



Phenolic composition and cell-based biological activities of ten coloured potato peels (*Solanum tuberosum* L.)

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ABSTRACT

The present study provides an in-depth characterisation of the non-anthocyanin and anthocyanin phenolic compounds of potato peels from ten coloured potato varieties. Furthermore, the underexplored bioactive potential (antioxidant, cytotoxic and anti-inflammatory capacities) of the studied peels is comprehensively analysed. Among non-anthocyanin phenolics, caffeic and a caffeoylquinic acid were found in the highest concentrations in all samples, which also showed the presence of O-glycosylated flavonol derivatives and polyamine derivatives. Acylated anthocyanins were identified in red and purple varieties, being pelargonidin, peonidin, and malvidin the most prominent aglycones. All samples revealed antioxidant and antitumor activities, and no toxic effect. The extract of the *Rosemary* variety presented the best antioxidant and antitumor outcomes and was the only sample to reveal anti-inflammatory activity. These results are valuable for the food-industry by adding value to an important bio-residue, particularly concerning its potential as natural ingredients in novel food and pharmaceutical formulations.

1. Introduction

The food and pharmaceutical industries have been intensively researching the use of natural matrices as sources of bioactive compounds to find alternatives for synthetic food additives and drugs. At the same time, the valorisation of bio-residues rich in bioactive compounds that are usually discarded, such as potato peels, could contribute to the creation of more economically and socially sustainable productive chains in the agro-industry sector (Pathak, Mandavgane, Puranik, Jambhulkar, & Kulkarni, 2018; Sampaio, Petropoulos et al., 2020).

Potato (*Solanum tuberosum* L.) is the most important vegetable crop, with more than 5000 known varieties, a global production of around 368 million tonnes and one of the largest food processing sectors throughout the world (Sampaio, Petropoulos et al., 2020). Peeling is usually the first step in the processing chain of raw tubers into added value food products, such as crisps, chips, mashed potatoes and frozen products (Pathak et al., 2018). This processing step results in the

generation of a great amount of bulky waste (15–40% of the original fresh weight depending on the processing procedure) that is usually discarded or used as low value animal feed (Schieber, Stintzing, & Carle, 2002). Annually, between 70 and 140 thousand tonnes of potato peels are generated worldwide (Hossain, Rawson, Aguiló-aguayo, Brunton, & Rai, 2015). Therefore, up-grading of this bio-residue to added value products could decrease the overall environmental impacts of the potato processing industry and add value to this production chain (Sampaio, Petropoulos et al., 2020).

Potato peels are rich sources of phytochemicals with known biological activities, such as phenolic acids and flavonoids. Moreover, purple-fleshed potatoes are rich sources of anthocyanins, and the amounts stored in peels are usually higher than the flesh when both flesh and peels are coloured (Chaves-Silva et al., 2018). Previous studies have highlighted the bioactive potential of potato peel extracts, for instance their antioxidant (Jeddou et al., 2018; Singh et al., 2011; Singh & Rajini, 2004; Yin et al., 2016), anti-inflammatory (Wahyudi, Ramadhan,

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Wijaya, Ardhani, & Utami, 2020), antimicrobial (Juneja, Friedman, Mohr, Silverman, & Mukhopadhyay, 2018) and anticancer properties (Reddivari, Vanamala, Chintharlapalli, Safe, & Miller, 2007).

In this study, an in-depth characterisation of the phenolic composition of potato peels was performed, obtained from ten red and purple-skinned varieties from five different countries of origin (Chile, Germany, Austria, United Kingdom and Finland). Furthermore, a comprehensive analysis of the underexplored bioactive potential of the studied peels was carried out, by assessing their antioxidant, cytotoxic and anti-inflammatory capacities. This work aims to provide valuable information that will support the valorisation of an important food processing industry bio-residue, particularly concerning its underexplored potential as a natural additive for application into functional food formulations. At the same time the presented information could help to alleviate the environmental burden that potato processing generates and increase the added value of this economically important crop.

2. Materials and methods

2.1. Plant material production and processing

Red- and purple-skinned potato tubers (*Solanum tuberosum* L.) of ten genotypes (Red-skinned: *Rosemary*, *Red Emmalie*, *Red Cardinal*; Purple-skinned: *Purple*, *Violetta*, *Kefermarkter Blaue*, *Salad Blue*, *Blaue aus Finnland*, *UACH 0917* and *Shetland Black*) from five different countries of origin (Chile, Germany, Austria, United Kingdom and Finland) were cultivated in the experimental farm of the University of Thessaly in Velesino, Greece (Table 1). Fresh harvested tubers of uniform size, depending on the prevalent size for each genotype, were transported to the Polytechnic Institute of Bragança, Portugal, where the samples were washed with cold tap water upon arrival to eliminate extraneous matter. In particular, tubers' mean size for each genotype was as follows: *Rosemary* (53.5 g), *Red Emmalie* (108.6 g), *Red Cardinal* (58.5 g); Purple-skinned: *Purple* (145.0 g), *Violetta* (49.6 g), *Kefermarkter Blaue* (60.5 g), *Salad Blue* (130.3 g), *Blaue aus Finnland* (59.1 g), *UACH 0917* (70.3 g) and *Shetland Black* (45.6 g). A colour assessment of the samples was carried out before the peels were manually separated from the flesh, using a Minolta spectrophotometer (model CR-400; Konica Minolta Sensing, Inc., Japan) using illuminant C and a measuring aperture of 8 mm. The L^* , a^* and b^* CIELab colour values were measured through the computerized system. The peel samples were then freeze-dried ($-49\text{ }^\circ\text{C}$, 0.08 bar, during 48 h, FreeZone 4.5 model 7750031, Labconco, Kansas, USA) and reduced to a fine and homogeneous powder.

2.2. Extracts preparation

The powdered freeze-dried peels were extracted twice with ethanol: water (80:20 v/v) under stirring for 1 h and filtered (Whatman paper No. 4). The obtained solutions were evaporated under reduced pressure at $40\text{ }^\circ\text{C}$ (rotary evaporator Büchi R-210, Flawil, Switzerland) until the total removal of the solvent. The obtained extracts were then freeze-dried. The freeze-dried extracts were dissolved in a hydroethanolic solution 80:20 (v/v) and filtered through a $0.22\text{ }\mu\text{m}$ nylon filter, followed by immediate characterization.

2.3. Non-anthocyanin and anthocyanin phenolic compounds characterisation

The ten extracts were characterised by high performance liquid chromatography (Dionex Ultimate 3000 UPLC, Thermo Fisher Scientific, San Jose, CA, USA) using the conditions previously described by the authors (Albuquerque et al., 2020). The compounds detection was performed using a diode-array detector linked to an electrospray ionization mass spectrophotometer (Linear Ion Trap LTQ XL, Thermo Scientific, San Jose, CA, USA). The preferred wavelengths used were 280, 330 and 370 nm, for non-anthocyanin compounds, and 520 nm for anthocyanins.

Data collection and analysis was carried out using the Xcalibur® program (Thermo Fisher Scientific, San Jose, CA, USA). The identification of the phenolic molecules was performed based on their retention time, UV-vis spectra, mass characteristics and literature data. The quantification of the compounds was performed using 7-level calibration curves and the results were expressed as mg per g of dry weight (dw).

2.4. Biological activities evaluation

2.4.1. Cell-based antioxidant activity (TBARS and OxHLIA)

The antioxidant activity of the obtained extracts was assessed in terms of their potential to inhibit the production of thiobarbituric acid reactive substances (TBARS) in porcine (*Sus scrofa*) brain homogenates, a cell-based *in vitro* method described in detail by Corrêa et al. (2015). The results were expressed as IC_{50} values, which correspond to the extract concentration that provides 50% of antioxidant activity ($\mu\text{g}/\text{ml}$). For the oxidative haemolysis inhibition assay (OxHLIA), a cell-based method described by Garcia et al. (2019) was followed. The results were also expressed as IC_{50} values ($\mu\text{g}/\text{mL}$), which correspond to the extract concentration able to promote a Δt haemolysis delay of 60 min. Trolox was used as positive control in both methods.

2.4.2. Anti-inflammatory activity

The anti-inflammatory activity of the extracts was evaluated by lipopolysaccharide (LPS)-induced nitric oxide (NO) production by mouse macrophages RAW 264.7, a procedure described in detail by Corrêa et al. (2015). Dexamethasone ($50\text{ }\mu\text{M}$) was used as positive control, and a negative control was prepared without the addition of LPS to observe possible effects on the basal levels of NO. The results were expressed as IC_{50} values ($\mu\text{g}/\text{mL}$), which correspond to the extract concentration that induced 50% of inhibition of NO production.

2.4.3. Anti-proliferative activity and cytotoxicity

The anti-proliferative activity of the hydroethanolic extracts was evaluated using four human tumour cell lines: NCI-H460 (lung carcinoma); MCF-7 (breast carcinoma); HepG2 (hepatocellular carcinoma); and HeLa (cervical carcinoma), according to the method described by Albuquerque et al. (2020). The results were expressed as GI_{50} values ($\mu\text{g}/\text{mL}$), which correspond to the extract concentration capable of inhibit 50% of cell proliferation.

In order to study the extracts safety and potential to be used as additives in food formulations, a cytotoxicity assay was carried out. A primary culture of non-tumour liver cells obtained from porcine liver (PLP2) was used, following the procedure previously described by the authors (Sampaio, Fernandes et al., 2020). The results were expressed as GI_{50} values, which correspond to the extract concentration capable of inhibit 50% of the net cell growth, and ellipticine (Sigma-Aldrich, St Louis, MO, USA) was used as a positive control.

2.5. Statistical analysis

Three samples were used for each assay. All assays were carried out in triplicate. The results were analysed using one-way analysis of variance (ANOVA) followed by Tukey's HSD Test with $p = 0.05$ and were expressed as mean values with standard deviations (SD).

3. Results and discussion

3.1. Colour assessment

A quantitative analysis of the outer colour of the tested potato peels was carried out. The results for the Hunter colour parameters L^* (lightness), a^* (green-redness) and b^* (blue-yellowness) are presented in Table 1. The three red-skinned varieties presented the highest values for the parameter a^* as expected, quantitatively confirming the presence of red tones in the peels (*Rosemary*: 24.8, *Red Emmalie*: 24.4 and *Red*


Table 1

Potato variety, country of origin, cultivation type, qualitative flesh colour and quantitative peel colour (Hunter scale parameters) of the studied potato peels (mean \pm SD).

Potato variety	Country of origin	Cultivation type	Flesh colour	Peel colour		
				L^*	a^*	b^*
Rosemary	Germany	Cultivated variety	Red	41 ± 1^b	24.8 ± 0.4^a	10.1 ± 0.4^c
Red Cardinal	United Kingdom	Landrace	Red	41 ± 2^b	20.1 ± 0.7^b	11.2 ± 0.2^b
Rote Emmalie (Red Emmalie)	Germany	Cultivated variety	Red	38 ± 2^c	24.4 ± 0.5^a	8.7 ± 0.7^d
Purple	–	–	Purple	27.3 ± 0.9^f	6.3 ± 0.7^e	$3.0 \pm 0.7^{f,g}$
Kefermarkter Blaue	Austria	Landrace	Purple	31.2 ± 0.5^d	7.3 ± 0.3^d	$3.3 \pm 0.3^{f,g}$
UACH 0917	Chile	Andean accession	Purple	28.4 ± 0.1^e	4.0 ± 0.6^f	1.6 ± 0.2^b
Salad Blue	United Kingdom	Cultivated variety	Purple	29.0 ± 0.4^e	5.9 ± 0.5^e	$2.48 \pm 0.2^{g,h}$
Blaue aus Finnland	Finland	Landrace	Purple	28.8 ± 0.6^e	5.3 ± 0.2^e	4.1 ± 0.9^f
Shetland Black (Ellenb.)	United Kingdom	Cultivated variety	Marble (purple/yellow)	46 ± 1^a	9.1 ± 0.6^c	18 ± 2^a

(continued on next page)

Table 1 (continued)

Potato variety	Country of origin	Cultivation type	Flesh colour	Peel colour		
				L*	a*	b*
	Germany	Cultivated variety	Purple	32 ± 2 ^d	1.6 ± 0.2 ^g	6.1 ± 0.7 ^e

In each column different Latin letters are significantly different according to Tukey's HSD test ($p = 0.05$), for each potato group peels.

Cardinal: 20.7). The peels from these three varieties also presented the highest values for b^* (*Rosemary*: 10.1, *Red Emmalie*: 8.7 and *Red Cardinal*: 11.2), after only the marble (purple/yellow) variety *Shetland Black*, which presented the highest b^* values (18) among all the tested varieties. This finding indicates that for this variety the presence of yellow tones was more prominent than blue tones. The purple varieties, in turn,

presented the lowest values for b^* , a result which is associated to the presence of blue tones in the peels. The *Shetland Black* variety also presented the highest values for L^* , meaning its peel had the lightest colour among the ten varieties. Significant differences in skin colour parameters among various potato cultivars have been also reported by [Seijo-Rodríguez et al. \(2018\)](#), while [Yang & Achaerandio \(2015\)](#) and

Table 2

Chromatographic properties, tentative identification, and quantification (mg/g dw) of the non-anthocyanin phenolic compounds found in the studied potato peels (mean ± SD).

Identification										
Peak	Rt (min)	λ_{max} (nm)	[M-H] ⁻ (m/z)	MS ²	Tentative identification					
1	6.87	325	353	191(19),179(53),173(100),135(5)	4-O-Caffeoylquinic acid					
2	9.97	323	179	135(100)	Caffeic acid					
3	13.66	328	313	269(100),159(5),109(5)	Salvianolic acid F					
4	15.35	311	755	593(21),285(55)	Kaempferol-O-hexoside-O-deoxyhexoside-hexoside					
5	19.71	317	593	285(100)	Kaempferol-O-deoxyhexoside-hexoside					
6	20	227,290,321sh	472	350(51),308(100)	Bis(dihydrocaffeoyl)spermidine					
7	21.12	324	593	285(100)	Kaempferol-3-O-rutinoside					
Quantification										
Peak	Rosemary	Red Cardinal	Red Emmalie	Purple	Kefermarkter Blaue	UACH 0917	Salad Blue	Blaue aus Finland	Shetland Black	Violetta
1	0.071 ± 0.001 ^e	0.049 ± 0.001 ^h	0.033 ± 0.002 ⁱ	0.090 ± 0.005 ^d	0.052 ± 0.001 ^g	0.097 ± 0.002 ^c	0.110 ± 0.001 ^b	0.031 ± 0.002 ^j	0.067 ± 0.001 ^f	0.31 ± 0.008 ^a
2	0.419 ± 0.004 ^g	0.722 ± 0.003 ^d	0.103 ± 0.003 ^h	1.06 ± 0.05 ^c	0.71 ± 0.02 ^d	1.443 ± 0.007 ^a	1.13 ± 0.03 ^b	0.683 ± 0.002 ^e	1.14 ± 0.02 ^b	0.65 ± 0.02 ^f
3	0.018 ± 0.001 ^g	0.058 ± 0.001 ^c	0.019 ± 0.001 ^g	0.027 ± 0.001 ^e	0.022 ± 0.001 ^f	0.117 ± 0.002 ^a	0.049 ± 0.001 ^d	0.023 ± 0.001 ^f	0.099 ± 0.002 ^b	nd
4	0.029 ± 0.001 ^d	nd	0.032 ± 0.001 ^c	nd	nd	0.097 ± 0.001 ^b	nd	nd	0.097 ± 0.001 ^b	0.119 ± 0.0001 ^a
5	nd	nd	0.024 ± 0.001	nd	nd	nd	nd	nd	nd	nd
6	tr	tr	nd	0.26 ± 0.01 ^a	0.211 ± 0.004 ^b	nd	0.165 ± 0.003 ^d	0.176 ± 0.006 ^c	tr	0.112 ± 0.001 ^e
7	0.036 ± 0.001 ^b	0.054 ± 0.001 ^a	0.054 ± 0.001 ^a	nd	nd	nd	nd	nd	nd	nd
TPA	0.508 ± 0.004 ⁱ	0.829 ± 0.003 ^f	0.16 ± 0.01 ^j	1.18 ± 0.05 ^d	0.79 ± 0.02 ^g	1.657 ± 0.007 ^a	1.29 ± 0.03 ^c	0.737 ± 0.001 ^h	1.30 ± 0.03 ^b	0.96 ± 0.02 ^e
TF	0.065 ± 0.001 ^d	0.054 ± 0.001 ^e	0.11 ± 0.001 ^b	nd	nd	0.097 ± 0.001 ^c	nd	nd	0.097 ± 0.001 ^c	0.119 ± 0.0001 ^a
TPd	tr	tr	nd	0.23 ± 0.01 ^a	0.211 ± 0.004 ^b	nd	0.165 ± 0.003 ^d	0.176 ± 0.006 ^c	tr	0.112 ± 0.001 ^c
TPCd	0.573 ± 0.004 ^h	0.882 ± 0.003 ^g	0.27 ± 0.01 ⁱ	1.44 ± 0.04 ^b	0.91 ± 0.03 ^e	1.755 ± 0.007 ^a	1.45 ± 0.02 ^b	0.913 ± 0.005 ^f	1.39 ± 0.03 ^c	1.19 ± 0.02 ^d

TPA – Total Phenolic Acids; TF – Total Flavonoids; TPd - Total Polyamine derivatives; TPCd - Total Phenolic Compounds and derivatives. tr - traces; nd – not detected. Standard Calibration Curves: chlorogenic acid ($y = 168823x - 161172$, $R^2 = 0.9999$, LOD = 0.20 µg/mL and LOQ = 0.68 µg/mL, peak 1); caffeic acid ($y = 388345x + 406369$, $R^2 = 0.9939$, LOD = 0.78 µg/mL and LOQ = 1.97 µg/mL, peak 2 and 6); rosmarinic acid ($y = 191291x - 652903$, $R^2 = 0.999$, LOD = 0.15 µg/mL and LOQ = 0.68 µg/mL, peak 3); and quercetin-3-O-rutinoside ($y = 13343x + 76751$, $R^2 = 0.9998$, LOD = 0.21 µg/mL and LOQ = 0.71 µg/mL, peaks 4, 5, and 7). In each line different Latin letters are significantly different according to Tukey's HSD test ($p = 0.05$), for each potato group peels.

Cabezas-Serrano et al. (2009) suggested that colour parameters can be affected by pre- and post-harvest factors, as well as by the genotype.

3.2. Phenolic compounds characterisation

3.2.1. Non-anthocyanin phenolics

The profiles of non-anthocyanin phenolic derivatives in the tested potato peels, including chromatographic characteristics, tentative identifications and quantification are shown in Table 2. Seven compounds were detected, of which three were tentatively identified as phenolic acid derivatives, three as flavonol glycosides and one as a caffeoyl-polyamine derivative, based on the observation of their absorption spectra, pseudomolecular ion, characteristic MS² fragments and literature data (Barros et al., 2013a, 2013b; Choi, Kozukue, Kim, & Friedman, 2016; Friedman, Kozukue, Kim, Choi, & Mizuno, 2017; Rommens et al., 2008; Svobodova et al., 2017; Yang, Wu, Rui, Guo, & Feng, 2015).

Peaks 1–3 were tentatively identified as phenolic acids. Peak 1 ([M–H][−] at *m/z* 353) was detected in all the tested potato peels and tentatively identified as 4-*O*-caffeoylquinic acid, i.e., the ester formed between caffeic acid and the 4-hydroxyl of *L*-quinic acid (Svobodova et al., 2017). Peak 2 ([M–H][−] at *m/z* 179) was the most abundant compound in all the tested varieties, with concentrations ranging from 0.42 (*Rosemary*) to 1.44 (*UACH 0917*) mg/g dw, being identified as caffeic acid by comparison with retention time, UV–vis, and chromatographic characteristics of the available commercial standard compound. Peak 3 ([M–H][−] at *m/z* 313) was identified as salvianolic acid F, based on its MS² fragmentation as previously reported in the literature (Barros et al., 2013a, 2013b; Yang et al., 2015). Peaks 4, 5 and 7 were identified as flavonols, all of which being kaempferol derivatives, after comparing the obtained LC-MS data with those reported by other authors (Rommens et al., 2008; Svobodova et al., 2017); their glycosylation patterns were assigned based on the pseudomolecular ions and mass fragmentation profiles. Finally, Peak 6 ([M–H][−] at *m/z* 472) was only detected in five purple-skinned varieties (*Purple*, *Kefermarkter Blaue*, *Salad Blue*, *Blaue aus Finnland* and *Violetta*) and was tentatively identified as bis(dihydrocaffeoyl) spermidine, a polyamine derivative, previously described by Svobodova et al. (2017) in the non-edible parts of *Solanum stramonifolium* Jacq. This polyamine derivative was described as a potent oxidative inhibitor (Ponasik et al., 1995), and it is also used as a molecular marker for the authentication of the origin of several potato varieties from Italy (Adamo et al., 2012). The concentration of total phenolic compounds and derivatives among the peels of the studied potato varieties showed a great variation and ranged from 0.27 (*Red Emmalie*) to 1.76 (*UACH 0917*) mg/g dw. In accordance with our results, literature data show that the total amount of phenolic compounds in potato peels can vary significantly among different varieties (Sampaio, Petropoulos et al., 2020; Torres et al., 2020), while the processing treatment and extraction method may also have an effect on the content of phenolic compounds (Camire, Kubow, & Donnelly, 2009).

3.2.2. Anthocyanins

The anthocyanins profile, chromatographic characteristics, tentative identifications, and quantifications for the red- and purple-skinned varieties are shown in Tables 3 and 4, respectively. All tentatively identified compounds were previously described in the literature (Kita, Bakowska-Barczak, Hamouz, Kulakowska, & Lisińska, 2013; Oertel et al., 2017; Su et al., 2016), and identified as acylated anthocyanins, owing to the presence of a shoulder around 310–330 nm in their UV–visible spectra. Six peaks were detected in the red varieties (*Rosemary*, *Red Cardinal* and *Red Emmalie*), comprising pelargonidin, peonidin, petunidin, malvidin and cyanidin derivatives, based on their molecular ions and characteristic fragments in the MS² spectra. Peak 1r ([M]⁺ at *m/z* 887) was only detected in the *Rosemary* peel extract and was tentatively associated to a pelargonidin-3-*O*-*p*-coumaroylrutinoside-5-*O*-glucoside isomer, based on the HPLC-DAD-MS results and previous literature reports (Kita et al., 2013; Oertel et al., 2017). Peak 2r ([M]⁺ at

Table 3

Chromatographic properties, tentative identification, and quantification (mg/g dw) of the anthocyanins found in the studied red-skinned potato peels (mean ± SD).

Identification					
Peak	Retention time	λ_{\max} (nm)	[M] ⁺ (<i>m/z</i>)	MS ² (<i>m/z</i>)	Tentative identification
1r	34.87	504	887	725 (100),433 (5),271(16)	Pelargonidin-3- <i>O</i> - <i>p</i> - <i>cis</i> -coumaroylrutinoside-5- <i>O</i> -glucoside
2r	36.45	519	903	449(100),287(18)	Cyanidin 3- <i>O</i> - <i>p</i> -coumaroylrutinoside-5- <i>O</i> -glucoside
3r	38.49	505	887	725 (100),433 (10),271 (13)	Pelargonidin-3- <i>O</i> - <i>p</i> - <i>trans</i> -coumaroylrutinoside-5- <i>O</i> -glucoside
4r	39.33	508	917	755 (100),463 (15),301 (38)	Peonidin-3- <i>O</i> - <i>p</i> -coumaroylrutinoside-5- <i>O</i> -glucoside
5r	39.8	517	947	785 (100),493 (19),331 (29)	Malvidin-3- <i>O</i> - <i>p</i> -coumaroylrutinoside-5- <i>O</i> -glucoside
6r	39.9	517	947	785 (100),463 (23),301 (38)	Peonidin-3- <i>O</i> -feruloylrutinoside-5- <i>O</i> -glucoside
Quantification					
Peak	Rosemary	Red Cardinal	Red Emmalie		
1r	0.0269 ± 0.0005	nd	nd		
2r	0.0474 ± 0.0001 ^a	0.045 ± 0.001 ^b	0.0437 ± 0.0001 ^c		
3r	0.2503 ± 0.005 ^a	0.099 ± 0.002 ^b	0.0581 ± 0.0006 ^d		
4r	0.248 ± 0.004 ^a	0.226 ± 0.001 ^b	0.212 ± 0.0003 ^c		
5r	nd	nd	0.205 ± 0.001		
6r	nd	0.2121 ± 0.0003	nd		
TA	0.5722 ± 0.0003 ^b	0.582 ± 0.004 ^a	0.518 ± 0.009 ^c		

TA – Total Anthocyanins. nd – not detected. Standard calibration curves: pelargonidin-3-*O*-glucoside ($y = 276117x - 480418$, $R^2 = 0.9979$, LOD = 0.24 µg/mL and LOQ = 0.76 µg/mL, peaks 1r and 3r), cyanidin-3-*O*-glucoside ($y = 243287x - 1E + 06$, $R^2 = 0.9986$, LOD = 0.25 µg/mL and LOQ = 0.83 µg/mL, peak 2r), and peonidin-3-*O*-glucoside ($y = 151438x - 3E + 06$, $R^2 = 0.9965$, LOD = 0.13 µg/mL and LOQ = 0.40 µg/mL, peaks 4r, 5r, and 6r). In each line, different Latin letters are significantly different according to Tukey's HSD test ($p = 0.05$), for each potato group peels.

m/z 903), identified as a cyanidin derivative (cyanidin 3-*O*-*p*-coumaroylrutinoside-5-*O*-glucoside), was detected in all the red varieties, but not in the purple ones. Peak 3r ([M]⁺ at *m/z* 887) was assigned as an isomer of Peak 1r and presented the highest concentration in the *Rosemary* peel extract. These two peaks might correspond to *cis/trans* *p*-coumaroyl isomers, as reported for similar anthocyanins present in grape and wine (Alcalde-Eon et al., 2006); *cis* isomers are expected to elute before the corresponding more common *trans* counterparts, which is coherent with the elution behaviour and levels of peaks 1r and 3r in the studied samples. Peaks 4r and 6r ([M]⁺ at *m/z* 917 and 947, respectively) were identified as peonidin acyl-glycosides, with Peak 4r being the main compound detected in the *Red Emmalie* peels. Finally, Peak 5r ([M]⁺ at *m/z* 947) was identified as an acylated malvidin glucoside (malvidin-3-*O*-*p*-coumaroylrutinoside-5-*O*-glucoside) detected only in the *Red Emmalie* peels. All the three red varieties showed very similar total anthocyanin concentration in the peels, ranging from 0.518 mg/g dw (*Red Emmalie*) to 0.583 mg/g dw (*Red Cardinal*).

Regarding the purple varieties, seven peaks were detected, two of which were tentatively identified as petunidin derivatives (Peaks 1p and 2p), two as peonidin derivatives (Peaks 4p and 6p), two as malvidin derivatives (Peaks 5p and 7p) and one as a pelargonidin derivative (Peak 3p). The molecular ions and fragmentation patterns of Peaks 1p

Table 4

Chromatographic properties, tentative identification and quantification (mg/g dw) of the anthocyanins found in the studied purple-skinned potato peels (mean \pm SD).

Identification							
Peak	Retention time	λ_{max} (nm)	[M] ⁺ (m/z)	MS ² (m/z)	Tentative identification		
1p	36.77	531	933	771(100),479(24),317(34)	Petunidin-3-O- <i>p</i> -coumaroylrutinoside-5-O-glucoside		
2p	37.76	531	963	801(100),479(25),317(38)	Petunidin-3-O-feruloylrutinoside-5-O-glucoside		
3p	38.59	507	887	725(100),433(10),271(13)	Pelargonidin-3-O- <i>p</i> -coumaroylrutinoside-5-O-glucoside		
4p	39.03	520	917	755(100),463(15),301(38)	Peonidin-3-O- <i>p</i> -coumaroylrutinoside-5-O-glucoside		
5p	39.21	532	947	785(100),493(19),331(29)	Malvidin-3-O- <i>p</i> -coumaroylrutinoside-5-O-glucoside		
6p	39.82	522	947	785(100),463(23),301(38)	Peonidin-3-O-feruloylrutinoside-5-O-glucoside		
7p	39.95	532	977	815(100),493(15),331(27)	Malvidin-3-O-feruloylrutinoside-5-O-glucoside		
Quantification							
Peak	Purple	Kefermarkter Blaue	UACH 0917	Salad Blue	Blaue aus Finland	Shetland Black	Violetta
1p	0.843 \pm 0.001 ^a	0.65 \pm 0.01 ^b	0.282 \pm 0.004 ^f	0.66 \pm 0.004 ^b	0.59 \pm 0.007 ^c	0.298 \pm 0.007 ^e	0.3952 \pm 0.004 ^d
2p	0.233 \pm 0.005 ^b	0.168 \pm 0.002 ^f	0.0963 \pm 0.0001 ^g	0.269 \pm 0.005 ^a	0.172 \pm 0.001 ^e	0.205 \pm 0.002 ^d	0.2186 \pm 0.0001 ^c
3p	nd	nd	0.0159 \pm 0.0002 ^c	nd	nd	0.0234 \pm 0.0004 ^b	0.0387 \pm 0.00002 ^a
4p	nd	nd	nd	nd	nd	0.241 \pm 0.005	nd
5p	0.171 \pm 0.001 ^d	0.1223 \pm 0.004 ^e	0.6559 \pm 0.001 ^a	0.2466 \pm 0.0001 ^b	0.123 \pm 0.002 ^e	nd	0.211 \pm 0.001 ^c
6p	nd	nd	nd	nd	nd	0.2183 \pm 0.0002	nd
7p	0.119 \pm 0.003 ^b	0.0937 \pm 0.0014 ^d	0.2118 \pm 0.0058 ^a	0.212 \pm 0.001 ^a	0.0985 \pm 0.0004 ^c	nd	nd
TA	1.368 \pm 0.001 ^b	1.04 \pm 0.02 ^d	1.26 \pm 0.01 ^c	1.39 \pm 0.01 ^a	0.98 \pm 0.01 ^e	0.99 \pm 0.02 ^e	0.863 \pm 0.005 ^f

TA – Total Anthocyanins. nd – not detected. Standard calibration curves: pelargonidin-3-O-glucoside ($y = 276117x - 480418$, $R^2 = 0.9979$, LOD = 0.24 μ g/mL and LOQ = 0.76 μ g/mL, peak 3p) and peonidin-3-O-glucoside ($y = 151438x - 3E + 06$, $R^2 = 0.9965$, LOD = 0.13 μ g/mL and LOQ = 0.40 μ g/mL, peaks 1p, 2p, 4, 5p, 6p, and 7p). In each lines different Latin letters are significantly different according to Tukey's HSD test ($p = 0.05$), for each potato group peels.

and 2p were coherent with derivatives of petunidin-3-O-rutinoside-5-O-glucoside acylated with *p*-coumaric and ferulic acids, respectively, as previously identified in coloured tubers of *Solanum tuberosum* (Kita et al., 2013). Peak 5p possessed the same molecular ion [M]⁺ at *m/z* 947 as Peak 6p, but different fragmentation pattern. Two compounds with this molecular ion were also reported by Kita et al. (2013), identified as malvidin-3-O-*p*-coumaroylrutinoside-5-O-glucoside and peonidin-3-O-feruloylrutinoside-5-O-glucoside, respectively, although the second appeared only in the flesh of red tubers; those identities are coherent with the respective release of MS² fragments at *m/z* 331 and 301, corresponding to malvidin and peonidin aglycones. Petunidin-3-O-coumaroylrutinoside-5-O-glucoside (Peak 1p) was the main anthocyanin found in the peels of all the purple varieties, except for UACH 0917 for which malvidin-3-O-*p*-coumaroylrutinoside-5-O-glucoside (Peak 5p) was the main compound (0.66 mg/g dw). The purple varieties showed a variable total anthocyanin content which ranged from 0.86 mg/g dw (Violetta) to 1.39 mg/g dw (Salad Blue).

Although potato peels are usually discarded, the present results suggest that these bio-residues could be used as sources of anthocyanins and other phenolic compounds. Yin et al. (2016) compared the flesh and peel of coloured potato varieties from China and found that on average the total anthocyanin contents in peels were 15.34 times higher than those of the respective flesh. Similarly, the total phenolic compounds content was 7.28 times higher in peels compared to the flesh. These results support the potential use of potato peels as sources of phenolic compounds with biological activity. However, despite the reports in the literature regarding the effect of pre- and post-harvest condition on colour parameters, it is important to note that the variability in the phenolic and anthocyanin profiles and contents of the peels herein found could be mainly attributed to inherited differences of the potato genotypes, as all samples were subjected to the same environmental factors (growing conditions, planting location and climate), transport and storage conditions, as well as the same extraction procedure.

3.3. Bioactive properties

3.3.1. Cell-based antioxidant and anti-inflammatory activities

The hydroethanolic extracts prepared from the tested potato peels were evaluated for their capacity to prevent lipid peroxidation of porcine brain tissues (TBARS assay) and haemolysis of sheep blood cells (OxHLIA assay). Additionally, the extracts' anti-inflammatory potential

of inhibiting the growth of RAW 264.7 mouse macrophages was assessed. The results are presented in Table 5.

All the tested extracts were effective in diminishing the production of TBAR substances, however the recorded results varied greatly among varieties (IC₅₀ = 26–230 μ g/mL). The peels from the *Rosemary* tubers presented the highest antioxidant capacity, as their extracts required the lowest concentration to diminish the lipid peroxidation in 50% compared to the control Trolox (IC₅₀ = 26 μ g/mL), whereas *Salad Blue* presented the weakest activity IC₅₀ with values being almost nine times lower than those of *Rosemary* cultivar (IC₅₀ = 230 μ g/mL).

Regarding the OxHLIA assay, almost all the tested potato varieties presented positive results in retarding the erythrocytes haemolysis process ($\Delta t = 60$ min), with the exception of *Red Emmalie*, that revealed no activity. *Violetta* and *Purple* were the varieties that presented the most prominent activity, as they recorded the lowest IC₅₀ values (16 μ g/mL for both varieties). In agreement with the results herein found in the TBARS assay, *Salad Blue* peels also presented antioxidant activity in the OxHLIA assay (IC₅₀ = 294 μ g/mL).

In agreement with our findings, several authors reported the antioxidant capacity of potato peel extracts in previous studies. For instance, positive results for antioxidant activity were obtained by the following assays: the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging capacity (Jeddou et al., 2018; Singh et al., 2011; Singh & Rajini, 2004; Yin et al., 2016); reducing power (Jeddou et al., 2018; Singh & Rajini, 2004), β -carotene bleaching inhibition activity (Jeddou et al., 2018), ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radical scavenging activity (Jeddou et al., 2018), lipid peroxidation in rat liver homogenates (Singh & Rajini, 2004) and iron ion chelation (Singh & Rajini, 2004), all of which indicate the antioxidant potential of this bio-residue. In some studies, potato peel extracts also exerted significantly higher radical scavenging activity ($p < 0.05$) than the respective flesh extracts indicating the presence of higher contents of antioxidant compounds in this part of the tubers (Albishi, John, Al-Khalifa, & Shahidi, 2013; Wu et al., 2012).

Regarding the anti-inflammatory assay, *Rosemary* was the only variety that presented significant capacity to inhibit the growth of RAW 264.7 mouse macrophages (IC₅₀ = 141 μ g/mL). It is important to mention that for the anti-inflammatory assay the maximum tested concentration of the extracts was 400 μ g/mL. In comparison with other studies, the *Rosemary* extract showed greater anti-inflammatory activity than, for example, *M. jaborcaba* epicarp (IC₅₀ = 299 μ g/mL)

Table 5

Antioxidant, anti-inflammatory and anti-proliferative activities and cytotoxicity ($\mu\text{g/mL}$ extract) of the studied potato peels (mean \pm SD).

Potato varieties	Antioxidant (IC ₅₀ values)		Anti-inflammatory (IC ₅₀ values)	Anti-proliferative (GI ₅₀ values)				Cytotoxicity (GI ₅₀ values)
	TBARS	OxHLLA	RAW 264.7	NCI-H460	HepG2	MCF-7	HeLa	PLP2
Rosemary	26 \pm 3 ^h	54 \pm 2 ^c	141 \pm 6	69 \pm 1 ^e	79 \pm 4 ^f	51 \pm 2 ^f	49 \pm 3 ^f	304 \pm 9
Red Cardinal	187 \pm 12 ^c	123 \pm 7 ^b	>400	241 \pm 3 ^c	305 \pm 11 ^d	315 \pm 10 ^a	333 \pm 17 ^b	>400
Rote Emmalie (Red Emmalie)	46 \pm 2 ^g	n.a.	>400	248 \pm 6 ^c	301 \pm 21 ^d	244 \pm 17 ^c	227 \pm 11 ^e	>400
Purple	114 \pm 8 ^f	16 \pm 1 ^{c,d}	>400	268 \pm 17 ^b	365 \pm 18 ^a	188 \pm 11 ^e	330 \pm 2 ^b	>400
Kefermarkter Blaue	208 \pm 12 ^b	32 \pm 2 ^{c,d}	>400	217 \pm 12 ^d	302 \pm 9 ^d	279 \pm 12 ^b	313 \pm 33 ^c	>400
UACH 0917	127 \pm 7 ^e	24 \pm 2 ^{c,d}	>400	280 \pm 7 ^a	319 \pm 1 ^c	224 \pm 10 ^d	346 \pm 10 ^a	>400
Salad Blue	230 \pm 6 ^a	294 \pm 8 ^a	>400	281 \pm 6 ^a	286 \pm 12 ^e	215 \pm 12 ^d	292 \pm 19 ^d	>400
Blaue aus Finnland	154 \pm 2 ^d	122 \pm 4 ^b	>400	276 \pm 2 ^{a,b}	281 \pm 10 ^e	281 \pm 66 ^b	333 \pm 12 ^b	>400
Shetland Black	190 \pm 6 ^c	53 \pm 2 ^c	>400	269 \pm 11 ^b	343 \pm 9 ^b	210 \pm 10 ^d	233 \pm 3 ^e	>400
Violetta (Blaue Elise)	144 \pm 5 ^d	16 \pm 1 ^{c,d}	>400	271 \pm 19 ^b	317 \pm 11 ^c	216 \pm 17 ^d	335 \pm 11 ^{a,b}	>400

IC₅₀: extract concentration corresponding to 50% of antioxidant activity against lipid peroxidation (TBARS) and haemolysis of sheep blood cells (OxHLLA; $\Delta t = 60$ min). n.a.: no activity. GI₅₀: values correspond to the sample concentration achieving 50% of growth inhibition in liver primary culture PLP2; maximum tested concentration: 400 $\mu\text{g/mL}$. In each column, different Latin letters are significantly different according to Tukey's HSD test ($p = 0.05$), for each potato group peels.

(Albuquerque et al., 2020). Moreover, Wahyudi et al. (2020) demonstrated the anti-inflammatory properties of potato peel extracts by conducting an *in vivo* study with rats, using carrageenan-induced paw edema and diclofenac as the reference drug. Their results showed that, compared with the negative control (distilled water), treatment doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg significantly reduced the edema volume increment.

3.3.2. Anti-proliferative activity and cytotoxicity

The *in vitro* anti-proliferative properties of the coloured potato peels were also investigated and the corresponding results are presented in Table 5. Additionally, a cytotoxicity assay was carried out to assess the safety of the extracts for incorporation into food formulations. Considering that potato peels may be rich in potentially toxic compounds such as glycoalkaloids (Friedman, Roitman, & Kozukue, 2003; Hossain et al., 2015; Sotelo & Serrano, 2000), this test is essential prior to suggesting the use of peel extracts for food purposes.

The inclusion of phytochemicals and functional foods in the diet has been proposed as a way of preventing the development of cancer cells (Albuquerque et al., 2020). In the present work, the capacity of the studied potato peels in inhibiting tumour cell growth was evaluated in four tumour cell lines. All the studied hydroethanolic extracts revealed anti-proliferative activity against all the tested tumour cell lines, with GI₅₀ values ranging from 69 $\mu\text{g/mL}$ to 281 $\mu\text{g/mL}$ for NCI-H460 (non-small cell lung carcinoma) cells, 79 $\mu\text{g/mL}$ to 365 $\mu\text{g/mL}$ for HepG2 (hepatocellular carcinoma) cells, 51 $\mu\text{g/mL}$ to 315 $\mu\text{g/mL}$ for MCF-7 (breast carcinoma) cells and 49 $\mu\text{g/mL}$ to 346 $\mu\text{g/mL}$ for HeLa (cervical carcinoma) cells. The extract from the *Rosemary* variety presented the highest anti-proliferative capacity for all the tested tumour cell lines, as it required the lowest concentrations to present activity in comparison with the other nine varieties. For comparison, Albuquerque et al. (2020) reported GI₅₀ values within the ranges found herein for the anti-proliferative activity of *M. jaboticaba* epicarp against three tumor cell lines (HepG2 = 258 $\mu\text{g/mL}$; MCF-7 = 300 $\mu\text{g/mL}$; HeLa = 278 $\mu\text{g/mL}$; NCI-H460 > 400 $\mu\text{g/mL}$). Moreover, Reddivari, Vanamala, Chintharlapalli, Safe, & Miller (2007) also found that the anthocyanin fraction from potato extracts exhibited anticancer properties, being cytotoxic to prostate cancer cells through the activation of caspase-dependent and caspase-independent pathways.

In order to assess the safety of the tested extracts, porcine liver was used as a model to study the hepatotoxicity effects of the extracts, due to its similarity with the human liver in terms of cellular and physiological functioning (Correia et al., 2018). The results showed that the extracts did not reveal toxicity for PLP2 cells up to the maximum tested concentration (GI₅₀ value >400 $\mu\text{g/mL}$), with the exception of the *Rosemary* extract. Nevertheless, the cytotoxic effect of this variety was recorded for a high concentration of the extract (GI₅₀ value = 304 $\mu\text{g/mL}$)

indicating low cytotoxic effects. This finding highlights the safety of potato peel extracts to be used as natural additives in food formulations in low concentrations which may exert antioxidant activity without cytotoxic effects to non-tumor cell lines.

4. Conclusion

The potato peels herein studied contained non-anthocyanin and anthocyanin phenolic compounds. Caffeic and caffeoylquinic acid were found in the highest concentrations among non-anthocyanin phenolics in all the samples, while *O*-glycosylated flavonoid derivatives and polyamine derivatives were also detected. Regarding anthocyanins, all the tentatively identified compounds were acylated with a hydroxycinnamic acid in the red-skinned varieties, pelargonidin-3-*p*-coumaroylrutinoside-5-glucoside isomer, peonidin-3-*p*-coumaroylrutinoside-5-glucoside, and malvidin-3-*p*-coumaroylrutinoside-5-glucoside presented the highest content; while in the purple-skinned varieties, petunidin-3-*p*-coumaroylrutinoside-5-glucoside was the most abundant compound. Positive results for the antioxidant capacity were recorded in the extracts of all the assayed potato peels, as well as significant antitumor activity. Particularly, the peels from the red-skinned variety *Rosemary* presented the best antioxidant and antitumor results and were the only to reveal anti-inflammatory activity. The studied potato peels also showed no hepatotoxic effects up to the maximum tested concentration of extract (400 $\mu\text{g/mL}$), except for the *Rosemary* peels that showed toxicity for concentrations above 304 $\mu\text{g/mL}$. In conclusion, the present results would support the use of potato peels as valuable sources of bioactive compounds and as natural additives in functional food formulations. However, further studies with more varieties are needed to reveal the genotypic variability, as well as to identify the effect of pre- and post-harvest factors on bioactive compounds content and bioactivities of potato processing bio-residues.

CRedit authorship contribution statement

Shirley L. Sampaio: Methodology, Investigation, Writing - original draft. **Spyridon A. Petropoulos:** Conceptualization, Writing - original draft. **Maria Inês Dias:** Methodology, Investigation, Writing - review & editing. **Carla Pereira:** Methodology, Investigation. **Ricardo C. Calhelha:** Methodology, Investigation. **Angela Fernandes:** Methodology, Investigation. **Camila M.M. Leme:** Methodology, Investigation. **Alexios Alexopoulos:** Methodology, Investigation. **Celestino Santos-Buelga:** Conceptualization, Methodology, Writing - review & editing. **Isabel C.F. R. Ferreira:** Conceptualization, Methodology, Writing - review & editing. **Lillian Barros:** Funding acquisition, Conceptualization, Methodology, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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