhibitor to suppress starch retrogradation | Wang et al. (2020)  |
| Biodegradable films                                                       | Peanut skin extract affected the film surface morphology and increased its surface hydrophobicity; also extracts at 1.0 g 100 mL⁻¹ exhibited a strong antioxidant capacity. These results demonstrate that the biodegradable films with peanut skin extracts can be utilized as an eco-friendly packaging material having an antioxidant activity | Ju and Song (2020)  |
water as solvent due to the high pressure and temperature conditions, which can reduce the solvent’s surface tension and viscosity, increasing the proanthocyanidin recovery.

The procyanidins isolated from peanut skins, obtained by deionized boiling water (7.55 mg g⁻¹ of peanut skin), also inhibited the degranulation of RBL-2H3 (rat basophilic leukemia cells), suggesting that peanut skin procyanidins are therapeutic effective against allergic diseases (Tomochika et al., 2011).

Liu et al. (2020) shows that procyanidin type B2 (Fig. 3(IV)) suppressed tumor cell proliferation and metabolism in vitro (docking) and in vivo (xenograft and diethylaminoethyl nitrosamine-induced hepatocellular carcinoma mouse models) assays. They indicate that procyanidin type B2 appears to bind the catalytically active kinase domain of AKT (protein kinase B) and regulatory pleckstrin homology domain (protein domain), associated with liver cancer pathogenesis, and locking the protein in closed conformation, avoiding cancer cell multiplication. Also, A-type proanthocyanidin dimers from peanut skin have a protective effect against oxidative stress damage in prostate cancer (DU145 cells) induced by H₂O₂, maintaining normal cell cycle, inhibiting apoptosis, increasing the levels of antioxidants (catalase, total super oxide dismutase, and reduced glutathione), and reducing the content of intracellular reactive oxygen species (Yan et al., 2021).

Camargo et al. (2017a) evaluated the inhibition of alpha-glucosidase and lipase activity by proanthocyanidin-rich extracts from peanut skin (pure and fractionated), obtained by shaker maceration with acetone solution (70%). The fractionated extract reached 76% inhibition of alpha-glucosidase activity, while the pure extract provided up to 94% inhibition of lipase activity. These results highlight the biological activities of peanut skin extracts, helping the control of the absorption of glucose and triglycerides by the inhibition of these enzymes.

Ho et al. (2019) evaluated the alpha-glucosidase inhibition by proanthocyanidins from peanut skin through in silico docking assays. The results show good inhibitory activity performance from A-type proanthocyanidins, with IC₅₀ (concentration required to reduce 50% the enzyme activity) of 9.72 µM against alpha-glucosidase, revealing hypoglycemic ability of proanthocyanidins.

Peanut skin extract, obtained by PLE with ethanol/water (60:40 v/v), containing 75% procyanidin dimers and 5% proanthocyanidin dimers, was tested by Rossi et al. (2020) in rat ileal epithelial cells (IEC-18), monkey kidney epithelial cells (Vero), and human peripheral blood mononuclear cells (PBMCs), for toxicity evaluations. Concentrations up to 300 µg mL⁻¹ for IEC-18 and Vero, and up to 250 µg mL⁻¹ for PBMCs, show no cytotoxic effects. These are very high concentrations compared to IC₅₀ between 3 and 12.5 µg mL⁻¹, representing the antioxidant activity by ABTS and DPPH methods. These promising results show that proanthocyanidin-rich extracts from peanut skin have high antioxidant activity, at safe concentrations for normal cells, suggesting its use as excellent and accessible alternative for therapeutic formulations.

Verstraeten et al. (2005) highlighted the ability of types A and B procyanidins (dimers and trimers) from peanut skin to interact with phosphatidyl choline liposomes (specifically the polar headgroup), avoiding membrane cell damages (maintaining bilayer integrity) by oxidants and other molecules. Also, trimer absorption from the stomach was extremely limited, while monomers and dimers were readily detected from blood plasma. As addressed before, high-pressure extractions increase the monomer and dimer fractions from proanthocyanidins, improving food and pharmaceutical applications.

The effect of proanthocyanidin-rich extracts from peanut skin on gastrointestinal absorption of vegetable oil in rats (male Wistar rats) was investigated by Bansode et al. (2015). Rats administered with the extracts showed reduced plasma triglycerides and lower plasma very-low-density-lipoprotein levels compared to rats without peanut skin extract administration, suggesting hypolipidemic properties of the extract.

Neagu et al. (2015) showed that ethanolic extracts from the plants Alchemilla vulgaris and Filipendula ulmaria, rich in proanthocyanidins (77.66 and 130.00 µg mL⁻¹, respectively), have acetylcholinesterase inhibitory activity (77.03–98.39% at 3 mg mL⁻¹), useful for the treatment of Alzheimer’s and degenerative diseases. In addition, Unusan (2020) indicated that proanthocyanidins from grape seed extracts are therapeutic agents for neuroinflammatory diseases such as Alzheimer’s. Therefore, considering the high proanthocyanidins content from peanut skins of 4.959 mg g⁻¹ founded by Camargo et al. (2017a), it may be of relevance to evaluate the acetylcholinesterase inhibitory activity, an attribute still not associated with peanut skin extracts.

The ethanolic extract from peanut skin exhibited antiviral in vitro activity against influenza types A and B (IC₅₀ of 1.3 µg mL⁻¹). The extract exhibited potent activity against the clinically isolate H1N1 virus from 2009 pandemic, with synergistic effect when combined with the approved anti-influenza drugs, oseltamivir and amantadine, implying that peanut skin extracts may have potential application in the development of new therapeutic approaches for influenza management (Makau et al., 2018).

Recent studies of dynamic molecular simulation (in silico, molecular docking) suggested the proanthocyanidins’ potential to inhibit the coronavirus disease (COVID-19 global pandemic), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Maroli et al., 2020; Zhu & Xie, 2020). The coronavirus infective cycle and the main virus structure are presented in Fig. 4 (adapted from Maroli et al., 2020; Zhu & Xie, 2020). Briefly, from Fig. 4A...
Fig. 4 Life cycle and the main structural features of coronavirus, SARS-CoV2 (A) schematic mechanism of action against SARS-CoV2 of proanthocyanidins (B). Source: Adapted from Maroli et al. (2020) and Zhu and Xie (2020)
(infective life cycle), the virus spike protein (S) binds to ACE2 enzyme receptor (angiotensin-converting enzyme), the lungs’ major binding receptor to SARS-CoV-2, which is activated by proteolytic cleavage with human type 2 transmembrane serine (TMPRSS2), allowing the virus entry into human cells (Fig. 4(A.1)). Then, the uncoated virus delivers RNA into the cytoplasm by translation and replication (Fig. 4(A.2, A.3)). Finally, the replicated RNA virus is expelled of the cell (Fig. 4(A.4, A.5)).

The inhibition mechanism of SARS-CoV-2, by therapeutic medicines such as proanthocyanidins/procyanidins, is still poorly elucidated, although molecular docking simulation strategies may justify the therapeutic use of proanthocyanidins/procyanidins (PA) against the COVID-19 virus, with action mechanism suggested at Fig. 4B (Adapted from Maroli et al., 2020; Zhu & Xie, 2020). This mechanism consists in the PA ability to bind with enzymes and proteins involved in the virus replication cycle (Fig. 4B), the SARS-CoV-2 spike protein (S), ACE2 receptor, and the transmembrane serine protein (TMPRSS2), destabilizing the binding between virus and human cell and preventing virus replication (Maroli et al., 2020; Zhu & Xie, 2020). Then, PA activity may alleviate the severity of COVID-19 symptoms and modulate the immune response.

**Food Applications** Proanthocyanidins have astringency, bitterness, sourness, and sweetness, and contribute to salivary viscosity, aroma, and color formation of food products. Therefore, these components are used as additives in food formulations, enhancing microbial stability, foamability, oxidative, and heat stability (Okino et al., 2021; Rauf et al., 2019). Table 3 also presents the studies related to food applications of proanthocyanidins recovered from peanut skin.

The use of proanthocyanidins from peanut skins successfully inhibited retrogradation properties of maize starch for 21-day storage (Wang et al., 2020). This powerful effect improves quality and extends shelf-life of starch-based food products, suggesting that proanthocyanidin-rich extracts from peanut skin can increase the quality of starch-based foods providing effects such as antioxidant and hypolipidemic.

Peanut skin extracts (methanol maceration), rich in proanthocyanidins, reduced 60% oxidation of ground beef storage for 14 days, reducing cooking loss and microbial growth, without an aroma effect (O’Keefe & Wang, 2006). Munekata et al. (2016) observed redness loss reduction, prevention of lipid and protein oxidation, and decreasing sensory attributes changes (red color intensity, superficial discoloration, and off-odor) in sheep patties added with peanut skin extract (proanthocyanidins rich in pentamers, tetramers, trimers, and oligomers), for 20 days of storage at 2 °C. These results suggest the extract potential as natural antioxidant, replacing synthetic ones such as butylated hydroxytoluene (BHT).

Camargo et al. (2014) shows that peanut skin improved the total phenolic content, fiber, antioxidant capacities, and moisture of cookies (at concentrations from 1.3 to 2.5%), while carbohydrate concentration was decreased. The cookies fortified by peanut skin were well accepted by sensorial analysis. In addition, procyanidin trimers and tetramers were identified by HPLC–DAD–ESI–MS from the phenolic fraction (extracted with acetone water solution 70:30 v/v) of the cookies.

Gamma irradiation of food products has been used to reduce and/or eliminate microorganisms, improving food safety, although it may affect sensory attributes by inducing oxidation. Then, Camargo et al. (2017a) compared antioxidant activity of peanut skin extracts, obtained by acetone:water solution (70:30 v/v), with 4.959 mg of proanthocyanidins g⁻¹ dry peanut skin, with that from BHA, a synthetic antioxidant. Then, the extract was added to salmon and submitted to gamma irradiation (3.0 kGy at 3.75 kGy h⁻¹). The results show the extract prevented oxidation up to 63% of non-irradiated salmon samples, and 37% of gamma-irradiated samples. No difference was found comparing the antioxidant activity from BHA and the extract, showing that natural proanthocyanidins can prevent gamma irradiation–induced oxidation. The same extract also inhibited the growth of gram-positive bacteria (Bacillus cereus, Staphylococcus aureus, Listeria monocytogenes, and Geobacillus stearothermophilus) and gram-negative bacteria (Pseudomonas aeruginosa, Pseudomonas fluorescens, Salmonella enteritidis, Salmonella typhimurium, and Escherichia coli) (Camargo et al., 2017b). Also, Levy et al. (2017) demonstrated the antimicrobial effect of peanut skin extracts, rich in proanthocyanidins, obtained by ultrasound with acetone, water, and acetic acid (70:28:2, v/v/v) from defatted sample, against the pathogens L. monocytogenes, E. coli, and S. typhimurium.

Undesirable non-enzymatic reaction, namely glycation (reaction of free amino groups from proteins with free carbonyl groups of reducing sugar), can occur in foods during processing, producing glycation end products (AGEs). Accumulation of AGEs in human tissues are directly related to diabetic complications, Alzheimer’s and cardiovascular disease, and kidney dysfunction. Then, Zhao et al. (2021) showed that peanut skin extracts (with proanthocyanidins content of 85.69%) strongly inhibited the AGE formation, serving as anti-glycation agent for food products. Then, considering the pharmaceutical and food applications of proanthocyanidins, their functions must be preserved for adequate use, for instance by encapsulation strategies (next section) that may avoid structural and functional changes during processing.
Encapsulation Strategies to Improve Proanthocyanidin/Procyanidin Bioavailability

Proanthocyanidin/procyanidin bioavailability affects their bio-accessibility and bioactivity (biological activities). Bio-accessibility makes proanthocyanidins bioavailable for absorption during gastrointestinal digestion (or assimilation through intestinal epithelium), and intestinal and hepatic metabolism. The bioactivity happens after epithelium assimilation and transport to specific tissue, generating the correspondent physiological responses, such as anti-inflammatory, antimicrobial, antioxidant, and others (Galanakis, 2021; Okino et al., 2021).

The in vivo biotransformation of proanthocyanidins, such as pH gastrointestinal degradation, rapid catabolism at upper gastrointestinal tract and liver (or monomer and dimer degradation during transport), fast urinary excretion, and bacterial gastrointestinal metabolism, affects potential bioactivity of proanthocyanidins. Also, they tend to interact with proteins, forming a complex, and with mucus and other intestine components (starches and digestive enzymes), reducing its availability and efficacy with progressing time (Ge et al., 2015).

The direct application of proanthocyanidins in foodstuff and pharmaceutical products can be hindered by their astrin- gent taste and susceptibility to changes induced by temperature, oxygen, extreme pH values, or light exposure (Okino et al., 2021; Xu et al., 2015). Also, the direct application can reduce storage stability, with progressive presence of brown color from oxidation and condensation reactions, affecting appearance and taste (Liu et al., 2017). Furthermore, proanthocyanidins have high water solubility, inhibiting their penetration into food oily systems (Chen et al., 2020b) and also into the cell membrane, since it mainly composed by lipids (specifically phospholipids).

To overcome these limitations and improve the proanthocyanidins’ functional properties for food and pharmaceutical applications, encapsulation strategies, by different techniques, have produced micro- or nanoparticles of peanut skin proanthocyanidins (Unusan, 2020). An efficient encapsulation process requires a careful selection of the wall material, followed by the appropriate encapsulation method and a proper characterization of the produced particles. Then, the incorporation of the loaded particles into the food or pharmaceutical matrices and kinetics of biocomponents released from the particles are also relevant to define the adequate strategy.

**GRAS Materials Derived From By-products—New Wall Barrier Tendency**

Appropriate wall materials should have the ability to isolate and protect the core product, such as proanthocyanidin-rich extracts, from external environmental conditions. It can contribute to incorporate the encapsulated particles (core + wall material) in different food systems, improving solubilization, reducing degradation (oxidation or hydrolysis), and, consequently, protecting its biological activity. The type of wall material also affects the particles’ stability and the encapsulation efficiency of loaded compounds, and, ultimately, controls the core release (Geranpour et al., 2020).

For proanthocyanidins, adequate wall materials should suppress the first-pass metabolism alterations, avoiding molecular changes, and allowing circulation to exert their bioactivity (Bora et al., 2018). The most common materials used to encapsulate proanthocyanidins are maltodextrin (Calomeni et al., 2017) vegetable fat (Hol kem & Favaro-Trindade, 2020), gum arabic, pectin, cashew gum, carboxymethylcellulose, and κ-carrageenan (Souza et al., 2018).

Besides, GRAS products are the preferential wall materials for food applications, but they also should be inexpensive, tasteless, soluble in typical solvents, biodegradable, and nonreactive with the target compound (Bora et al., 2018; Geranpour et al., 2020).

Recent sustainable policies have encouraged the use of biopolymers, derived from industrial co-products, which stimulate the circular economy, as green alternatives for wall materials (Geranpour et al., 2020). Sorita et al. (2020) suggested the recovery, by green methods, of proteins, carbohydrates, and fibers from peanut meal, by-product from peanut oil production. Then, these recovered products (proteins, carbohydrates, and fibers) can be applied as wall materials to encapsulate proanthocyanidins from peanut skin, a strategy that contributes to the biorefinery concept, and industrial “zero waste.”

**Trends and Recent Advancements in Encapsulation Methods**

The literature reports three classes of methods that have been used for micro- or nanoparticle formulations. The method used to produce the particles affects the encapsulation efficiency and can be classified as (i) physical methods: spray-drying and freeze-drying (Geranpour et al., 2020; Okino et al., 2021; Sorita et al., 2021; Waterhouse et al., 2017); (ii) physical–chemical methods: coacervation, emulsification, and supercritical fluid micronization (Mendonça et al., 2019; Rudke et al., 2019); and (iii) chemical methods: interfacial polymerization and complexation by molecular inclusion (Vakilinezhad et al., 2019).

Spray-drying is the most common physical method used for the encapsulation of peanut skin extracts rich in proanthocyanidins (or procyanidins), probably due to its feasibility, easy operation, and scale-up, with no organic solvent needed, and good benefit–cost ratio (Geranpour et al., 2020). Calomeni et al. (2017) used a spray-dryer to encapsulate procyanidin-rich extract from peanut skin using maltodextrin as encapsulating agent. The
resulting particles (proanthocyanidin powder) show remarkable 120-day stability, suggesting its use as a natural additive (colorant) in food formulation. A solubility increase, compared to non-encapsulated power, was observed by Constanza et al. (2012) for procyanidin-rich extract, from peanut skin, encapsulated in maltodextrin by spray-dryer.

Complex coacervation was also applied to protect proanthocyanidins and/or procyanidins from peanut skin by Razola-Díaz et al. (2021), with high load capacity and low temperature, avoiding component degradation. Solid-lipid microparticles, composed of proanthocyanidins and probiotics (Lactobacillus paracasei and Bifidobacterium animali subsp. Lactis), were produced by Holkem and Favaro-Trindade (2020) to improve proanthocyanidin solubility in oil systems. These studies show the benefits of encapsulation to improve the use of procyanidin- and/or proanthocyanidin-rich extracts as natural additive for food industries, although complementary data about digestibility, bioavailability, and release from the particles are necessary for specific applications.

**Future Perspectives for Proanthocyanidin-Based Products from Peanut Skin**

Food by-products are gaining increasing attention as alternative biomasses, within the new biorefinery approach, because they can be converted into high-value chemical components, besides reducing industrial residues. Then, extraction and encapsulation strategies can enable adequate uses of the recovered products in food and pharmaceutical industries. Therefore, green extraction techniques, which have been stimulated by the environmental politics, can provide proanthocyanidin-rich extracts from peanut skin, with high quality and functionalities, as discussed in the “Encapsulation Strategies to Improve Proanthocyanidin/Procyanidin Bioavailability” section. Then, the viability evaluation of extraction and encapsulation methods, based on bioeconomy strategies, is necessary to innovate the peanut industry.

The production of high-value and innovative chemicals from agro-food by-products is an urgent objective, within the Sustainable Development Goals from United Nations (SDG-UN), although the polices are mainly focused on the use of biomasses to obtain bioenergy. Also, the use of by-products in conventional industries presents some resistance, and requires new procedures and equipment, complicating the implementation. To overcome these inconveniences, innovative and long-term wide polices are necessary, such as tax reduction and subsidies for recycling, and increase in research investments to promote the circular economy and by-product industrial use. Additionally, the creation of regional companies or cooperatives for by-product processing would be a promising strategy, reducing initial investments and increasing profitability, adding value to underused by-products (Langen et al., 2021). These strategies for peanut industry may help the circular economy, with the production of proanthocyanidin-rich extracts and other chemical from peanut skin, with several applications.

**Conclusions**

Phenolic fractions (rich in proanthocyanidins/procyanidins) are health-benefit molecules, valuable for food and pharmaceutical industries, due to effects as antioxidant, anti-inflammatory, neuroprotective, anticancer, lipid-lowering, bacteriostatic, and hypotensive. The valorization of peanut skin is relevant for circular economy due to their high proanthocyanidin content, which can be recovered from the biomass, that otherwise would be underused, and reintegrated in the processing chain. Unconventional extractions techniques such as SFE, PLE, MAE, and SWE can overcome the current drawbacks of conventional methods, leading to a greener process. Also, incorporating proanthocyanidins in micro/nanocapsules can improve their bioavailability and solubility in different systems. Then, the use of proanthocyanidins, in micro- or nanoparticles, in foods or medicines, must be validated by large double-blind clinical trials, to attest the nontoxic effect of proanthocyanidins from peanut skin.

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**Declarations**

**Competing Interests** The authors declare no competing interests.

**References**

Ameer, K., Shahbaz, H. M., & Kwon, J. H. (2017). Green extraction methods for polyphenols from plant matrices and their byproducts: A review. Comprehensive Reviews in Food Science and Food Safety, 16(2), 295–315. https://doi.org/10.1111/1541-4337.12253

An, Q., Gong, X., Le, L., Zhu, D., Xiang, D., Geng, F., et al. (2021). Prospects for proanthocyanidins from grape seed: Extraction
Camargo, A. C., Regitano-d’Arce, M. A. B., & Shahidi, F. (2017b). Phenolic profile of peanut by-products: Antioxidant potential and inhibition of alpha-glucosidase and lipase activities. *JAOC*.*S, 94(7), 959–971. https://doi.org/10.1016/s1174-017-2996-9

Camargo, A. C., Vidal, C. M. M., Canniatti-Brazaca, S. G., & Shahidi, F. (2014). Fortification of cookies with peanut skins: Effects on the composition, polyphenols, antioxidant properties, and sensory quality. *Journal of Agricultural and Food Chemistry*, 62(46), 11228–11235. https://doi.org/10.1021/jf503625p

Candela, F. M., Giordano, W. F., Quiroga, P. L., Escobar, F. M., Mañas, F., Roma, D. A., et al. (2020). Evaluation of cellular safety and the chemical composition of the peanut Arachis hypogaea L. ethanolic extracts. *Heliyon*, 6(10), e05119. https://doi.org/10.1016/j.heliyon.2020.e05119

Chemat, F., Abert-vian, M., Fabiano-tixier, A. S., Strube, J., Uhlenbrock, L., Gunev, V., & Cravotto, G. (2019). Green extraction of natural products. Origins, current status, and future challenges. *Trends in Analytical Chemistry*, 118, 248–263. https://doi.org/10.1016/j.trac.2019.05.037

Chen, F., Du, X., Zuo, Y., Yang, L., & Wang, F. (2016). Microwave-assisted method for distillation and dual extraction in obtaining essential oil, proanthocyanidins and polysaccharides by one-pot process from Cinnamonom Cortex. *Separation and Purification Technology*, 164, 1–11. https://doi.org/10.1016/j.seppur.2016.03.018

Chen, J., Thilakaratna, W. P. D. W., Astatkie, T., & Rupasinghe, H. P. V. (2020a). Optimization of catechin and proanthocyanidin recovery from grape seeds using microwave-assisted extraction. *Biomolecules*, 10(2), 243. https://doi.org/10.3390/biom1002243

Chen, S., Shen, X., Tao, W., Mao, G., Wu, W., Zhou, S., et al. (2020). Preparation of a novel emulsifier by self-assembling of proantho- cyanidins from Chinese bayberry (Myrica rubra Sieb. et Zucc.) leaves with gelatin. *Food Chemistry*, 319, 126570.

Chukwumah, Y., Walker, L., Vogler, B., & Verghe, M. (2012). Profiling of bioactive compounds in cultivars of Runner and Valencia peanut market-types using liquid chromatography/APCI mass spectrometry. *Food Chemistry*, 132(1), 525–531. https://doi.org/10.1016/j.foodchem.2011.10.050

Chupin, L., Maunu, S. L., Reynaud, S., Pizzini, A., Charrier, B., & Charrier-Industrial Crops and Products, 65, 142–149. https://doi.org/10.1016/j.indcrop.2014.11.052

Constanza, K. F., White, B. L., Davis, J. P., Sanders, T. H., & Dean, L. L. (2012). Value-added processing of peanut skins: Antioxidant capacity, total phenolics, and proanthocyanidin content of spray-dried extracts. *Journal of Agricultural and Food Chemistry*, 60, 10776–10783. https://doi.org/10.1021/jf3035258

Dean, L. L. (2020). Extracts of peanut skins as a source of bioactive compounds: Methodology and applications. *Applied Sciences (switzerland)*, 10(23), 1–26. https://doi.org/10.3390/app10238546

Dean, L. L., Klevorn, C. M., & Hess, B. J. (2016). Minimizing the negative flavor attributes and evaluating consumer acceptance of chocolate fortified with peanut skin extracts. *Journal of Food Science*, 81, S2824–S2830. https://doi.org/10.1111/1750-3841.13533

Dong, X., Zou, B., Zhang, Y., Ge, Z. Z., Du, J., & Li, C. M. (2017). Prepartion of A-type proanthocyanidin dimers from peanut skins and persimmon pulp and comparison of the antioxidant activity of A-type and B-type dimers. *Fitoterapia*, 91, 128–139. https://doi.org/10.1016/j.fitote.2013.08.019

Dudek, M. K., Gliński, V. B., Davey, M. H., Sliva, D., Kaźmierski, S., & Gliński, J. A. (2017). Trimeric and tetrameric A-type procyanidins from peanut skins. *Journal of Natural Products*, 80(2), 415–426. https://doi.org/10.1021/acs.jnatprod.6b00946

Appeldoorn, M. M., Sanders, M., Vincken, J. P., Cheynier, V., le Guernevé, C., Hollman, P. C. H., & Gruppen, H. (2009). Efficient isolation of major procyanidin A-type dimers from peanut skins and B-type dimers from grape seeds. *Food Chemistry*, 117(4), 713–720. https://doi.org/10.1016/j.foodchem.2009.04.047

Bansode, R. R., Randolph, P., Ahmeda, M., Hurley, S., Hanner, T., Baxter, S. A. S., et al. (2014). Bioavailability of polyphenols from peanut skin extract associated with plasma lipid lowering function. *Food Chemistry*, 148, 24–29. https://doi.org/10.1016/j.foodchem.2013.09.129

Bansode, R. R., Randolph, P., Ahmeda, M., Williams, L. L., & Yu, J. (2014). Bioavailability and hypolipidemic effects of peanut skin polyphenols. *Journal of Medicinal Food*, 18(3), 265–272. https://doi.org/10.1089/jmf.2014.0060

Belwal, T., Chemat, F., Venskutonis, P. R., Cravotto, G., Jaiswal, D. K., Bhatt, I. D., et al. (2020). Recent advances in scaling-up of non-conventional extraction techniques: Learning from successes and failures. *TrAC - Trends in Analytical Chemistry*, 127, 115895. https://doi.org/10.1016/j.trac.2020.115895

Benvenuti, L., Zielinski, A. A. F., & Ferreira, S. R. S. (2021). Jaboticaba (Myrtaceae cauliflora) fruit and its by-products: Alternative sources for new foods and functional components. *Trends in Food Science and Technology*, 112(April), 118–136. https://doi.org/10.1016/j.tifs.2021.03.044

Blade, C., Arola, L., & Salvado, M. (2010). Hypolipidemic effects of proanthocyanidins and their underlying biochemical and molecular mechanisms. *Molecular Nutrition & Food Research*, 54, 37–59. https://doi.org/10.1002/mnfr.200900476

Bodoira, R., Rossi, Y., Montenegro, M., Maestri, D., & Velez, A. (2017). Extraction of antioxidant polyphenolic compounds from peanut skin using water-ethanol at high pressure and temperature conditions. *Journal of Supercritical Fluids*, 128, 57–65. https://doi.org/10.1016/j.supflu.2017.05.011

Bodoira, R., Velez, A., Maestri, D., & Herrera, J. (2019). Bioactive compounds obtained from oilseed by-products with subcritical fluids: Effects on Fusarium verticillioides growth. *Waste and Biomass Valorization*, 10, 1327–1343. https://doi.org/10.1007/s12649-019-00839-y

Bora, A. F. M., Ma, S., Li, X., & Liu, L. (2018). Application of microencapsulation for the safe delivery of green tea polyphenols in food systems: Review and recent advances. *Food Research International*, 105(59), 241–249. https://doi.org/10.1016/j.foodres.2017.11.047

Calomeni, A., de Souza, V. B., Tulini, F. L., Thomazini, M., Oroschi, L. C., de Alencar, S. M. E., et al. (2017). Characterization of antioxidant and antimicrobial properties of spray-dried extracts from peanut skins. *Food and Bioprocess Technology Processing*, 105, 215–223. https://doi.org/10.1016/j.fbp.2017.08.001

Camargo, A. C., de Souza Vieira, T. M. F., Regitano-D’Arce, M. A. B., Calori-Domingues, M. A., & Canniatti-Brazaca, S. G. (2012). Gamma radiation effects on peanut skin antioxidants. *International Journal of Molecular Sciences*, 13(3), 3073–3084. https://doi.org/10.3390/ijms13033073

Camargo, A. C., Regitano-d’Arce, M. A. B., Rasera, G. B., Canniatti-Brazaca, S. G., do Prado-Silva, L., Alvarenga, V. O., et al. (2017a). Phenolic acids and flavonoids of peanut by-products: Antioxidant capacity and antimicrobial effects. *Food Chemistry*, 237, 538–544. https://doi.org/10.1016/j.foodchem.2017.05.046
Le Bourvellec, C., & Renard, C. M. G. C. (2018). Interactions between polyphenols and macromolecules: Effect of tannin structure. Elsevier. https://doi.org/10.1016/B978-0-08-100596-5.52148-6

Lee, C. H., Kang, J. H., Woo, H. J., & Song, K. B. (2021). Inactivation of Listeria monocytogenes and Escherichia coli O157:H7 inoculated on fresh-cut romaine lettuce by peanut skin extract/benzenthionium chloride emulsion washing. Food Control, 119, 107479. https://doi.org/10.1016/j.foodcont.2020.107479

Levy, J., Boyer, R. R., Neilson, A. P., O’Keeffe, S. F., Chu, H. S. S., Williams, R. C., et al. (2017). Evaluation of peanut skin and grape seed extracts to inhibit growth of foodborne pathogens. Food Science and Nutrition, 5(6), 1130–1138. https://doi.org/10.1002/fsn3.503

Lewis, W. E., Harris, G. K., Sanders, T. H., White, B. L., & Dean, L. L. (2013). Antioxidant and anti-inflammatory effects of peanut skin extracts. Food and Nutrition Sciences, 04(08), 22–32. https://doi.org/10.4236/fns.2013.48a003

Liu, C., Li, M., Yang, J., Xiong, L., & Sun, Q. (2017). Fabrication and characterization of biocompatible hybrid nanoparticles from spontaneous co-assembly of casein/gliadin and proanthocyanidin. Food Hydrocolloids, 73, 74–89. https://doi.org/10.1016/j.foodhyd.2017.06.036

Liu, G., Shi, A., Wang, N., Li, M., He, X., Yin, C., et al. (2020). Polyphenolic proanthocyanidin-B2 suppresses proliferation of liver cancer cells and hepatocellular carcinogenesis through directly binding and inhibiting AKT activity. Redox Biology, 37, 101701. https://doi.org/10.1016/j.redox.2020.101701

Liu, Y., Yang, L., Zu, Y., Zhao, C., Zhang, L., Zhang, Y., et al. (2012). Development of an ionic liquid-based microwave-assisted method for simultaneous extraction and distillation for determination of proanthocyanidins and essential oil in Cortex cinnamonomi. Food Chemistry, 135(4), 2514–2521. https://doi.org/10.1016/j.foodchem.2012.07.001

Lorenzo, J. M., Munekata, P. E. S., Sant’Ana, A. S., Carvalho, R. B., Barba, F. J., Toldrá, F., et al. (2018). Main characteristics of peanut skin and its role for the preservation of meat products. Trends in Food Science and Technology, 77, 1–10. https://doi.org/10.1016/j.tifs.2018.04.007

Lou, H., Yuan, H., Yamazaki, Y., Sasaki, T., & Oka, S. (2001). Alkaloids and flavonoids from peanut skins. Planta Medica, 67, 345–349. https://doi.org/10.1055/s-2001-14319

Ma, Y., Kerr, W. L., Cavender, G. A., Swanson, R. B., Hargrove, J. L., & Pegg, R. B. (2013). Effect of peanut skin incorporation on the color, texture and total phenolics content of peanut butters. Journal of Food Process Engineering, 36, 316–328. https://doi.org/doi:10.1111/j.1745-4530.2012.00693.x

Makau, J. N., Watanabe, K., Mohammed, M. M. D., & Nishida, N. (2018). Antiviral activity of peanut (Arachis hypogaea L.) skin extract against human influenza viruses. Journal of Medicinal Food, 21(8), 777–784. https://doi.org/10.1089/jmf.2017.4121

Maroli, N., Bhasuran, B., Natarajan, J., & Kolandaivel, P. (2020). The potential role of procyanidin as a therapeautic agent against SARS-CoV-2: A text mining, molecular docking and molecular dynamics simulation approach. Journal of Biomolecular Structure and Dynamics, 40(3), 1230–1245. https://doi.org/10.1080/07391102.2020.1823887

Martins, C. M., Ferro, D. M., de Brito, E. S., & Ferreira, S. R. S. (2020). Industrial relevance of Tamarindus indica L. by-products as source of valuable active metabolites. Innovative Food Science and Emerging Technologies, 66, 102518. https://doi.org/10.1016/j.ifset.2020.102518

Mazzuotti, S., Riehl, C. A. S., Ibañez, E., & Ferreira, S. R. S. (2017). Green-based methods to obtain bioactive extracts from Plantago major and Plantago lanceolata. Journal of Supercritical Fluids, 119, 211–220. https://doi.org/10.1016/j.supflu.2016.09.018

Francisco, M. L. D. L., & Resurreccion, A. V. A. (2009). Development of a reversed-phase high performance liquid chromatography (RP-HPLC) procedure for the simultaneous determination of polyphenolic compounds in peanut skin extracts. Food Chemistry, 117(2), 356–363. https://doi.org/10.1016/j.foodchem.2009.03.110

Galanakis, C. M. (2021). Functionality of food components and emerging technologies. Foods, 10(1), 1–26. https://doi.org/10.3390/foods10010128

Ge, Z. Z., Dong, X. Q., Zhu, W., Zhang, Y., & Li, C. M. (2015). Metabolites and changes in antioxidant activity of A-type and B-type proanthocyanidin dimers after incubation with rat intestinal microbiota. Journal of Agricultural and Food Chemistry, 63(41), 8991–8998. https://doi.org/10.1021/jacs.jfa.5b03657

Geranpour, M., Assadpour, E., & Jafari, S. M. (2020). Recent advances in the spray drying encapsulation of essential fatty acids and functional oils. Trends in Food Science & Technology. https://doi.org/10.1016/j.tifs.2020.05.028

Hamed, A. M., Taha, S. H., Darwish, A. A., & Aly, E. (2021). Antioxidant activity and some quality characteristics of buffalo yoghurt fortified with peanut skin extract powder. Journal of Food Science and Technology, 58(6), 2431–2440. https://doi.org/10.1007/s13197-020-04835-2

He, F., Pan, Q. H., Shi, Y., & Duan, C. Q. (2008). Biosynthesis and genetic regulation of proanthocyanidins in plants. Molecules, 13(10), 2674–2703. https://doi.org/10.3390/molecules13102674

Ho, S. L., Lin, Y., Tsai, S., & Lee, S. (2019). In-silico docking analysis of A-type proanthocyanidins to alpha-glucosidase constructed by correlation with in vitro bioassay. Journal of Drug Design and Medicinal Chemistry, 5(4), 47. https://doi.org/10.11648/j.jddmc.20190504.11

Hol kem, A. T., & Favaro-Trindade, C. S. (2020). Potential of solid lipid nanoparticles covered by the protein-polsaccharide complex for protection of probiotics and proanthocyanidin-rich cinnamon extract. Food Research International, 136(June), 109520. https://doi.org/10.1016/j.foodres.2020.109520

Ju, A., & Song, K. B. (2020). Active biodegradable films based on water soluble polysaccharides from white jelly mushroom (Tramella fuciformis) containing roasted peanut skin extract. Lwt, 126(January), 109293. https://doi.org/10.1016/j.lwt.2020.109293

Kandhare, A. D., Bodhankar, S. L., Singh, V., Mohan, V., & Thakurdesai, P. A. (2013). Anti-asthmatic effects of type-A procyandin polyphenols from cinnamon bark in ovalbumin-induced airway hyperresponsiveness in laboratory animals. Biomedicine and Aging Pathology, 3(1), 23–30. https://doi.org/10.1016/j.bmap.2013.01.003

Katiyar, S. K., Sciences, E. H., Obesity, N., & Affairs, V. (2017). Dietary proanthocyanidins inhibit UV radiation-induced skin tumor development through functional activation of the immune system. Molecular Nutrition & Food Research, 60(6), 1374–1382. https://doi.org/10.1002/mnfr.201501026.Dietary

Kitryté, V., Kavaliauskaitė, A., Tamkutė, L., Pukalskiënė, M., Syrpa, M., & Rimantas Venskutonis, P. (2020). Zero waste biofining of lingonberry (Vaccinium vitis-idaea L.) pomace into functional ingredients by consecutive high pressure and enzyme assisted extractions with green solvents. Food Chemistry, 322, 126767. https://doi.org/10.1016/j.foodchem.2020.126767

Lan, X., Qiang, W., Yang, Y., Gao, T., Guo, J., Du, L., et al. (2020). Physicochemical stability of safflower oil body emulsions during food processing. Lwt, 132(June), 109838. https://doi.org/10.1016/j.lwt.2020.109838

Larrauri, M., Zunino, M. P., Zygadlo, J. A., Grosso, N. R., & Nepote, V. (2016). Chemical characterization and antioxidant properties of fractions separated from extract of peanut skin derived from different industrial processes. Industrial Crops and Products, 94, 964–971. https://doi.org/10.1016/j.indcrop.2016.09.066
Souza, V. B., Thomazini, M., Echalar Barrientos, M. A., Nalin, C. M., Ferro-Furtado, R., Genovese, M. I., & Favaro-Trindade, C. S. (2018). Functional properties and encapsulation of a proanthocyanidin-rich cinnamon extract (Cinnamomum zeylanicum) by complex coacervation using gelatin and different polysaccharides. Food Hydrocolloids, 77, 297–306. https://doi.org/10.1016/j.foodhyd.2017.09.040

Sun, Y. A. N., Xiu, C., Liu, W. E. L., Tao, Y., Wang, J., & Qu, Y. I. (2016). Grape seed proanthocyanidin extract protects the retina against early diabetic injury by activating the Nr12 pathway. Experimental and Therapeutic Medicine, 11, 1253–1258. https://doi.org/10.3892/etm.2016.3033

Tamkutė, L., Liepuoniūtė, R., Pukalskienė, M., & Venskutonis, R. P. (2020). Recovery of valuable lipophilic and polyphenolic fractions from cranberry pomace by consecutive supercritical CO2 and pressurized liquid extraction. Journal of Supercritical Fluids, 159, 104755. https://doi.org/10.1016/j.supflu.2020.104755

Tatsuno, T., Jinno, M., Arima, Y., Kawabata, T., Hasegawa, T., & Yahagi, N., et al. (2019). Anti-inflammatory and anti-melanogenic proanthocyanidin oligomers from peanut skin. Biological and Pharmaceutical Bulletin, 35(6), 909–916. https://doi.org/10.1248/bpb.35.909

Tomochika, K., Ibuca, A. S., Tamura, T., Mura, K., Abe, N., Onose, J. I., & Arai, S. (2011). Effects of peanut-skin procyandin A1 on degranulation of RBL-2H3 cells. Bioscience, Biotechnology and Biochemistry, 75(9), 1644–1648. https://doi.org/10.1067/bbb.110085

Unusan, N. (2020). Proanthocyanidins in grape seeds: An updated review of their health benefits and potential uses in the food industry. Journal of Functional Foods, 67, 103861. https://doi.org/10.1016/j.jff.2020.103861

USDA. (2022). Major Vegetable Oils: World Supply and Distribution. Retrieved June 23, 2022, from https://www.fas.usda.gov/data/oilseeds-world-markets-and-trade

Vakilinezhad, M. A., Amini, A., Dara, T., & Alipour, S. (2019). Methotrexate and Curcumin co-encapsulated PLGA nanoparticles as a potential breast cancer therapeutic system: In vitro and in vivo evaluation. Colloids and Surfaces B: Biointerfaces, 184, 110515. https://doi.org/10.1016/j.colsurfb.2019.110515

van Langen, S. K., Vassillo, C., Ghisellini, P., Restaino, D., Passaro, R., & Uligati, S. (2021). Promoting circular economy transition: A study about perceptions and awareness by different stakeholders groups. Journal of Cleaner Production, 110516. https://doi.org/10.1016/j.jclepro.2021.120816

Vazquez-Flores, A. A., Martinez-Gonzalez, A. I., Alvarez-Parrilla, E., Diaz-Sanchez, A. G., de la Rosa, L. A., Gonzalez-Aguilar, G. A., & Aguilar, C. N. (2018). Proanthocyanidins with a low degree of polymerization are good inhibitors of digestive enzymes because of their ability to form specific interactions: A hypothesis. Journal of Food Science, 83(12), 2895–2902. https://doi.org/10.1111/1750-3841.14386

Verstraeten, S. V., Hammerstone, J. F., Keen, C. L., Fraga, C. G., & Oteiza, P. I. (2005). Antioxidant and membrane effects of procyanidin dimers and trimers isolated from peanut and cocoa. Journal of Agricultural and Food Chemistry, 53(12), 5041–5048. https://doi.org/10.1021/jf058018m

Wang, L., Wang, Y., Qin, Y., Liu, B., & Zhou, Y. (2022). Extraction and determination of protein from edible oil using aqueous biphasic systems of ionic liquids and salts. Food and Bioprocess Technology, 15(1), 190–202. https://doi.org/10.1007/s11947-021-02738-4

Wang, M., Chen, J., Chen, S., Ye, X., & Liu, D. (2020). Inhibition effect of three common proanthocyanidins from grape seeds, peanut skins and pine barks on maize starch retrogradation. Carbohydrate Polymers, 252, 117172. https://doi.org/10.1016/j.carbpol.2020.117172

Waterhouse, G. I. N., Sun-Waterhouse, D., Su, G., Zhao, H., & Zhao, M. (2017). Spray-Drying of antioxidant-rich blueberry waste extracts; interplay between waste pretreatments and spray-drying process. Food and Bioprocess Technology, 10(6), 1074–1092. https://doi.org/10.1007/s11947-017-1880-9

Xie, D. Y., & Dixon, R. A. (2005). Proanthocyanidin biosynthesis - Still more questions than answers? Phytochemistry, 66(18), 2127–2144. https://doi.org/10.1016/j.phytochem.2005.01.008

Xu, M., Lv, C., Wang, H., Lu, Q., Ye, M., Zhu, X., & Liu, R. (2022). Peanut skin extract ameliorates high-fat diet-induced atherosclerosis by regulating lipid metabolism, inflammation reaction and gut microbiota in ApoE−/− mice. Food Research International, 154, 111014. https://doi.org/10.1016/j.foodres.2022.111014

Xu, Z., Wei, L., & hong, Ge, Z. zhen, Zhu, W., & Li, C. mei. (2015). Comparison of the degradation kinetics of A-type and B-type proanthocyanidins dimers as a function of pH and temperature. European Food Research and Technology, 240(4), 707–717. https://doi.org/10.1007/s00214-017-2375-9

Yan, F., Chen, L., Chen, W., Zhao, L., Lu, Q., & Liu, R. (2021). Protective effect of procyanidin A-type dimers against H2O2-induced oxidative stress in prostate DU145 cells through the MAPKs signaling pathway. Life Sciences, 266, 118908. https://doi.org/10.1016/j.lfs.2020.118908

Ye, L., & Neilson, A. (2016). Comparison of A-type proanthocyanidins in cranberry and peanut skin extracts using matrix-assisted laser desorption ionization-time of flight mass spectrometry. Journal of Molecular and Genetic Medicine, 10(2). https://doi.org/10.4172/1747-0862.1000209

Yu, J., Ahmedna, M., & Goktepe, I. (2010). Potential of peanut skin phenolic extract as antioxidative and antibacterial agent in cooked and raw ground beef. International Journal of Food Science and Technology, 45(7), 1337–1344. https://doi.org/10.1111/j.1365-2621.2010.02241.x

Yu, J., Ahmedna, M., Goktepe, I., & Dai, J. (2006). Peanut skin procyandins: Composition and antioxidant activities as affected by processing. Journal of Food Composition and Analysis, 19(4), 364–371. https://doi.org/10.1016/j.jfca.2005.08.003

Zhang, H., Yerigui, Y., & Ma, C. (2013). Structures and anti-oxidative and intestinal disaccharidase inhibitory activities of A-type proanthocyanidins from peanut skin. Journal of Agricultural and Food Chemistry, 61(37), 8814–8820. https://doi.org/10.1021/jf402518k

Zhao, C., Yang, X., Tian, H., & Yang, L. (2020). An improved method to obtain essential oil, flavonols and proanthocyanidins from fresh Cinnamomum japonicum Sieb. leaves using solvent-free microwave-assisted distillation followed by homogenate extraction. Arabian Journal of Chemistry, 13(1), 2041–2052. https://doi.org/10.1016/j.arabjc.2018.03.002

Zhao, L., Zhu, X., Yu, Y., He, L., Li, Y., Zhang, L., & Liu, R. (2021). Comprehensive analysis of the anti-glycation effect of peanut skin extract. Food Chemistry, 362, 130169. https://doi.org/10.1016/j.foodchem.2021.130169

Zhu, Y., & Xie, D. Y. (2020). Docking characterization and in vitro inhibitory activity of flavan-3-ols and dimeric proanthocyanidins against the main protease activity of SARS-Cov-2. Frontiers in Plant Science, 11, 1–14. https://doi.org/10.3389/fpls.2020.601316

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