Article

Not peer-reviewed version

Spray-Drying Microencapsulation of Phenolic Compounds from *Bauhinia ungulata* L. Var. Obtusifolia Aqueous Extract: A Comparative Study Using Different Wall Materials

Myrth Soares do Nascimento Remigio , Teresa Greco , José-Otávio Carrera Silva-Júnior , Attilio Converti , Roseane Maria Ribeiro-Costa , Alessandra Rossi , Wagner Luiz Ramos Barbosa *

Posted Date: 4 January 2024

doi: 10.20944/preprints202401.0343.v1

Keywords: Phytotherapy; Medicinal plants; Radical scavenger; Phenolic compounds; Medicinal tea

Article

Spray-Drying Microencapsulation of Phenolic Compounds from *Bauhinia ungulata* L. var. *obtusifolia* Aqueous Extract: A Comparative Study Using Different Wall Materials

Myrth Soares do Nascimento Remígio [1], Teresa Greco [2], José Otávio Carréra Silva Júnior [3], Attilio Converti [4], Roseane Maria Ribeiro-Costa [5], Alessandra Rossi [2,*] and Wagner Luiz Ramos Barbosa [1,*]

[1] Laboratory of Chromatography and Mass Spectrometry, Graduate Program in Pharmaceutical Innovation, Institute of Health Sciences, Federal University of Pará, Belém, 66075-110, Pará, Brazil
[2] Food and Drug Department, University of Parma, Parco Area delle Scienze 27/A, 43124, Parma, Italy.
[3] Laboratory of R&D Pharmaceutical and Cosmetic, Graduate Program in Pharmaceutical Innovation, Institute of Health Sciences, Federal University of Pará, Federal University of Pará, Belém, 66075-110, Pará, Brazil.
[4] Department of Civil, Chemical and Environmental Engineering, Pole of Chemical Engineering, University of Genoa, Via Opera Pia 15, I-16145, Genoa, Italy.
[5] Laboratory of Nanotechnology, Graduate Program in Pharmaceutical Innovation, Institute of Health Sciences, Federal University of Pará, Belém, 66075-110, Pará, Brazil
* Correspondence: **authors:** Wagner Luiz Ramos Barbosa. Laboratory of Chromatography and Mass Spectrometry, Graduate Program in Pharmaceutical Innovation, Institute of Health Sciences, Federal University of Pará, 66075-110 Belém, Pará, Brazil; barbosa@ufpa.br

Abstract: Species belonging to the *Bauhinia* genus, usually known as "pata-de-vaca", are popularly used to treat diabetes. Among them is *Bauhinia ungulata* var. *obtusifolia* (Ducke) Vaz, whose leaves are used, as a tea, for medicinal purposes in the Amazon region. The microencapsulation of the aqueous extract of its leaves, containing phenolic compounds, using five different wall materials (maltodextrin: DE11-14, and DE4-7; β-cyclodextrin; pectin, and sodium carboxymethylcellulose) is described in this paper. The microstructure, particle size, thermal behavior, yield, and encapsulation efficiency were investigated and compared using different techniques. Using high-performance liquid chromatography, phenolics, and flavonoids were detected and quantified in the microparticles. Microparticles, obtained with yield and phenolics encapsulation efficiency ranging between 60-83 % and 35-57 %, respectively, showed a particle size distribution between 1.15 and 5.54 μm, spherical morphology, and wrinkled surface. Among them, those prepared with sodium carboxymethylcellulose and pectin proved to be thermally the most stable. They had the highest flavonoid content (23.07 and 21.73 mgRUTE/g Extract) and total antioxidant activity by both the $DPPH^{\cdot}$ (376.55 and 367.86 μmolTrolox/g Extract) and $ABTS^{+}$ (1085.72 and 1062.32 μmolTrolox/ g Extract) assays. The chromatographic analyses allowed for quantification, in the microparticles, chlorogenic acid (1.67-1.98 mg/g Extract), *p*-coumaric acid (0.06-0.08 mg/g Extract), rutin (11.1-12.9 mg/g Extract) and isoquercitrin (0.47-0.53 mg/g Extract), compounds considered responsible for the antidiabetic property attributed to the species.

Keywords: phytotherapy; medicinal plants; radical scavenger; phenolic compounds; medicinal tea

1. INTRODUCTION

Bauhinia ungulata L. var. *obtusifolia* (Ducke) Vaz, vernacular "pata-de-vaca", is a tree from the Leguminosae family, considered endemic to Brazil, whose occurrence has been confirmed in the Brazilian North - Amazonia - and Northeast regions (Vaz and Tozzi, 2003; Tropicos, 2021, Flora do Brasil em Construção, 2019). The leaves, like those of other species of the genus, are empirically used as an infusion to treat diabetes (Van den Berg and Silva, 1988; Scoles, 2006). The chemical constitution and biological activities of this infusion have scarcely been investigated, with only one report

 doi:10.20944/preprints202401.0343.v1

describing its antioxidant activity detected by the DPPH· and β-carotene/linoleic acid radical methods as the likely result of the presence of phenolic compounds (Port's et al. 2013).

Phenolic compounds are considered the main group of substances synthesized by the secondary metabolism of plants (Li et al. 2014). Due to their chemopreventive/protective roles, consumption of these compounds reduces the incidence of many chronic diseases induced by oxidative stress, such as neurodegenerative and cardiovascular diseases, cancer, inflammation, infections, and diabetes. Products rich in polyphenols can modulate carbohydrate and lipid metabolism, attenuate hyperglycemia and dyslipidemia, improve the function of pancreatic β-cells, stimulate insulin secretion, and reduce resistance to this hormone (Rudrapal et al. 2022).

However, phenolic compounds are sensitive to adverse environmental conditions, including light, temperature, pH, moisture, and oxygen, thus being susceptible to degradation during processing and storage (Fang and Bhandari, 2011). In this sense, it is important to protect them to preserve their biological activities and properties. Improving their bioaccessibility and bioavailability, as well as promoting their transport for absorption by the human body, is also of great interest (Escobar-Avello et al. 2021).

To this purpose, various microencapsulation strategies have been introduced, among which spray-drying is one of the most commonly used since it ensures high-quality products besides being a relatively low-cost process (Poomkokrak et al. 2015; Lu et al. 2021). This technique has proven to be an effective method to dry and microencapsulate phenolic compounds rich materials, such as extracts from *Litsea glaucescens*, *Camellia sinensis*, *Prunus salicina*, *Crocus sativus* and *Laurus nobilis*, among others (Medina-Torres et al. 2016; Wang et al. 2016; Li et al. 2018; Ahmadian et al. 2019; Chaumun et al. 2020).

Overall, an appropriate wall material should have high solubility, low hygroscopicity, effective emulsification, flavor masking capability, good film formation, and low cost (Gallo et al 2012; Lu et al. 2021). Its selection should also take into account the specific characteristics of the natural bioactive substance, such as sensory properties, physicochemical stability, bioactive retention, loading, and release. The most used wall materials include polysaccharides, such as maltodextrin (MD) with different dextrose equivalent (DE) values (Pourashouri et al. 2014; Medina-Torres et al. 2016; Caliskan and Dirim, 2013; Gallegos-Infante et al. 2013; Vidovic et al. 2014; Vladic et al. 2016), β-cyclodextrin (βCD) (Rita et al. 2011; Chordiya and Senthikumaran, 2012; Poomkokrak et al. 2015; Nadeem et al. 2011; Ahmad et al. 2018; Li et al. 2018), pectin (Pec) (Srivastava and Rishabha, 2011; Freitas et al. 2021; Diaz-Bandera et al. 2015; Li et al. 2018; Pudziuvelyte et al. 2019), and cellulose or its derivatives like sodium carboxymethylcellulose (NaCMC) (Kamel et al. 2008; Tchabo et al. 2018). Furthermore, when it comes to prepare pharmaceutical formulations such as tablets from the encapsulated extracts, the percentage of excipients to be added becomes a critical manufacturing issue, as tablets often contain a high dose of dry plant extract.

To the best of our knowledge, there is no available information on an eligible wall material for the encapsulation of aqueous extract, containing phenolic compounds, from *B. ungulata*. Therefore, since the coating behavior of each wall material is different, its suitability for encapsulation needs to be experimentally assessed.

So, this work reports the preparation of microparticles loaded with the dried aqueous extract of *B. ungulata* var. *obtusifolia* leaves by spray-drying, using different wall materials aiming to stabilize it and its active compounds and to improve their bioavailability, if orally administrated. The microstructure, particle size, thermal behavior, yield, and encapsulation efficiency of microparticles was evaluated.

2. RESULTS

2.1. Properties of extracts and spray-drying solutions

The lyophilized extract obtained by freeze-drying the aqueous extract, Bu-L, presented 7.9 % w/w of residual moisture. The solutions used for spray-drying contained 51 mg of wall material,

 doi:10.20944/preprints202401.0343.v1

showed a solid content of approximately 9.1 g/L (Table 2), and viscosity for all samples quite similar, except for Bu-CMC, whose value was higher ($p<0.0001$).

Table 2. Solids content and viscosity of solutions for atomization without (Bu-A) or with wall material (Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec e Bu-CMC) (mean values ± standard deviation, n = 3) and spray-drying process yield of the corresponding extracts (mean values ± standard deviation, n = 2).

Solution	Wall material	Solids content (g/L)	Viscosity (mPa.s)	YD (%)
Bu-A	None	8.234 ± 0.001	1.45 ± 0.03^{a}	64.20 ± 0.72^{a}
Bu-MD4	Maltodextrin DE 4-7	9.146 ± 0.003	1.44 ± 0.04^{a}	88.52 ± 0.72^{b}
Bu-MD11	Maltodextrin DE 11-14	9.142 ± 0.003	1.43 ± 0.03^{a}	77.41 ± 4.63^{ab}
Bu-βCD	β-Cyclodextrin	9.139 ± 0.002	1.43 ± 0.02^{a}	78.93 ± 7.11^{ab}
Bu-Pec	Pectin LM-22-CG	9.162 ± 0.005	1.41 ± 0.01^{a}	73.19 ± 1.01^{a}
Bu-CMC	Sodium Carboxymethylcellulose	9.145 ± 0.004	3.46 ± 0.03^{b}	76.31 ± 1.54^{ab}

YD (%): Yield of drying, in percentage.

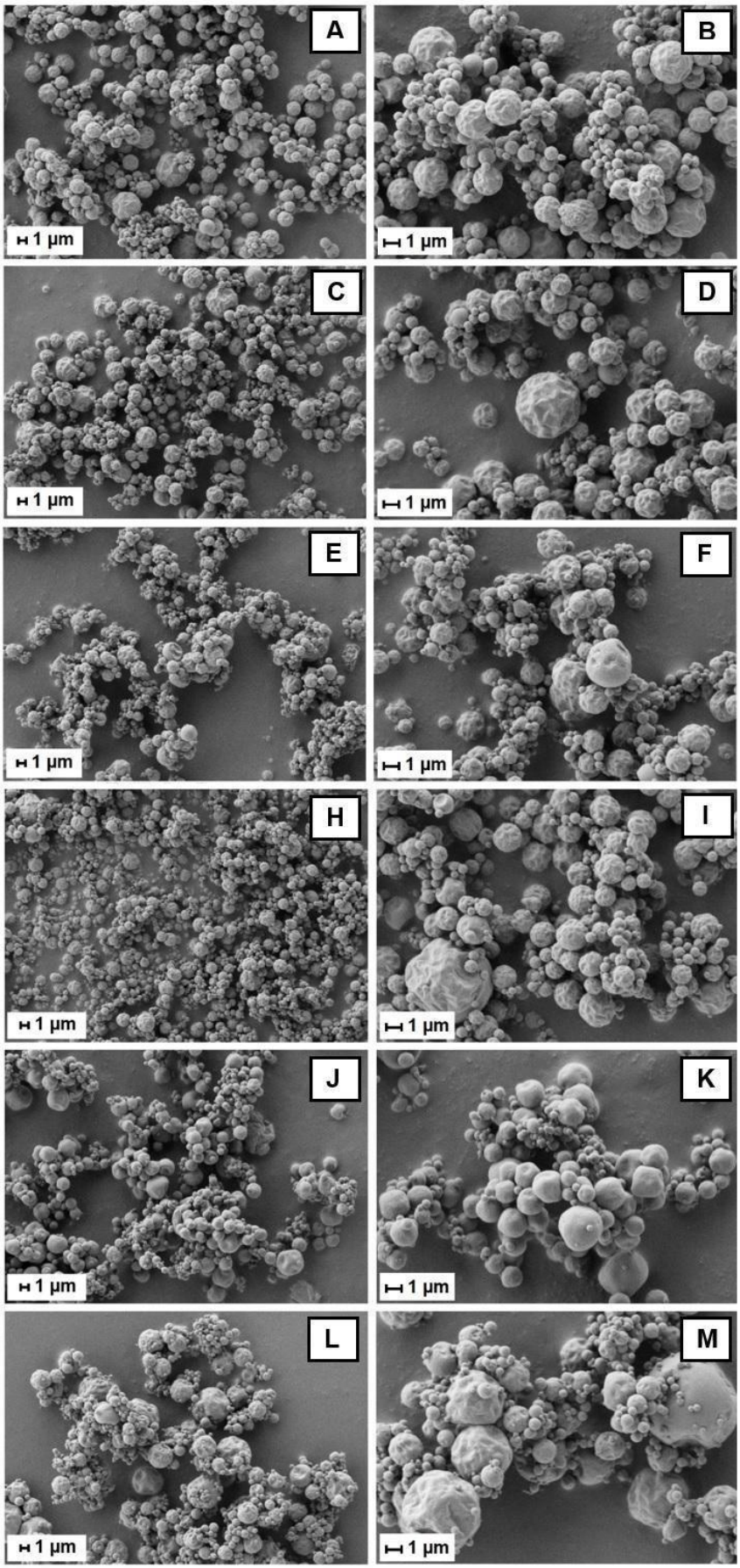
2.2. Yield of drying (YD)

All samples had a YD greater than 60% (Table 2), with no statistical difference between microparticles and Bu-A ($p>0.05$). The powder without wall material (64.20%) and Bu-MD4 (88.52%) showed the lowest and highest yield, respectively. Therefore, the following microparticle types: Bu-βCD, Bu-Pec, and Bu-CMC showed similar drying yields.

2.3. Morphology and particle size

Bu-A, Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec, and Bu-CMC were analyzed by SEM (Figure 1), and it was observed that their particles were somewhat agglomerated and had a non-porous and undamaged surface. Considering the surface morphology, the particles are heterogeneous, predominating rough structures with many shrinkages and dents in all samples.

 doi:10.20944/preprints202401.0343.v1



Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 4 January 2024 doi:10.20944/preprints202401.0343.v1

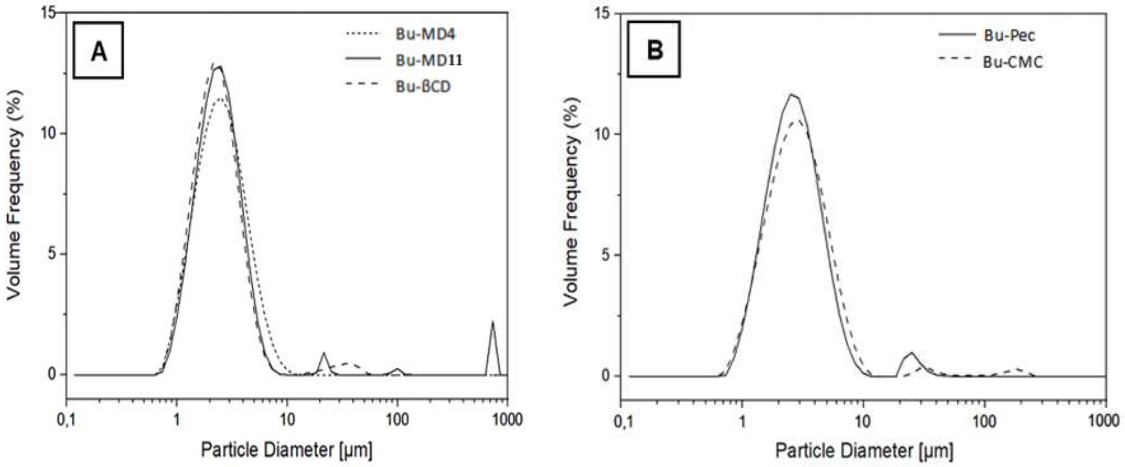
Figure 1. Micrographs of Bu-A (A/B), Bu-MD4 (C/D), Bu-MD11 (E/F), Bu-βCD (G/H), Bu-Pec (I/J) and Bu-CMC (K/L), in magnifications of 5,000 x (left) and 10,000 x (right).

All microparticles showed a spherical shape of variable size, ranging from 1.15 to 5.54 μm, with a volumetric average particle diameter (Dv50) in the range of 2.01-2.87 μm, with Bu-βCD and Bu-CMC particles showing the smallest and largest particle diameters, respectively ($p < 0.05$) (Table 3).

Table 3. Particle size distribution of the microparticles, expressed as mean ± standard deviation of 3 independent batches).

Sample	Dv_{10} (μm)	Dv_{50} (μm)	Dv_{90} (μm)	Span (μm)
Bu-MD4	1.22 ± 0.02^{a}	2.23 ± 0.17^{abc}	4.66 ± 0.71^{abc}	1.53 ± 0.21^{a}
Bu-MD11	1.19 ± 0.08^{a}	2.41 ± 0.39^{abc}	4.54 ± 0.79^{abc}	1.40 ± 0.30^{a}
Bu-βCD	1.15 ± 0.07^{a}	2.01 ± 0.13^{b}	3.76 ± 0.40^{b}	1.29 ± 0.10^{a}
Bu-Pec	1.29 ± 0.02^{a}	2.50 ± 0.02^{abc}	4.82 ± 0.11^{abc}	1.41 ± 0.04^{a}
Bu-CMC	1.29 ± 0.07^{a}	2.87 ± 0.25^{c}	5.54 ± 0.34^{c}	1.50 ± 0.23^{a}

All the samples tended to polydispersion, as seen by the peaks corresponding to the particle diameter of all analyzed microparticles, where each peak represented a predominant particle size, except for Bu-MD4, which showed only one peak (Figure 2). Regarding the particle size distribution range, represented by the span values, similar values were found among themselves ($p>0.05$), according to the analysis of variance performed.



(**a**) (**b**)

Figure 2. Particle size distribution of Bu-MD4, Bu-MD11, Bu-βCD (A), Bu-Pec and Bu-CMC (B).

2.4. Thermal behavior of the microparticles

TGA/DTG and DSC techniques allowed to evaluate the thermal behavior of the microparticles. Two representative stages were observed in the thermogravimetric curves (Figure 3). The first significant weight loss occurred between 30 and 120 °C and the determination of the percentage related to this weight loss allowed to estimate the residual moisture content of the samples, which ranged between 2.90 and 4.25% (Table 4). The use of wall materials promoted an increase in the residual water content of the microencapsulated extracts compared to Bu-A, but only for Bu-MD11,

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 4 January 2024 doi:10.20944/preprints202401.0343.v1

Bu-Pec and Bu-CMC this difference was statistically significant ($p<0.05$). After the initial water removal event from the samples, a pronounced mass loss was observed in the TGA/DTG curves at 150 °C (Bu-A, EBu-MD4, Bu-MD11 and Bu-βCD) or at 190 °C (Bu-CMC and Bu-Pec).

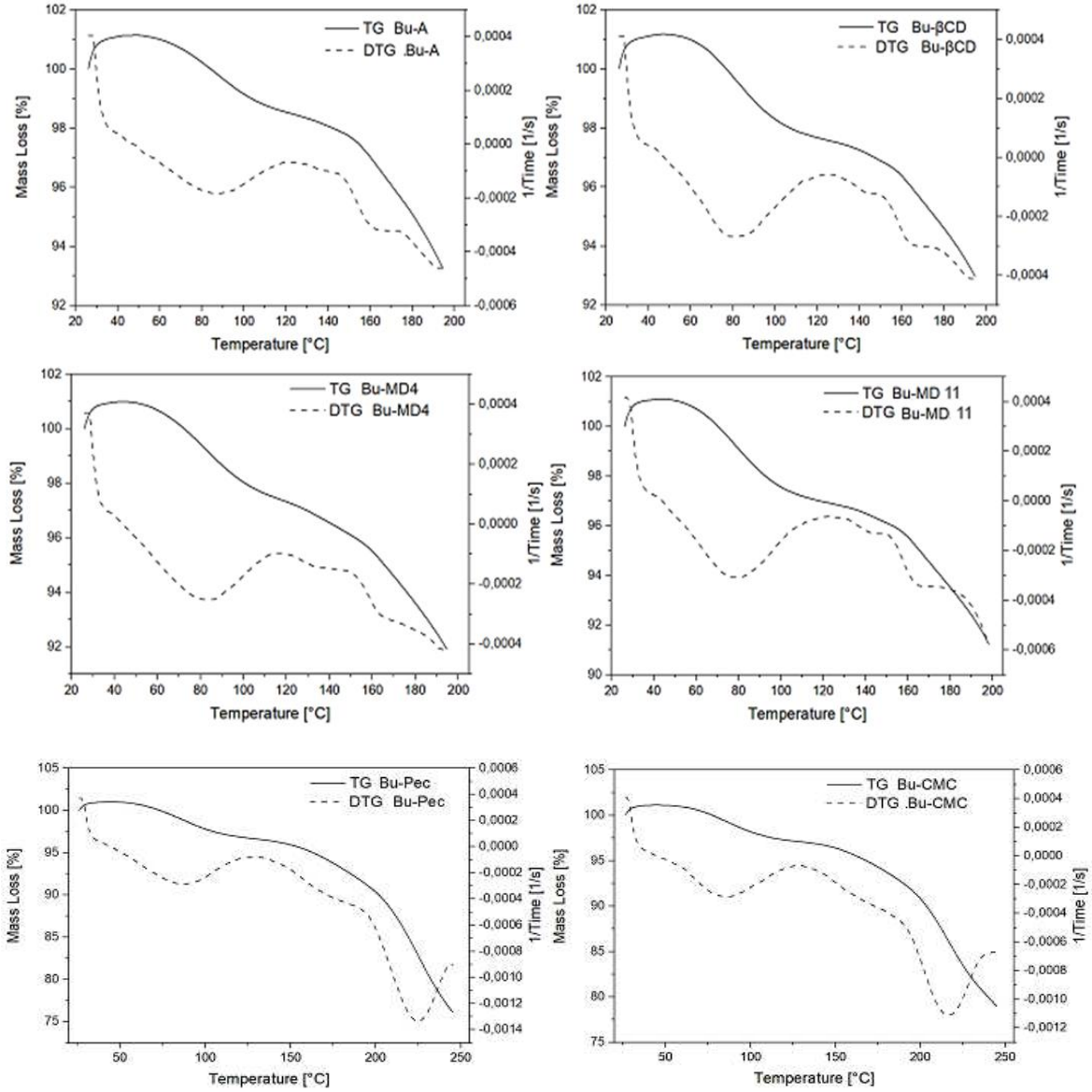


Figure 3. Thermograms by TG/DTG of Bu-A, Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec and Bu-CMC.

The thermograms of the samples analyzed by DSC show two main thermal events (Figure 4). The first event, which generally occurred between 50 and 80 °C and is represented by a variation of the baseline in the endothermic direction, corresponds to the glass transition (T_g) of the microparticles. This event was then examined using STARe evaluation software (Mettler-Toledo) to determine its midpoint temperature, which was the T_g (Fang and Bhandari, 2012). Although the extracts have different mean T_g values, statistical analysis showed that there was no significant difference between the T_g values recorded ($p>0.05$).

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 4 January 2024 doi:10.20944/preprints202401.0343.v1

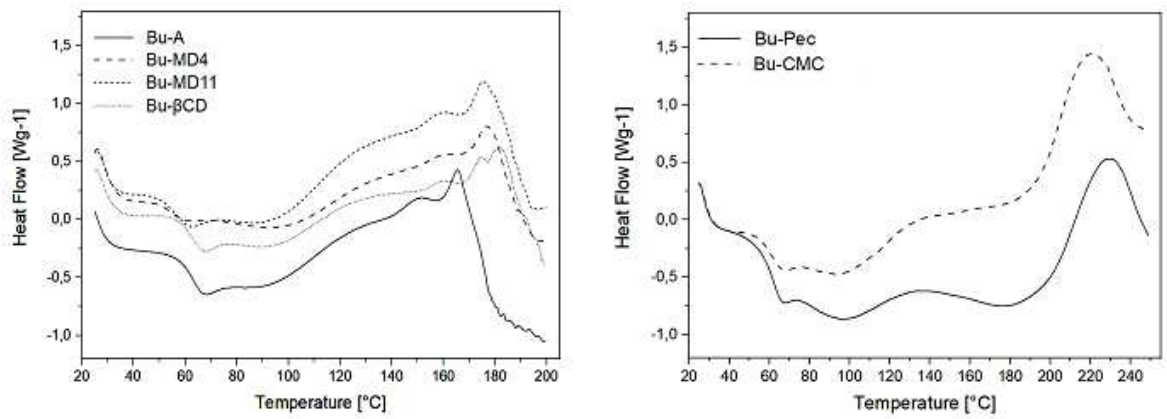


Figure 4. DSC thermograms of Bu-MD4, Bu-MD11, Bu-βCD (A), Bu-Pec and Bu-CMC (B).

Table 4. Moisture content, glass transition and initial decomposition temperature of the spray dried extracts.

Sample	Moisture content (%)	T_g (°C)	$T_{initial}$ decomposition (ºC)
Bu-A	2.90 ± 0.10^{a}	60.4 ± 3.5^{a}	160.2 ± 1.6^{a}
Bu-MD4	3.43 ± 0.16^{ab}	56.8 ± 2.9^{a}	165.8 ± 3.6^{a}
Bu-MD11	3.89 ± 0.27^{b}	57.6 ± 2.4^{a}	163.6 ± 3.9^{a}
Bu-βCD	3.63 ± 0.27^{ab}	61.5 ± 0.4^{a}	162.6 ± 6.4^{a}
Bu-Pec	4.05 ± 0.40^{b}	58.4 ± 4.8^{a}	191.4 ± 0.9^{b}
Bu-CMC	4.25 ± 0.48^{b}	57.8 ± 5.6^{a}	188.2 ± 1.1^{b}

Different letters in the same column indicate significant differences between microparticles ($p< 0.05$). The values represent the mean of three determinations ± standard deviation.

The second event recorded in the thermograms occurs in the exothermic direction. For Bu-A, Bu-MD4, Bu-MD11 and Bu-βCD (Figure 4A), this event starts at temperatures around 160 ºC (Table 4), which are not statistically different from each other ($p>0.05$). In the curves of the extracts prepared with Pec and NaCMC (Figure 4B), this event starts at 191 and 188 °C, respectively, temperatures similar to each other ($p>0.05$) and significantly higher than those recorded for the other samples ($p<0.0001$).

2.5. Total Flavonoid Content (TFC), Total Phenolic Content (TPC), Yield of encapsulation (YE) and encapsulation efficiency (EE)

The samples were analyzed for the content of phenolic compounds present by determining TFC and TPC. For comparison purposes, all values were adjusted according to the residual moisture content determined for each extract. The TPC and TFC, in the extract, ranged from 69.98-101.43 mgGAEq/g Extract and 12.69-23.07 mgRUTE/g Extract, respectively. Therefore, the determination of total phenolic content in the microparticle (PME) and total phenolic content on the surface of the microparticle (PS) allowed to calculate the encapsulation efficiency (EE) of the microencapsulated extracts. Among them, Bu-MD11, Bu-CMC, and Bu-βCD showed a higher encapsulation efficiency

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 4 January 2024 doi:10.20944/preprints202401.0343.v1

of phenolics. In terms of yield of encapsulation (YE), the microparticles obtained with MD4-7, MD11-14, and βCD had better results (83.09, 89.71, and 83.59%, respectively), with values statistically similar to each other (p>0.05) (Table 5)

Table 5. Total flavonoid content (TFC), total phenolic content in the microparticles (PME), total phenolic content on the surface (PS), encapsulation efficiency (EE), and encapsulation yield (YE_{TPC}) of the extracts.

Sample	TFC (mgRUTE/g Extract)	PME ($mgGA_{Eq}$/g Extract)	PS ($mgGA_{Eq}$/g Extract)	EE (%)	YE (%)
Bu-L	21.93 ± 0.30^{a}	101.43 ± 1.68^{a}	–	–	–
Bu-A	22.69 ± 0.45^{ac}	101.28 ± 1.65^{a}	–	–	–
Bu-MD4	12.75 ± 0.57^{b}	84.28 ± 5.47^{b}	38.69 ± 0.64^{a}	44.95 ± 5.17^{a}	83.09 ± 5.40^{a}
Bu-MD11	12.69 ± 0.21^{b}	90.99 ± 2.31^{b}	32.82 ± 2.51^{ab}	57.35 ± 2.24^{b}	89.71 ± 2.28^{a}
Bu-βCD	12.69 ± 0.31^{b}	84.78 ± 1.70^{b}	33.57 ± 1.28^{ab}	50.49 ± 2.92^{ab}	83.59 ± 1.68^{a}
Bu-Pec	21.73 ± 0.34^{a}	69.98 ± 3.44^{c}	33.59 ± 3.87^{ab}	35.87 ± 3.49^{c}	68.99 ± 3.39^{b}
Bu-CMC	23.07 ± 0.50^{c}	75.15 ± 3.13^{c}	27.96 ± 1.99^{b}	46.53 ± 1.13^{a}	74.09 ± 3.09^{b}

Data are expressed as mean ± standard deviation of three determinations.

2.6. Antioxidant activity

The samples were able to scavenge the radicals tested, showing different percentages of inhibition and total antioxidant activity (TAA) depending on the method used or the sample considered (Table 6). In the evaluation of DPPH· scavenging, Bu-L was the sample with the lowest total antioxidant activity compared to the others, with only 308.67 ± 2.64 μmTEq/g Extract. Still, the statistical analysis of the data showed that this value was not significantly different from Bu-A (p>0.05). The data also show that all microencapsulated extracts had a higher AAT than that calculated for the unencapsulated samples. In terms of ABTS·+ radical scavenging, Bu-CMC and Bu-Pec were the most active.

Table 6. Scavenging percentages of DPPH· and ABTS·+ radicals by extracts and total antioxidant activity (TAA)..

Sample	DPPH·		ABTS·+	
	Percentage scavenging (%)	TAA (μMTEq/gExtract)	Percentage scavenging (%)	TAA (μMTEq/gExtract)
Bu-L	22.09 ± 0.66^{a}	308.67 ± 2.64^{a}	23.97 ± 0.22^{a}	956.40 ± 2.81^{a}
Bu-A	25.65 ± 0.25^{b}	323.45 ± 1.07^{a}	29.49 ± 0.55^{b}	1031.33 ± 8.04^{b}

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 4 January 2024 doi:10.20944/preprints202401.0343.v1

Bu-MD4	30.41 ± 0.60^{c}	345.58 ± 2.98^{b}	23.84 ± 1.89^{a}	955.17 ± 23.65^{a}
Bu-MD11	38.34 ± 1.04^{d}	390.06 ± 6.66^{c}	25.24 ± 1.34^{a}	972.82 ± 17.26^{a}
Bu-βCD	38.22 ± 0.43^{d}	389.26 ± 2.72^{c}	24.58 ± 1.26^{a}	964.31 ± 16.12^{a}
Bu-Pec	34.61 ± 1.17^{e}	367.86 ± 6.65^{d}	31.54 ± 0.77^{bc}	1062.32 ± 11.94^{bc}
Bu-CMC	36.10 ± 1.74^{de}	376.55 ± 10.16^{cd}	33.02 ± 0.92^{c}	1085.72 ± 14.84^{c}

*Data expressed as mean ± standard deviation of three determinations.

2.7. Characterization and quantification of phenolics in the microparticles by high-performance liquid chromatography (HPLC-DAD)

The analysis of Bu-A and microparticles by HPLC-DAD showed peaks corresponding to those observed in Bu-L (Remígio, 2023). The average contents of *p*-coumaric acid and isoquercitrin, determined in the extract, are also observed in the microparticles, regardless of the drying process or the use of encapsulating agents in obtaining the samples, showing no statistically significant difference between the calculated means ($p>0.05$). In contrast, the content of chlorogenic acid and rutin was variable (Table 7). The extract nebulized without wall materials, Bu-A, showed 1.975 ± 0.052 and 12.886 ± 0.115 mg/g Extract of the phenolic acid and flavonoid, respectively, values significantly higher than those determined for all the samples ($p<0.05$). Among the microparticles, Bu-Pec and Bu-CMC had the highest content of chlorogenic acid and rutin, significantly different from all the other samples ($p<0.05$), except for Bu-βCD, which showed comparable levels of these compounds.

Table 7. Content (μg/mL or mg/g Extract) of chlorogenic acid, *p*-coumaric acid, rutin, and isoquercitrin in the extracts.

Sample	Content	Compound			
		Chlorogenic acid	***p*-coumaric acid**	**Rutin**	**Isoquercitrin**
Bu-L	μg/mL	15.38 ± 0.22^{a}	0.60 ± 0.05^{a}	102.02 ± 2.52^{a}	4.30 ± 0.21^{a}
Bu-A		19.17 ± 0.51^{b}	0.76 ± 0.08^{a}	125.13 ± 1.12^{b}	5.17 ± 0.67^{a}
Bu-MD4		17.08 ± 0.06^{cd}	0.58 ± 0.11^{a}	108. 30 ± 0.60^{c}	4.82 ± 0.27^{a}
Bu-MD11		16.72 ± 0.46^{d}	0.69 ± 0.01^{a}	110.19 ± 1.58^{cd}	4.66 ± 0.40^{a}
Bu-βCD		17.43 ± 0.15^{cde}	0.60 ± 0.04^{a}	113.07 ± 0.94^{de}	4.90 ± 0.42^{a}
Bu-Pec		17.90 ± 0.12^{e}	0.70 ± 0.04^{a}	115.10 ± 0.76^{e}	5.01 ± 0.12^{a}
Bu-CMC		17.80 ± 0.15^{ce}	0.68 ± 0.10^{a}	112.59 ± 1.47^{de}	4.84 ± 0.30^{a}

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 4 January 2024 doi:10.20944/preprints202401.0343.v1

Bu-L		1.669 ± 0.024[a]	0.066 ± 0.005[a]	11.077 ± 0.274[a]	0.466 ± 0.022[a]
Bu-A		1.975 ± 0.052[b]	0.078 ± 0.008[a]	12.886 ± 0.115[b]	0.533 ± 0.069[a]
Bu-MD4		1.769 ± 0.007[c]	0.060 ± 0.012[a]	11.216 ± 0.062[a]	0.500 ± 0.029[a]
Bu-MD11	mg/g Extract	1.740 ± 0.048[ac]	0.072 ± 0.001[a]	11.465 ± 0.164[ac]	0.485 ± 0.041[a]
Bu-βCD		1.808 ± 0.016[cd]	0.062 ± 0.004[a]	11.724 ± 0.098[cd]	0.508 ± 0.044[a]
Bu-Pec		1.867 ± 0.013[d]	0.073 ± 0.004[a]	12.003 ± 0.080[d]	0.522 ± 0.013[a]
Bu-CMC		1.858 ± 0.016[d]	0.070 ± 0.011[a]	11.755 ± 0.153[cd]	0.505 ± 0.032[a]

Data expressed as mean ± standard deviation of three determinations.

3. DISCUSSION

The viscosity of the solutions for spray drying influences the drop formation and consequently modifies the particle size at the process end. Furthermore, less viscous solutions demand lower pressure to form the spray, saving energy (Oliveira and Petrovick, 2010; Patel et al., 2009). Among the solutions prepared for atomization, only Bu-CMC differed from the others in terms of viscosity, inferring that the solids content did not significantly influence the viscosity of the solutions. The viscosity value determined for Bu-A, with lower solids content, was similar to those measured for Bu-MD4, Bu-MD-11, Bu-βCD, and Bu-Pec, which infers that the viscosity is strongly influenced by the type of encapsulating agent used, since the solution with NaCMC showed an increased viscosity due to the thickening property of this excipient that, and like other cellulose derivatives, it acts as a modifier of viscosity (Kono et al. 2016; Komorowska et al. 2017). Although pectin has thickening and gelling properties too, its addition to solutions did not lead to any significant change in viscosity, likely since the low methoxylated pectin used in this work would have required calcium ions to display such functions (Urias-Orona et al. 2010; Picot-Allain et al. 2020). Despite the difference observed in this property between the solution prepared with NaCMC and the others, all had suitable viscosity for atomization, since they flowed easily through the equipment during drying.

The applied method can be considered efficient since the YD values are higher than 50%, a value that defines the efficiency of a bench spray-drying process (Bhandari et al. 1997; Vidovic et al. 2014). The lowest yield of Bu-A suggests that using wall materials favors a higher solids recovery by this drying process, especially when using MD4-7, whose average yield was 88.52%. It was an expected result since the addition of these agents to solutions of plant extracts to be sprayed decreases the viscosity of the sample, favoring less deposition of atomized material on the walls of the drying chamber, increasing the process yield (Tonon et al. 2008; Krishnaiah et al. 2014). The viscosity of solutions is related to the high content of low molecular weight sugars and organic acids, and this reduces its glass transition temperature (Tg), promoting cohesion between particles or their adhesion to dry surfaces. The addition of excipients, such as maltodextrins, induces a material Tg increase, thus facilitating its transit through the cyclone chamber, consequently increasing the yield of the process (Truong et al., 2005; Caliskan and Dirim, 2013; Krishnaiah et al., 2014).

A similar result was described by Vidovic et al. (2014) when drying a liquid *Satureja montana* extract and observed a significant amount of material deposition in the drying chamber during the aspersion. Additioning DE-16 maltodextrin at 10 %, 30 %, and 50 % to the extract improved the efficiency of the process and promoted similar yields to each other, ranging from 66 to 68 %. Cid-Ortega and Guerrero-Beltrán (2020) also reported higher yielding in the microencapsulation of

Hibiscus sabdariffa (Roselle) extract after adding maltodextrin. The authors recorded 58.19 % solid recovery without the encapsulating agent and reached 56.46, 59.81, and 72.07 after adding 3, 5, and 10 % of the material, respectively.

Vladic et al. (2016) spray-dried a liquid extract from *Achillea millefolium* with and without maltodextrin DE16.5-19.5, performing similar drying efficiencies (around 70%), differently from those observed by the other authors. A lower recovery was registered just by the atomization of the extract concentrated before drying, a step which, according to the authors, could reduce the efficiency of the process due to the higher solids content. Increasing the solids content in a solution alters its viscosity and may decrease the microparticle yield, as Tonon et al. (2008) reported by obtaining *Euterpe oleraceae* Mart. microparticle, using maltodextrin DE9-12 by spray-drying.

The average yield values of Bu-MD4 and Bu-MD11, higher than 70%, are in agreement with those observed by Caliskan and Dirim (2013). They spray-dried *Rhus coriaria* L. extract with maltodextrin DE 10-12, yielding 70.21%, 86.77%, 97.45%, and 98.5% for solutions with soluble solids contents of 10, 15, 20, and 25%, respectively, indicating that higher amounts of wall material increase the efficiency of spray drying. Similar yields were obtained by Farias-Cervantes et al. (2020) when spraying raspberry or blackberry juices with maltodextrin, with values ranging from 52-66% and 64-78%, respectively. Nevertheless, the reported drying yields were higher than those observed by Costa and collaborators (2019) for the microencapsulation of a cupuassu seeds by-product extract with maltodextrin that ranged from 11 to 19% with 5, 7.5, and 10% (w/v) of wall material. Besides the different chemical composition of the extracts, the distinct results can be due to the operating conditions of the spray dryer used in the process, the degree of dextrinization, the proportion of maltodextrin added to the solutions, and the core:wall ratio of the microparticles obtained (Rajabi et al., 2015).

The yield recorded for Bu-MD4 (88.52%), the highest registered in this work, could be due to the low dextrinization grade (DE) of the maltodextrin used, which are mainly composed by long polysaccharides of high molecular weight and a small fraction of oligomers and so can form less sticky solutions, favoring the yield of microparticles prepared by spray drying, as observed by Siemons et al. (2020).

The similar drying yields of Bu-βCD, Bu-Pec, and Bu-CMC were higher than those described in other works using the same wall materials. In the case of Bu-CMC, the average yielding (76.31%) is higher than those observed by Sansone et al. (2014) and Tchabo et al. (2018) for the encapsulation of *Lannea microcarpa* (46.7%) and *Morus alba* (53.47-61.87%) extracts. Also Nadeem et al. (2011) and Jovanovic et al. (2021), who used β-CD and Pec to obtain atomized extracts of *Sideritis stricta* and *Gentiana asclepiadea*, report yields of 33.07 % and 49.51-62.12 %, respectively, indicating lower drying efficiencies, in comparison to the present work. These variations can be due to the different compositions of the feed solutions and the conditions set for the spray-drying process.

Regarding the characterization of the microcapsule structure, this is a relevant parameter as it reveals the protective capacity of different polymers and reflects the quality of the microparticles obtained. Desirable morphological characteristics of the particles produced by spray drying, which affect the stability of the encapsulated compounds, include a smooth surface without structural defects, compounds in the core of the particles, and a size as large as possible (Labuschagne, 2018). The size of the particles varies according to the pharmaceutical form pretended from the microparticles obtained by spraying: for example, microparticles for direct compression tend to have particles in the range of 100-200 μm, while for inhalation, it is desirable that this size be between 1-5 μm (Shekunov et al. 2007).

The agglomeration of some particles in Bu-A, Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec and Bu-CMC by SEM (Figure 1) is a phenomenon that can occur when the glass transition temperature (Tg) of the material is lowered by the influence of its plasticization with water. As a result, the material becomes sticky on the surface, which promotes particle cohesion (Takeiti et al. 2010) after the spraying process (Bhandari and Howes, 2005).

The spherical shape of the analyzed particles is a characteristic attribute of spray-dried products (Vehring 2008; Tonon et al. 2008; Poomkokrak et al. 2015). The integrity of the particles in the samples

 doi:10.20944/preprints202401.0343.v1

and the absence of pores on their surface can be considered a technical advantage, as they increase the retention and protection of the active compounds inside the particles. The occurrence of pores or fissures on the wall can expose the particle core to the atmosphere and allow leaching or migration of actives to the surface where in contact with oxygen can undergo degradation (Pourashouri et al., 2014; Poomkokrak et al., 2015). Regarding the surface morphology, the wrinkling of the microparticle may be due to the drastic moisture loss by the droplets during the drying process, followed by cooling. Nadeem et al. (2011) and Pasrija et al. (2015) observed similar aspects on microparticles prepared with maltodextrin, cyclodextrin, or a combination of these encapsulant agents (Rezende et al., 2018).

Sansone et al. (2014) described the obtention of spherical particles with a smooth surface using 50% (w/w) NaCMC for the *Lannea microcarpa* encapsulation by spray-drying. Bu-CMC surface differs from them probably because the amount of wall material used to encapsulate *B. ungulata* extract represents only 10% of the Bu-CMC total solids content. In addition, the drying parameters and composition of both extracts play decisive roles in those differences on the microparticles surface.

The larger particles observed in the Bu-CMC microparticles were foreseen because of the higher viscosity of the feed solutions prepared with this excipient when compared to others microparticles, since the higher the viscosity of the liquid, the larger the droplets formed during atomization and, therefore, the larger the particles obtained after drying (Tonon et al. 2008). This result correlates to that published by Jinapong et al. (2008) for instant powdered soymilk produced by ultrafiltration and spray drying. Keogh et al. (2003) also observed a linear increase in the particle size, as the viscosity of the feed solution, an ultrafiltered concentrate integral milk, increased. In both studies, the authors attributed the large particle size to the high viscosity of the feed solutions.

Based on the particle size distribution data, the tendency of a monomodal behavior for Bu-MD4 can be inferred, while for the other microparticles, a multimodal one. It is worth noting that smaller particles can penetrate the spaces among the larger ones, occupying less space and increasing the density of the microparticles. The presence of "populations" of larger particles can be attributed to agglomeration suggested by SEM (Tonon et al. 2009). Regarding the particle size distribution range, the data indicate a narrow distribution in all the microencapsulated extracts obtained, since the values are close to 1 (Sarrate et al. 2015) and show that the type of encapsulating agent added to the extracts did not significantly affect the particle size distribution of the microparticles.

The microparticles were also evaluated for their thermal behavior. This evaluation is important as it provides information on the stability of the sample in the face of temperature variations, providing useful data for the quality control process. The first significant weight loss (30-120°C) observed on the thermogravimetric curves by TGA/DTG corresponds to the elimination of water and volatile compounds by the samples (Costa et al. 2020) and the values of residual moisture content (2.90-4.25%) associated with this event were considered typical for microparticles obtained by spray-drying (GAVARIC et al. 2019). Similar results were observed in the microencapsulation of *Litsea glaucescens* infusions using maltodextrin DE 10 (1.82 - 4.32%) (Medina-Torres et al. 2016) and for the encapsulated extract of *Hibiscus sabdariffa* using carboxymethylcellulose as encapsulating agent (4.53%) (Díaz-Bandera et al. 2015). This range of values have also been reported for microencapsulated extracts obtained from soybean using β-cyclodextrin, maltodextrin or gum arabic as wall material (2.07 - 4.63%) (Niamnuy et al. 2019) and for microencapsulation of bioactive compounds from *Camellia sinensis* using different biopolymers as encapsulating agents, including pectin (less than 2.40%) (Belščak-Cvitanović et al. 2015).

Despite the increase in the residual water content of the microencapsulated extracts (3.43-4.25%) compared to Bu-A (2.90%), all the samples had low levels of residual moisture, which tends to increase shelf life and reduce the possibility of microbiological contamination of powders (Vidović et al. 2014; Jovanovic et al. 2021). The statistical difference observed for Bu-MD11, Bu-Pec and Bu-CMC compared to Bu-A ($p<0.05$), can be attributed to the properties of these encapsulants such as chemical structure and hygroscopicity. For example, MD11-14, composed of a mixture of glucose, disaccharides, and polysaccharides, has many hydroxyl groups capable of interacting with water, making this sugar more hygroscopic than MD4-7. According to Negrão-Murakami et al. (2017), this

 doi:10.20944/preprints202401.0343.v1

difference appears because maltodextrins with higher DE values, being more hydroxylated saccharides, show a chemical structure favorable for interaction with water. In the case of pectin, this interaction is possibly due to the presence of hydroxyl, carboxyl, and amide groups (amidated Pectins), which also gives this excipient a certain degree of hygroscopicity (Einhorn-Stoll et al. 2012; Einhorn-Stoll et al. 2016). Similarly, NaCMC is considered to be a highly hygroscopic excipient and can adsorb a large amount of water (> 50%) under high relative humidity conditions (Durig and Karan, 2019). According to Tonon et al. (2008), microparticles with many hydrophilic groups can easily bind water molecules from the ambient during sample handling after spray-drying, which could justify the higher residual moisture in the extracts prepared with these wall materials. The authors recorded similar results for *Euterpe oleraceae* microparticles obtained by atomization with maltodextrin DE 20 and Arabic gum.

The second event recorded in the TGA/DTG curves at 150 °C (Bu-A, EBu-MD4, Bu-MD11 and Bu-βCD) or at 190 °C (Bu-CMC and Bu-Pec) corresponds to the decomposition process of the samples. These results indicate that the microparticles obtained with Pec or NaCMC have a higher thermogravimetric stability than the others, since they require a higher temperature to initiate the thermal decomposition step. These results are different from those observed by Nunes et al. (2015), who described an increase in the thermal stability of a concentrated extract of *Ilex paraguariensis* when encapsulated with different concentrations of maltodextrin. However, it is noteworthy that the excipient concentrations chosen by the authors (20, 30, and 40%) were higher than the one used in the present work, which was only 10%. The loss of mass of the materials in this temperature range can be understood as a degradation due to thermal decomposition of organic compounds and subsequent volatilization, a behavior also observed in the analysis of the by-product of cupuassu seeds and their respective crude extract, when analyzed by TGA/DTG (Costa et al. 2020).

Regarding the thermograms obtained by DSC, the first event (50-80 °C) corresponds to the glass transition (T_g) of the microparticles, characteristic of amorphous materials, as is the case of dried plant extracts (Roos and Karel, 1991; Shrestha et al. 2007; Gallo et al. 2012). The statistical similarity between these values ($p>0.05$), suggests that the encapsulating agents used did not modify this property of the microparticles. However, it should be considered that T_g is influenced by the amount of water present in the material analyzed, which occurs at lower temperatures as the moisture content increases (Goula et al. 2008). In the case of the extracts obtained, which had different levels of residual water and were hygroscopic, the moisture adsorbed after spray drying or during the preparation of the samples for analysis may have made it impossible to determine their glass transition temperatures accurately, so that the values are statistically similar, which would justify the observed results. The determination of T_g is important because the values of this parameter are directly related to the stability of the microparticle during storage (Kuck and Noreña, 2016). According to Gallo et al. (2015), structural changes occur in amorphous microparticles when stored at temperatures above the T_g (temperature at which these materials transform from a glassy to a rubbery state). Therefore, microparticles with low moisture content and T_g above the storage temperature can be considered stable. For the samples analyzed, the glass transition temperature was always above room temperature, and then all microparticles showed adequate physical stability.

The second event in the thermograms may correspond to the onset of sample decomposition. The temperatures recorded for Bu-A, Bu-MD4, Bu-MD11, and Bu-βCD (around 160ºC) indicate that the addition of encapsulating agents MD4-7, MD11-14, and βcD did not modify the thermal stability of Bu-L compared to the sample obtained without excipients, Bu-A. In contrast, the temperatures observed for Bu-Pec and Bu-CMC (191 and 188°C, respectively), suggest that microencapsulated extracts obtained with Pec and NaCMC are thermally more stable since their degradation process starts at higher temperatures. When these data are related to those obtained by TG/DTG, it is observed that the changes in the baseline of the DSC curves are accompanied by mass loss in the same temperature ranges, which reinforces the understanding that the second event corresponds to degradation samples.

Among the metabolites present in the samples, phenolic compounds were quantified at 69.98-101.43 mgGAEq/g Extract. These values are lower than those determined for extracts obtained from

 doi:10.20944/preprints202401.0343.v1

congeneric species, such as *B. vahlii* (237 mgGAEq/g) (Sowndhararajan and Kang, 2013) and *B. pulchella* (201.89 mgGAEq/g) (CARVALHO et al. 2018). On the other hand, the levels were higher than those determined for extracts of *B. forficata* (5.81-58.58 mgGAEq/g Extract) (Palsikowski et al. 2019), *B. scandens* (47.33 mgGAEq/g Extract) (Hossain et al. 2016) and *B. variegata* (69.39 mgGAEq/g Extract) (Vyas and Braganza, 2019). These differences may be justified not only by the fact that they are different plant species, but also by the type of solvent and extraction method used to obtain each sample. For example, in the works of Alothman et al. (2009), Boeing et al. (2014), and Palsikowsk et al. (2019), it was shown that the use of different solvents and extraction methods favored the obtaining of samples with different levels of phenolic compounds.

Regarding the TFC, the values determined (12.69-23.07 mgRUTE/g Extract) were similar or higher than those recorded for aqueous extracts prepared with leaves of *B. variegata* (3.86-18.40 mgRUTE/g Extract) (Vyas and Braganza, 2019). In contrast, these values can be considered low compared to those determined for aqueous extracts prepared with leaves of other species of the genus *Bauhinia*, such as *B. vahlii* (59 mgRUTE/g Extract) (Sowndhararajan and Kang, 2013) and *B. pulchella* (221.71 mgRUTE/g Extract) (Carvalho et al., 2018).

The similarity between the phenolic and flavonoid content of lyophilized extract - Bu-L - and Bu-A ($p>0.05$) allows us to affirm that the parameters used in the spray-drying process ensured the preservation of the phenolic compounds present. The observed result agrees with that reported by Cunha et al. (2010), who obtained from the leaves of *B. forficata* a spray-dried extract with preserved flavonoid profile, under operating conditions similar to those used in the present work. Moreover, the result confirms the applicability, widely discussed in the literature, of the spray-drying technique for the atomization of thermosensitive samples (Jain et al., 2012; Tobar-Grande et al., 2013; Anish et al., 2014; Balducci et al., 2014; Sosnik and Seremeta, 2015), since it contributes preserving the phenolic compounds present in the extract.

As for the microencapsulated extracts, different behaviors were observed in the encapsulation of flavonoids and phenolic compounds by Dextrin and the other encapsulating agents. Considering that Bu-L was added to the feed solutions to represent 90% of the present solids content, this was the maximum YE value expected after the drying process. The microparticles obtained with MD4-7, MD11-14, and βCD presented a TPC of 84.28, 90.99, and 84.78 mgGAEq/g Extract, corresponding to a YE of 83.09, 89.71, and 83.59%, respectively, values statistically similar to each other ($p>0.05$), indicating the preservation of most of the phenolic compounds added to the atomized solution. In terms of TFC, the values obtained for the same samples were the lowest among those recorded, around 12 mgRUTE/g Extract, with no statistically significant difference between them ($p>0.05$). However, it is possible that this interaction occurred mainly with non-flavonoids, since Bu-MD4, Bu-MD11, and Bu-βCD were also the samples with the lowest TFC, suggesting a loss of part of these compounds during atomization or even during the process of extraction from the particles for the quantification of the phenolics present.

As reviewed by Jakobek and Matić (2019), Dextrin can bind to phenolic compounds, but there are still unknowns about this process. For example, hydrogen bonds formed between the oxygen atoms of glycosidic bonds present in Dextrin, and the hydrogens of hydroxyl groups of phenolic compounds are possible interactions between maltodextrins and polyphenols. However, it should be considered that these interactions may vary depending on the affinity between the phenolic compounds and the encapsulating agents, as well as on properties such as water solubility, molecular size, conformational mobility, and shape of the polyphenol. All these factors could justify the observed difference in the interaction between Dextrin and flavonoid and non-flavonoid phenolic compounds present in the samples (Mahdavi et al. 2016; Navarro-Flores et al. 2020).

The TPC and TFC values recorded for Bu-Pec and Bu-CMC were exactly the opposite of those obtained for the Dextrin: lower levels of phenolic compounds (69.98 and 75.15 mgGAEq/g Extract, respectively), resulting in a lower YE compared to the other extracts, a difference considered significant ($p<0.05$); and higher TFC values among those obtained for the microencapsulated extracts, amounts comparable or even higher than those obtained for Bu-L and Bu-A. In this case, a greater interaction of the wall materials with the flavonoids is suggested, resulting in the loss of part of the

 doi:10.20944/preprints202401.0343.v1

non-flavonoid phenolic compounds during the spraying or extraction of substances from the particles for quantification, since the TPC is reduced and the TFC is maintained in these extracts after drying.

As for pectin and NaCMC, both considered dietary fibers, their interaction with polyphenols can occur through hydrogen bonding, van der Waals forces, and hydrophobic interactions. It can be said that polyphenols and fibers share some important general characteristics in these interactions. For fibers, OH and other functional groups are important, along with the degree of saturation, molecular weight, degree of aggregation, structural and conformational organization. In the case of phenolic compounds, the presence of OH, CH_3, and galloyl groups, sugar molecules in the aglycone, flexibility and number of phenolic rings, molecular size, and spatial configuration have been suggested to influence dietary polyphenol-fiber interactions. In addition, their hydrophilic or hydrophobic character is important. Regarding the molecular size and the number of phenolic rings present in polyphenols, which favor their interaction with Pec and NaCMC (Jakobek and Matić, 2019), flavonoids, due to their structural characteristics, have a greater possibility of interaction compared to phenolic acids, which could justify the found result.

Despite the differences observed between the samples, the TPC values recorded for all the extracts obtained in this work were higher than those found by Port's et al. (2013), who, when analyzing an infusion obtained from leaves of the same variety of *B. ungulata*, quantified the phenolics present in the sample at 23.67 mgAG/g. However, it should be considered that the infusion prepared by the authors (500 mg in 25 mL of boiling water) produced a less concentrated aqueous extract than the one used in this work (1.25 g in 25 mL of boiling water), so a lower content of total phenolic compounds was expected.

Regarding the encapsulation efficiency (EE) of the microencapsulated extracts, Bu-MD11, Bu-CMC, and Bu-βCD showed a higher encapsulation efficiency of phenolics, indicating that in these extracts a greater amount of such substances is located inside the particle, which favors their preservation and tends to increase the stability of the microparticles (Labuschagne, 2018; Etzbach et al. 2020).

Unexpectedly, the microparticles obtained with MD11-14 showed a higher encapsulation efficiency than that observed for Bu-MD4. The fact that maltodextrin DE 11-14 presents a higher amount of low molecular weight sugars compared to MD4-7 suggests that its ability to retain phenolic compounds inside the particles is lower, which would reduce its encapsulation efficiency, as already reported by other authors (Negrão-Murakami et al. 2017; Ding et al., 2020; Zhu et al. 2022). However, it was observed that this polymer had a lower TPC_S/TPC_{ME} ratio, resulting in a higher encapsulation efficiency of the phenolic compounds of *B. ungulata*. This phenomenon may be due to the agglomeration of the particles resulting from the use of MD11-14, as demonstrated by SEM and observed in the particle size distribution analysis. This agglomeration hinders the extraction of compounds present on the surface, since it tends to form larger structures with less contact surface, where phenolic compounds tend to be trapped. Similar results were found by Etzbach et al. (2020) in the encapsulation of *Physalis peruviana* L. by spray drying using different encapsulating agents. The authors observed that the particle size had a strong influence on the encapsulation efficiency, as the fine microparticles produced showed significantly lower encapsulation efficiencies compared to agglomerated microparticles, due to their higher surface area.

Encapsulation efficiency is an important indicator in particle analysis and refers to the potential of wall materials to encapsulate or maintain the material in the core of the formed structure (Mahdavi et al. 2016). In terms of this parameter, Bu-MD11, Bu-CMC and Bu-βCD proved to be the most advantageous, also showing a high encapsulation yield of phenolic compounds. Among these samples, Bu-CMC was the microencapsulated extract that, in addition to the advantages already described, presented the highest content of total flavonoids, presenting itself as an interesting alternative in the microencapsulation of the aqueous extract of *B. ungulata* var. *obtusifolia*.

The samples scavenged DPPH· and ABTS-+ radicals with different scavenging percentages and TAA. This difference was expected due to the different affinities of the radicals used by the substances present in the extracts. While ABTS-+ radicals have an affinity for hydrophilic, lipophilic, and

hydrogen atom donor compounds, DPPH· interacts more with lipophilic compounds, showing a lower affinity for compounds containing aromatic rings with only hydroxyl groups (Kim et al. 2002; Perez-Perez et al. 2021). In this sense, AAT tends to be higher with the ABTS·+ radical scavenging method and lower when the radical used is DPPH·, which agrees with what was observed in the present work. Similar results were found by Floegel et al. (2011), who compared the antioxidant activity of 50 antioxidant-rich fruits, vegetables, and beverages most popular in the U.S. diet using ABTS and DPPH assays and reported that the ABTS assay better reflected the antioxidant activity in various foods than the DPPH assay.

About DPPH· scavenging, Bu-L had lowest total antioxidant activity compared to the others (308.67 ± 2.64 μmTEq/g Extract), but this value was not significantly different from Bu-A ($p>0.05$), indicating the preservation of this property in the atomized extract without wall materials. All microencapsulated extracts had higher TAA than the unencapsulated samples, indicating that the addition of encapsulating agents increased the ability of the extract to scavenge DPPH· radicals. This result may be justified by the fact that the wall materials used are described in the literature as antioxidants or secondary antioxidants, capable of interacting with different types of radicals, each with different intensities and through different mechanisms (Moseley et al. 2002; Moseley et al. 2003; Fan et al. 2014; Wathoni et al. 2019; Sun et al. 2020; Ma et al. 2016; López-Ncolás et al. 2014). In this sense, these agents, together with the compounds present in Bu-L, may have contributed to the scavenging of DPPH· radicals.

Bu-MD11, Bu-βCD, and Bu-Pec were the most active samples, with no statistically significant difference between the first three and the last two microparticles ($p>0.05$). The best results obtained for the samples prepared with MD11-14, βCD, and NaCMC may be related to the higher encapsulation efficiency determined for these extracts (Mahdavi et al. 2016; Labuschagne, 2018), which, due to this property, were able to preserve inside the particles the phenolic compounds proposed to be involved in the scavenging of DPPH· radicals.

In terms of ABTS·+ radical scavenging, Bu-CMC and Bu-Pec were the most active, showing that the use of NaCMC and Pec increased the TAA of these samples concerning the others. Contrary to what was expected, these microparticles presented the lowest TPC, an unusual result since phenolic compounds have been positively correlated with the antioxidant capacity of plant extracts by different analytical methods (Melo et al. 2011; Augusto et al. 2014; Bratu et al. 2018). However, it is important to note that this correlation is not always observed. For example, in the work of Rivero-Pérez et al. (2007), which consisted of the analysis of 321 wine samples, many of those with a high content of phenolic compounds showed low values of total antioxidant capacity. It was suggested that this result could be justified by the fact that the antioxidant capacity of wine is more related to the type of phenolic compounds present in wines than to their total content. According to the authors, this property is due to the flavonoids present in the beverage, especially tannins and anthocyanins, and the samples tested contain low levels of these compounds due to their method of preparation, which affects their antioxidant activity.

Similarly, Bu-CMC and Bu-Pec, despite having the lowest TPC values, contain high TFC, which leads to the understanding that their higher AAT may be mainly related to the flavonoids present in these samples. As reviewed by Rice-Evans et al. (1996), flavonoids are electron/H+ donors due to the reduction of several hydroxyl groups present in their structure, which is directly related to the antioxidant activity of these phenolics. In addition, among the structural characteristics that contribute to the action of flavonoids as antioxidants are the presence of the catechol or dihydroxy structure in the B ring, the presence of a double bond in the C ring between carbons C2-C3, in conjugation with the ketone function in C4, and the presence of hydroxyl groups in C3 and C5. These factors allow the stability of the molecule since they favor an extensive delocalization of electrons in the aromatic nuclei, different from that observed in other phenolic compounds, such as phenolic acids derived from hydroxybenzoic or hydroxycinnamic acids. These structural characteristics of the flavonoids could explain the observed result.

Microparticles obtained with NaCMC and Pec showed better antioxidant activity, even with low TPC such data allowed to conclude that the phenolic compounds, present in lower amounts in these

 doi:10.20944/preprints202401.0343.v1

samples, are non-flavonoids. Based on these results, it is possible to affirm that among the microencapsulated extracts, Bu-CMC and Bu-Pec proved to be worthwhile antioxidants. This characterization reinforces the antioxidant potential of the genus and suggests that this variety of *B. ungulata* can be employed as a natural antioxidant. As a plant popularly used as a hypoglycemic agent, this activity becomes even more important, since oxidative stress resulting from the generation of free radicals in diabetes is related to the development of secondary complications in patients with the disease, arousing interest in new therapeutic options that, in addition to acting as hypoglycemic agents, are capable of protecting the body from the action of these radicals (Azevedo and Manso, 1992; Rocha et al. 2006).

Since the presence of phenolic compounds in the samples was known, HPLC was used to characterize and quantify these substances. Bu-A and all microencapsulated extracts showed peaks corresponding to those observed in Bu-L, indicating that the drying process and the encapsulating agents used did not produce detectable qualitative changes, preserving phenolic compounds that may be related to the antidiabetic activity attributed to the species (Remígio, 2023). This result is important because it confirms the application of the spray-drying technique in the drying of thermosensitive materials (Agnihotri et al. 2012), since even using a high inlet temperature (150 °C) in the atomization of Bu-A and microencapsulated extracts, these phenolic compounds were preserved. This is possible due to the rapid contact between the drying chamber and the sample during aspersion, since the microparticle produced is subsequently stored in a collector with temperatures lower than the outlet temperature, avoiding thermal degradation of the product (Sosnik and Seremeta, 2015).

In quantitative terms, only the content of chlorogenic acid and rutin was variable. The extract nebulized without wall materials, Bu-A, showed values significantly higher than those determined for the microparticles ($p<0.05$), but this result was expected since the addition of encapsulating agents reduces the content of the compounds present in the microparticles, which are composed of 90% (w/w) of Bu-L and 10% (m/m) of wall material. In the case of Bu-A, the values determined were expected to be equivalent to those obtained for the extract, since the microparticle was obtained from the lyophilized extract. However, regarding that plant extracts are heterogeneous samples, even considering the sample moisture, the dry extract weighed to obtain the analytical solution could contain residual moisture values higher than that assessed (7.9%), which could explain the lower content of chlorogenic acid and rutin in the lyophilized extract. Among the microparticles, Bu-Pec and Bu-CMC were the samples with the highest content of chlorogenic acid and rutin, significantly different from all the other samples (Tukey test, $p<0.05$), except for Bu-βCD, which showed comparable levels of these compounds.

The chlorogenic acid content determined in the samples (1.669 to 1.975 mg/g Extract) is close to that observed in a polyphenolic fraction obtained from *Catharanthus roseus* stems (0.216%, corresponding to 2.16 mg/g). This sample was effective in reducing the glycemia of normal or diabetic mice 6 h after its administration, in addition to stimulating insulin secretion in RINm5F cells (Espejel-Nava et al. 2018). Similarly, an aqueous extract of *Cecropia obtusifolia* leaves standardized in chlorogenic acid (5.2 µg/g) promoted, among other effects, the increase of insulin secretion in vitro and the acute and subacute reduction of glucose levels in diabetic mice. In addition, daily administration of *C. obtusifolia* increased hepatic glycogen storage and glycogen synthase levels in animals without apparent changes in gluconeogenesis (Fortis-Barrera et al. 2019). It is worth noting that the chlorogenic acid content determined by the authors was much lower than that found for the aqueous extract of *Bauhinia ungulata* var. *obtusifolia*.

As for *p*-coumaric acid, the levels determined in the aqueous extract in its various preparations (0.060-0.078 mg/g extract) were higher than the value determined for an aqueous extract obtained from *Cucurbita ficifolia* fruits, which contained this phenolic as one of its five main compounds (58 µg/g). This sample showed an acute and sub-chronic hypoglycemic effect when administered to normal or diabetic mice, also promoting a greater accumulation of glycogen in the liver of the animals, increased levels of glycogen synthase, and decreased glycogen phosphorylase enzyme (Garcia et al. 2017).

The values of rutin determined in the samples (11.077-12.886 mg/g extract) were similar to those found by Gandhi et al. (2011), who quantified the flavonoid at 1.36% (m/m) (equivalent to 13.6 mg/g) in the methanolic extract prepared from the fruit of *Solanum torvum* Swartz, characterized as hypoglycemic after administration to diabetic rats by induction with streptozotocin. These values were even higher than those determined in extracts obtained from the leaves of *Cnidoscolus chayamansa* (2.00 mg/g) (Loarca-Piña et al. 2010) and *Bauhinia variegata* (4.38 mg/g) (Hago et al. 2019), both of which were able to reduce fasting blood glucose when administered to diabetic rats.

Regarding isoquercitrin, the contents (0.466-0.533 mg/g Extract) are in the range of values determined in derivatives obtained from *Ribes meyeri* leaves (0.09-14.64 mg/g). These samples were effective in increasing glucose uptake in 3T3-L1 adipocytes, suggesting their potential use as a functional food ingredient for the prevention of type 2 Diabetes (Zhao et al. 2021).

4. MATERIALS AND METHODS

4.1. Materials

The extract used in this study was obtained from a plant material collected in November 2017 at Castanhal, Pará state, Brazil (coordinates 1.3115937890195082, -47.946452657345034), botanically described by Manoel dos Reis Cordeiro (Empresa Brasileira de Pesquisa Agropecuária – EMBRAPA, Belém, Brazil), one herborized specimen of which was deposited at the Herbarium of Embrapa Amazônia Oriental (IAN), under the number 196.015.

Rutin, chlorogenic acid, *p*-coumaric acid, isoquercitrin, gallic acid, 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2-azinobis (3-ethylbenzothiazoline-6) sulfonic acid (ABTS), 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox), maltodextrin DE 4-7 and Folin-Ciocâlteu reagent were obtained from Sigma Aldrich (St. Louis, MI, USA). Potassium persulphate and aluminum chloride were purchased from LabSynth (São Paulo, Brazil), while maltodextrin Lycatab DSH DE 11-14 and β-cyclodextrin were obtained from Roquette (Lestrem, France). Pectin LM-22-CG and sodium carbonate were purchased from CP Kelco GENU (Großenbrode, Germany) and A.C.E.F. (Fiorenzuola D'Arda, Italy), respectively, and sodium carboxymethylcellulose was donated by Lisapharma (Erba, Italy). Acetic acid was obtained from VWR Chemicals (Fontenay-sous-Bois, France), while formic acid was purchased from Vetec (Duque de Caxias, Brazil). All high-performance liquid chromatography (HPLC) grade solvents were purchased from VWR Chemicals and Merck (Darmstadt, Germany).

4.2. Preparation of the encapsulated samples

Solutions containing 51 mg of each of the encapsulating agents, namely maltodextrin DE 4-7 (MD4), maltodextrin DE 11-14 (MD11), β-cyclodextrin (βCD), pectin (Pec), and sodium carboxymethylcellulose (CMC) were prepared with 56 mL of purified water. To each of them 500 mg of the extract were added under stirring, while a solution without an encapsulating agent was used as control. All solutions were stored under refrigeration at 4 °C.

Determination of the solutions viscosity

The viscosity of the above-described solutions was measured in triplicate at 20 °C using a viscosimeter (Rotational Smart R, Fungi-Lab, Barcelona, Spain) equipped with a spindle LCP at 100 rpm.

Spray-drying of the solutions

Solutions were spray-dried, in duplicate, in a MiniSpray-Dryer (model B-290, Büchi, Milan, Italy) equipped with an inert-loop (model B-295), under nitrogen atmosphere, using a two-fluid nozzle, with a 1.4-mm diameter orifice. The temperature of the inlet drying air was 150 °C, the feed volumetric flow rate 4 mL/min, the drying air volumetric flow rate 742 L/h, and the aspiration rate of 90 % (Cunha *et al.*, 2010), while the outlet air temperature ranged from 60 to 75 °C. The samples

 doi:10.20944/preprints202401.0343.v1

obtained were labeled as Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec, Bu-CMC, and Bu-A (without any wall material) and stored in sealed glass vials, with a rubber stopper and aluminum cap, in a desiccator at room temperature (25±1 ºC) to avoid moisture absorption.

4.3. . Yield of drying (YD)

The spray-dried microparticles were quantitatively recovered from the product collection vessel and cyclone and weighed on analytical balance. The yield of the spray drying process (*YD*) was determined as a percentage, considering the weight of total solids in the solution and that of dry microparticle obtained after each drying cycle (GABBAY-ALVES et al 2017).

4.4. Characterization of the microparticles

Morphology of the particles

Morphological and surface characteristics of Bu-A, Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec and Bu-CMC microparticles were examined by scanning electron microscopy (SEM, Zeiss AURIGA, Oberkochen, Germany), at extra high tension of 1.00 kV. Samples were placed on a double-sided adhesive tape premounted on an aluminum stub and analyzed after 30 min depressurization.

Particle size distribution

Samples were prepared suspending 5 mg of each microparticle in 10 mL of cyclohexane, containing 1% (w/v) of sorbitan trioleate (Span 85) and were then dispersed in an ultrasonic bath (mod. 8510, Branson Ultrasonics Corporation, Brookfield, CT, USA) at high potency for 2 min. The particle size distribution was measured, in triplicate, at an obscuration threshold of at least 10%, using a laser light diffractometer (model Spraytec, Malvern Instruments Ltd, Malvern, UK). The results were expressed in median volumetric particle diameter (Dv50) and in 10th (Dv10) and 90th (Dv90) percentiles, i.e., the values of each diameter to which 50, 10, and 90% of the population are below, respectively. The span value was also calculated as $(Dv_{90} - Dv_{10})/Dv_{50}$.

4.5. Sample preparation for quantitative spectroscopic analyses

Total Phenolics Retained in the microparticles

Aliquots of 20 mg of Bu-MD4, Bu-MD11, and Bu-βCD were suspended in 2 mL of a 50:8:42 (v/v/v) methanol/acetic acid/water solution, stirred (Vortex Velp Scientifica, Milan, Italy) for 1 min, sonicated for 40 min (Branson 8510 Ultrasonic Cleaner, Sterling Heights, MI, USA), centrifuged at 18,670 g for 30 min (Scilogex D3024 Centrifuge, Giorgio Bormac, Capri, Italy), and the resulting supernatants filtered on a 0.45 μm hydrophilic membrane (Robert *et al.*, 2010, with modifications). The same procedure was applied to Bu-Pec, Bu-CMC, and Bu-A but using a 50:50 (v/v) methanol/water solution as a solvent. Membranes with 0.45-μm pore diameter were used for filtration, except for Bu-Pec for which a 0.22 μm membrane was needed. Total Phenolics Retained (TPR) in the particles were quantified according to Dewanto *et al.* (2002).

Total phenolic compounds on the microparticle surface

Aliquots of 20 mg of each type of microparticles were treated with 2 mL of ethanol/methanol (50:50 v/v), stirred in Vortex for 1 min, filtered on a 0.45 μm hydrophilic membrane, 0.22 μm for Bu-P, then analyzed by UV-Vis spectrophotometry (Robert et al. 2010, with modifications). Total phenolic compounds on the surface of microparticles (PS) were quantified, (according to Dewanto et al. 2002).

All the quantitative analyses were performed using a Perkin Elmer Lambda 25 spectrophotometer (Monza, Italy), using the total phenolic content in the extract as reference-TCE, according to the parameter to be calculated (Remigio, 2023).

 doi:10.20944/preprints202401.0343.v1

Determination of total phenolic content in the samples

Aliquots of 125 µL of each solution prepared to determine TPR and 125 µL of Folin-Ciocalteu reagent were added to 0.5 mL of ultrapure water and let stand for 6 minutes; then, 1.25 mL of aqueous sodium carbonate and 1 mL of water were added. The samples stood for 90 min at room temperature and were then analyzed by UV-Vis spectrophotometry at 760 nm to determine their Total Phenolic Content (TPC), according to Dewanto et al. (2002), using gallic acid as standard. AEBu and Bu-A sample solutions were diluted at 20:80 (v/v), and those used for PS determination at 1:1 (v/v), both in methanol/water at (50:50 v/v) to set their absorbance values into the calibration curve range. Bu-A sample solution was diluted at 20:80 (v/v), and those used for PS determination at 1:1 (v/v), both in methanol/water at (50:50 v/v) to adequate their absorbance values to the calibration curve range.

Determination of Total flavonoid content

Aliquots of 20 mg of Bu-MD11 and Bu-βCD, suspended in 2 mL of methanol/acetic acid/water (50:8:42 v/v/v), and of Bu-Pec, Bu-CMC, and Bu-A, in 2 mL of methanol/water (50:50 v/v), were used for quantifying the total flavonoids in each sample, based on Costa et al. (2019), with modifications. The resulting dispersions were stirred in Vortex for 1 min, sonicated for 40 min (Cristófoli Cleaner, Campo Mourão, PR, Brazil), and centrifuged at 7,043 g for 15 min (Eppendorf Centrifuge 5804, Hamburg, Germany). The supernatants were filtered on a 0.22 µm hydrophilic membrane, and then 400 µL of each sample received 500 µL of 2.5% aluminum chloride solution and 4.1 mL of distilled water. The mixtures were stored in the dark for 30 min before being analyzed at 425 nm using a Shimadzu UV-1800 spectrophotometer (Kyoto, Japan). The reference value was determined for the extract (Remígio, 2023).

Total antioxidant Activity

The solutions used to quantify flavonoids had their total antioxidant activity evaluated against the free radicals $DPPH^{\cdot}$ and $ABTS^{\cdot+}$ after dilution to 1 mg/mL with methanol/water (50:50 v/v) and were analyzed in a spectrophotometer (Shimadzu UV 1800, Kyoto, Japan), and the results expressed as a percentage of inhibition (equation 1) and activity total antioxidant (TAA).

$$\% \text{ Inhibition} = \frac{\text{Abs control} - \text{Abs sample}}{\text{Abs control}} \times 100 \qquad \text{(eq. 1)}$$

Using DPPH

To 150 µL of each diluted sample were added 5850 µL of DPPH radical (2,2-diphenyl-1-picrylhydrazyl at 0.06 mM in methanol), the mixtures incubated in absence of light for 30 min, and then analyzed at 515 nm, in triplicate. The antioxidant activity was calculated with a Trolox standard curve (50 µM-800 µM), and the results were expressed as µM Trolox equivalent (µmTEq/g Extrato) (RUFINO et al. 2007).

The same method used to analyze their microparticles was applied to the extract and to Bu-A. The results were expressed as percentage of inhibition (equation 3) and activity total antioxidant (TAA).

Using ABTS

Aliquots of 30 µL of each diluted sample were added to 3000 µL of an ABTS radical solution (obtained from 88 µL of 1.40 mM potassium persulfate solution and 5 mL of 7 mM ABTS solution, kept in the dark, at room temperature for 16 h) and incubated in the absence of light for 6 min and then analyzed at 734 nm, in triplicate. The antioxidant activity was calculated using a Trolox standard curve (100-1500 µM). The results are expressed as µM Trolox equivalent (µmTEq/g Extract) (Re et al. 1999). The same method used to analyze their microparticles was applied to EABu and Bu-A, and the result was expressed as a percentage of inhibition (equation 3) and activity total antioxidant (TAA).

Encapsulation efficiency

 doi:10.20944/preprints202401.0343.v1

The encapsulation efficiency (EE) corresponds to the percentual of phenolics within each microparticle and was calculated for Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec, and Bu-CMC from the amounts of phenolic compounds retained by the microparticles (PME) minus those present on their surface (PS) in relation to the phenolic content of the extract (TPC) (equation 2) (Pashazadeh et al. 2021):

$$EE = \frac{PME - PS}{TPC} \times 100 \quad \text{(eq. 2)}$$

Yield of phenols encapsulation

The yield of the encapsulation process (YE) corresponds to the percentage of phenolics encapsulated by each wall material (TCP), in relation to the phenolic compounds content recorded for the extract (equation 3) (Zaidel et al. 2015; Gabbay-Alves et al 2017):

$$YE = \frac{TPCi}{TPC_A} \times 100 \quad \text{(eq. 3)}$$

4.6. Thermogravimetric analysis/derivative thermogravimetry

Approximately 3 to 6 mg of each encapsulated sample were placed in a 70 μL aluminum pan and heated at a rate of 20 ºC/min under N_2 atmosphere (80 mL/min) from 25 to 200 °C using a TGA/DSC1 equipment (Mettler Toledo, Milan, Italy) driven by STARe System.

4.7. Differential scanning calorimetry

Samples of 3 to 6 mg of each type of microparticle were placed in a 40 μL aluminum pan, sealed and pierced twice to evaluate their phase change behavior and decomposition. Differential scanning calorimetry (DSC) measurements were performed using a DSC 821e instrument (Mettler Toledo, Schweiz, Switzerland) driven by the STARe System scans were performed between 25 and 200 °C at a rate of 20 °C/min under a N2 atmosphere (100 mL/min).

4.8. Quali-quantitative analyses of microparticles using high performance liquid chromatography

Chromatographic conditions. (Remígio, 2023)

Detection and quantification of phenolic compounds present Bu-A, and in the microparticles were performed at 40 ºC in an Agilent 1260 Infinity (Delaware, USA) equipment for high-performance liquid chromatography with a diode array detector (HPLC-DAD) using a Zorbax SB-Aq C18 (150 x 4.6 mm) column, particle size of 5 μm. The mobile phase consisted of (A) aqueous formic acid 0.1 % (v/v), pH= 3, and (B) acetonitrile, and the gradient elution was 0–60 min. 1-20 % B; and 60-65 min 20-1 % B. The flow rate was 1 mL/min, the injection volume was 20 μL, and the detection wavelength was 330 nm.

Qualitative analyses - Detection and Characterization of compounds. (Remigio, 2023)

The presence of gallic acid, caffeic acid, chlorogenic acid, ferulic acid, p-coumaric acid, 2-hydroxycinnamic acid, sinapic acid, tannic acid, apigenin, hyperoside, isoquercitrin, isorhamnetin, quercetin, quercitrin, and rutin in the microencapsulated samples was investigated using solutions at 0.1 mg/mL of them, by comparison of their UV spectra, with those relative to different peaks in the extract, at the corresponding retention times. Chlorogenic acid, p-coumaric acid, rutin, and isoquercitrin were detected and co-eluted with the extract in determined amounts, and the increased peak areas corresponding to each compound registered and compared to the peak areas in the not enriched extract.

Quantitative analyses of microparticles - Preparation of stock and work solutions (Remígio, 2023)

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 4 January 2024 doi:10.20944/preprints202401.0343.v1

Stock solutions (in methanol:water 50:50; v/v, at 1 mg/mL) of chlorogenic acid and p-coumaric acid, and isoquercitrin (0.2 mg/mL) and rutin (1 mg/mL) in pure methanol were blended to provide a work solution containing 10, 30, 100, and 400 µg/mL of p-coumaric acid, rutin, chlorogenic acid, and Isoquercitrin, respectively. The work solution used for quantitative analyses was diluted in methanol to the concentrations listed in Table 1. The calibration curves were plotted using the average peak areas, registered in triplicate, from which the regression equation, linearity, coefficient of determination (R2), limit of detection (LOD), and limit of quantification (LOQ) were determined. The equations were then used to determine the concentration of these compounds in the microparticles.

Table 1. The concentration of standard compounds in the working solutions.

Solution	Concentration (µg/mL)			
	Chlorogenic acid	*p*-Coumaric acid	Rutin	Isoquercitrin
1	50	5.00	200	15.00
2	25	2.50	100	7.50
3	10	1.00	40	3.00
4	5	0.50	20	1.50
5	2.5	0.25	10	0.75

4.9. Statistical analysis

Statistical analysis was performed using GraphPad Prism 9.00 (California, USA, 2020). One-way analysis of variance (ANOVA) and Tukey's multiple comparisons test were conducted to detect statistically significant differences ($p < 0.05$) among values.

CONCLUSIONS

In this work, the aqueous extract of *Bauhinia ungulata* var. *obtusifolia* was analyzed and microencapsulated by spray drying using different wall materials, i.e., maltodextrin DE 11-14 and 4-7, β-cyclodextrin, pectin and sodium carboxymethylcellulose (NaCMC), with the aim of protecting their phenolic compounds with recognized antioxidant and antidiabetic activities. Samples exhibited contents of four phenolic compounds, namely p-coumaric acid, chlorogenic acid, rutin and isoquercitrin, similar or even higher than those described for other hypoglycemic species, which allowed to infer that such a plant species variety could be an interesting option in diabetes treatment consistently with literature data on its popular use. In this sense, one of the next stages of the study will be the use of these phenolic compounds as quality markers of pharmacologically tested derivatives.

The data comparison of the lyophilized extract and the microparticles evidenced the efficiency of the encapsulation process, where NaCMC was shown to be very suitable for the microencapsulation of the aqueous extract of *B. ungulata* var. obtusifolia, which can be combined with MD4-7 to overcome limitations detected, based on the analyses reported.

All tested samples demonstrated antioxidant capacity, which can be attributed, above all, to the flavonoids detected and quantified. The description of this activity reinforces the antioxidant potential of the genus species, inferring that this variety of *B. ungulata* is used as a natural antioxidant whose activity increases its effectivity since oxidative damage is considered a secondary complication of diabetes.

The results reported in the present work provide relevant data on *Bauhinia ungulata* var. obtusifolia (Ducke) Vaz, a plant species on which, to date, hasn't been published in the literature

knowledge about the investigation of its leaves' aqueous extracts under the various aspects analyzed, including microencapsulation, chemical constitution, antidiabetic activity and use safety.

Author Contributions: The authors of this paper have contributed as follows, according to the dimensioning proposed by Pharmaceutics: Wagner Barbosa, responsible for the conceptualization of the thesis here reported, the funding acquisition for the used equipment, the project administration by the sponsor and by the university, the supervision of the experimental work, and the writing – review & editing during a recent post-doctoral fellowship. Attilio Converti, who contributed with critical insight by writing - review & editing the manuscript, performed the data curation as post-doctor supervisor. Contributions to the investigation of the samples, in associated laboratories, were made by José Otávio Silva-Júnior and Roseane Maria Ribeiro-Costa. Myrth Remigio developed the conceptualized methodology as her doctoral thesis. At the UNIPR, important contributions to the methodology was made by Teresa Greco, and Alessandra Rossi, who supervised the general work at that institution. Roseane Maria Ribeiro-Costa made her contribution by data validation. The writing of the original draft, as her doctoral thesis, was in charge of Myrth Remigio.

Funding: This research was funded by Coordination for the Improvement of Higher Education Personnel (CAPES, MSNR for the institutional scholarship), National Council for Scientific and Technological Development (CNPq, JOCSJ, WLRB for postdoctoral grant nr. 200015/2023-0). Postgraduate Program in Pharmaceutical Innovation-Federal University of Para (PPGIF-UFPA), and Food and Drug Department, University of Parma for laboratories facilities. Financing Agency of Studies and Projects (FINEP, WLRB for financing project, Grant nr. 1792/2010).

Acknowledgments: The authors thank the Coordination for the Improvement of Higher Education Personnel (CAPES, MSNR for the scholarship), National Council for Scientific and Technological Development (CNPq, JOCSJ, WLRB for postdoctoral grant), Postgraduate Program in Pharmaceutical Innovation (PPGIF) and Financing Agency of Studies and Projects (FINEP, WLRB for financing project), and Federal University of Pará (UFPA), University of Genoa (UNIGE) and University of Parma (UNIPR, MSNR for the scholarship), Italy, for the experimental facilities.

Conflicts of Interest: The authors declare no conflict of interest.

Bauhinia ungulata Lyophilized extract (Bu-L)
Microparticles (*Bauhinia ubgulata*-Wall material): Bu-MD4, Bu-MD11, Bu-βCD, Bu-Pec, Bu-CMC, and Bu-A (without excipients)
Total Flavonoid Content (TFC)
Total Phenolic content in the Microencapsulated Extracts (PME)
Total Phenolic Content of the extract (TPC)
Total Phenolic compounds on the Surface of microparticles (PS)
Encapsulation Efficiency (EE)
Yield Encapsulation (YE)

References

AGUIAR, J., COSTA, R., ROCHA, F., ESTEVINHO, B. N., SANTOS, L. Design of microparticles containing natural antioxidants: Preparation, characterization and controlled release studies. **Powder technology**, v. 313, p. 287-292, 2017.

AHMADIAN, Z., NIAZMAND, R., POURFARZAD, A. Microencapsulation of saffron petal phenolic extract: Their characterization, in vitro gastrointestinal digestion, and storage stability. **Journal of food science**, v. 84, n. 10, p. 2745-2757, 2019.

AHMAD, M., ASHRAF, B., GANI, A., GANI, A. Microencapsulation of saffron anthocyanins using β glucan and β cyclodextrin: Microcapsule characterization, release behaviour & antioxidant potential during *in-vitro* digestion. **International journal of biological macromolecules**, v. 109, p. 435-442, 2018.

ALOTHMAN, M., BHAT, R., KARIM, A. A. Antioxidant capacity and phenolic content of selected tropical fruits from Malaysia, extracted with different solvents. **Food Chemistry**, v. 115, n. 3, p. 785-788, 2009.

ANISH, C., UPADHYAY, A. K., SEHGAL, D., PANDA, A. K. Influences of process and formulation parameters on powder flow properties and immunogenicity of spray dried polymer particles entrapping recombinant pneumococcal surface protein A. **International Journal of Pharmaceutics**, v. 466, p. 198-210, 2014.

AUGUSTO, T. R., SALINAS, E. S. S., ALENCAR, S. M., D'ARCE, M. A. B. R., CAMARGO, A. C. D., VIEIRA, T. M. F. D. S. Phenolic compounds and antioxidant activity of hydroalcoholic extracts of wild and cultivated murtilla (*Ugni molinae* Turcz.). **Food Science and Technology**, v. 34, p. 667-679, 2014.

AZEVEDO, M. S., MANSO, C. Oxygen free radicals and complications of diabetes mellitus. **Acta Medica Portuguesa**, v. 5, n. 4, p. 201-207, 1992.

BALDUCCI, A. G., CAGNANI, S., SONVICO, F., ROSSI, A., BARATA, P., COLOMBO, G., COLOMBO, P., BUTTINI, F. Pure insulin highly respirable powders for inhalation. **European Journal of Pharmaceutical Sciences**, v. 51, p. 110-117, 2014.

BELŠČAK-CVITANOVIĆ, A., LEVIĆ, S., KALUŠEVIĆ, A., ŠPOLJARIĆ, I., ĐORĐEVIĆ, V., KOMES, D., MRŠIĆ, G., NEDOVIĆ, V. Efficiency assessment of natural biopolymers as encapsulants of green tea (*Camellia sinensis* L.) bioactive compounds by spray drying. **Food and bioprocess technology**, v. 8, n. 12, p. 2444-2460, 2015.

BHANDARI, B., HOWES, T. Relating the stickiness property of foods undergoing drying and dried products to their surface energetics. **Drying Technology**, v. 23, n. 4, p. 781-797, 2005.

BHANDARI, B. R., DATTA, N., HOWES, T. Problems associated with spray drying of sugar-rich foods. **Drying technology**, v. 15, n. 2, p. 671-684, 1997.

BOEING, J. S., BARIZÃO, É. O., MONTANHER, P. F., DE CINQUE ALMEIDA, V., VISENTAINER, J. V. Evaluation of solvent effect on the extraction of phenolic compounds and antioxidant capacities from the berries: application of principal component analysis. **Chemistry Central Journal**, v. 8, n. 1, p. 1-9. 2014.

BRASIL. **Farmacopeia Brasileira**. 1ª edição, 1926.

BRASIL. Agência Nacional de Vigilância Sanitária (ANVISA). **Farmacopeia Brasileira**, 6ª edição, Brasília: Editora do Ministério da Saúde, 2019.

BRATU, M. M., BIRGHILA, S., POPESCU, A., NEGREANU-PIRJOL, B. S., NEGREANU-PIRJOL, T. Correlation of antioxidant activity of dried berry infusions with the polyphenols and selected microelements contents. **Bulletin of the Chemical Society of Ethiopia**, v. 32, n. 1, p. 1-12, 2018.

CALISKAN, G., DIRIM, S. N. The effects of the different drying conditions and the amounts of maltodextrin addition during spray drying of sumac extract. **Food and bioproducts Processing**, v. 91, n. 4, p. 539-548, 2013.

CARVALHO, A. A., SANTOS, L. R. D., FARIAS, R. R. S. D., CHAVES, M. H., FEITOSA, C. M., VIEIRA JÚNIOR, G. M., ARAÚJO, M. R. S., FERREIRA, P. M. P., PESSOA, C. D. Ó. Phenolic derivatives and antioxidant activity of polar extracts from *Bauhinia pulchella*. **Química Nova**, v. 41, p. 405-411, 2018.

CHAUMUN, M., GOËLO, V., RIBEIRO, A. M., ROCHA, F., ESTEVINHO, B. N. *In vitro* evaluation of microparticles with *Laurus nobilis* L. extract prepared by spray-drying for application in food and pharmaceutical products. **Food and Bioproducts Processing**, v. 122, p. 124-135, 2020.

CHORDIYA, M. A., SENTHILKUMARAN, K. Cyclodextrin in drug delivery: A review. **Research and Reviews in Pharmacy and Pharmaceutical Sciences**, v. 1, p. 19-29, 2012.

CID-ORTEGA, S., GUERRERO-BELTRÁN, J. Á. Microencapsulation of *Hibiscus sabdariffa* (Roselle) extracts by spray drying using maltodextrin and gum arabic as carriers. **Journal of Food Research**, v. 9, n. 5, p. 53-66, 2020.

COSTA, R. S., TEIXEIRA, C. B., GABBAY ALVES, T. V., RIBEIRO-COSTA, R. M., CASAZZA, A. A., ALIAKBARIAN, B., CONVERTI, A., SILVA JÚNIOR, J. O. C., PEREGO, P. Optimization of spray drying conditions to microencapsulate cupuassu (*Theobroma grandiflorum*) seed by-product extract. **Natural Product Research**, v. 33, n. 18, p. 2600-2608, 2019.

COSTA, R. S., PINHEIRO, W. B. D. S., ARRUDA, M. S. P., COSTA, C. E. F., CONVERTI, A., RIBEIRO COSTA, R. M., SILVA JÚNIOR, J. O. C. Thermoanalytical and phytochemical study of the cupuassu (*Theobroma grandiflorum* Schum.) seed by-product in different processing stages. **Journal of Thermal Analysis and Calorimetry**, p. 1-10, 2020.

CUNHA, A. M., MENON, S., MENON, R., COUTO, A. G., BÜRGER, C., BIAVATTI, M. W. Hypoglycemic activity of dried extracts of *Bauhinia forficata* Link. **Phytomedicine**, v. 17, n. 1, p. 37-41, 2010.

DEWANTO, V., WU, X., ADOM, K. K., LIU, R. H. Thermal processing enhances the nutritional value of tomatoes by increasing total antioxidant activity. **Journal of agricultural and food chemistry**, v. 50, n. 10, p. 3010-3014, 2002.

DÍAZ-BANDERA, D., VILLANUEVA-CARVAJAL, A., DUBLÁN-GARCÍA, O., QUINTERO-SALAZAR, B., DOMINGUEZ-LOPEZ, A. Assessing release kinetics and dissolution of spray-dried Roselle (*Hibiscus sabdariffa* L.) extract encapsulated with different carrier agents. **LWT-Food Science and Technology**, v. 64, n. 2, p. 693-698, 2015.

DING, Z., TAO, T., WANG, X., PRAKASH, S., ZHAO, Y., HAN, J., WANG, Z. Influences of different carbohydrates as wall material on powder characteristics, encapsulation efficiency, stability and degradation kinetics of microencapsulated lutein by spray drying. **International Journal of Food Science & Technology**, v. 55, n. 7, p. 2872-2882, 2020.

DÜRIG, T., KARAN, K. Binders in wet granulation. In: **Handbook of Pharmaceutical Wet Granulation**. Academic Press, 2019. p. 317-349.

EINHORN-STOLL, U., HATAKEYAMA, H., HATAKEYAMA, T. Influence of pectin modification on water binding properties. **Food Hydrocolloids**, v. 27, n. 2, p. 494-502, 2012.

EINHORN-STOLL, U., VASILEVA, E., HECHT, T., DRUSCH, S. Investigation of pectin-water interactions: A practical approach. In: **Gums and Stabilisers for the Food Industry 18: Hydrocolloid Functionality for Affordable and Sustainable Global Food Solutions**, 2016. p. 3-12.

ESCOBAR-AVELLO, D., AVENDAÑO-GODOY, J., SANTOS, J., LOZANO-CASTELLÓN, J., MARDONES, C., VON BAER, D., LUENGO, J., LAMUELA-RAVENTÓS, R. M., VALLVERDÚ-QUERALT, A., GÓMEZ-GAETE, C. Encapsulation of phenolic compounds from a grape cane pilot-plant extract in hydroxypropyl beta-cyclodextrin and maltodextrin by spray drying. **Antioxidants**, v. 10, n. 7, p. 1130, 2021.

ESPEJEL-NAVA, J. A., VEGA-AVILA, E., ALARCON-AGUILAR, F., CONTRERAS-RAMOS, A., DIAZ-ROSAS, G., TREJO-AGUILAR, G., ORTEGA-CAMARILLO, C. A phenolic fraction from Catharanthus roseus L. stems decreases glycemia and stimulates insulin secretion. **Evidence-Based Complementary and Alternative Medicine**, v. 2018, p. 1-9, 2018.

ETZBACH, L., MEINERT, M., FABER, T., KLEIN, C., SCHIEBER, A., WEBER, F. Effects of carrier agents on powder properties, stability of carotenoids, and encapsulation efficiency of goldenberry (*Physalis peruviana* L.) powder produced by co-current spray drying. **Current Research in Food Science**, v. 3, p. 73-81, 2020.

FAN, L., PENG, M., ZHOU, X., WU, H., HU, J., XIE, W., LIU, S. Modification of carboxymethyl cellulose grafted with collagen peptide and its antioxidant activity. **Carbohydrate polymers**, v. 112, p. 32-38, 2014.

FANG, Z., BHANDARI, B. Effect of spray drying and storage on the stability of bayberry polyphenols. **Food Chemistry**, v. 129, n. 3, p. 1139-1147, 2011.

FARÍAS-CERVANTES, V. S., SALINAS-MORENO, Y., CHÁVEZ-RODRÍGUEZ, A., LUNA-SOLANO, G., MEDRANO-ROLDAN, H., ANDRADE-GONZÁLEZ, I. Stickiness and agglomeration of blackberry and raspberry spray dried juices using agave fructans and maltodextrin as carrier agents. **Czech Journal of Food Sciences**, v. 38, n. 4, p. 229-236, 2020.

FLOEGEL, A., KIM, D. O., CHUNG, S. J., KOO, S. I., CHUN, O. K. Comparison of ABTS·+/DPPH· assays to measure antioxidant capacity in popular antioxidant-rich US foods. **Journal of food composition and analysis**, v. 24, n. 7, p. 1043-1048, 2011.

FLORA DO BRASIL EM CONSTRUÇÃO, 2019 - Algas, fungos e plantas. Disponível em:http://floradobrasil.jbrj.gov.br/reflora/listaBrasil/PrincipalUC/PrincipalUC.do;jsessionid=5923F194BDA7DA1448013CFF9EB8DC9A#CondicaoTaxonCP. Acesso em: 14 de fevereiro de 2019.

FORTIS-BARRERA, M. D. L. Á., ALARCÓN-AGUILAR, F. J., BECERRIL-GARCÍA, A., FLORES-SÁENZ, J. L. E., ALMANZA-PÉREZ, J. C., GARCÍA-LORENZANA, M., ROBERTO CARLOS LAZZARINI-LECHUGA, R. C., ROMÁN-RAMOS, R., BLANCAS-FLORES, G. Mechanism of the hypoglycemic activity and hepatoprotective effect of the aqueous extract of Cecropia obtusifolia Bertol. **Journal of medicinal food**, v. 23, n. 7, p. 783-792, 2019.

FREITAS, C. M. P., COIMBRA, J. S. R., SOUZA, V. G. L., SOUSA, R. C. S. Structure and applications of pectin in food, biomedical, and pharmaceutical industry: A review. **Coatings**, v. 11, n. 8, 922, p. 1-22, 2021.

GABBAY ALVES, T. V., SILVA DA COSTA, R., ALIAKBARIAN, B., CASAZZA, A. A., PEREGO, P., CARRERA SILVA JUNIOR, J. O., RIBEIRO-COSTA, R. M., CONVERTI, A. Microencapsulation of *Theobroma cacao* L. waste extract: optimization using response surface methodology. **Journal of microencapsulation**, v. 34, n. 2, p. 111-120, 2017.

GALLEGOS-INFANTE, J. A., ROCHA-GUZMÁN, N. E., GONZÁLEZ-LAREDO, R. F., MEDINA-TORRES, L., GOMEZ-ALDAPA, C. A., OCHOA-MARTÍNEZ, L. A., MARTÍNEZ-SÁNCHEZ, A. E., HERNÁNDEZ-SANTOS, B., RODRÍGUEZ-RAMÍREZ, J. Physicochemical properties and antioxidant capacity of oak (*Quercus resinosa*) leaf infusions encapsulated by spray-drying. **Food Bioscience**, v. 2, p. 31-38, 2013.

GALLO, L., RAMÍREZ-RIGO, M. V., PIÑA, J., BUCALÁ, V. A comparative study of spray-dried medicinal plant aqueous extracts. Drying performance and product quality. **Chemical Engineering Research and Design**, v. 104, p. 681-694, 2015.

GALLO, L., RAMÍREZ-RIGO, M. V., PIÑA, J., PALMA, S., ALLEMANDI, D., BUCALÁ, V. *Valeriana officinalis* dry plant extract for direct compression: preparation and characterization. **Scientia pharmaceutica**, v. 80, n. 4, p. 1013-1026, 2012.

GANDHI, G. R., IGNACIMUTHU, S., PAULRAJ, M. G. *Solanum torvum* Swartz. fruit containing phenolic compounds shows antidiabetic and antioxidant effects in streptozotocin induced diabetic rats**. Food and Chemical Toxicology**, v. 49, n. 11, p. 2725-2733, 2011.

GARCIA, J. G., GARCIA, M. L., ZAMILPA, A., PEREZ, C. J. A., VILLAGOMEZ, I. E. J., ROMAN, R. R., ALARCON-AGUILAR, J. F. Chemical characterization of a hypoglycemic extract from *Cucurbita ficifolia* Bouche that induces liver glycogen accumulation in diabetic mice. **African Journal of Traditional, Complementary and Alternative Medicines**, v. 14, n. 3, p. 218-230, 2017.

GAVARIĆ, A., VIDOVIĆ, S., ZEKOVIĆ, Z., VLADIĆ, J. Influence of storage time on quality of spray-dried extracts of basil (*Ocimum basilicum* L.). **Hrana u zdravlju i bolesti: znanstveno-stručni časopis za nutricionizam i dijetetiku**, v. 8, n. 1, p. 6-12, 2019.

GOULA, A. M., KARAPANTSIOS, T. D., ACHILIAS, D. S., ADAMOPOULOS, K. G. Water sorption isotherms and glass transition temperature of spray dried tomato pulp. **Journal of Food Engineering**, v. 85, n. 1, p. 73-83, 2008.

HAGO, S., MAHROUS, E. A., MOAWAD, M., ABDEL-WAHAB, S., ABDEL-SATTAR, E. Evaluation of antidiabetic activity of *Morus nigra* L. and *Bauhinia variegata* L. leaves as Egyptian remedies used for the treatment of diabetes. **Natural Product Research,** v. 35, n. 5, p. 829-835, 2019.

HOSSAIN, M. A., PERVIN, R. Current antidiabetic drugs: review of their efficacy and safety. **Nutritional and Therapeutic Interventions for Diabetes and Metabolic Syndrome**, p. 455-473, 2018

JAIN, M. S., LOHARE, G. B., BARI, M. M., CHAVAN, R. B., BARHATE, S. D., SHAH, C. B. Spray drying in pharmaceutical industry: A review. **Research Journal of pharmaceutical dosage forms and technology**, p. 4, n. 2, p. 74-79, 2012.

JAKOBEK, L., MATIĆ, P. Non-covalent dietary fiber-polyphenol interactions and their influence on polyphenol bioaccessibility. **Trends in Food Science & Technology**, 83, 235-247, 2019.

JINAPONG, N., SUPHANTHARIKA, M., JAMNONG, P. Production of instant soymilk powders by ultrafiltration, spray drying and fluidized bed agglomeration. **Journal of food engineering**, v. 84, n. 2, p. 194-205, 2008.

JOVANOVIĆ, M., ĆUJIĆ-NIKOLIĆ, N., DRINIĆ, Z., JANKOVIĆ, T., MARKOVIĆ, S., PETROVIĆ, P., ŠAVIKIN, K. Spray drying of *Gentiana asclepiadea* L. root extract: Successful encapsulation into powders with preserved stability of bioactive compounds. **Industrial Crops and Products**, v. 172, 114044, 2021.

KEOGH, M. K., MURRAY, C. A., T O'KENNEDY, B. Effects of ultrafiltration of whole milk on some properties of spray-dried milk powders. **International Dairy Journal**, v. 13, n. 12, p. 995-1002, 2003.

KIM, D. O., LEE, K. W., LEE, H. J., LEE, C. Y. Vitamin C equivalent antioxidant capacity (VCEAC) of phenolic phytochemicals. **Journal of Agricultural and food chemistry**, v. 50, n. 13, p. 3713-3717, 2002.

KOMOROWSKA, P., ROZANSKA, S., ROZANSKI, J. Effect of the degree of substitution on the rheology of sodium carboxymethylcellulose solutions in propylene glycol/water mixtures. **Cellulose**, v. 24, n. 10, p. 4151-4162, 2017.

KONO, H., OSHIMA, K., HASHIMOTO, H., SHIMIZU, Y., TAJIMA, K. NMR characterization of sodium carboxymethyl cellulose: Substituent distribution and mole fraction of monomers in the polymer chains. **Carbohydrate Polymers**, v. 146, p. 1-9, 2016.

KRISHNAIAH, D., NITHYANANDAM, R., SARBATLY, R. A critical review on the spray drying of fruit extract: Effect of additives on physicochemical properties. **Critical reviews in food science and nutrition**, v. 54, n. 4, p. 449-473, 2014.

KUCK, L. S., NOREÑA, C. P. Z. Microencapsulation of grape (*Vitis labrusca* var. Bordo) skin phenolic extract using gum Arabic, polydextrose, and partially hydrolyzed guar gum as encapsulating agents. **Food chemistry**, v. 194, p. 569-576, 2016.

KWON, O., ECK, P., CHEN, S., CORPE, C. P., LEE, J. H., KRUHLAK, M., LEVINE, M. Inhibition of the intestinal glucose transporter GLUT2 by flavonoids. **The FASEB Journal**, v. 21, n. 2, p. 366-377, 2007.

LABUSCHAGNE, P. Impact of wall material physicochemical characteristics on the stability of encapsulated phytochemicals: A review. **Food Research International**, v. 107, p. 227-247, 2018

LI, Y., GAO, F., SHAN, F., BIAN, J., ZHAO, C. Study on the interaction between 3 flavonoid compounds and a-amylase by fluorescence spectroscopy and enzymatic kinetics. **Journal of Food Science**, v. 74, p. 199-203, 2009.

LI, Y. Q., ZHOU, F. C., GAO, F., BIAN, J. S., SHAN, F. Comparative evaluation of quercetin, Isoquercetin and Rutin as inhibitors of a-glucosidase. **Journal of Agricultural and Food Chemistry, v.** 57, p. 11463-11468, 2009.

LI, A. N., LI, S., ZHANG, Y. J., XU, X. R., CHEN, Y. M., LI, H. B. Resources and biological activities of natural polyphenols. **Nutrients**, v. 6, n. 12, p. 6020-6047, 2014

LOARCA-PIÑA, G., MENDOZA, S., RAMOS-GÓMEZ, M., REYNOSO, R. Antioxidant, antimutagenic, and antidiabetic activities of edible leaves from *Cnidoscolus chayamansa* Mc. Vaugh. **Journal of Food science,** p. 75, n. 2, p. 68-72, 2010.

LÓPEZ-NICOLÁS, J. M., RODRÍGUEZ-BONILLA, P., GARCÍA-CARMONA, F. Cyclodextrins and antioxidants. **Critical reviews in food science and nutrition**, v. 54, n. 2, p. 251-276, 2014.

LU, W., YANG, X., SHEN, J., LI, Z., TAN, S., LIU, W., CHENG, Z. Choosing the appropriate wall materials for spray-drying microencapsulation of natural bioactive ingredients: Taking phenolic compounds as examples. **Powder Technology**, v. 394, p. 562-574, 2021.

MA, Y., HOU, C. J., FA, H. B., HUO, D. Q., YANG, M. Synthesis and antioxidant property of hydroxycinnamoyl maltodextrin derivatives. **International Journal of Food Science & Technology**, v. 51, n. 11, p. 2450-2459, 2016.

MAHDAVI, S. A., JAFARI, S. M., ASSADPOOR, E., DEHNAD, D. Microencapsulation optimization of natural anthocyanins with maltodextrin, gum Arabic and gelatin. **International journal of biological macromolecules**, v.85, p. 379-385, 2016.

MEDINA-TORRES, L., SANTIAGO-ADAME, R., CALDERAS, F., GALLEGOS-INFANTE, J. A., GONZÁLEZ-LAREDO, R. F., ROCHA-GUZMÁN, N. E., NÚÑEZ-RAMIREZ, D. M., BERNAD-BERNAD, M. J, MANERO, O. Microencapsulation by spray drying of laurel infusions (*Litsea glaucescens*) with maltodextrin. **Industrial Crops and Products**, v. 90, p. 1-8, 2016.

MELO, P. S., BERGAMASCHI, K. B., TIVERON, A. P., MASSARIOLI, A. P., OLDONI, T. L. C., ZANUS, M. C., PEREIRA, G. E., ALENCAR, S. M. D. Composição fenólica e atividade antioxidante de resíduos agroindustriais. **Ciência Rural**, v. 41, p. 1088-1093, 2011.

MOSELEY, R., LEAVER, M., WALKER, M., WADDINGTON, R. J., PARSONS, D., CHEN, W. Y. J., EMBERY, G. Comparison of the antioxidant properties of HYAFF®-11p75, AQUACEL® and hyaluronan towards reactive oxygen species *in vitro*. **Biomaterials**, v. 23, n. 10, p. 2255-2264, 2002.

MOSELEY, R., WALKER, M., WADDINGTON, R. J., CHEN, W. Y. J. Comparison of the antioxidant properties of wound dressing materials - carboxymethylcellulose, hyaluronan benzyl ester and hyaluronan, towards polymorphonuclear leukocyte-derived reactive oxygen species. **Biomaterials**, v. 24, n. 9, p. 1549-1557, 2003.

NADEEM, H. Ş., TORUN, M., ÖZDEMIR, F. Spray drying of the mountain tea (*Sideritis stricta*) water extract by using different hydrocolloid carriers. **LWT-Food Science and Technology**, v. 44, n. 7, p. 1626-1635, 2011.

NAVARRO-FLORES, M. J., VENTURA-CANSECO, L. M. C., MEZA-GORDILLO, R., AYORA-TALAVERA, T. D. R., ABUD-ARCHILA, M. Spray drying encapsulation of a native plant extract rich in phenolic compounds with combinations of maltodextrin and non-conventional wall materials. **Journal of Food Science and Technology**, v. 57, n. 11, p. 4111-4122, 2020.

NEGRÃO-MURAKAMI, A. N., NUNES, G. L., PINTO, S. S., MURAKAMI, F. S., AMANTE, E. R., PETRUS, J. C. C., PRUDÊNCIO, E. S., AMBONI, R. D. Influence of DE-value of maltodextrin on the physicochemical properties, antioxidant activity, and storage stability of spray dried concentrated mate (*Ilex paraguaiensis* A. St. Hil.). **LWT-Food Science and Technology**, v. 79, p. 561-567, 2017.

NIAMNUY, C., POOMKOKRAK, J., DITTANET, P., DEVAHASTIN, S. Impacts of spray drying conditions on stability of isoflavones in microencapsulated soybean extract. **Drying Technology**, v. 37, n. 14, p. 1844-1862, 2019.

NUNES, G. L., BOAVENTURA, B. C. B., PINTO, S. S., VERRUCK, S., MURAKAMI, F. S., PRUDÊNCIO, E. S., AMBONI, R. D. D. M. C. Microencapsulation of freeze concentrated *Ilex paraguaiensis* extract by spray drying. **Journal of Food Engineering**, v. 151, p. 60-68, 2015.

OLIVEIRA, O. W., PETROVICK, P. R. Spray drying of plant extracts: basic remarks and application. **Revista Brasileira de Farmacognosia**, v. 20, n. 4, p. 641-650, 2010.

PALSIKOWSKI, P. A., BESEN, L. M., SANTOS, K. A., SILVA, C., SILVA, E. A. Supercritical CO2 oil extraction from *Bauhinia forficata* link subsp. *pruinosa* leaves: Composition, antioxidant activity and mathematical modeling. **The Journal of Supercritical Fluids**, v. 153, 104588, p. 1-9, 2019.

Pashazadeh, H., Zannou, O., Ghellam, M., Koca, I., Galanakis, C. M., Aldawoud, T. M. Optimization and encapsulation of phenolic compounds extracted from maize waste by freeze-drying, spray-drying, and microwave-drying using maltodextrin. **Foods**, v. 10, n. 6. 2021

PASRIJA, D., EZHILARASI, P. N., INDRANI, D., ANANDHARAMAKRISHNAN, C. Microencapsulation of green tea polyphenols and its effect on incorporated bread quality. **LWT-Food Science and Technology**, v. 64, n. 1, p. 289-296, 2015.

PATEL, R. P.; PATEL, M. P.; SUTHAR, A. M. Spray drying technology: an overview. **Indian Journal of Science and Technology**, v. 2, n. 10, p. 44-47, 2009.

PEI, K., OU, J., HUANG, J., OU, S. p-Coumaric acid and its conjugates: dietary sources, pharmacokinetic properties and biological activities. **Journal of the Science of Food and Agriculture**, v. 96, n. 9, p. 2952-2962, 2016.

PEREZ-PEREZ, L. M., HUERTA-OCAMPO, J. Á., RUIZ-CRUZ, S., CINCO-MOROYOQUI, F. J., WONG-CORRAL, F. J., RASCÓN-VALENZUELA, L. A., ROBLES-GARCÍA, M. A., GONZÁLEZ-VEGA, R. I., ROSAS-BURGOS, E. C., CORELLA-MADUEÑO, M. A. G., DEL-TORO-SÁNCHEZ, C. L. Evaluation of quality, antioxidant capacity, and digestibility of chickpea (*Cicer arietinum* L. cv Blanoro) stored under N2 and CO2 atmospheres. **Molecules**, v. 26, n. 9, 2773, 2021.

PICOT-ALLAIN, M. C. N., RAMASAWMY, B., EMMAMBUX, M. N. Extraction, characterisation, and application of pectin from tropical and sub-tropical fruits: a review. **Food Reviews International**, v. 38, n. 3, p. 282-312, 2020.

POOMKOKRAK, J., NIAMNUY, C., CHOICHAROEN, K., DEVAHASTIN, S. Encapsulation of soybean extract using spray drying. **Journal of Food Science and Agricultural Technology**, v. 1, p. 105-110, 2015.

PORT'S, P. S., CHISTÉ, R. C., GODOY, H. T., PRADO, M. A. The phenolic compounds and the antioxidant potential of infusion of herbs from the Brazilian Amazonian region. **Food Research International**, v. 53, n. 2, p. 875-881, 2013.

POURASHOURI, P., SHABANPOUR, B., RAZAVI, S. H., JAFARI, S. M., SHABANI, A., AUBOURG, S. P. Oxidative stability of spray-dried microencapsulated fish oils with different wall materials. **Journal of aquatic food product technology**, v. 23, n. 6, p. 567-578, 2014.

PUDZIUVELYTE, L., MARKSA, M., JAKSTAS, V., IVANAUSKAS, L., KOPUSTINSKIENE, D. M., BERNATONIENE, J. Microencapsulation of *Elsholtzia ciliata* Herb Ethanolic Extract by Spray-Drying: Impact of resistant-maltodextrin complemented with sodium caseinate, skim milk, and beta-cyclodextrin on the quality of spray-dried powders. **Molecules**, v. 24, n. 8, p. 1461, 2019.

RAJABI, H., GHORBANI, M., JAFARI, S. M., MAHOONAK, A. S., RAJABZADEH, G. Retention of saffron bioactive components by spray drying encapsulation using maltodextrin, gum Arabic and gelatin as wall materials. **Food hydrocolloid**s, v. 51, p. 327-337, 2015.

RE, R., PELLEGRINI, N., PROTEGGENTE, A., PANNALA, A., YANG, M., RICE-EVANS, C. Antioxidant activity applying an improved ABTS·+ radical cation decolorization assay. **Free Radical Biology and Medicine**, v. 26, n. 9-10, p. 1231-1237, 1999.

REZENDE, Y. R. R. S., NOGUEIRA, J. P., NARAIN, N. Microencapsulation of extracts of bioactive compounds obtained from acerola (*Malpighia emarginata* DC) pulp and residue by spray and freeze drying: Chemical, morphological and chemometric characterization. **Food Chemistry**, v. 254, p. 281-291, 2018.

RICE-EVANS, C. A., MILLER, N. J., PAGANGA, G. Structure-antioxidant activity relationships of flavonoids and phenolic acids. **Free radical biology and medicine**, v. 20, n. 7, p. 933-956, 1996.

RIVERO-PÉREZ, M. D., MUNIZ, P. I. L. A. R., GONZÁLEZ-SANJOSÉ, M. L. Antioxidant profile of red wines evaluated by total antioxidant capacity, scavenger activity, and biomarkers of oxidative stress methodologies. **Journal of Agricultural and Food Chemistry**, v. 55, n. 14, p. 5476-5483, 2007.

ROBERT, P., GORENA, T., ROMERO, N., SEPULVEDA, E., CHAVEZ, J., SAENZ, C. Encapsulation of polyphenols and anthocyanins from pomegranate (*Punica granatum*) by spray drying. **International Journal of Food Science & Technology**, v. 45, n. 7, p. 1386-1394, 2010.

ROCHA, F. D., TEIXEIRA, V. L., PEREIRA, R. C., KAPLAN, M. A. C. Diabetes mellitus e estresse oxidativo: produtos naturais como alvo de novos modelos terapêuticos. **Revista Brasileira de Farmacognosia**, v. 87, n. 2, p. 49-54, 2006.

ROOS, Y., KAREL, M. Phase transitions of mixtures of amorphous polysaccharides and sugars. **Biotechnology Progress**, v. 7, n. 1, p. 49-53, 1991.

RUDRAPAL, M., KHAIRNAR, S. J., KHAN, J., DUKHYIL, A. B., ANSARI, M. A., ALOMARY, M. N., ALSHABRMI, F. M., PALAI, S., DEB, P. K., DEVI, R. Dietary polyphenols and their role in oxidative stress-induced human diseases: insights into protective effects, antioxidant potentials and mechanism (s) of action. **Frontiers in pharmacology**, v. 13, 2022.

RUFINO, M. D. S. M., ALVES, R. E., DE BRITO, E. S., DE MORAIS, S. M., SAMPAIO, C. D. G., PÉREZ-JIMENEZ, J., SAURA-CALIXTO, F. D. Metodologia científica: determinação da atividade antioxidante total em frutas pela captura do radical livre DPPH·. **Embrapa Agroindústria Tropical - Comunicado Técnico 127**, p. 1-4, 2007.

SANSONE, F. F., MENCHERINI, T., PICERNO, P., ESPOSITO, T., DEL GAUDIO, P., RUSSO, P., PEPE, G., LAURO, M. R., AQUINO, R. P. Microencapsulation by spray drying of *Lannea microcarpa* extract: Technological characteristics and antioxidant activity. **Journal of Pharmacy & Pharmacognosy Research**, v. 2, n. 4, p. 100-109, 2014.

SARRATE, R., TICÓ, J. R., MIÑARRO, M., CARRILLO, C., FÀBREGAS, A., GARCÍA-MONTOYA, E., PÉREZ-LOZANO, P., SUÑÉ-NEGRE, J. M. Modification of the morphology and particle size of pharmaceutical excipients by spray drying technique. **Powder Technology**, v. 270, p. 244-255, 2015.

SCOLES, R. Sabiduría popular y plantas medicinales: el ejemplo de la comunidad negra de Itacoã, Acará, Pará. **Boletim do Museu Paraense Emílio Goeldi Ciências Naturais**, v. 1, n. 2, p. 79-102, 2006.

SHEKUNOV, B. Y., CHATTOPADHYAY, P., TONG, H. H., CHOW, A. H. Particle size analysis in pharmaceutics: principles, methods and applications. **Pharmaceutical research**, v. 24, n. 2, p. 203-227, 2007.

SHIBANO, M., KAKUTANI, K., TANIGUCHI, M., YASUDA, M., BABA, K. Antioxidant constituents in the dayflower (*Commelina communis* L.) and their α-glucosidase-inhibitory activity. **Journal of Natural Medicines**, v. 62, n. 3, p. 349-353, 2008.

SHRESTHA, A. K., UA-ARAK, T., ADHIKARI, B. P., HOWES, T., BHANDARI, B. R. Glass transition behavior of spray dried orange juice powder measured by differential scanning calorimetry (DSC) and thermal mechanical compression test (TMCT). **International Journal of Food Properties**, v. 10, n. 3, p. 661-673, 2007.

SIEMONS, I., POLITIEK, R. G. A., BOOM, R. M., VAN DER SMAN, R. G. M., SCHUTYSER, M. A. I. Dextrose equivalence of maltodextrins determines particle morphology development during single sessile droplet drying. **Food Research International**, v. 131, 108988, 2020.

SOSNIK, A., SEREMETA, K. P. Advantages and challenges of the spray-drying technology for the production of pure drug particles and drug-loaded polymeric carriers. **Advances in colloid and interface science**, v. 223, p. 40-54, 2015

SRIVASTAVA, P., MALVIYA, R. Sources of pectin, extraction and its applications in pharmaceutical industry–An overview. **Indian Journal of Natural Products and Resources**, v. 2, n. 1, p. 10-18, 2011.

SOWNDHARARAJAN, K., KANG, S. C. Free radical scavenging activity from different extracts of leaves of *Bauhinia vahlii* Wight & Arn. **Saudi journal of biological sciences**, v. 20, n. 4, p. 319-325, 2013.

SUN, D., CHEN, X., ZHU, C. Physicochemical properties and antioxidant activity of pectin from hawthorn wine pomace: A comparison of different extraction methods. **International Journal of Biological Macromolecules**, v. 158, p. 1239-1247, 2020

TAKEITI, C. Y., KIECKBUSCH, T. G., COLLARES-QUEIROZ, F. P. Morphological and physicochemical characterization of commercial maltodextrins with different degrees of dextrose-equivalent. **International Journal of Food Properties**, v. 13, n. 2, p. 411-425, 2010.

TCHABO, W., MA, Y., KAPTSO, G. K., KWAW, E., CHENO, R. W., XIAO, L., OSAE, R., WU, M., FAROOQ, M. Process analysis of mulberry (*Morus alba*) leaf extract encapsulation: Effects of spray drying conditions on bioactive encapsulated powder quality. **Food and Bioprocess Technology**, v. 12, n. 1, p. 122-146, 2018.

TOBAR-GRANDE, B., GODOY, R., BUSTOS, P., VON PLESSING, C., FATTAL, E., TSAPIS, N., OLAVE, C., GOMEZ-GAETE., C. Development of biodegradable methylprednisolone microparticles for treatment of articular pathology using a spray-drying technique. **International Journal of Nanomedicine**, v. 8, p. 2065-2076, 2013.

TONON, R. V., BRABET, C., HUBINGER, M. D. Influence of process conditions on the physicochemical properties of açai (*Euterpe oleraceae* Mart.) powder produced by spray drying. **Journal of food engineering**, v. 88, n. 3, p. 411-418, 2008.

TONON, R. V., BRABET, C., PALLET, D., BRAT, P., HUBINGER, M. D. Physicochemical and morphological characterisation of açai (*Euterpe oleraceae* Mart.) powder produced with different carrier agents. **International journal of food science & technology**, v. 44, n. 10, p. 1950-1958, 2009.

TROPICOS. Disponível em: https://www.tropicos.org/Name/100297284. Acesso em 15 de maio de 2019.

TRUONG, V., BHANDARI, B. R., HOWES, T. Optimization of co-current spray drying process of sugar-rich foods. Part I - Moisture and glass transition temperature profile during drying. **Journal of Food Engineering**, v. 71, n. 1, p. 55-65, 2005.

URIAS-ORONA, V., RASCÓN-CHU, A., LIZARDI-MENDOZA, J., CARVAJAL-MILLÁN, E., GARDEA, A. A., RAMÍREZ-WONG, B. A novel pectin material: extraction, characterization and gelling properties. **International journal of molecular sciences**, v. 11, n. 10, p. 3686-3695, 2010.

VALENTOVÁ, K., VRBA, J., BANCÍŘOVÁ, M., ULRICHOVÁ, J., KŘEN, V. Isoquercitrin: pharmacology, toxicology, and metabolism. **Food and Chemical Toxicology**, v. 68, p. 267-282, 2014.

VAN DEN BERG, M. E., SILVA, M. H. L. D. Contribuição ao conhecimento da flora medicinal de Roraima. **Acta amazônica**, v. 18, p. 23-35, 1988.

VAZ, A. M. S. F., TOZZI, A. M. G. A. *Bauhinia* Ser. *Cansenia* (Leguminosae: Caesalpinioideae) in Brazil. **Rodriguesia**, v. 54, n. 83, p. 55-143, 2003.

VEHRING, R. Pharmaceutical particle engineering via spray drying. **Pharmaceutical research**, v. 25, n. 5, p. 999-1022., 2008.

VIDOVIĆ, S. S., VLADIĆ, J. Z., VAŠTAG, Ž. G., ZEKOVIĆ, Z. P., POPOVIĆ, L. M. Maltodextrin as a carrier of health benefit compounds in *Satureja montana* dry powder extract obtained by spray drying technique. **Powder technology**, v. 258, p. 209-215, 2014.

VLADIĆ, J., AMBRUS, R., SZABÓ-RÉVÉSZ, P., VASIĆ, A., CVEJIN, A., PAVLIĆ, B., VIDOVIĆ, S. Recycling of filter tea industry by-products: Production of *A. millefolium* powder using spray drying technique. **Industrial Crops and Products**, v. 80, p. 197-206, 2016.

VYAS, P., BRAGANZA, V. J. Effect of solvents and extraction methods on the phenolic content, flavonoid content, and antioxidant activity of and *Bauhinia variegata* Leptadenia reticulata. **Asian Journal of Pharmacy and Pharmacology**, v. 5, n. 4, p. 834-840, 2019.

WANG, J., LI, H., CHEN, Z., LIU, W., CHEN, H. Characterization and storage properties of a new microencapsulation of tea polyphenols. **Industrial Crops and Products**, v. 89, p. 152-156, 2016

WATHONI, N., SHAN, C. Y., SHAN, W. Y., ROSTINAWATI, T., INDRADI, R. B., PRATIWI, R., MUCHTARIDI, M. Characterization and antioxidant activity of pectin from Indonesian mangosteen (*Garcinia mangostana* L.) rind. **Heliyon**, v. 5, n. 8, e02299, 2019.

ZAIDEL, N. D. A., MAKHTAR, N. A., JUSOH, Y. M. M., MUHAMAD, I. I. Efficiency and thermal stability of encapsulated anthocyanins from red dragon fruit (*Hylocereus polyrhizus* (Weber) Britton & Rose) using microwave-assisted technique. **Chemical Engineering Transactions**, v. 43, p. 127-132, 2015.

ZHANG, L., ZHANG, S. T., YIN, Y. C., XING, S., LI, W. N., FU, X. Q. Hypoglycemic effect and mechanism of Isoquercitrin as an inhibitor of dipeptidyl peptidase-4 in type 2 diabetic mice. **RSC advances**, v. 8, n. 27, p. 14967-14974, 2018.

ZHAO, Y., LU, H., WANG, Q., LIU, H., SHEN, H., XU, W., GE, J., HE, D. Rapid qualitative profiling and quantitative analysis of phenolics in *Ribes meyeri* leaves and their antioxidant and antidiabetic activities by HPLC-QTOF-MS/MS and UHPLC-MS/MS. **Journal of Separation Science**, v. 44, n. 7, p. 1404-1420, 2021.

 doi:10.20944/preprints202401.0343.v1

ZHU, J., LI, X., LIU, L., LI, Y., QI, B., JIANG, L. Preparation of spray-dried soybean oil body microcapsules using maltodextrin: Effects of dextrose equivalence. **LWT**, v. 154, 112874, p. 1-10, 2022.