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Effect of spray drying process parameters on *Uncaria tomentosa* (Willd. ex Schult.) DC. dried extracts

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Abstract

Uncaria tomentosa (Willd. ex Schult.) DC. (Cat's claw) is a plant member of the Rubiaceae family, from the Amazon region, and used in traditional medicine as raw material for phytomedicines indicated for arthritis and osteoarthritis. This study aimed to evaluate the spray drying process parameters on the properties of different extracts obtained from *Uncaria tomentosa*. A reduced 2^{4-1} multifactorial design was applied to evaluate the importance of the equipment variables (pump speed, spray nozzle diameter, air inlet temperature, and atomization airflow rate) in the process. Maltodextrin and acacia gum were used as carriers in a 1:1 (m/m) ratio, considering the solid residue content of the liquid plant extract. Process yield, moisture, and hygroscopicity were evaluated as dependent variables. Higher atomization airflow rate led to higher process yield for powdered dried extracts with maltodextrin. Higher temperature led to lower moisture contents regarding powdered dried extracts with acacia gum. No variable, for any carrier, was considered significant for hygroscopicity. The best spray drying configuration for the desired characteristics (*i.e.* lower hygroscopicity and moisture) used the larger spray nozzle with a diameter of 1.2 mm and the higher temperature of 150 °C, with both carriers.

Keywords: Traditional medicine. Design of experiments. Spray drying. Phytomedicine Development.

Introduction

Uncaria tomentosa (Willd. ex Schult.) DC. is popularly known as Cat's claw due to its curved spines. It is a member of the Rubiaceae family and a native medicinal plant of South America[1]. It is commonly used in the form of liquid extracts and herbal teas, as a natural anti-inflammatory phytomedicine. In Brazil, the coated tablets and the capsules containing powdered dried extract of *U. tomentosa* are provided by the Brazilian Unified National Health System (SUS), and they are indicated for the treatment of arthritis and osteoarthritis[2].

Spray drying is a common technique used to obtain the plant's powdered dried extracts for production of its phytomedicines. Due to the hygroscopic characteristics of the plant's powdered dried extract as an active pharmaceutical ingredient (API), a coating procedure is required to increase the stability of the tablets. Certain compounds, called carriers or wall materials, can be added before the drying procedure to adjust the extract's properties such as its morphological and granulometric characteristics, chemical, physicochemical properties, and its stability. Also, they may be influenced by the equipment variables[3].

Since it is not possible to infer to the operating conditions of the spray drying process, based on previous results from similar studies with other plant/carrier systems[4], this study aims to evaluate the variables related to the drying apparatus to obtain a powdered dried extract of *U. tomentosa* with high yield, and low values of hygroscopicity, and moisture using separately maltodextrin and acacia gum as carriers. Hence, a dry extract with these characteristics could enable direct compression and possibly dismiss the coating procedure for tablets.

Material and methods

Barks of *Uncaria tomentosa* (Willd. ex Schult.) DC. of Rubiaceae family, received from the supplier (Florien Pharmaceutical Supplier, Brazil, batch 053626), were initially cut and partially crushed in a Fortinox Star ft 51/1 cyclone knife mill to obtain smaller particles. Liquid extracts were obtained by static maceration with 40% v/v (1:10 m/v) hydroalcoholic solution for four days with occasional agitation. After supernatant filtration, the vegetal material was subjected to remaceration (1:5 m/v), and the combined extracts were partially concentrated in a rotary evaporator. The solid residue was determined by solvent evaporation at 105°C, to constant weight (10 mL, n = 3)[5].

Maltodextrin and acacia gum were separately used as carriers in a 1:1 m/m proportion regarding the solid residue of the plant extracts. The experimental conditions of the process were evaluated by a 2^{4-1} multifactorial design applied to each carrier, considering pump speed, spray nozzle diameter, air inlet temperature, and atomization airflow rate as independent variables (**TABLE 1**), and process yield, moisture and hygroscopicity as dependent variables.

TABLE 1: Summary of the experiments.

Extract identification	Carrier	Pump speed (L/h)	Spray nozzle (mm)	Air inlet temperature (°C)	Atomization airflow rate (m³/min)
E1	Maltodextrin	0.3	1.2	150	0.64
E2	Maltodextrin	0.7	1.2	150	1.07
E3	Maltodextrin	0.3	0.7	150	1.07
E4	Maltodextrin	0.3	1.2	110	1.07
E5	Maltodextrin	0.7	1.2	110	0.64
E6	Maltodextrin	0.7	0.7	110	1.07
E7	Maltodextrin	0.3	0.7	110	0.64
E8	Maltodextrin	0.7	0.7	150	0.64
E9	Acacia gum	0.3	1.2	150	0.64
E10	Acacia gum	0.7	1.2	150	1.07
E11	Acacia gum	0.3	0.7	150	1.07
E12	Acacia gum	0.3	1.2	110	1.07

E13	Acacia gum	0.7	1.2	110	0.64
E14	Acacia gum	0.7	0.7	110	1.07
E15	Acacia gum	0.3	0.7	110	0.64
E16	Acacia gum	0.7	0.7	150	0.64

A co-current supply spray dryer (Labmaq do Brasil MSDi 1.0), was fed with the liquid extract mixed with the carrier under constant magnetic stirring after homogenization for 5 minutes at approximately 18.000 RPM (speed 3) in a DragonLab D-500 ultraturrax. The powdered dried extracts (0.1 g) obtained were heated at 105°C to constant weight (n = 3) to evaluate moisture[5]. The hygroscopicity test was performed in a desiccator with controlled atmosphere (constant relative moisture (RH) = 75%) using a saturated sodium chloride solution. The mass gain from the powdered dried extracts was verified for 2 h (n = 3). The percentage of hygroscopicity (%H) was calculated according to Equation 1. The powders with less than 10% hygroscopicity were classified as non-hygroscopic; 10.1 – 15% as slightly hygroscopic; 15.1 – 20% as hygroscopic; 20,1 – 25% as very hygroscopic; > 25% as extremely hygroscopic[6].

$$\%H = \frac{(WI+\%M)x100}{100+WI}, and\ WI = \frac{m_{absorbed\ water}}{(initial\ mass)}\ x100 \quad \text{(Equation 1)}$$

Where WI = percentage of water intake; %M = moisture content of the sample after the test.

The statistical evaluation of the results was carried out by analysis of variance (ANOVA). Statistical significance was established through p-value. P-values < 0.05 were considered statistically significant. The analysis was performed using the Statistica® software, version 12.5 from TIBCO Software Inc. (California, United States).

Results and Discussion

Two powdered dried extracts (E5 and E8) that used maltodextrin provided insignificant amounts of powder, which were visibly moist. These experiments were repeated, and the same results were observed, indicating that the process was not efficient under such conditions. Therefore, we used the most unwanted results to calculate a value that was used as input for the software. The percentage of hygroscopicity (%H) and the percentage of moisture (%M) were calculated according to the Equation 2, by summing the amplitude (w) of each category values for maltodextrin, with the highest value (z) obtained. A 5% rate was added to the final result.

$$\%H \lor \%M = (w+z)\ x\ 1,05 \quad \text{(Equation 2)}$$

Thus, the %H results for extracts E5 and E8 were 23.17%, and 16.40% for %M. To fill in the results (**TABLE 2**), the acronym VMM (visually moisture material) was adopted since these numbers do not reflect the actual results for these extracts.

TABLE 2: Summary of the results.

Extract identification	Yield (%)	Moisture (%)	Hygroscopicity (%)	Classification
E1	18.82	5.55	14.60	Slightly hygroscopic
E2	30.16	5.60	12.77	Slightly hygroscopic
E3	39.88	4.37	14.83	Slightly hygroscopic
E4	34.64	8.60	15.33	Hygroscopic
E5	9.88	VMM*	VMM	VMM
E6	40.87	9.99	14.23	Slightly hygroscopic
E7	24.88	8.25	17.42	Hygroscopic
E8	13.11	VMM	VMM	VMM
E9	39.01	5.83	22.76	Very Hygroscopic

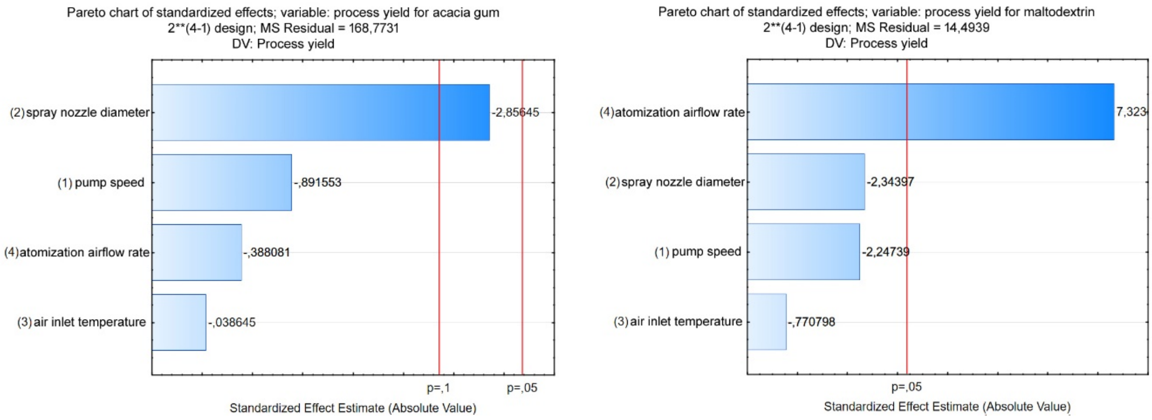
E10	25.59	5.35	16.68	Hygroscopic
E11	44.88	4.86	17.46	Hygroscopic
E12	40.08	5.53	13.14	Slightly hygroscopic
E13	14.37	10.88	22.67	Very hygroscopic
E14	53.85	11.63	23.55	Very hygroscopic
E15	63.94	12.23	28.80	Extremely hygroscopic
E16	61.34	7.43	18.56	Hygroscopic

* VMM = visually moisture material.

The extraction procedure was performed twice, providing two different liquid extracts, which presented 1.21 and 1.27% m/v of dry residue, 0.974 and 0.978 g/mL of density (measured with a pycnometer), and pH ≈ 5 measured with universal pH indicator paper. These extracts were used to manufacture the powdered dried extracts. Regarding the spray drying procedure, the highest yield was 63.94% (E15) – spite of its extreme hygroscopicity –, while the lowest yield was 9.88% (E5).

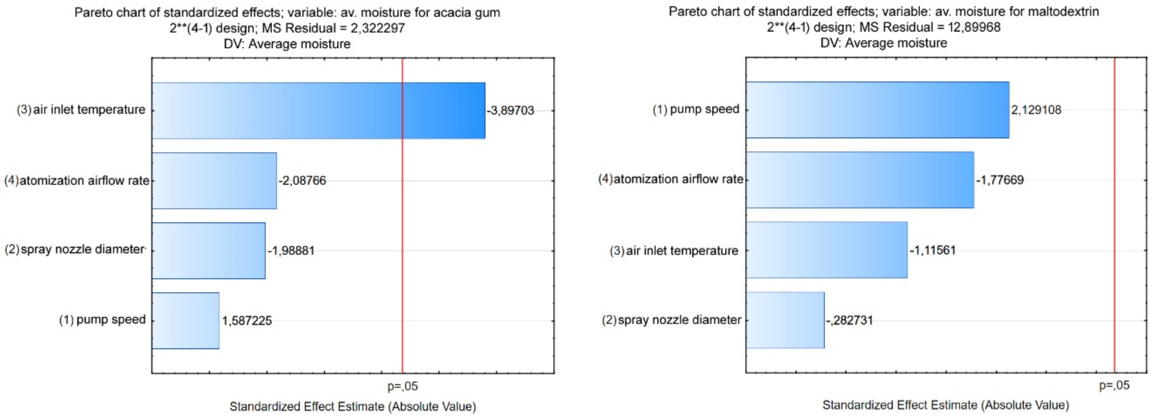
However, no variable was statistically significant for the yield results using acacia gum (E9 - E16). The parameter atomization airflow rate was significant (p = 0.005259), which influence the yield of the spray drying process with maltodextrin (**FIGURE 1**), where a higher aiflow rate led to a higher yield. As higher airflow leads to greater availability of hot air and heat transfer, there is a possibility that a higher airflow could lower the initial diameter of the droplet and, therefore, significantly reduce the drying time[7]. As a result, drying is more effective, and yield can increase.

FIGURE 1: Pareto charts of standardized effects for the yield of extracts with acacia gum (left) and maltodextrin (right).



Regarding moisture, the results obtained from extracts with acacia gum showed no significant influence. The lowest moisture value was 4.37% (E3), while the highest was 12.23% (E15). The results from extracts with maltodextrin, showed significant negative influence of air inlet temperature (p = 0.029980) (**FIGURE 2**), where a higher temperature led to lower moisture content.

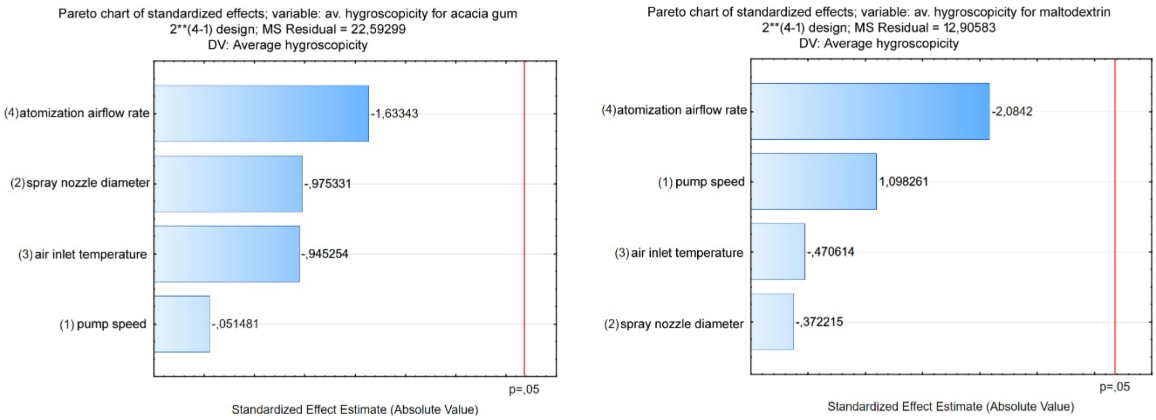
FIGURE 2: Pareto charts of standardized effects for the moisture of extracts with acacia gum (left) and maltodextrin (right).



Similar studies[4,8-10] also found significance for air inlet temperature, since higher temperatures facilitate water evaporation, and consequently, the samples tend to present less moisture content. The best results for moisture (< 5%) were obtained from extracts E3 (maltodextrin) and E11 (acacia gum), which were produced with the same equipment variables (**TABLES 1, 2**).

For hygroscopicity, the lowest value found was 12.77% (E2) and the highest was 28.80% (E15). No significant influence was observed (**FIGURE 3**).

FIGURE 3: Pareto charts of standardized effects for the hygroscopicity of extracts with acacia gum (left) and maltodextrin (right).



However, it was possible to experimentally notice that a higher atomization airflow helped to obtain a less hygroscopic powder. This observation is also based on the classification of the extracts (**TABLE 2**), where 80% (4 out of 5) of them, classified as slightly hygroscopic, had the airflow at its highest level as the common variable.

Conclusion

Higher atomization airflow rate led to higher process yield for powdered dried extracts with maltodextrin. Higher temperature led to lower moisture contents regarding powdered dried extracts with acacia gum. No variable, for any carrier, was considered significant for hygroscopicity. The best dried extracts in terms of lower hygroscopicity and moisture were E1 and E2 (maltodextrin), and E10 and E12 (acacia gum). E1, E2, and E10 had in common the highest tested temperature (150°C). All of them presented the spray nozzle as the common variable at its largest tested diameter (1.2 mm). Therefore, a larger spray nozzle and a higher temperature could help the development of a tablet that dismiss the currently necessary coating procedure.

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