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Ficus carica L.: Metabolic and biological screening

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ABSTRACT

Ficus carica L. is one of the earliest cultivated fruit trees. In this work, metabolite profiling was performed on the leaves, pulps and peels of two Portuguese white varieties of *F. carica* (Pingo de Mel and Branca Tradicional). Phenolics and organic acids profiles were determined by HPLC/DAD and HPLC/UV, respectively. All samples presented a similar phenolic profile composed by 3-*O*- and 5-*O*-caffeoylquinic acids, ferulic acid, quercetin-3-*O*-glucoside, quercetin-3-*O*-rutinoside, psoralen and bergapten. 3-*O*-Caffeoylquinic acid and quercetin-3-*O*-glucoside are described for the first time in this species. Leaves' organic acids profile presented oxalic, citric, malic, quinic, shikimic and fumaric acids, while in pulps and peels quinic acid was absent. The antioxidant potential of the different plant parts was checked. All materials exhibited activity against DPPH and nitric oxide radicals in a concentration-dependent way. However, only the leaves presented capacity to scavenge superoxide radical. Leaves were always the most effective part, which seems to be related with phenolics compounds. Additionally, acetylcholinesterase inhibitory capacity was evaluated, but no effect was observed. Antimicrobial potential was also assessed against several bacterial species, although no activity was noticed. This is the first study comparing the chemical composition and biological potential of *F. carica* pulps, peels and leaves.

1. Introduction

Ficus carica L., a deciduous tree belonging to the Moraceae family, is one of the earliest cultivated fruit trees. Mediterranean diets are characterized by abundant intake of this fruit (Solomon et al., 2006), which can be eaten fresh, dried or used as jam. Figs are an excellent source of minerals, vitamins and dietary fibre; they are fat and cholesterol-free and contain a high number of amino acids (Veberic et al., 2008; Solomon et al., 2006). Figs have been traditionally used for its medicinal benefits as laxative, cardiovascular, respiratory, antispasmodic and anti-inflammatory remedies (Guarrera, 2005).

Some studies have described the presence of several phenolic compounds in this species (Teixeira et al., 2006; Vaya and Mahmood, 2006; Guarrera, 2005), phytosterols and fatty acids in fruits and branches of fig trees (Jeong and Lachance, 2001) and its antioxidant activity (Solomon et al., 2006). However, leaf, pulp and peel's metabolic profile and biological activity have not been compared.

Biomolecules from plants have attracted a great deal of attention, mainly concentrated on their role in preventing diseases. Epidemiological studies have consistently shown that there is a clear significant positive association between intake of these natural products and reduced rate of heart disease mortalities, common cancers and other degenerative diseases. Free radicals present in human organism cause oxidative damage to various molecules, such as lipids, proteins and nucleic acids, being involved in the initiation of those diseases (García-Alonso et al., 2004). Antioxidant compounds, such as phenolics, organic acids, vitamin E and carotenoids, scavenge free radicals, thus inhibiting the oxidative mechanisms that lead to degenerative illnesses (du Toit et al., 2001; Silva et al., 2004). Additionally, growing interest has been devoted to natural antimicrobial agents, in order to avoid chemical preservatives and because of increasing antibiotics resistance.

Phenolic compounds are secondary metabolites that are quite widespread in nature. These compounds play many physiological roles in plants and some of them are also favourable to human health, since they are able to act as antioxidants by different ways: as reducing agents, hydrogen donators, free radicals scavengers, and singlet oxygen quenchers and, therefore, as cell saviours (Merken and Beecher, 2000; Costa et al., 2009; Fattouch et al., 2007).

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Organic acids are primary metabolites, which can be found in great amounts in all plants, especially in fruits. These compounds also have antioxidant properties (Silva et al., 2004; Valentão et al., 2005a, 2005b). Citric, malic and tartaric acids are commonly found in fruits and berries, while oxalic acid is present in higher amounts in green leaves (Oliveira et al., 2008). Ascorbic acid is probably the most widely distributed water soluble antioxidant in vegetables (Naidu, 2003; Seabra et al., 2006; Sousa et al., 2009).

Recently, several studies have been developed to assess the ability of natural compounds inhibition of acetylcholinesterases, since it is directly related with the treatment of neurological disorders, such as Alzheimer's disease, senile dementia, ataxia and *myasthenia gravis* (Mukherjee et al., 2007). Acetylcholinesterase breaks down the ester bond in the molecule of acetylcholine, thus leading to the loss of stimulatory activity. Inhibition of acetylcholinesterases will, as far as nervous transmission is concerned, result in a prolongation of the existence, and therefore of the activity, of acetylcholine (Houghton et al., 2006).

The aim of the present work was to characterise the phenolics and organic acids composition of the material obtained from two Portuguese *F. carica* varieties (Pingo de Mel and Branca Tradicional), using HPLC coupled to diode array and UV detectors, respectively, and to assess their biological potential, namely as antioxidant, acetylcholinesterase inhibitor and antimicrobial agent. To our knowledge this is the first report comparing chemical composition and bioactivity of several materials from *F. carica*. In addition, no previous study involved the above mentioned varieties.

2. Materials and methods

2.1. Standards and reagents

Quercetin 3-*O*-rutinoside, bergapten, psoralen, oxalic, malic, fumaric, shikimic, quinic and citric acids, ferulic acid, dimethyl sulfoxide (DMSO) and carbachol were from Sigma–Aldrich (St. Louis, MO, USA) and 5-*O*-caffeoylquinic acid was from Extrasynthése (Genay, France). Sodium nitroprussiate dihydrate was from Riedel-de Haën (St. Louis, MO). N-(1-Naphthyl)ethylene-diamine dihydrochloride, phosphoric acid and methanol were from Merck. Sulfanilamide, β-nicotinamide adenine dinucleotide (NADH), nitroblue tetrazolium chloride (NBT), phenazine methosulfate (PMS), 2,2-diphenyl-1-picrylhydrazyl (DPPH), acetylthiocoline iodide and acetylcholinesterase were obtained from Sigma–Aldrich. The water was treated in a Milli-Q water purification system (Millipore, Bedford, MA, USA). The Chromabond C18 SPE columns (70 mL/10,000 mg) were purchased from Macherey–Nagel (Duren, Germany).

2.2. Plant material

F. carica (var. Pingo de Mel and var. Branca Tradicional) leaves and fruits were collected in Mirandela region (Northeast Portugal), in August 2008. Fruit peel and pulp were separated. All materials were frozen and lyophilized. Voucher specimens were deposited at Department of Pharmacognosy, Faculty of Pharmacy, Porto University.

2.3. Extracts preparation

Fig leaves, peels and pulps (2 g) were boiled for 15 min in 500 ml of water. The resulting extracts were filtered over a filtration funnel and then lyophilized in a Labconco Freezone 4.5 apparatus (Kansas City, MO, US). The lyophilized extracts were kept in a desiccator, in the dark, until analysis.

2.4. HPLC/DAD for phenolic compounds analysis

Each lyophilized extract was redissolved in water, filtered and 20 μL were analysed on an analytical HPLC unit (Gilson), using a Spherisorb ODS2 (25.0 × 0.46 cm; 5 μm, particle size) column, according to a described procedure (Oliveira et al., 2007). The solvent system used was a gradient of water-formic acid (19:1) (A) and methanol (B), starting with 5% methanol and installing a gradient to obtain 15% B at 3 min, 25% B at 13 min, 30% B at 25 min, 35% B at 35 min, 45% B at 39 min, 45% B at 42 min, 50% B at 44 min, 55% B at 47 min, 70% B at 50 min, 75% B at 56 min and 80% B at 60 min, at a solvent flow rate of 0.9 mL/min. Detection was achieved with a Gilson Diode Array Detector (DAD). Spectral data from all peaks were accumulated in the range 200–400 nm, and chromatograms were recorded at 320 nm and 350 nm. The data were processed on an Unipoint® System software (Gilson Medical Electronics, Villiers le Bel, France).

The compounds in each extract were identified by comparing their retention times and UV–vis spectra in the 200–400 nm range with authentic standards and with the library of spectra previously compiled by the authors.

Phenolic compounds quantification was achieved by the absorbance recorded in the chromatograms relative to external standards. Phenolic acids and furanocoumarins were determined at 320 nm and flavonoids at 350 nm. 3-*O*-Caffeoylquinic acid was quantified as 5-*O*-caffeoylquinic acid and the other compounds were quantified as themselves.

2.5. HPLC/UV for organic acids analysis

Before HPLC analysis, each lyophilized extract was dissolved in acid water (pH 2 with HCl). The solution obtained was passed through an SPE C18 column, previously conditioned with 30 mL of methanol and 70 mL of acid water. The aqueous solution was then evaporated to dryness under reduced pressure (40 °C), redissolved in sulphuric acid 0.01 N (1 mL) and 20 μL were analysed on an analytical HPLC unit (Gilson), using an ion exclusion column Nucleogel® Ion 300 OA (300 × 7.7 mm), in conjunction with a column heating device at 30 °C. Elution was carried out at a solvent flow rate of 0.2 mL/min, isocratically, with sulphuric acid 0.01 N as the mobile phase. Detection was performed with a Gilson UV detector at 214 nm. Organic acids quantification was achieved by the absorbance recorded in the chromatograms relative to external standards.

2.6. Antioxidant activity

2.6.1. DPPH scavenging activity

The aqueous lyophilized extract of each sample was dissolved in water (five different concentrations). Antiradical activity was determined spectrophotometrically in a Multiskan Ascent plate reader (Thermo; electron corporation), by monitoring the disappearance of DPPH at 515 nm, according to a described procedure (Costa et al., 2009). The reaction mixtures in the sample wells consisted of extract and 150 μM DPPH. The plate was incubated for 30 min at room temperature after the addition of DPPH. Three experiments were performed in triplicate.

2.6.2. Nitric oxide scavenging activity

The aqueous lyophilized extract of each sample was dissolved in 0.1 M phosphate buffer (pH 7.4). The antiradical activity was determined in a Multiskan Ascent plate reader (Thermo; electron corporation), according to a described procedure (Sousa et al., 2008). Sodium nitroprusside (20 mM) was incubated with each extract (five different concentrations) for 60 min, at room temperature, under light. All solutions were prepared in phosphate buffer. After incubation, Griess reagent, containing 1% sulphanilamide and 0.1% naphthylethyldiamine in 2% phosphoric acid, was added to each well. The mixture was incubated at room temperature for 10 min, and the absorbance of the chromophore formed during the diazotization of nitrite with sulphanilamide and subsequent coupling with naphthylethylenediamine was read at 562 nm. Three experiments were performed in triplicate.

2.6.3. Superoxide radical scavenging activity

The aqueous lyophilized extract of each sample was dissolved in 19 mM phosphate buffer (pH 7.4). Superoxide radicals were generated by NADH/PMS system according to a described procedure (Valentão et al., 2001). All components were dissolved in buffer. In each well, sample (five different concentrations), NADH, NBT and PMS were added. The absorbances were read at 560 nm. Three experiments were performed in triplicate.

2.7. Acetylcholinesterases inhibitory activity

2.7.1. Buffers

The following buffers were used. Buffer A: 50 mM Tris–HCl, pH 8; buffer B: 50 mM Tris–HCl, pH 8, containing 0.1% bovine serum albumin (BSA); buffer C: 50 mM Tris–HCl, pH 8, containing 0.1 M NaCl and 0.02 M $MgCl.6H_2O$.

2.7.2. Enzyme

Acetylcholinesterase was from *Electrophorus electricus* – electric eel – (type VI-s, lyophilized powder, 425 U/mg, 687 mg/protein). Lyophilized enzyme was dissolved in buffer A to make 1000 U/mL stock solution, and further diluted with buffer B to get 0.44 U/mL enzyme for the microplate assay.

2.7.3. Microplate assay

Acetylcholinesterase inhibitory activity was determined spectrophotometrically in a Multiskan Ascent plate reader (Thermo; electron corporation) based on Ellman's method, according to a described procedure (Pereira et al., 2009). In each well the mixture consisted of acetyltiocholine in water, DTNB in buffer C, buffer B and sample dissolved in a solution of 10% methanol in buffer A. The absorbance was read at 405 nm. After this step acetylcholinesterase was added and the

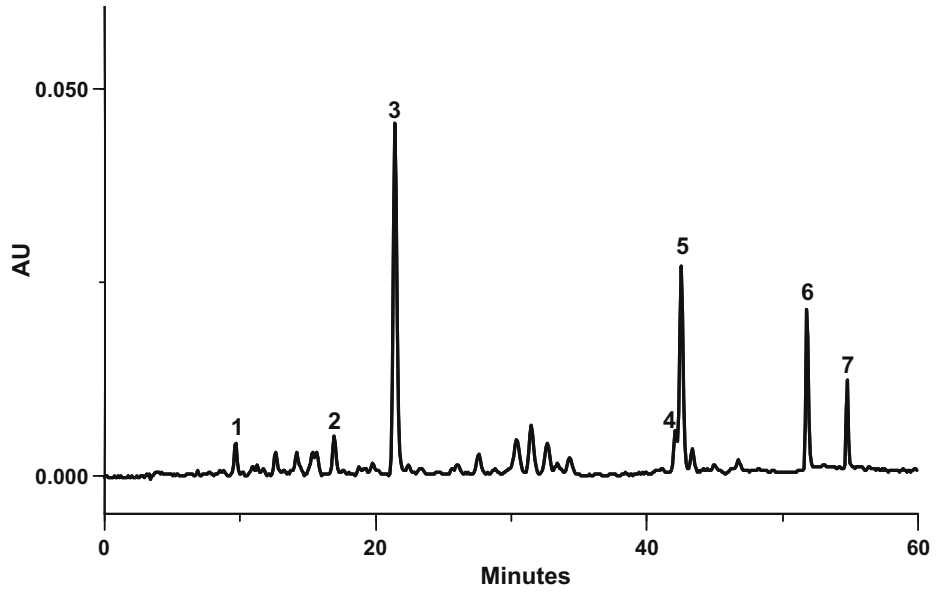

Fig. 1. HPLC phenolic profile of *Ficus carica* leaves. Detection at 320 nm. Peaks: (1) 3-*O*-caffeoylquinic acid; (2) 5-*O*-caffeoylquinic acid; (3) ferulic acid; (4) quercetin 3-*O*-glucoside; (5) quercetin 3-*O*-rutinoside; (6) psoralen; (7) bergapten.

Table 1
Phenolic composition of Portuguese *Ficus carica* L. varieties (mg/kg lyophilized extract).[a]

Phenolics	Pingo de mel			Branca Tradicional		
	Peel	Pulp	Leaves	Peel	Pulp	Leaves
3-CQA	3.2 ± 0.9	nq	nq	nq	nq	nq
5-CQA	43.8 ± 3.8	32.9 ± 23.2	1158.8 ± 7.4	8.3 ± 0.5	2.8 ± 0.0	473.6 ± 9.5
Ferulic acid	20.5 ± 0.1	–	11983.8 ± 241.5	9.2 ± 0.0	–	nq
Q-3-Glu	31.4 ± 2.1	nq	1633.9 ± 11.1	30.8 ± 1.2	nq	611.1 ± 29.0
Q-3-Rut	499.1 ± 1.2	nq	14585.8 ± 1164.9	629.6 ± 18.3	64.6 ± 1.7	17440.4 ± 1709.6
Psoralen	2.6 ± 0.0	3.7 ± 0.5	3774.7 ± 237.7	18.4 ± 2.6	17.0 ± 0.2	9259.7 ± 29.3
Bergapten	nq	nq	1336.7 ± 78.7	26.8 ± 11.1	45.8 ± 11.2	4627.2 ± 361.7
∑	600.6	36.6	34473.6	723.0	130.3	32412.0

[a] Values are expressed as mean ± standard deviation of three assays; nq, not quantified; ∑, sum of the determined phenolic compounds; 3-CQA: 3-*O*-caffeoylquinic acid; 5-CQA: 5-*O*-caffeoylquinic acid; Q-3-Glu: quercetin 3-*O*-glucoside; Q-3-rut: quercetin 3-*O*-rutinoside.

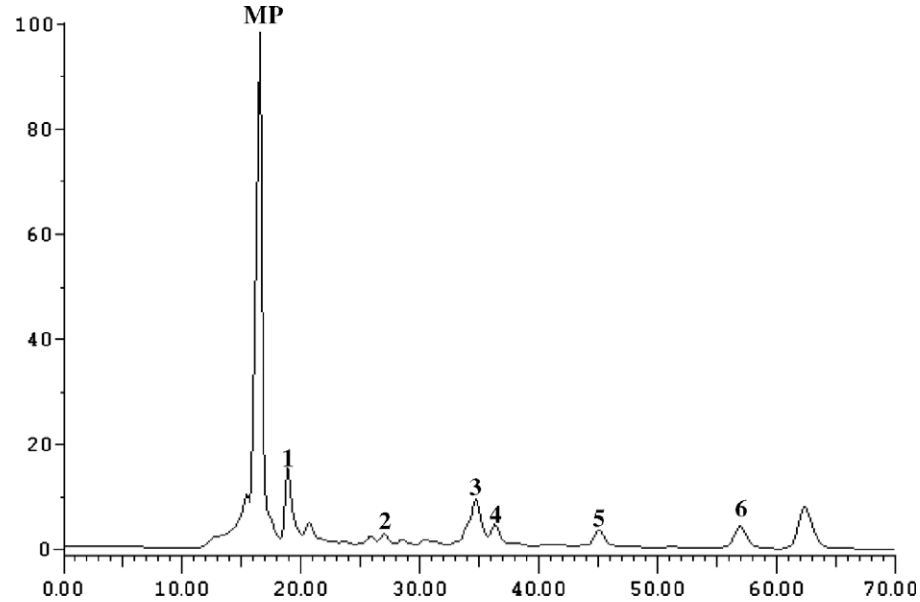

Fig. 2. HPLC organic acid profile of *Ficus carica* leaves. Detection at 214 nm. Peaks: (MP) mobile phase; (1) oxalic acid; (2) citric acid; (3) malic acid; (4) quinic acid; (5) shikimic acid; (6) fumaric acid.

absorbance was read again. The rates of reactions were calculated by Ascent Software version 2.6 (Thermo Labsystems Oy). The rate of the reaction before adding the enzyme was subtracted from that obtained after adding the enzyme in order to correct eventual spontaneous hydrolysis of substrate. Percentage of inhibition was calculated by comparing the rates of the sample with the control (10% methanol in buffer A). Three experiments were performed in triplicate.

2.8. Antimicrobial activity

F. carica aqueous lyophilized extracts were tested for antimicrobial activity by diffusion assay against *Bacillus cereus*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas fluorescens*. Water and aqueous garlic extract (1:1) were used as negative and positive references standards, respectively. The antibacterial susceptibility tests were performed on Muller–Hinton Agar media plates which were inoculated by streaking over the surface of the media a suspension of bacterial cells containing 10^6 CFU/mL. All extracts were diluted with 0.5% dimethyl sulfoxide (DMSO), being tested at concentrations of 1.5 mg/mL for leaves and 50 mg/mL for pulps and peels. About 10 μL of all materials solutions were placed in contact with the inoculated agar surface. Finally, the inoculated plates were incubated at 25 and 37 °C for 24–48 h, before screening for inhibition zones.

2.9. Statistical analysis

The evaluation of statistical significance was determined by ANOVA, followed by Newman–Keuls test. The level of significance was set at $p < 0.05$.

3. Results and discussion

3.1. Phenolic compounds

In fig materials, three hydroxycinnamic acids (3-*O*- and 5-*O*-caffeoylquinic acids and ferulic acid), two flavonoid glycosides (quercetin 3-*O*-glucoside and quercetin 3-*O*-rutinoside) and two furanocoumarins (psoralen and bergapten) (Fig. 1 and Table 1) were characterized. With the exception of ferulic acid that was not found in pulps, all of the remaining phenolics were present in the three analysed matrices. As far as we know, 3-*O*-caffeoylquinic acid and quercetin 3-*O*-glucoside are described for the first time in this species.

In quantitative terms, aqueous lyophilized extracts of leaves presented the highest quantities of these compounds and pulps the lowest ones (Table 1). Indeed, the total phenolic content is significantly different among the three vegetal materials, following the order leaves ≫ peels ≫ pulps. This fact is not surprising since these compounds, especially flavonoids, act as UV filters, protecting some cell structures, like chloroplasts, from harmful effects of UV radiation (Treutter, 2006; Macheix et al., 1990). Among these compounds, flavonols, like quercetin derivatives, should be highlighted (Oliveira et al., 2007). For pulp and peel, Branca Tradicional was the variety with higher amounts of phenolic compounds, while the leaves of Pingo de Mel exhibited higher phenolics contents (Table 1).

In all samples, quercetin 3-*O*-rutinoside was the major compound, representing 42–87% of total identified phenolics, with the exception of Pingo de Mel pulp in which chlorogenic acid was present at the highest amount (90%). Quercetin 3-*O*-rutinoside content in peels was significantly higher than that found in pulps and leaves. 3-*O*-Caffeoylquinic acid was a vestigial com-

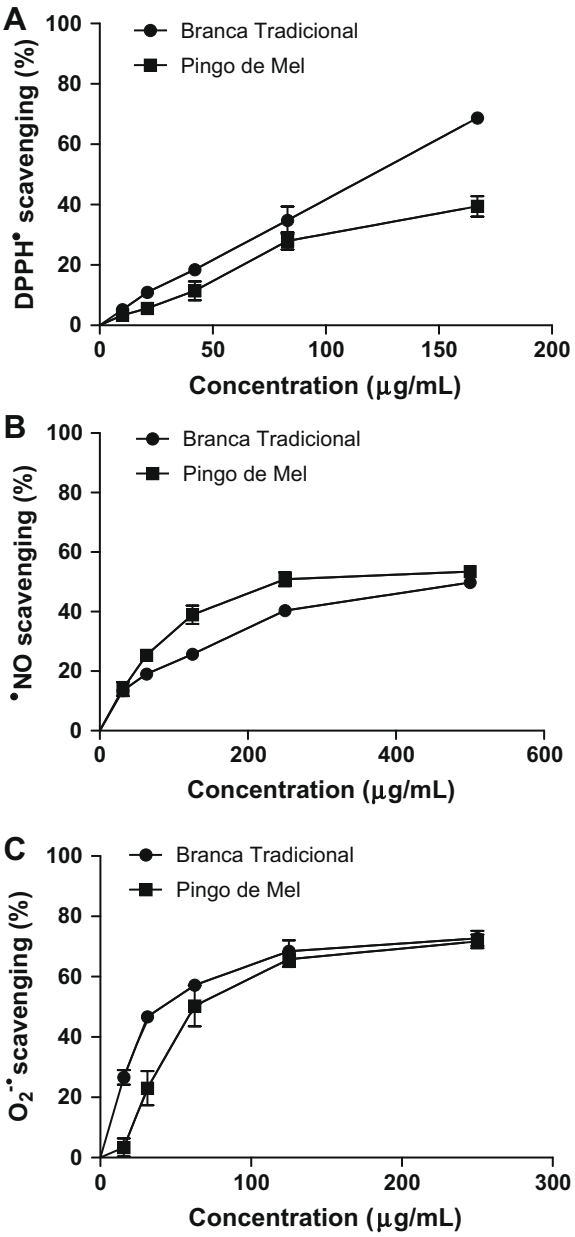

Fig. 3. Effects of *Ficus carica* leaves varieties Branca Tradicional and Pingo de Mel aqueous lyophilized extracts against: (A) DPPH, (B) nitric oxide and, (C) superoxide radical. Values show mean ± SE from three experiments performed in triplicate.

Table 2
Organic acids of Portuguese *Ficus carica* L. varieties (mg/kg lyophilized extract).[a]

Organic acids	Pingo de mel			Branca Tradicional		
	Peel	Pulp	Leaves	Peel	Pulp	Leaves
Oxalic	155.5 ± 4.8	79.4 ± 1.1	2406.1 ± 16.3	nq	nq	983.4 ± 58.8
Citric	nq	2280.3 ± 80.5	nq	2002.5 ± 216.9	2663.2 ± 58.6	nq
Malic	8704.1 ± 133.3	6851.2 ± 109.9	24171.1 ± 1106.5	3648.4 ± 212.5	5442.9 ± 224.2	7684.4 ± 167.8
Quinic	–	–	10502.5 ± 97.1	–	–	5183.3 ± 116.5
Shikimic	142.2 ± 2.3	80.7 ± 0.1	99.1 ± 0.5	158.1 ± 8.7	136.0 ± 5.2	nq
Fumaric	23.0 ± 0.4	24.2 ± 4.0	81.1 ± 3.9	31.4 ± 4.2	58.3 ± 1.0	nq
∑	9024.9	9315.8	37260.0	5840.4	8300.3	13851.1

[a] Values are expressed as mean ± standard deviation of three assays; nq, not quantified; ∑, sum of the determined organic acids.

pound in all samples, excepting in the peel of Pingo de Mel variety (Table 1).

Psoralen occurred in pulps at significantly higher levels when compared with peels. Psoralen and bergapten (5-methoxypsoralen) are two photoactive furanocoumarins already reported in *F. carica* leaves (Teixeira et al., 2006). These compounds, especially psoralen, are utilized in association with UV radiation in the treatment of skin conditions, such as skin depigmentation (psoriasis and vitiligo), mycosis fungoides, polymorphous dermatitis, and eczema (Baumgart et al., 2005; Kulkosky and Diawara, 2003).

3.2. Organic acids

Organic acids profile of fig leaves is composed by six organic acids: oxalic, citric, malic, quinic, shikimic and fumaric acids (Fig. 2). In pulps and peels quinic acid was absent (Table 2). As far as we know, quinic and shikimic acids are reported for the first time in *F. carica*. The other compounds were already reported in fig juice (Shiraishi et al., 1996).

As it happened for phenolics, leaves are characterized by higher quantities of organic acids than the other materials. Peels exhibited the lowest contents (Table 2). This may be explained by the fact that leaves proctect fruits from UV radiation and they have an important role in the photosynthesis process: they are able to convert light energy in chemical energy (glucose and ATP) by scavenging CO_2 and producing O_2. After this, glucose can be used in the synthesis of various metabolites, including organic acids, amino acids, polysaccharides, phenolic compounds, among others, according to plant needs (Oliveira et al., 2008).

Malic acid was the main compound in all matrices, representing 56–96% of the total organic acids content. In pulps and peels it was followed by citric acid (24–34%), excepting Pingo de Mel peel, in which it was present in vestigial amounts (Table 2). Quinic acid was detected only in leaves samples, being the second organic acid (28–37%). Thus, this compound may be useful as chemical marker for fig leaves. Oxalic, shikimic and fumaric acids were present in lower quantities.

Pingo de Mel was the variety with higher organic acids contents (Table 2).

3.3. Antioxidant activity

Pulps, peels and leaves extracts exhibited DPPH scavenging capacity, in a concentration-dependent way (Figs. 3A, 4A and 5A), being the leaves the most effective material (Table 3). The different samples also revealed to have nitric oxide scavenging ability, being the effect concentration-dependent (Figs. 3B, 4B and 5B). As it happened for DPPH, leaves showed the strongest capacity (Table 3). In what concerns to superoxide anion, leaves were the only material displaying a protective effect (Fig. 3C).

Overall, the results obtained in the three assays revealed that leaves possess the strongest antioxidant potential and pulps the weakest one (Table 3). These facts may be partially explained by the highest amounts of phenolic compounds occurring in leaves. In a general way, Branca Tradicional was the variety with stronger ability to scavenge free radicals (Table 3), which can be related with the highest flavonoids relative content comparing with the leaves of Pingo de Mel variety. The antioxidant capacity of phenolic compounds is based on their ability to scavenge free radicals, chelate pro-oxidant metal-ions and to inhibit some enzymes (Silva et al., 2004; Halliwell et al., 2000). Nevertheless, the contribution of organic acids cannot be ignored.

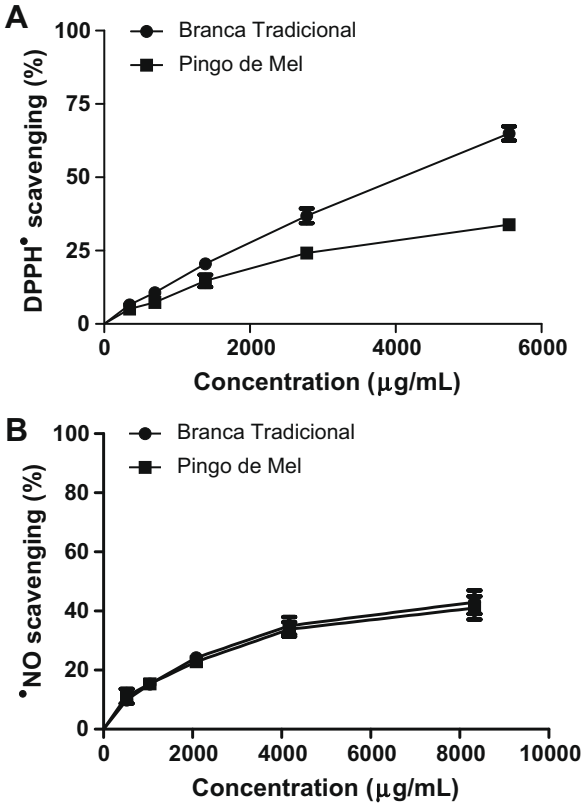

Fig. 4. Effects of *Ficus carica* peel varieties Branca Tradicional and Pingo de Mel aqueous lyophilized extracts against: (A) DPPH and, (B) nitric oxide. Values show mean ± SE from three experiments performed in triplicate.

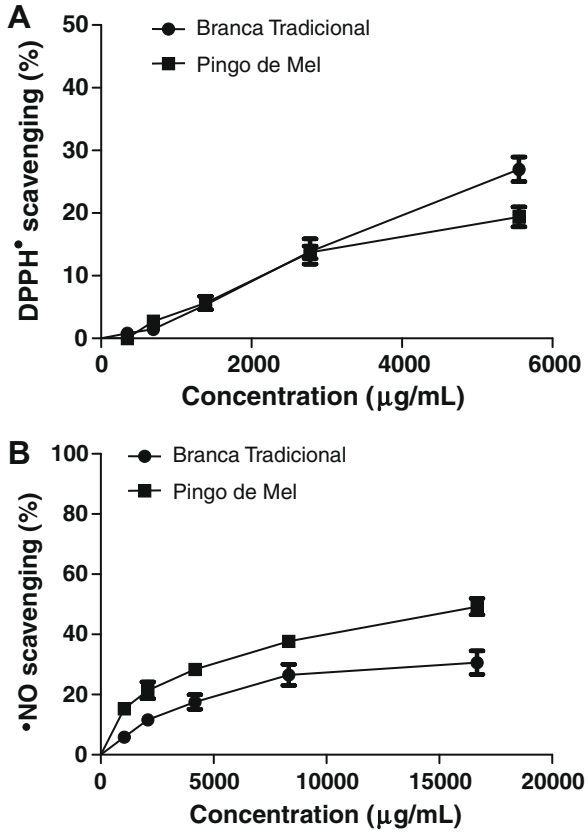

Fig. 5. Effects of *Ficus carica* pulp varieties Branca Tradicional and Pingo de Mel aqueous lyophilized extracts against: (A) DPPH and, (B) nitric oxide. Values show mean ± SE from three experiments performed in triplicate.

Table 3
IC_{25} values obtained in antioxidant activity assays (μg/mL).

	Pingo de Mel			Branca Tradicional		
	Peel	Pulp	Leaves	Peel	Pulp	Leaves
DPPH·	2948.7	>5556	75.2	1724.3	4056.4	59.6
·NO	2425.5	3154.8	63.2	2195.7	7623.2	118.5
O_2^{-}	–	–	33.0	–	–	<15.6

3.4. Acetylcholinesterase inhibitory activity

The acetylcholinesterase inhibitory activity is, usually, the first of a number of requirements for the development of medicines for treating some neurological disorders, such as Alzheimer's disease (Pereira et al., 2009). These compounds are recently used in ophthalmology for the treatment of glaucoma and for the treatment of myasthenia gravis (Houghton et al., 2006).

According to Houghton et al. (2006), compounds like alkaloids, flavonoids, terpenoids, furano- and isocoumarins have the capacity to inhibit this enzyme. Although, our samples presented high quantities of flavonoids, namely quercetin 3-*O*-rutinoside, and furanocoumarins (psoralen and bergapten), they had no effect on acetylcholinesterase, in the tested concentrations. May be the lack of acethylcholinesterase inhibition might be related with the chemical structure of the identified compounds (Brühlmann et al., 2004). In addition, also the interactions between phenolics and other compounds present in the tested aqueous extract, namely antagonisms, may result in the absence of activity. Carbachol, tested as positive control under the same conditions, exhibited a IC_{50} of 81 μg/mL.

3.5. Antimicrobial activity

None of the aqueous lyophilized extracts of *F. carica* materials produced an inhibition zone against the assayed bacterial species; therefore, no antimicrobial activity was found.

4. Conclusion

This is the first study comparing *F. carica* leaves, pulps and peels. Data obtained indicate that chemical composition and bioactivity are dependent on the variety. 3-*O*-Caffeoylquinic acid and quercetin 3-*O*-glucoside were described for the first time, which adds to the knowledge of this species. Leaves may constitute an excellent dietary and economical source of bioactive compounds, namely, phenolics. The consumption of this fruit may contribute to the prevention of diseases in which homeostasis is impaired by oxidative features. In addition, as leaves are characterized by higher quantities of psoralen and bergapten their use by cosmetic and pharmaceutical industries for the treatment of some dermatologic diseases, such as psoriasis and vitiligo, may deserve to be explored.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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