Journal of Ethnopharmacology 139 (2012) 228–233

Contents lists available at SciVerse ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Antioxidant and anti-inflammatory properties of *Capsicum baccatum*: From traditional use to scientific approach

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ARTICLE INFO

Article history:
Received 27 July 2011
Received in revised form 29 October 2011
Accepted 2 November 2011
Available online 9 November 2011

Keywords:
Capsicum baccatum
Antioxidant
Anti-inflammatory
Capsaicinoids
Phenolic compounds

ABSTRACT

Ethnopharmacological relevance: Peppers from *Capsicum* species (Solanaceae) are native to Central and South America, and are commonly used as food and also for a broad variety of medicinal applications.
Aim of the study: The red pepper *Capsicum baccatum* var. *pendulum* is widely consumed in Brazil, but there are few reports in the literature of studies on its chemical composition and biological properties. In this study the antioxidant and anti-inflammatory activities of *Capsicum baccatum* were evaluated and the total phenolic compounds and flavonoid contents were determined.
Materials and methods: The antioxidant property was assayed by scavenging abilities using DPPH and the anti-inflammatory activity was tested through the carrageenan-induced pleurisy model in mice. The total phenolic compounds and flavonoid contents were determined spectrophotometrically.
Results: The ethanolic and butanol extracts (200 mg/kg, p.o.) presented a significant anti-inflammatory activity toward carrageenan-induced pleurisy model in mice in comparison to dexamethasone (0.5 mg/kg, s.c.). Among the parameters evaluated, the treatment with these samples inhibited leukocyte migration and reduced the formation of exudate. The contents of flavonoids and total phenolic compounds could be correlated with the antioxidant and anti-inflammatory activities observed for *Capsicum baccatum*.
Conclusions: Our findings suggest that *Capsicum baccatum* contains potential antioxidant and anti-inflammatory compounds which could be tested as drug candidates against oxidative and inflammation-related pathological processes in medicinal chemistry studies.

1. Introduction

Inflammation and oxidative stress plays an important role in various diseases, such as cancer, rheumatoid arthritis, asthma, diabetes, and cardiovascular and neurodegenerative diseases including atherosclerosis, Alzheimer's disease, and other age-related degenerative disorders, which show a high prevalence worldwide. In the past few years, there has been a renewed interest in studying and quantifying the antioxidant and anti-inflammatory constituents of plants in terms of their potential health functionality through action against these various pathological processes (Menichini et al., 2009; Mueller et al., 2010).

The genus *Capsicum* comprises more than 200 varieties, and the fruits vary widely in size, shape, flavor and sensory heat. Five main species are cited in literature: *Capsicum annuum*, *Capsicum baccatum*, *Capsicum chinense*, *Capsicum frutescens* and *Capsicum pubescens*. Peppers from *Capsicum* species are native to the tropical and humid zones of Central and South America and belong to the Solanaceae family, which includes peppers of important economic value (Govindarajan, 1986; Menichini et al., 2009). They are commonly used as a spice or food and also for a broad variety of therapeutic applications in Indian, Native American and Chinese medicinal traditions for the treatment of arthritis, rheumatism, stomach ache, skin rashes, dog/snake bite and wounds (Meghvansi et al., 2010).

Capsicum annuum, *Capsicum chinense* and *Capsicum frutescens* have a wide array of phytochemicals with well-known antioxidant properties (Hervert-Hernandez et al., 2010) such as carotenoids (Deli et al., 2001), capsaicinoids (Kirschbaum-Titze et al., 2002;

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0378-8741
doi:10.1016/j.jep.2011.11.005

Rosa et al., 2002; Ochi et al., 2003; Pino et al., 2007), and phenolic compounds particularly flavonoids, quercetin and luteolin (Howard et al., 2000; Marin et al., 2004; Materska and Perucka, 2005; Kappel et al., 2008). Capsaicin, the main representative of the pungent components, is a lipophilic alkaloid and because of its analgesic and anti-inflammatory activity has been used in clinical practice (The Capsaicin Study, 1991).

Capsicum annuum showed hypocholesterolemic properties in animal assays (Srinivasan, 2005; Aizawa and Inakuma, 2009). Recent studies demonstrated that hyperlipidemia, inflammation and oxidative stress are closely linked to the pathogenesis of atherosclerosis and, consequently, to the increased risk of cardiovascular diseases (Libby, 2002; Arroyo and Iruela-Arispe, 2010). Thus, an agent that has antioxidant and anti-inflammatory activities will be useful in the prevention of these pathologies. The red pepper *Capsicum baccatum* var. *pendulum* is widely consumed in Brazil, and the few reports found in the literature focus on its carotenoid and capsaicinoid compositions and the antioxidant activity of its crude juice (Kappel et al., 2008; Rodriguez-Burruezo et al., 2010; Kollmannsberger et al., 2011). In a preliminary study about the anti-inflammatory activity, Spiller et al. (2008) assayed a crude extract of *Capsicum baccatum* via i.p. and s.c. in rodents at doses of 0.2, 2 and 20 g/kg. The latter two doses presented activity.

In the present study, *Capsicum baccatum* was fractionated to obtain an enriched bioactive extract with the aim of identifying the compounds responsible for the antioxidant and anti-inflammatory activities. In addition, we measured the content of total phenolic compounds and flavonoids, and the presence of capsaicin in the extracts in order to correlate them with the assayed activities.

2. Materials and methods

2.1. Chemicals and solvents

The following reagents were purchased from Sigma–Aldrich Chemicals Company (St. Louis, MO): gallic acid, quercetin, rutin, capsaicin, ascorbic acid, carrageenan, dexamethasone, Folin-Ciocalteau reagent, 1,1-diphenyl-2-picrylhydrazyl (DPPH). Heparin (Liquemine®), isoflurane (Forane®) and Evans blue dye were obtained from Roche (Brazil), Abbot (Brazil) and Merck (Germany), respectively. Acetonitrile and methanol HPLC grade were obtained from Merck (Darmstat, Germany) and water was purified in a Millipore Milli-Q system (Bedford, MA).

2.2. Plant material and extract preparation

Capsicum baccatum var. *pendulum* (Willd.) Eshbaugh (Solanaceae) fruit was obtained from a cultivated area in Turuçu, Rio Grande do Sul, Brazil. A voucher specimen (number P278) was identified and deposited at the Herbarium of the Brazilian Government Research Institute EMBRAPA (Empresa Brasileira de Pesquisa Agropecuária, Pelotas, RS, Brazil). The seeds were removed from a fresh fruit sample. The fruit without seeds and the seeds were left to dry, separately, in a circulating air oven (40 °C) for seven days and then triturated to powders. To obtain the ethanolic extract the plant material (1 kg of fruits or 0.2 kg of seeds) was extracted with 70% ethanol (plant:solvent, 1:10, w/v) under reflux for 4 h. The fruit and seeds of *Capsicum baccatum* (5 kg of fruits or 1 kg of seeds) were also submitted, separately, to successive extractions in a soxhlet apparatus using dichloromethane, *n*-butanol and water until complete exhaustion, in order to obtain the dichloromethane, butanol and aqueous extracts, respectively. The organic solvents were evaporated under reduced pressure to dryness and, the aqueous extract was lyophilized, to obtain the respective residues from fruit and seeds named CE (crude ethanol extract), DCM (dichloromethane extract), BUT (butanol extract) and RAq (residual aqueous extract).

2.3. Determination of total phenolic compounds and flavonoid content

The total phenolic content in the extracts obtained from *Capsicum baccatum* fruit and seeds were estimated using the Folin-Ciocalteau method described by Singleton et al. (1999), customized for 96-well microplates. Samples were prepared in a concentration of 1.0 mg/ml dissolved in methanol. Gallic acid was used for the calibration curve in concentrations ranging from 10.0 to 100.0 μg/ml for which the regression equation was $y = 0.0098x + 0.1418$ ($R = 0.9967$). Thirty microliters of samples were added to 50 μl of 1.0 mol/l Folin-Ciocalteau reagent and mixed with 100 μl of sodium carbonate (Na_2CO_3) 7.5% after 10 min. Absorbance at 760 nm was read after 2 h of incubation at room temperature in a Spectramax® M5 (Molecular Devices, USA). Results were expressed as milligrams of gallic acid equivalents (GAE) per gram of sample (dry weight). The experiment was conducted in triplicate.

The aluminum chloride colorimetric method described by Chang et al. (2002), adapted for 96-well microplates, was used to determine the total content of flavonoids. Samples were prepared in a concentration of 1.0 mg/ml, whereas quercetin solutions were prepared ranging from 10.0 to 100.0 μg/ml for which the regression equation was $y = 0.0069x - 0.0132$ ($R = 0.9956$). Sixty microliters of samples were diluted with 60 μl of methanol, and 6 μl of 10% aluminum chloride, 6 μl of 1 mol/l potassium acetate, and 130 μl of distilled water were added. The absorbance at 415 nm was determined after 30 min. Results were expressed as milligrams of quercetin equivalents (QE) per gram of sample (dry weight). The experiment was conducted in triplicate.

2.4. HPLC analysis of Capsicum baccatum extracts

The characterization of the phenolic compounds (quercetin and rutin) and capsaicin in *Capsicum baccatum* was performed by HPLC with an Agilent Instrument (series 1200), equipped with a photodiode array detector (G1322A), autosampler (G1329A), and Agilent ChemStation software. Chromatographic separation was performed on an Ace® RP-18 column (250 mm × 4.0 mm i.d., particle size 5 μm). A linear gradient was run starting from 15:15:70 methanol:acetonitrile:water and changing to 30:30:40 methanol:acetonitrile:water over 19 min. This composition was held for a further 6 min in isocratic mode. The temperature was set at 30 °C in the column oven. The flow rate was 1.2 ml/min, the injection volume was 25 μl and the run time was 25 min. The presence of phenolic compounds and capsaicin were determined by comparison of the retention time and UV spectra of samples and standards. Capsaicin was determined at 280 nm and rutin and quercetin at 254 nm. All standards (rutin, quercetin and capsaicin) were dissolved in methanol:water (1:1, v/v) to obtain 50 μg/ml. The experiment was conducted in triplicate.

2.5. Antioxidant assay

The free radical scavenging capacity of the standards and samples were determined using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) method (Brand-Williams et al., 1995). Sample solutions of 100–400 μg/ml were prepared in methanol and a 0.5 ml aliquot was then added to a tube containing 1.5 ml of DPPH solution (150 μM). The reaction mixtures were kept in the dark for 60 min. The absorbance was measured using a Perkin–Elmer Lambda 40 UV/vis spectrophotometer at 517 nm. A DPPH solution (1.5 ml) and methanol (0.5 ml) were used as the negative control. Ascorbic acid, quercetin and capsaicin were used in five concentrations (100 to

400 μg/ml) in methanol to obtain the calibration curves. All tests were run in triplicate and the mean values calculated. The antioxidant activity (AA) was expressed according to the ability of an extract to scavenge DPPH free radicals and was determined using the following equation:

$$\%AA = [1 - (A_1 - A_2)/A_0)] \times 100$$

where % AA is the antioxidant activity, A_0 the absorbance of the negative control (original DPPH solution without sample), A_1 the absorbance of the test sample (DPPH solution in the presence of sample), and A_2 the absorbance of the sample without DPPH.

The EC_{50}, which is the concentration (in μg/ml) of samples or standards necessary to reduce the absorbance of DPPH by 50% compared to the negative control, is typically employed to express the antioxidant activity and to compare it with that of other samples. The EC_{50} was determined by interpolation from linear regression analysis of the antioxidant activity (%AA) against sample concentration (μg/ml) and the EC_{50} value decreases as a function of increasing antioxidant activity of samples. Results were also expressed as AEAC (ascorbic acid equivalent antioxidant capacity) in grams and calculated as follows:

$$\text{AEAC (g)} = \frac{EC_{50\ \text{(ascorbic acid)}}}{EC_{50\ \text{(sample)}}} \times 1\ \text{g}$$

2.6. Animals and anti-inflammatory activity

Non-fasted 1-month-old adult Swiss mice of both sexes (20–25 g) were used (n = 6–8). The animals were maintained in a controlled environment at 22 ± 2 °C and 55 ± 10% humidity with 12 h light–dark cycle. All the animals were allowed free access to tap water and standard animal feed. This study was carried out in accordance with the international standards of animal protection and with the ethical principles of the Brazilian College of Animal Experimentation, and was approved by the Ethics Committee on Animal Use (CEUA) of the Pontificia Catholic University of Rio Grande do Sul (PUCRS, Brazil, protocol 10/00159). The anti-inflammatory activity was tested through the experimental model of carrageenan-induced pleurisy according to Saleh et al. (1996). Twenty-four hours prior to the experiments, the animals were challenged with a solution of Evans blue dye (25.0 mg/kg, 0.2 ml, i.v.) in order to evaluate the degree of exudation in the pleural space. On the following day, animals were anaesthetized with isoflurane, and 0.1 ml of carrageenan (1%) was injected into the right pleural space. After 4 h, the animals were sacrificed using isoflurane. The chest was then carefully opened and the pleural cavity was rinsed with 1 ml of saline solution containing 1% EDTA. The exudate and rinse solution were removed by aspiration of the total volume. Exudates containing blood were discarded. Total leukocyte counts were performed in Neubauer chambers by means of an optical microscope after diluting the pleural fluid with Thoma solution (1:20). A sample of the fluid collected from the pleural space was separated and stored at −20 °C until the determination of Evans blue dye concentration by colorimetry on a Spectramax® M5 (Molecular Devices, USA) at 600 nm and interpolation of the standard curve using Evans blue in the range of 0.78–25.00 μg/ml. In the animals of the treated groups, all samples of *Capsicum baccatum* tested were administered orally (200 mg/kg) 1 h before the inflammatory stimulus. In the inflammation group (CG), saline solution was administered orally 1 h before the intrapleural (i.pl.) injection of carrageenan. In the control group (SAL), saline solution was administered orally 1 h before the i.pl. injection of saline. The ethanolic and the residual aqueous extracts were solubilized in saline (NaCl 0.9%). The dichloromethane and butanol extracts were solubilized with 1.0% of dimethyl sulfoxide (DMSO) in saline. Dexamethasone in saline (DEXA, 0.5 mg/kg, s.c., 2 h before inflammatory stimulus) was used as a positive control.

2.7. Statistical analysis

Results were expressed as mean ± SEM. Statistical analysis was performed by one-way analysis of variance (ANOVA) followed by the Bonferroni's test for multiple comparisons. Differences were considered significant at $P < 0.05$.

3. Results

Initially, yields of the extracts obtained from the fruit and seeds of *Capsicum baccatum* were evaluated. One gram of dried red pepper fruit produced 0.109 g of dried ethanolic extract, 0.074 g of dichloromethane extract, 0.163 g of butanol extract and 0.136 g of residual aqueous extract. In relation to the seeds, 1 g of dried red pepper seeds produced 0.095 g of dried ethanolic extract, 0.057 g of dichloromethane extract, 0.015 g of butanol extract and 0.032 g of residual aqueous extract.

3.1. Phenolic analysis

The samples investigated were analyzed for total phenolic compounds and flavonoid contents, compounds which are largely responsible for the antioxidant activity of plant extracts (Havsteen, 2002; Materska and Perucka, 2005). Total phenolic content was quantified using the Folin-Ciocalteau reagent, which is a widely used method for estimating total phenolic compounds. The results of the total phenolic content of *Capsicum baccatum* ranged from 149.28 to 187.51 mg of GAE/g (dry weight) for fruit extracts, and 53.97 to 223.38 mg of GAE/g (dry weight) for seed extracts (Table 1). The crude ethanol extract of seeds presented the highest total phenolic content among all samples tested, and the respective dichloromethane extract presented the lowest. Regarding the total flavonoid content (Table 1), the highest amount was found in the dichloromethane extract of the fruit.

3.2. Antioxidant activities

To calculate the EC_{50} in relation to the DPPH assay, the curves for each standard and the samples of *Capsicum baccatum* were calculated using five data points in the range of 100–400 μg/ml (Fig. 1). These curves were linear and resulted in a correlation coefficient (r) > 0.98 (Table 2). The antioxidant activities (AEAC) of the extracts of *Capsicum baccatum* showed a wide range, from 0.071

Table 1
The total flavonoid and phenolic contents, and presence of capsaicin in extracts of the fruit and seeds of *Capsicum baccatum*.

Samples	Total flavonoid content (mg QE/g extract)	Total phenolic content (mg GAE/g extract)	Capsaicin[a]
Fruit			
Ethanol	34.36 ± 4.04c	180.08 ± 3.76b	+
Dichloromethane	102.48 ± 6.38a	149.28 ± 2.46c	+
Butanol	54.68 ± 2.92b	187.51 ± 2.34b	–
Residual aqueous	20.80 ± 1.56d	186.00 ± 6.82b	–
Seeds			
Ethanol	20.21 ± 0.38d	223.38 ± 4.64a	+
Dichloromethane	18.28 ± 8.80d	53.97 ± 8.15e	+
Butanol	26.21 ± 3.29d	75.77 ± 14.64d	+
Residual aqueous	21.81 ± 4.82d	70.29 ± 21.01d	–

Values are expressed as mean ± SEM (n = 3); means in the same column followed by different letters are significantly different at $P < 0.05$ using Tukey's multiple range tests. *Abbreviation*: QE, quercetin equivalents; GAE, gallic acid equivalents.

[a] +, capsaicin was detected; –, capsaicin was not detected at 50 μg/ml.

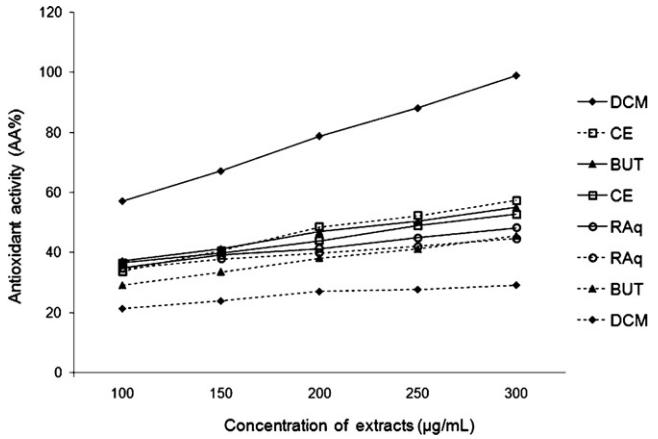

Fig. 1. Dose-dependent antioxidant activity of extracts of *Capsicum baccatum* fruit (––) and seeds (––) evaluated *in vitro* using the DPPH assay. The experiment was conducted in triplicate. CE, crude ethanolic extract; DCM, dichloromethane extract; BUT, butanol extract; RAq, residual aqueous extract.

to 0.006 μg g^{-1} (Table 2). The dichloromethane extract of the fruit exhibited the greatest free radical scavenging activity, followed by the crude ethanolic extract of seeds and the butanol extract of the fruit in a dose-dependent manner (Table 2 and Fig. 1). The dichloromethane extract of the seeds presented the lowest antioxidant capacity among samples (Table 2). The greatest antioxidant activity of the standards was observed for ascorbic acid, followed by quercetin, and capsaicin.

3.3. HPLC analysis

HPLC analysis detected capsaicin (R_t = 14.20 min) in all samples obtained from the seeds of *Capsicum baccatum*, except in the aqueous extract (Fig. 2B). In relation to the fruit, only the ethanolic and dichloromethane extracts contained capsaicin (Fig. 2A). The flavonoids quercetin and rutin were not identified in any of the samples obtained from *Capsicum baccatum* (Fig. 2C and D).

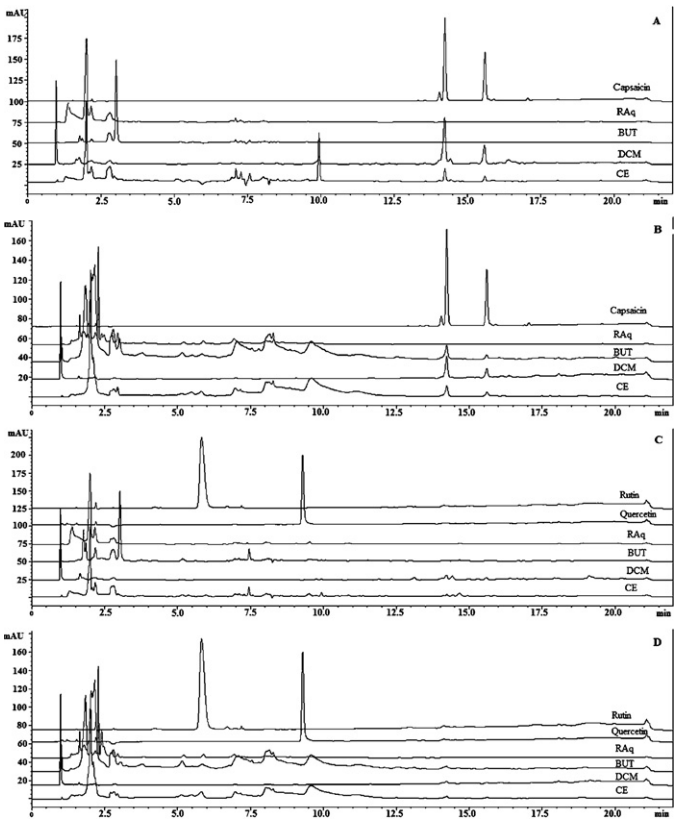

Fig. 2. HPLC chromatograms of samples from *Capsicum baccatum* fruit and seeds at the concentration of 50 μg/ml. Detection was at 280 nm to capsaicin (R_t = 14.20 min; A and B), and 254 nm to rutin and quercetin (R_t = 5.80 and 9.26 min, respectively; C and D). CE, crude ethanolic extract; DCM, dichloromethane extract; BUT, butanol extract; RAq, residual aqueous extract. The *y*-axis represents mAU and *x*-axis represents time (min).

3.4. Anti-inflammatory activities

The number of total leukocytes in the exudate in the inflammation group (CG) was significantly higher when compared to the number of cells collected from the pleural space of the negative control group (SAL). Treatment with the butanol (BUT) and the crude ethanolic (CE) extracts of the fruit of *Capsicum baccatum* showed an anti-inflammatory effect on carrageenan-induced mice pleurisy considering that the total cell number of the pleural exudate was significantly attenuated (reductions of 45% and 41%, respectively; Fig. 3). There was also a significant reduction in the protein level in the groups pre-treated with the butanol (BUT) and the crude ethanolic (CE) extracts of the fruit of *Capsicum baccatum* (reductions of 45 and 48%, respectively; Fig. 4). These later samples (BUT and CE) of fruit showed similar anti-inflammatory action when compared to dexamethasone ($P < 0.05$).

Table 2
Data used to calculate the EC_{50} in DPPH assay of extracts obtained from *Capsicum baccatum*.

Samples	Slope[a]	Intercept[a]	r^2	EC_{50} (μg/ml)	AEAC (μg g^{-1})
Ascorbic acid	5.0434	26.398	0.9997	4.68 ± 0.58a	1a
Quercetin	1.7794	23.473	0.9980	14.91 ± 2.74b	0.31 ± 0.09b
Capsaicin	0.8488	35.042	0.9870	17.62 ± 1.84b	0.27 ± 0.03b
Fruit					
Ethanol	0.0827	27.871	0.9950	267.58 ± 29.08d	0.017 ± 0.002d
Dichloromethane	0.2098	36.11	0.9991	66.21 ± 8.50c	0.071 ± 0.010c
Butanol	0.0898	28.301	0.9960	241.64 ± 26.12d	0.019 ± 0.002d
Residual aqueous	0.0651	28.688	0.9933	327.37 ± 35.26d,e	0.014 ± 0.001d,e
Seeds					
Ethanol extract	0.1168	23.169	0.9956	229.72 ± 32.83d	0.020 ± 0.004d
Dichloromethane	0.0390	18.032	0.9879	819.67 ± 86.78f	0.006 ± 0.001f
Butanol	0.0756	22.253	0.9964	367.02 ± 50.12d,e	0.013 ± 0.002d,e
Residual aqueous	0.0485	30.152	0.9943	409.24 ± 37.05e	0.011 ± 0.001e

Values are expressed as mean ± SEM (n = 3); means in the same column followed by different letters are significantly different at $P < 0.05$ using Tukey's multiple range tests.
Abbreviation: AEAC, ascorbic acid equivalent antioxidant capacity.
[a] Linear range (μg/ml): ascorbic acid = 1.56–12.5; quercetin = 1.25–20.0; capsaicin = 8.3–50.0; extracts of samples of fruit and seeds = 100–400.

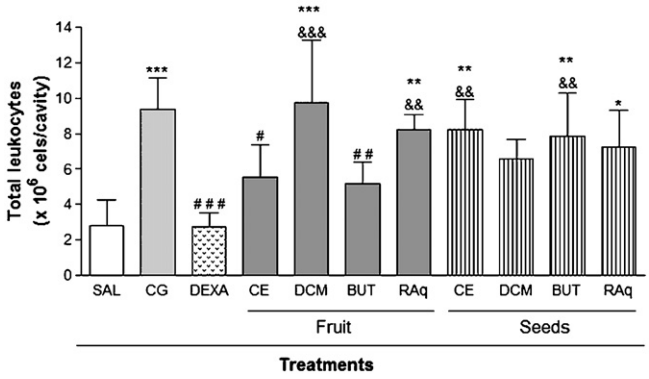

Fig. 3. Effects of the extracts of the fruit and seeds of *Capsicum baccatum* (200 mg/kg, *per os*) upon total leukocytes in the pleural cavity in carrageenan-induced pleurisy in mice. SAL, saline; CG, carrageenan; DEXA, dexamethasone; CE, crude ethanolic extract; DCM, dichloromethane extract; BUT, butanol extract; RAq, residual aqueous extract. The experiment was conducted in triplicate. Statistical differences determined by ANOVA followed the Bonferroni's test. Data are expressed as mean ± SD. $^{***}P < 0.001$, $^{**}P < 0.01$, $^{*}P < 0.05$ when compared to SAL group; $^{###}P < 0.001$, $^{##}P < 0.01$, $^{#}P < 0.05$ when compared to CG group; $^{\&\&\&}P < 0.001$, $^{\&\&}P < 0.01$, $^{\&}P < 0.05$ when compared to DEXA.

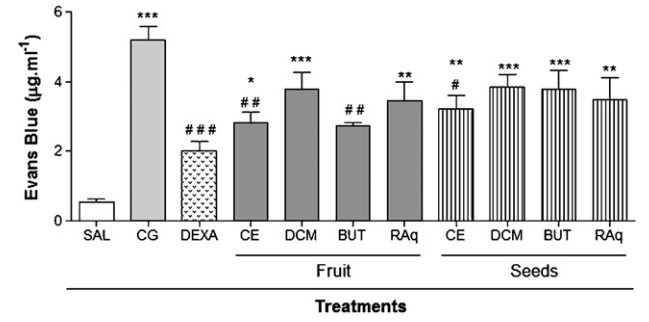

Fig. 4. Effects of *Capsicum baccatum* extracts of the fruit and seeds (200 mg/kg, *per os*) on plasmatic exudation (Evans blue content) in the pleural cavity in carrageenan-induced pleurisy in mice. SAL, saline, negative control; CG, carrageenan, inflammation group; DEXA, dexamethasone; CE, crude ethanolic extract; DCM, dichloromethane extract; BUT, butanol extract; RAq, residual aqueous extract. The experiment was conducted in triplicate. Statistical differences determined by ANOVA followed the Bonferroni's test. Data are expressed as mean ± SD. $^{***}P < 0.001$, $^{**}P < 0.01$, $^{*}P < 0.05$ when compared to SAL group; $^{###}P < 0.001$, $^{##}P < 0.01$, $^{#}P < 0.05$ when compared to CG group.

4. Discussion

The ethanolic and butanol extracts of *Capsicum baccatum* presented a significant anti-inflammatory activity toward carrageenan-induced pleurisy model in mice. The contents of flavonoids and total phenolic compounds could be correlated with the antioxidant and anti-inflammatory activities observed for *Capsicum baccatum*.

The phenolic and flavonoid contents determined in *Capsicum baccatum* samples were higher than values for other *Capsicum* species reported in the literature (Howard et al., 2000; Marin et al., 2004; Menichini et al., 2009; Hervert-Hernandez et al., 2010). These differences can be attributed to the botanical variety, plant maturity, extraction and analytical methods, and geographic origin of the plants. The dichloromethane extract of the fruit, which showed the highest antioxidant activity, presented the highest content of flavonoids. The dichloromethane extract of the seeds presented the lowest phenolic compounds and flavonoid contents, and correspondingly the lowest antioxidant capacity among samples. The fruit of *Capsicum baccatum* presented higher flavonoid and phenolic contents than the seeds, and these contents could be correlated with the DPPH antioxidant activity. The dichloromethane extract of the fruit had the highest amount of capsaicin. Considering that capsaicin showed high antioxidant activity in the DPPH assay, it could be inferred that capsaicin contributed significantly to the higher antioxidant effect of the dichloromethane extract of the fruit (Table 2).

The injection of carrageenan into the pleural cavity of mice elicited an acute inflammatory response characterized by the accumulation of fluid (edema) with a large amount of polymorphonuclear leukocytes (PMNs). During acute inflammation serum proteins and leukocytes migrate to areas of tissue injury. The recruitment of cells to inflammatory sites is dependent on the release of vasoactive and chemotactic factors that increase regional blood flow and microvascular permeability and promote the migration of leukocytes from the intravascular space into the tissues (Suffredini et al., 1999). Considering a reduction in cell migration, both samples of the fruit (BUT and CE) showed significant differences to the inflammation group (CG) and did not differ from the negative control group (SAL) and the group treated with dexamethasone (DEXA). However, considering the degree of plasma exudation, both extracts significantly differed from the inflammation group (CG), but only the butanol extract of the fruit did not differ from the control group (SAL) and the group treated with dexamethasone (DEXA). This result indicates that the butanol extract of the fruit was more efficient than the ethanolic extract of fruit in the reduction of exudation. This effect could be assigned to the presence of flavonoids and phenolic compounds in the butanol extract which have a pronounced antioxidant activity and can modulate several enzymes and cell receptors. In addition, some flavonoids inhibit phosphodiesterases involved in specific cell activation (Havsteen, 2002).

Several fruits, vegetables and their compounds, such as polyphenols, ascorbic acid and capsaicinoids, have been found to inhibit the inflammation process in experimental animals, and are considered to be potential candidate drugs against the inflammation-related pathological processes (Calixto et al., 2003). *Capsicum baccatum* is the most consumed pepper in Brazil and phenolic compounds, capsaicinoids and ascorbic acid were significantly greater in the *Capsicum baccatum* fruit compared to other peppers species such as *Capsicum annuum* or *Capsicum frutescens* (Howard et al., 2000; Antonious et al., 2006; Hervert-Hernandez et al., 2010). These compounds present in red pepper exhibit anti-inflammatory or antioxidant properties (Surh, 2002).

An important mechanism in inflammation is the recruitment of macrophages and the released of interleukins, such as IL-1 which induces the expression of the COXgene. Flavonoids can inhibit the production of eicosanoids, formed from arachidonic acid by a series of enzymes, particularly PG COX, having also an important effect on the intricate regulatory processes of cardiovascular diseases and markedly improving the condition of patients suffering from these progressive illnesses (Havsteen, 2002). The results of many anti-inflammatory experiments involving *Capsicum* species extracts, including *Capsicum baccatum*, have suggested, but not proved, that capsaicin might be the major compound responsible for the observed anti-inflammatory effects (Surh, 2002; Spiller et al., 2008; Mueller et al., 2010). Several authors have demonstrated that capsaicin has anti-inflammatory properties, such as the inhibition of the production of pro-inflammatory mediators as IL-6, TNF-α, PGE2 and nitric oxide (Surh, 2002; Kim et al., 2003; Liu and Nair, 2010). However, the results reported herein demonstrate that the butanol extract obtained from *Capsicum baccatum* fruit, which did not show detectable amounts of capsaicin (Fig. 2A), was the most active extract in the experimental model of pleurisy in mice. Moreover, the sample richest in capsaicin, the dichloromethane extract of the fruit showed no anti-inflammatory effect. Thus, there are other compounds present in the *Capsicum baccatum* fruit that have potent anti-inflammatory activity in addition to capsaicinoids.

The present study demonstrated that the butanol extract obtained from the fruit of *Capsicum baccatum* presented the best antioxidant and anti-inflammatory activities. In this sense, *Capsicum baccatum* has potential antioxidant and anti-inflammatory compounds which could be used as prototypes in medicinal chemistry studies in order to design new drugs.

Acknowledgements

We would like to thank Dr. Rosa Lía Barbieri from the Brazilian Government Research Institute EMBRAPA (Empresa Brasileira de Pesquisa Agropecuária, Pelotas, RS, Brazil) for the identification of the plant and the Brazilian Government Agency CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico, Brazil) for financial support.

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