© 2024 Journal of Pharmacy & Pharmacognosy Research, 12 (6), 1056-1066, 2024
ISSN 0719-4250
https://jppres.com

DOI: https://doi.org/10.56499/jppres24.2009_12.6.1056

Original Article

Optimization of spray-drying conditions and quality assessment of dry extract from *Perilla frutescens* (L.) Britton leaves

[Optimización de las condiciones de secado por atomización y evaluación de la calidad del extracto seco de hojas de *Perilla frutescens* (L.) Britton]

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Abstract

Context: *Perilla frutescens* and its dried extract have been employed in food and pharmaceutical manufacturing due to the plant's biological activities, which include antibacterial, anti-allergic, anticancer, antiviral, antioxidant, and antidepressant properties. Despite numerous studies on preparing dry extracts from various medicinal herbs, no research has been conducted to optimize spray-drying conditions specifically for *P. frutescens*.

Aims: To optimize the spray-drying parameters using BCPharSoft software and evaluate the quality of *P. frutescens* dry extract.

Methods: D-optimal design based on four independent variables carrier type (Glucidex, Glucidex: Arabic gum 9:1, Glucidex: Arabic gum 8:2), carrier mass (10, 15, and 20 g), inlet air temperature (160, and 180℃) and flow rate (12, and 14 rpm/min) was applied to investigate the cause-effect relations and optimized preparation process. The drying performance, moisture content, total phenol, and total flavonoid content were investigated as four dependent variables.

Results: All independent variables had significant effects on the dependent variables. The optimal parameters of the preparation process included using carrier Glucidex: Arabic gum at a ratio of 9:1, carrier mass of 19 g, inlet air temperature of 161°C, and flow rate of 12 rpm/min. The drying performance, moisture content, total phenol, and flavonoid content of the optimized *P. frutescens* dry extract were found to be 10.42%, 4.80%, and 90.57 mg GA/g, and 53.55 mg QE/g, respectively.

Conclusions: Dried *P. frutescens* extract has been efficiently produced using the spray-drying technique, establishing a foundation for future manufacturing of pharmaceuticals and functional foods derived from *P. frutescens*.

Keywords: BCPharSoft software; dry extract; *Perilla frutescens*; spray-drying.

Resumen

Contexto: La *Perilla frutescens* y su extracto seco se han utilizado en la fabricación de alimentos y productos farmacéuticos debido a las actividades biológicas de la planta, que incluyen propiedades antibacterianas, antialérgicas, anticancerígenas, antivirales, antioxidantes y antidepresivas. A pesar de numerosos estudios sobre la preparación de extractos secos de varias hierbas medicinales, no se ha realizado ninguna investigación para optimizar las condiciones de secado por pulverización específicamente para la *P. frutescens*.

Objetivos: Optimizar los parámetros de secado por pulverización utilizando el software BCPharSoft y evaluar la calidad del extracto seco de *P. frutescens*.

Métodos: Se aplicó un diseño D-óptimo basado en cuatro variables independientes: tipo de portador (Glucidex, Glucidex: goma arábiga 9:1, Glucidex: goma arábiga 8:2), masa del portador (10, 15 y 20 g), temperatura del aire de entrada (160 y 180℃) y velocidad de flujo (12 y 14 rpm/min) para investigar las relaciones causa-efecto y optimizar el proceso de preparación. El rendimiento de secado, el contenido de humedad, el contenido total de fenoles y el contenido total de flavonoides fueron investigados como cuatro variables dependientes.

Resultados: Todas las variables independientes tuvieron efectos significativos en las variables dependientes. Los parámetros óptimos del proceso de preparación incluyeron el uso de un portador Glucidex: goma arábiga en una proporción de 9:1, una masa de portador de 19 g, una temperatura del aire de entrada de 161°C y una velocidad de flujo de 12 rpm/min. El rendimiento de secado, el contenido de humedad, el contenido total de fenoles y el contenido total de flavonoides del extracto seco de *P. frutescens* optimizado fueron de 10,42%; 4,80% y 90,57 mg de ácido gálico/g y 53,55 mg de equivalente de quercetina/g, respectivamente.

Conclusiones: El extracto seco de *P. frutescens* se ha producido de manera eficiente mediante la técnica de secado por aspersión, estableciendo una base para la futura fabricación de productos farmacéuticos y alimentos funcionales derivados de *P. frutescens*.

Palabras Clave: extracto seco; *Perilla frutescens*; secado por pulverización; software BCPharSoft.

ARTICLE INFO
Received: March 6, 2024.
Accepted: May 14, 2024.
Available Online: June 2, 2024.

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INTRODUCTION

Perilla, also known as *Perilla frutescens* (L.) Britton, is a plant species belonging to the *Lamiaceae* family, commonly found across diverse regions worldwide. *P. frutescens* serves not only as a nutritious herb but also as a medicinal remedy for various ailments in East Asian countries like China, Japan, Korea, Taiwan, and Vietnam (Ahmed, 2018; Yu et al., 2017). In traditional folk remedies, *P. frutescens* is commonly used to treat a range of ailments such as colds, headaches, coughs, indigestion, stomach disorders, seafood poisoning, and gout. (Ahmed et al., 2022; Liu et al., 2020). With advancements in the fields of science and technology, researchers have become increasingly interested in *P. frutescens*, prompting them to explore the plant's pharmacological properties further. This involves investigating its antioxidative, antibacterial, antidepressant, anti-inflammatory, and anti-allergic effects (Ahmed et al., 2022). Furthermore, *P. frutescens* has been found to possess capabilities in reducing anxiety (Ahmed and Tavaszi-Sarosi, 2019), preventing and combating cancer (Osakabe et al., 2004), regulating the immune system, and inhibiting the spread of the SARS-CoV-2 virus for prevention or treatment of COVID-19 (Tang et al., 2021). Studies have demonstrated that *P. frutescens* exhibits a broad array of diverse biological activities due to the abundance of secondary metabolites in different parts of the plant. These compounds encompass terpenoids, flavonoids, phenolic compounds, steroids, alkaloids, and quinines (Yu et al., 2017), offering potential applications in various sectors such as pharmaceuticals, functional foods, agricultural chemicals, biopesticides, flavors, fragrances, colors, and food additives.

With its numerous significant health benefits, the emphasis on researching and manufacturing products derived from *P. frutescens* herb is steadily increasing in both the pharmaceutical and functional food industries to develop preventive and therapeutic products (Bao and Huy, 2019; Nguyen et al., 2021). Typically, finished products derived from medicinal herbs are manufactured from intermediate products, such as liquid, soft, and dry extracts. Among these, dry extracts provide several advantages in terms of preservation, transportation, and diversification of modern manufacturing methods like tablets, capsules, and coatings (Pham et al., 2023). Therefore, the utilization of the spray-drying method for formulating dry extract products is becoming increasingly popular and widely applied. Dry extracts produced through this method achieve stability in physicochemical properties, extend shelf life, mitigate the risk of bacterial contamination, enhance solubility, and maintain low moisture content (Patel et al., 2009). Furthermore, this method is suitable for heat-sensitive compounds like phenolic compounds, flavonoids present in *P. frutescens*, given that the spray-drying process takes place at low temperatures and for a brief duration (Oliveira et al., 2010).

Presently, ongoing studies are concentrating on preparing dry extracts from various medicinal herbs like bitter melon, ginger, and licorice using the spray-drying method (Jangam and Thorat, 2010; Karaaslan and Dalgıç, 2014; Tan et al., 2015). However, no research has been conducted to optimize the spray-drying conditions specifically for *P. frutescens*. This research aimed to optimize the spray-drying process and assess the quality of the resulting product.

MATERIAL AND METHODS

Materials

Dried *P. frutescens* leaves with a moisture content of 12% were acquired from Le Hoang medicinal store in Ho Chi Minh City, Vietnam, and delivered to the Department of Pharmacognosy for testing in accordance with the Vietnamese Pharmacopoeia V (Vietnam Ministry of Health, 2018). Following this, the dried *P. frutescens* leaves were ground through a 1.0 mm sieve and then stored in sealed nylon bags at 24-26°C at the Department of Pharmacognosy, Faculty of Pharmacy, Can Tho University of Medicine and Pharmacy (code H102023).

Maltodextrin (Glucidex®) with 12DE (Roquette, France) and Arabic gum (AG) (Himedia, India) were purchased from Phuong Tram Chemical Company (Ho Chi Minh city, Vietnam).

Process of preparing dried *P. frutescens* extract using the spray-drying method

Accurately were weighed about 150 g of *P. frutescens* leaves into 2000 mL Erlenmeyer flask, extracts by heat reflux method with distilled water as the solvent and medicinal herbs/solvent ratio of 1:16 (w/v) at a temperature of 60 ± 2°C in 60 minutes in two times. All extracts were combined, mixed with a carrier under homogenization at 1500 rpm for 5 minutes, and dried by Mini Spray Drier DHSL.SD303 (DHSL, Korea) to obtain the dry extract. The parameters of the independent and dependent variables are presented in Table 1 (Nguyen et al., 2022).

Effects of variables on drying performance (Y_1)

The performance of spray-drying for each experiment was calculated as the ratio of the weight of the dry extract obtained and the initial total solids (raw

Table 1. Variables in experimental design.

Independent variables	**Level 1**	**Level 2**	**Level 3**
X_1: carrier type	Glucidex	Glucidex: Arabic gum 9:1	Glucidex: Arabic gum 8:2
X_2: carrier mass (g)	10	15	20
X_3: inlet air temperature (°C)	160	180	-
X_4: flow rate (rpm/min)	12	14	-
Dependent variables	**Constraints**		
Y_1: drying performance (%)	Maximum		
Y_2: moisture content (%)	Minimum and less than 5%		
Y_3: total phenol content (mg GA/g)	Maximum		
Y_4: total flavonoid content (mg QE/g)	Maximum		

material and carrier mass) in the prepared feed solution (Nguyen et al., 2022).

Effects of variables on moisture content (Y_2)

The moisture content of the sample was gravimetrically determined with a moisture analyzer MA35 (Sartorius AG, Germany) at 105°C. According to Vietnamese Pharmacopeia V, the moisture content should not be more than 5% (Vietnam Ministry of Health, 2018).

Effects of variables on total phenol content (Y_3)

Total phenol content was determined by the Folin-Ciocalteu (FC) method, and gallic acid was used as standard material (Nguyen et al., 2022). FC 10% reagent was diluted with distilled water. The sample powder was diluted in methanol solution with a 1000 µg/mL concentration. 1 mL of the sample, 6 mL of distilled water, and 0.5 mL of FC reagent were added to a 10 mL volumetric flask and shaken well. After 5 min, 1.5 mL Na_2CO_3 20% were added, shaken well, and distilled water was added until the total volume of 10 mL. The samples were kept in the dark at ambient temperature for 30 min. The absorbance of samples was determined by a Shimadzu UV2100 spectrophotometer at 760 nm (Shimadzu, Japan). The total polyphenol content in dry extract was expressed as mg GA per g of dry extract (mg GA/g) and calculated by the formula [1].

$$Y_3 = \frac{C \times V}{m} \quad [1]$$

Where C: x value from calibration curve with gallic acid (mg/mL); V: volume of test solution (mL); m: mass of dry extract present in volume V (g).

Effects of variables on total flavonoid content (Y_4)

Total flavonoid content was determined by the aluminum chloride colorimetry method, and quercetin was used as the standard material (Nguyen et al., 2022). The powder sample was diluted in methanol solution with a 1000 µg/mL concentration. 1 mL of the sample and 4 mL of distilled water were added to a 10 mL volumetric flask. Then, 0.3 mL $NaNO_2$ 5%, 0.3 mL $AlCl_3$ 10%, and 2 mL NaOH 1 M were added, shaken well, and distilled water was added to bring the volume to 10 mL. The absorbance of samples was determined with a wavelength of 510 nm. The total flavonoid content in dry extract was expressed as mg QE per g of dry extract (mg QE/g) and calculated by the formula [2].

$$Y_4 = \frac{C \times V}{m} \quad [2]$$

Where C: x value from calibration curve with quercetin (mg/mL); V: volume of test solution (mL); m: mass of dry extract present in volume V (g).

Optimizing the preparation process of dry extract

Twenty experiments (F_1-F_{20}) were designed according to the D-optimal model using Design-Expert software (version 6.0.6, Stat-Ease Inc., Minneapolis, USA). The data were analyzed using BCPharSoft software to investigate cause-effect relations and optimize preparation.

Physical properties of dry extract

Particle morphology

The particle morphology was assessed in a field-emission scanning electron microscope (SEM) Hitachi S-4800 (Hitachi, Japan) at a voltage of 10 kV. A small amount of each sample was placed on a carbon double-sided adhesive tab, mounted onto a brass sample holder, sputter-coated with gold practical, and observed under the microscope. The SEM images were captured at magnifications of 2500× and 5000× (Tan et al., 2015).

Bulk density and tapped density

The bulk and tapped density were determined using the USP 43 – NF38 (The United States Pharmacopoeia Convention, 2020).

Flowability

The flowability of powder was expressed as Carr-index (CI) in terms of tapped density and bulk density as formula [3] (Jangam and Thorat, 2010).

$$CI = \frac{\rho_{tapped} - \rho_{bulk}}{\rho_{tapped}} \times 100 \quad [3]$$

Quality evaluation of dry extract

Some of the criteria that were evaluated included appearance, moisture content, and active ingredient content, in which total phenol content and total flavonoid content were determined with the formula [1] and [2].

Statistical analysis

All analyses were done in triplicate, and results were expressed as mean ± standard deviations. The statistical software SPSS 26 (SPSS, Inc., Chicago, IL, USA) was employed to compare observed and predicted data. One-sample t-test analysis indicated no significant difference between the expected and observed data ($p>0.05$), confirming the consistency of the ideal outcomes with the results predicted by the BCPharSoft program.

RESULTS

Process of preparing dried *P. frutescens* extract using the spray-drying method

The preparation process for dried *P. frutescens* extract was designed using Design-Expert software and included 20 experiments. These results corresponding to the experiments are summarized in Table 2.

Table 2. The independent variables of 20 experiments (F1-F20) and their responses.

Run	Independent variables				Dependent variables			
	X_1	X_2 (g)	X_3 (°C)	X_4 (rpm/min)	Y_1 (%)	Y_2 (%)	Y_3 (mg GA/g)	Y_4 (mg QE/g)
F_1	Glucidex	20	180	14	12.28	7.75	86.02	48.09
F_2	Glucidex	20	160	12	10.35	5.8	82.24	44.01
F_3	Glucidex: Arabic gum 9:1	10	180	14	5.4	5.31	74.21	55.96
F_4	Glucidex: Arabic gum 9:1	15	160	14	8.17	5.15	65.20	49.38
F_5	Glucidex	20	160	14	9.98	6.52	60.21	44.39
F_6	Glucidex	10	180	12	5.83	5.96	67.43	50.62
F_7	Glucidex	10	160	14	4.5	5.67	91.08	53.91
F_8	Glucidex	15	180	12	7.14	5.72	59.36	47.94
F_9	Glucidex: Arabic gum 9:1	10	160	12	4.86	4.85	69.12	51.66
F_{10}	Glucidex: Arabic gum 9:1	20	180	12	4.27	6.11	91.82	55.66
F_{11}	Glucidex	15	160	12	6.53	4.84	88.22	49.5
F_{12}	Glucidex: Arabic gum 8:2	20	160	12	11.13	4.21	83.23	39.36
F_{13}	Glucidex: Arabic gum 8:2	15	180	14	7.34	6.78	90.34	45.4
F_{14}	Glucidex: Arabic gum 9:1	15	180	12	7.12	4.85	93.63	51.63
F_{15}	Glucidex: Arabic gum 8:2	20	180	12	8.56	6.12	86.52	40.73
F_{16}	Glucidex: Arabic gum 8:2	10	160	12	4.36	7.56	98.51	50.79
F_{17}	Glucidex: Arabic gum 8:2	20	160	14	8.35	5.6	86.20	39.6
F_{18}	Glucidex: Arabic gum 9:1	20	160	14	10.04	4.29	87.26	38.69
F_{19}	Glucidex: Arabic gum 8:2	10	180	14	4.85	5.18	102.11	50.23
F_{20}	Glucidex: Arabic gum 8:2	15	160	12	7.33	6.35	100.42	51.59

Table 3. Model statistics from BCPharSoft outputs.

Dependent variables	Y_1	Y_2	Y_3	Y_4
R^2 training	0.99	1.00	0.97	0.97
R^2 test	0.95	0.95	0.96	0.99

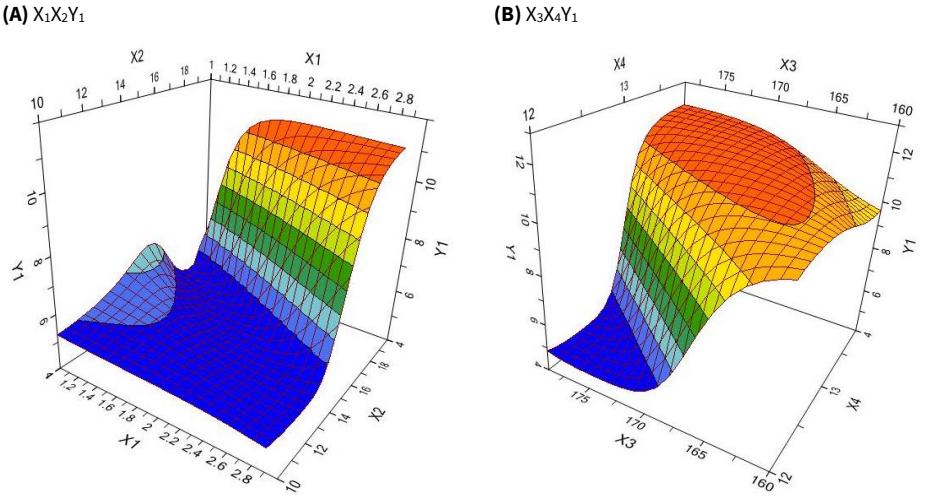


Figure 1. Response surface plots showing the effects of **(A)** carrier type (X_1) and carrier mass (X_2); **(B)** inlet air temperature (X_3) and flow rate (X_4) on drying performance (Y_1).

The data from Table 2 served as inputs for BCPharSoft to investigate the cause-effect relations and optimize the process. The results of the accuracy of model statistics from BCPharSoft outputs are presented in Table 3.

Table 3 demonstrated that all R^2 training and R^2 test values were more than 0.9, suggesting the high reliability of the models. These models exhibited potential for application in multivariate optimization.

To enhance comprehension of the cause-effect linkages between the independent and dependent variables, three-dimensional (3D) response surface plots of the fit models were showcased. Each 3D figure simultaneously depicted the impacts of two independent factors on the dependent variables while maintaining the third variable constant.

Effects of variables on drying performance (Y_1)

Given the ideal circumstances, as shown in Table 1, drying performance (percent) – Y_1 needs to be maximized. When all X factors were considered in the 3D diagram in Fig. 1, it can be seen that the carrier type – X_1 is used on levels 2–3 (in a combination form), the carrier mass (g) – X_2 should be high (20 g), the inlet air temperature (°C) - X_3 is at a medium level, and the flow rate (rpm/min) – X_4 maintains at a low level (12 rpm/min).

Effects of variables on moisture content (Y_2)

Moisture content (percent) – Y_2 should be as low as feasible and less than 5% under the specified conditions outlined in Table 1. If all X factors are taken into account in the 3D diagram in Fig. 2, the carrier type – X_1 is at a medium level (level 2 - Glucidex: Arabic gum 9:1), the carrier mass (g) – X_2 needs to be high 20 g, the inlet air temp (°C) – X_3 is around 161°C, and the flow rate (rpm/min) – X_4 is at a low level (12 rpm/min).

Effects of variables on total phenol content (Y_3)

To achieve the desired conditions in Table 1, the total phenol content (mg GA/g) needs to be as high as possible. X factors are considered in the 3D diagram in Fig. 3, which can be seen that the carrier type (X_1) is used on levels 2–3 (Glucidex: Arabic gum 9:1 - Glucidex: Arabic gum 8:2), the carrier mass (X_2) is high ≥ 16 g, inlet air temperature (X_3) and the flow rate (X_4) are on a low level (160°C and 12 rpm/min, respectively) giving the increase of total phenol content (mg GA/g).

Effects of variables on total flavonoid content (Y_4)

According to conditions in Table 1, total flavonoid content (mg QE/g) also needs to be as high as possible (Fig. 4). The carrier type (X_1) is used on level 2 (Glucidex: Arabic gum 9:1), with a high carrier mass (X_2) of ≥ 18 g, while maintaining the inlet air tempera-

ture (X_3) and the flow rate (X_4) at low levels (160°C and 12 rpm/min, respectively), leading to an enhancement in the total flavonoid content (Y_4).

Optimizing the preparation process of dry extract

BCPharSoft program optimized the preparation process by setting variables X_1, X_2, X_3, and X_4 to Glucidex: Arabic gum 9:1, 19 g, 161°C, and 12 rpm/min, respectively. Three replicated batches of the improved method were created to validate the optimization approach. The experimental outcomes are presented in Table 4.

Physical properties of dry extract

The particle morphology of the optimal samples was assessed using SEM, as illustrated in Fig. 5.

The bulk density, tapped density, and flowability of the dry extract in three analytical batches demonstrated good precision with average values of 0.329 ± 0.022 g/mL, 0.409 ± 0.009 g/mL, and 0.020 ± 0.004, respectively.

Quality evaluation of dry extract

Appearance

The dried *P. frutescens* extract was a homogeneous pale-yellow powder, susceptible to moisture absorption when left outdoors for an extended period and readily soluble in water, resulting in a pale yellow solution (Fig. 6).

Moisture content

The average moisture content of the dry extract was 4.80 ± 0.17%, which fell within the 5% limit specified by Vietnamese Pharmacopoeia V (Vietnam Ministry of Health 2017).

Active ingredient content

The results displayed in Table 4 suggested that the average total phenol content and total flavonoid content analyzed from 3 batches demonstrated a narrow range of fluctuation, with each test's result being at 90.57 ± 0.90 mg GA/g and 53.55 ± 2.21 mg QE/g, respectively.

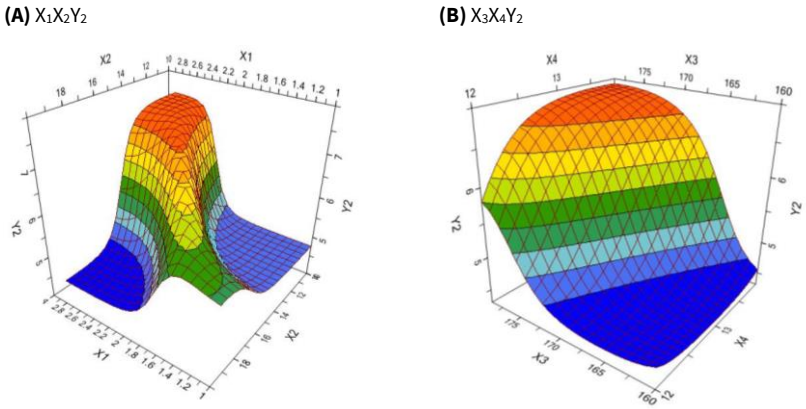


Figure 2. Response surface plots showing the effects of **(A)** carrier type (X_1) and carrier mass (X_2) and **(B)** inlet air temperature (X_3) and flow rate (X_4) on moisture content (Y_2).

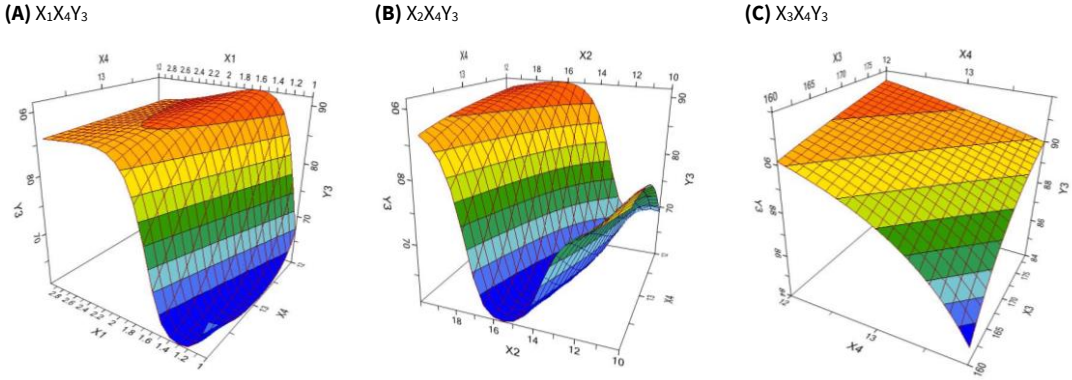


Figure 3. Response surface plots showing the effects of **(A)** carrier mass (X_2) and inlet air temperature (X_3); **(B)** carrier mass (X_2) and flow rate (X_4); and **(C)** inlet air temperature (X_3) and flow rate (X_4) on total phenol content (Y_3).

(A) $X_1X_4Y_4$ **(B)** $X_2X_3Y_4$ **(C)** $X_3X_4Y_4$

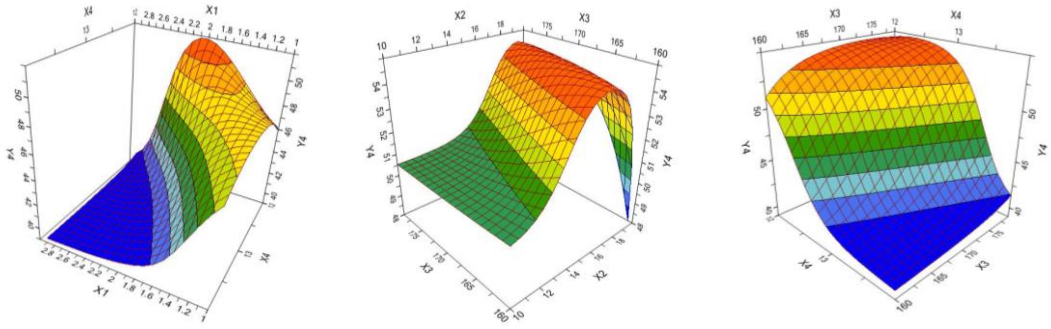
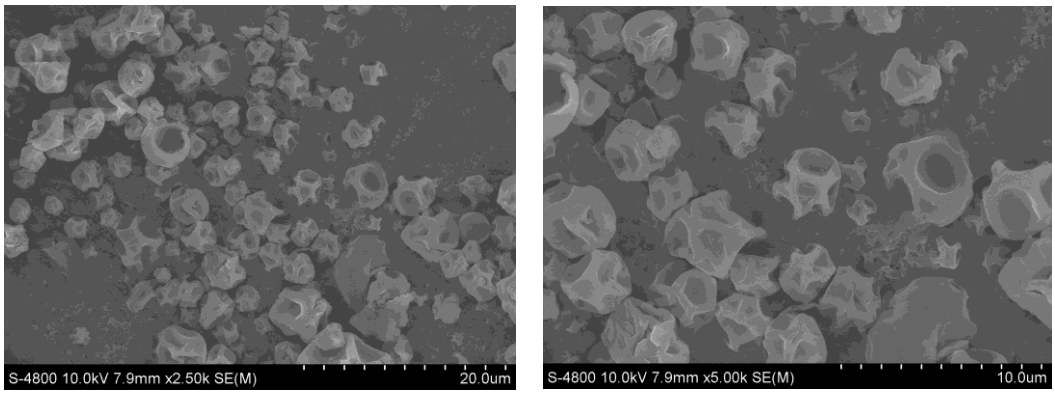


Figure 4. Response surface plots showing the effects of **(A)** carrier type (X_1) and flow rate (X_4); **(B)** carrier mass (X_2) and inlet air temperature (X_3); **(C)** inlet air temperature (X_3) and flow rate (X_4) on total flavonoid content (Y_4).

Table 4. Comparison of the predicted and observed responses (n = 3).

Responses	Y_1 (%)	Y_2 (%)	Y_3 (mg GA/g)	Y_4 (mg QE/g)
Predicted	10.84	4.56	90.23	51.85
Observed	10.42 ± 0,30	4.80 ± 0.17	90.57 ± 0.90	53.55 ± 2.21
P-value*	0.136	0.147	0.584	0.313

*One-sample t-test.



(magnification 2500×) (magnification 5000×)

Figure 5. SEM images of the dried *P. frutescens* extract.

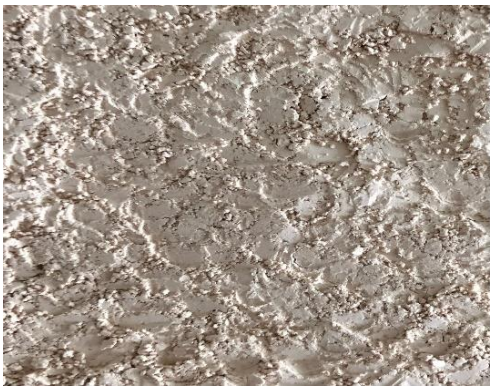


Figure 6. The dried *P. frutescens* extract.

DISCUSSION

Spray-drying is among the most frequently utilized methods in the pharmaceutical and food sectors. The physical characteristics and quality of the *P. frutescens* dry extract produced depend on various spray-drying conditions, including the type and mass of the carrier substance, inlet air temperature, and flow rate, among others (Cortés et al., 2017; Gallo et al., 2015; Tan and Thuy, 2017).

Furthermore, in the context of the spray-drying process, powders frequently tend to agglomerate due to their substantial surface area and adhere to various encountered surfaces, like drying chambers and cyclones. This phenomenon inevitably results in diminished product recovery efficiency. To tackle the aforementioned issue, researchers typically incorporate various carriers into the liquid extract to decrease adhesion and prevent settling in the collection vessel during the spray-drying process, ultimately enhancing drying performance (van Boven et al., 2023).

The main carriers employed are biomolecule-based substances, such as carbohydrate polymers, proteins, and lipids. Of these, carbohydrate polymers are particularly favored as carriers due to their remarkable properties, including high solubility, oxidative and thermal stability, film-forming ability, and low viscosity. Carbohydrate polymers are classified into three types: (1) Starch and its derivatives (starches, modified starch, wheat, dextrin, maltodextrin, cyclodextrin, pectin, chitosan, modified chitosan); (2) Cellulose and its derivatives (cellulose, microcrystalline cellulose, carboxymethyl cellulose, methylcellulose, hydroxypropyl methylcellulose); (3) Gums (Arabic gum, guar gum, cashew gum, mesquite gum, xanthan gum, sodium alginate, carrageenan) (Tontul and Topuz, 2017).

Different types of carriers can influence drying performance and moisture content, as well as the total phenol and flavonoid contents (Bednarska and Janiszewska-Turak, 2020; Pui et al., 2020; Tran and Nguyen, 2018). In this study, we opted to utilize standalone Glucidex and a combination of Glucidex with Arabic gum at ratios of 9:1 and 8:2.

Glucidex comprises a diverse array of maltodextrins with unique powder characteristics and is widely utilized as a carrier in the majority of spray-drying processes. It effectively mitigates powder adhesion and enhances the glass transition temperature. Glucidex offers relatively low cost and low viscosity at high solid concentrations. However, the moisture content of the dry extract tends to be relatively high, exceeding 5%, as shown in experiments F_1, F_5, and Fig. 2A. This illustrates that relying solely on a single type of carrier cannot fulfill the desired functional properties of the product. Therefore, it is advisable to combine it with recommended carriers to enhance the synergistic effects between them, thereby optimizing drying performance and the quality of the final product (Kalušević et al., 2017; Karrar et al., 2021; Lee et al., 2018; Mazuco et al., 2018).

Arabic gum is introduced to stabilize emulsions, addressing the low viscosity issue commonly encountered in water solutions with maltodextrin. The findings from Table 2, specifically in experiment F_{18}, in conjunction with Figs. 1A and 2A indicate that the combination of carriers Glucidex and Arabic gum leads to the highest drying performance (Y_1), lowest moisture content (Y_2), and while simultaneously enhancing the retention of total phenol and total flavonoid content levels (Y_3, Y_4). However, increasing the proportion of Arabic gum in experiments F_{13}, F_{15}, and F_{20} is expected to correlate with a reduction in drying performance (Y_1) and a rise in moisture content (Y_2). This phenomenon might be attributed to Arabic gum's propensity to heighten the viscosity of the extract solution, thereby potentially causing nozzle obstruction during the spray-drying operation (Azhar et al., 2021).

Experiments featuring low carrier mass (X_2), such as F_7, F_{16}, and F_{19}, commonly show a significant propensity for clumping, high moisture content, and reduced drying performance. On the contrary, there is a simultaneous increase in drying performance (Y_1) and a decrease in moisture content (Y_2) as the carrier mass (X_2) increases. This phenomenon can be clarified by the rise in dry matter concentration, which increases solid content and decreases overall moisture available for evaporation (Figs. 1A and 2A).

Additionally, according to Pham et al. (2023), an increase in carrier mass leads to a decrease in the active ingredient content in the product. This finding is also supported by the research results depicted in Figs. 3B and 4B. Therefore, selecting the optimal carrier mass is essential to attaining the highest achievable total phenol and flavonoid levels.

The inlet air temperature also plays a crucial role in determining the quality of the dried extract (Corrêa-Filho et al., 2019; Jafari et al., 2017; Santhalakshmy et al., 2015; Shishir et al., 2017). The data in Table 2 suggests that the chosen temperature of 160°C results in a dried product with low moisture content, as evidenced by experiments F_{12} and F_{18}, which recorded moisture levels of 4.21 and 4.29, respectively. On the other hand, drying at a higher temperature of 180°C leads to product burning and adhesion onto the product collector, thereby

diminishing drying performance (Y_1) and raising moisture content (Y_2). The elevated inlet air temperature notably decreases the total phenol content (F_8 59.36 mg GA/g). This aligns perfectly with the research conducted by Sinh et al. (2019).

The flow rate has a significant impact on the productivity and the outlet air temperature of the equipment (Özdikicierler et al., 2019). As the flow rate increases (14 rpm), the residence time of the extract solution in the drying chamber decreases, resulting in particles being likely to adhere to the drying chamber. Consequently, drying performance decreases and moisture content increases (4.85% and 5.18%, respectively, in experiment F_{19}). This is demonstrated in Fig. 2B. Furthermore, the rise in flow rate results in a reduction of total phenol content (60.21 mg GA/g in F_5) and total flavonoid content (39.60 mg QE/g in F_{17}), which aligns with the findings of the study conducted by Tan et al. (2015).

The BCPharSoft OPT program optimizes the following parameters: carrier material with Glucidex: Arabic gum 9:1, carrier mass of 19 g, inlet air temperature of 161°C, and flow rate of 12 rpm. The R^2 test and R^2 train values are used to examine the cause-effect relationship. Generally, if the R^2 training value exceeds 95% and the R^2 test value exceeds 70%, the model is considered acceptable. If the R^2 test value surpasses 100%, it indicates an enhancement in the model's predictability. According to Table 3, the values Y_1, Y_2, Y_3, and Y_4 exhibited high compatibility based on the R^2 test (R^2 training = 97% > 95%). The values Y_1, Y_2, Y_3, and Y_4 have strong predictability (R^2 test = 95% > 85%) based on the value of R^2 test.

CONCLUSION

The successful preparation of dried *P. frutescens* extract using the spray-drying method offers valuable insights for both the pharmaceutical and food industries. This research outcome provides a foundation for manufacturing medications, functional foods, and instant tea from *P. frutescens* herbal materials while facilitating the diversification of finished products.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

The authors would like to express their gratitude to Assoc. Prof. Do Quang Duong from the University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam, and colleagues from Can Tho University of Medicine and Pharmacy, Vietnam, for their support in this research. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Contribution	Tuyen NTL	Linh NTT	Lien PTT	Duong DQ
Concepts or ideas	x		x	
Design	x			x
Definition of intellectual content	x		x	x
Literature search	x	x	x	
Experimental studies	x	x		
Data acquisition	x	x		x
Data analysis	x			x
Statistical analysis	x			
Manuscript preparation	x			
Manuscript editing	x			
Manuscript review	x	x	x	x

Citation Format: Tuyen NTL, Linh NTT, Lien PTT, Duong DQ (2024) Optimization of spray-drying conditions and quality assessment of dry extract from *Perilla frutescens* (L.) Britton leaves. J Pharm Pharmacogn Res 12(6): 1056–1066. https://doi.org/10.56499/jppres24.2009_12.6.1056