A Multi-Objective Optimization of Artichoke (*Cynara Scolymus* L.) Leaves Aqueous Extraction Dehydration Through a Novel Spray Drying Approach Using Response Surface Methodology

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ABSTRACT: *In this study, Cynara scolymus L. leaves aqueous extract powder was produced using a novel spray drying approach by incorporation of ongoing ultrasonic atomization and vacuumed drying chamber. A Response Surface Methodology (RSM)-based central composite face-centered design was employed for optimization of the operating conditions of ultrasonic vacuum spray dryer. The independent variables of the prepared mode include inlet temperature, the vacuum pressure in drying chamber and concentration of extract solution. Drying experiments were carried out with an inlet temperature range of 55–75 °C, a vacuum pressure range of 20–40kPa and extract solution concentration of 2–3%. The responses were Moisture Content (MC), Solubility Index (SI), the bulk density of extract powder, Total Phenolic Content (TPC) and DPPH scavenging capacity. Optimum operating conditions were found to be an inlet temperature of 70.58 ℃, a vacuum pressure of 20kPa, and an extract solution concentration of 3%. In this optimum condition, Moisture Content (MC), Solubility Index (SI), bulk density of extract powder, Total Phenolic Content (TPC) and DPPH scavenging activity were found to be 6.73%, 58.5%, 0.5838 g/cm^3, 13.53 mg of GAE/g of spray dying extract powder and 18.43%, respectively. The morphology of microstructures analyzed with Scanning Electron Microscopy (SEM) also showed spherical and smooth particles in optimum condition.*

KEYWORDS: *Cynara scolymus; Spray drying; Response surface methodology; Extract powder; Total phenol content; Antioxidant capacity*.

INTRODUCTION

Cynara scolymus (Asteraceae) is a native plant of the Mediterranean region (southern Europe and North Africa) and is also seen in subtropical climates such as Brazil, where it is known as artichoke. The *C. scolymus* is a plant rich in nutritious and possesses numerous medicinal properties. In other words, it is not only cultivated all around the world because of being a healthy tasty; rather, it is viewd also as an herbal drug [1,2]. Currently,

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the artichoke is cultivated in different countries such as the United States (mainly in California), South America, North Africa, Near East Turkey, Iran and China [1-4]. Artichoke is consumed as a fresh, frozen, or canned vegetable [1, 5].

Atichoke Leaf Extracts (ALEs) are extensively used alone or in association with other herbs to prepare herbal teas [6]. Polyphenolic compositions, as an active component of this plant exist significantly from its leaf rather than its heads. Biological composition of an extract of artichoke leaf shows a low fat content and a high amount of minerals (phosphorus, sodium and potassium), vitamin C, fibers, polyphenols, flavones, inulin and caffeoylquinic acid derivatives [3, 7, 8]. Due to anti-cancer properties of these compounds, they play an important role in human nutrition. Hence researcher suggest taking into account the‘‘functionalization’’ of foodstuffs by adding artichoke by-product extracts [9, 10].

Regarding the demands of modern therapeutic operation, ease of standardization and handling, and producing a homogenized products make herbal dried extracts suitable for medicinal applications. The dehydration of a concentrated solution extracted from herbal materials (roots, leaf, seeds, whole plant, inflorescence and fruits) results in a dried extract powder. For this purpose, many drying techniques including spray drying, freeze-drying and spouted bed drying have been proposeed [11-13]. Whereas most of the dried extracts and nutraceuticals are intended for oral utilization, there are acceptable restricts of bacterial. Many researchers investigated the microbial impurity of spray-dried extracts of plants and the process effects on product quality [14]. The results show a low microbial contamination in spray-dried extracts. Several procedures have been examined to provide rapid beverages from artichoke. In this regard, spray-drying is an adequate technique to provide microspheres comprising artichoke extract [15].

Spray drying is mostly applied in dairy industry where original properties can be preserved. Also it is widely used for transforming an extensive range of liquid nutrition products into the powder form. The main assumption of spray drying is that the cell viability at the end of the drying and/or storage stages will enhance remarkably by reducing the oxidative and thermal stresses during the drying process. The process includes spraying of atomized solutions into a chamber where hot dry air rapidly vaporizes the solution leaving the spray dried particles. Spray-dried powders can be stored at room temperature for a long time without endangering the powder stability [16]. According to the cheap and easy transportation of powders and handling in plants manufacturing, spray-dried powders are economical to produce compared to other processes, such as freeze-drying [17].

One of the newly developed spray drying techniques is ultrasonic vacuum method, which enjoys the strengths of spray drying by incorporation of ultrasonic atomizer and vacuum chamber [18]. The ultrasonic vacuum spray dryer is expected to be achieved by the short residual time of the monotonic droplets generated by the ultrasonic atomizer, and also through a low temperature and vacuum atmosphere in the drying chamber [19, 20].

Generally, plant leaf extracts have higher contents of sugars, carbohydrates, and organic acids [21, 22]. Therefore, the drying aids addition to the extractive solution before drying can improve the product properties and drying efficiency bacause to the significant presence of reducing sugars is almost compulsory. Drying aids with a wide usage in the dehydration process of herbal extracts include: cassava, corn and rice starches, modified starches, gum Arabic, cyclodextrins, maltodextrins, colloidal silica and κ-carrageenan. In order to prepare micro-particles by a spray-drying technique, lactose can be applied as carrier materials [15, 23, and 24].

The Response Surface Methodology (RSM) has been proved as a strong tool for characterizing the effects of each factor and the interactions among them since it allows process optimization to be performed effectively [25]. RSM includes a combination of experimental strategy, mathematical methods and statistical inference, making an efficient empirical exploration of the system of interest [26].

The main benefit of the RSM is that it significantly reduces the number of experiments required for evaluation, analysis and optimization. Beside, it is a fast and more cost-effective method for data collection of compared to the classic one-variable or full-factor experiments.

The effects of spray drying conditions on some physicochemical properties of hydroalcoholic extract powder of artichoke leaf have been studied by many

researchers [15, 27]. However, to the best of our knowledge, no study is available about optimization of the ultrasonic vacuum spray drying conditions on extract aqueous powder of artichoke leaf. The aim of this study is to find the optimal parameters of ultrasonic vacuum spray-drying process to create microencapsulated powder of *Cynara scolymus* L. leave aqueous extract with the lowest value of Moisture Content (MC) and the highest values of Solubility Index (SI), bulk density of extract powder, Total Phenolic Content (TPC) and Free Radical Scavenging Capacity (FRSC) through applying RSM. The inlet temperature, vacuum pressure inside the chamber and concentration of solution were considered as the independent variables of the process.

EXPERIMENTAL SECTION

Chemicals

Methanol and Folin Ciocalteau reagent were prepared from Merck, Germany. Sodium carbonate, 2; 2-diphenyl picryl hydrazyl (DPPH) and lactose monohydrate were purchased from Sigma-Aldrich, Germany. Distilled water was used as a solvent all over the experiments.

Extract preparation

Fresh leaves of artichoke were purchased from herb garden in Hamedan, Iran. After washing with distilled water, artichoke leaves were dried in shade and grounded with a laboratory grinder (Artisan M.D 5000, Iran). Powdered leaves of artichoke were extracted with distilled water boiling through stirring in 900rpm for 3h. The obtained decoction was centrifuged and filtered through Whatman no.4 filter paper. This method was performed in duplicate and the combined filtrates were evaporated on a rotary evaporator (IKA-RV 10, Germany) to dry under the vacuum pressure. Then the solution of desired concentration was reached by adding the distilled water to the extract. Extract concentration was determined by a refractometer (Kruss Optronic DR 101-60, Germany) having a variability range of 0-60% and resolution of 0.1%. Afterward, lactose monohydrate as an excipient was mixed with Cynara scolymus leaf extract at a specified volume ratio (1:2) and then stirred to form an aqueous solution. Various concentrations of solution were as per experimental design condition of RSM. The mixture was spray-dried with ultrasonic vacuum spray dryer (UVSD) developed in the post-harvest processing laboratory (of Bu-Ali Sina University, Hamedan, Iran) and operated under vacuum conditions.

Experimental setup

In the current research, a new ultrasonic vacuum spray dryer was developed. The main components of this apparatus are the feeding system of the artichoke leaf extract consisting of a peristaltic pump and a fluid atomizer system with a specially designed ultrasonic atomizer that can operate in a vacuum space, dispersing the solution equal to the vacuum drying zone. UVSD includes a vacuum cylindrical chamber (12 cm in diameter and 80 cm in height) with electrical heaters controlling the temperature of the drying chamber. Coil heater (1300W) wrapped around the cylindrical chamber was used to heat the vacuum chamber. The internal temperature of the chamber was controlled via a temperature control unit with type k sensor and the accuracy of ±0.1℃ (Lutron TM-903, Taiwan). Vacuum condition was created by a vacuum pump (DV-285N-250- PLATINUM, USA). To regulate the absolute pressure during the experiments, a pressure controller with an accuracy of 0.001 bars (Sensys PSCH0001 BCIJ, Korea) was used (Fig. 1). The atomized drops were directed into a vacuum chamber by Silicone hoses from the ultrasonic atomizer. Finally, a product control system (cyclone) and paper filter before vacuum pump were employed. The heating of the falling drops into the drying chamber occurred through heat convection of the chamber wall towards the atomized drops. The solution feeding was maintained at 0.5-1 ml/min and the vacuum was adjusted from 20-40kPa in the drying chamber. Internal temperature and vacuum pressure in the drying chamber are the other experimental design conditions of RSM. Several UVSD runs were carried out to investigate the effects of the internal temperature and vacuum pressure of the drying chamber for various concentration of the solution (extract/excipient). Further analyses were performed to determine the Moisture Content (MC), Solubility Index (SI), the bulk density of extract powder, Total Phenolic Content (TPC), and DPPH scavenging capacity of the microencapsulated powder.The SEM analyses were performed with a maximum acceleration potential of the primary electrons between 10 and 15 kV and few milligrams of the samples were placed on a SEM aluminium holder, which was supported on conductive carbon tape.

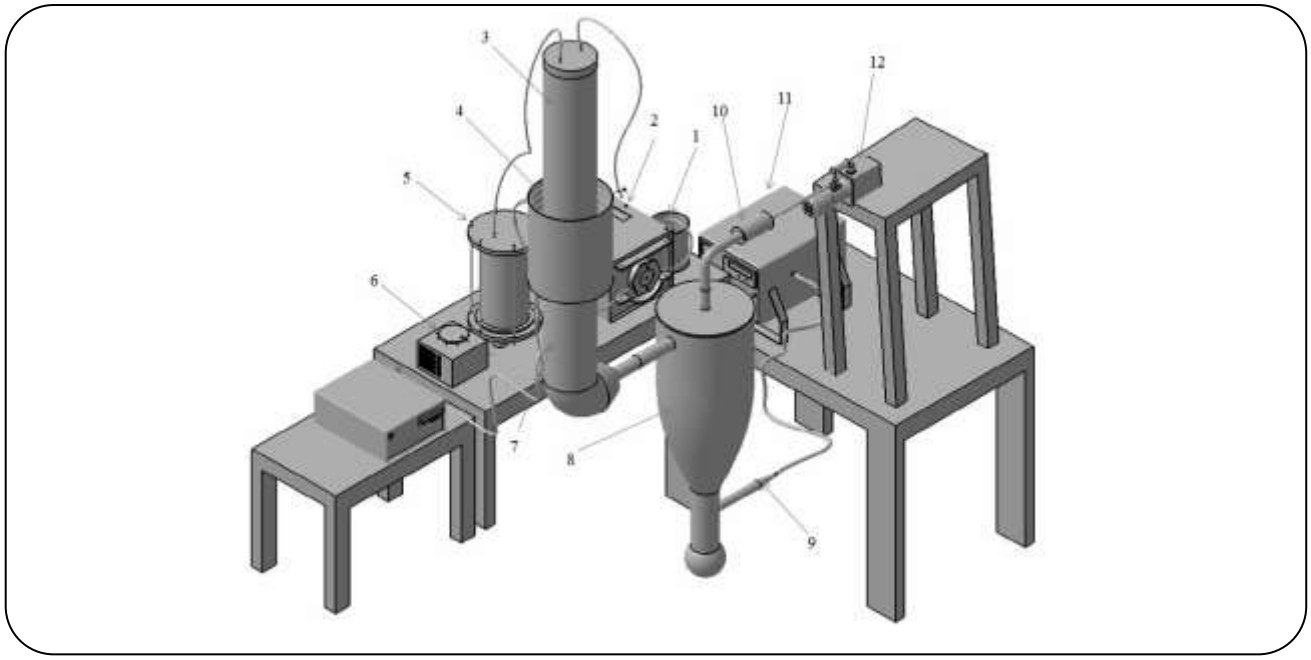

Fig. 1: A schematic diagram of the ultrasonic vacuum spray dryer used in this study: (1) solution container, (2) peristaltic pump, (3) vacuum chamber, (4) coil-heater-element, (5) ultrasonic atomizer, (6) thermometer, (7) temperature sensor, (8) cyclone chamber, (9) pressure sensor, (10) paper filter, (11) pressure controller, and (12) vacuum pump.

Moisture content

The moisture content of artichoke extract powder as a physical property was analyzed according to AOAC [28]. Samples treated with nano-particles with predetermined masses were put in an oven (Memmert UNE-500, Germany), heated up to 102℃, and weighed on a digital balance (AND GF-600, Japan) until a constant mass was reached. According to Eq. (1), dry basis moisture content (M_{db}) is described by the percentage equivalent of the ratio of the weight of water to the weight of the dry matter (M_t).

$$M_{d.b} = \frac{M_0 - M_t}{M_t} \times 100 \quad (1)$$

M_{db}: Dry basis moisture content (%).

M_0: initial mass of the sample (g).

M_t: the sample mass after drying in the oven (g).

Bulk density

For bulk density determination of powder, 0.6g of the sample was poured into a graduated cylinder, then packed bulk density was calculated according to the volume occupied by the powder and the weight of powder contained in the cylinder after being tapped 10 times by hand on a bench from a height of 10 cm (Eq. (2)) [29].

$$\rho = \frac{m}{v} \quad (2)$$

ρ: bulk density (g/cm^3)

m: the mass of powder (g)

v: the volume of graduated cylinder occopied by the powder (cm^3).

Solubility

The method of *Eastman* and *Moore* [30] modified by *Goncalves et al.* [31] was used to measure the solubilitypercentage. About 0.2 g of each sample was suspended in 5 mL of water at room temperature in a centrifuge tube. Before centrifuging at 9500 rpm for 10 min, the suspension was stirred for 30 min. The supernatant was completely drained into an evaporating dish and dried to fixed weight at 105 °C. The solubility index in water (%) was calculated from the weight of the solids recovered after drying.The solubility was calculated according to the following equation:

$$\text{solubility} = \frac{m_s}{m_p} \times 100 \quad (3)$$

m_s: the mass (g) obtained by drying of the supernatant.

m_p: the mass (g) of the powder taken into analysis.

Total phenol content

The Total Phenolic Content (TPC) of spray-dried *Cynara scolymus*L. Leaves aqueous extract was determined based on the Folin-Ciocalteau procedure described by Gamil et al. [32] with some modifications. The sample solution was prepared by dissolving 10 mg of spray-dried powder in 1 mL of distilled water and centrifuging it for 10 min using a scientific centrifuge (DAIHAN Promicro centrifuge Set, CF-10, Korea). The reaction mixture was composed of 0.1 mL supernatant of the solution, 7.9 mL distilled water, 0.5 mL Folin–Ciocalteu reagent, and 1.5 mL sodium carbonate 20%. The mixture was put in anhydrous turbid flasks, followed by addingFolin-Ciocalteau reagent 2 min after. Next, it was allowed to stand for 2 h. The optical density of the blue-solution was measured at 765 nm. The total phenolic content was characterized as Gallic Acid Equivalents (GAE) and values were expressed as mg of Gallic acid/per a gram of spray-dried *Cynara scolymus.L* extract (in GAE).

DPPH radical scavenging capacity

DPPH is a free radical that interacts with compounds and is capable of donating a hydrogen atom. Thus, the hydrogen donating abilities of spray-dried *Cynara scolymus* L. aqueous extract powder was determined from the change in the absorbance at 517 nm [32]. The antioxidant capacity of the extract powder was measured as described by Gebhard [33] using the 2, 2–diphenyl– 1–picrylhydrazyl ($DPPH^0$) free radical scavenging capacity. A solution of samples was prepared by dissolving 10 mg of spray-dried powder in 2 ml of methanol and centrifuging for 10 min. The supernatant was added to 3 mL of solution 0.004% DPPH in methanol. The change in absorbance was read after 40 min at 30℃ employing a spectrometer (T80 UV/VIS double beam, USA). The radical scavenging capacity of the samples (antioxidant capacity) was defined as the percent inhibition of $DPPH^0$ radical as follows:

$$\text{I\%inhibition} = \left[\frac{\left(A_{blank} - A_{sample}\right)}{A_{blank}}\right] \times 100 \quad (4)$$

A_{blank}: the absorbance of the control reaction (containing of the reagents except the test compound).

A_{sample}: the absorbance of the test compound.

Experimental uncertainty

Errors and uncertainties in experiments can arise from instrument condition, selection, calibration, environment, observation and reading, test planning, and reading [34]. In drying experiments in UVSD, inlet temperatures, vacuum pressure inside the chamber, concentration of solution were measured with appropriate instruments clarified before, and uncertainties for all these parameters were calculated using the method described by *Akpinar* [35], and *Chayjan et al.* [34].

If a set of measurements is made and the uncertainty in each measurement is expressed with the same odds, these measurements can be applied to calculate some desired result of the experiments (Table 1). The uncertainty in the calculated result can be estimated based on the uncertainties in the primary measurements. The result R is a given function of the independent variables $x_1, x_2, x_3, \ldots, x_n$. Thus,

$$R = R\left(X_1, X_2, X_3 ..., X_n\right) \quad (5)$$

If the uncertainties in the independent variables are all given with the same odds, then the uncertainty in the result having these odds is given as [34]:

$$W_R = \left(\left(\frac{\partial R}{\partial X_1} W_1\right)^2 + \left(\frac{\partial R}{\partial X_2} W_2\right)^2 + ... + \left(\frac{\partial R}{\partial X_n} W_n\right)^2\right)^{\frac{1}{2}} \quad (6)$$

where w_R is the uncertainty in the result and w_1, w_2,...,w_n be the uncertainties in the independent variables.

Experimental design

The Design-Expert version 7.0.0 was applied to recognize the optimum levels of the three variables of inlet temperature (℃), the concentration of extract solution (%) and vacuum pressure (kPa) using RSM.

Using the RSM methodology, the effect of three independent variables on five response variables was evaluated in order to find the benefits of the newly developed process and the quality of the powder. The inlet temperature to the drying chamber (x_1, 55–75 ℃), the concentration of the solution (x_2, 2-3 extraction with lactose) and vacuum pressure in the drying chamber (x_3, 20–40 kPa) were selected as independent variables. The response variables to be considered were moisture content (Y_1), solubility (Y_2), bulk density (Y_3), total phenolic content (Y_4), and DPPH scavenging capacity (Y_5)

Table 1: Measurements uncertainty during ultrasonic vacuum spray drying of artichoke leaves aqueous extraction.

Description	Unit	Value
Uncertainty in the temperature measurement	°C	±1.005
Uncertainty in vacuum pressure measurement	bar	±0.001
Uncertainty in solution concentration measurement	%	±0.1
Uncertainty in spectrophotometer absorbance	-	±0.002
Uncertainty in the moisture quantity measurement	g	±0.00141
Total uncertainty for moisture content	%	±0.5
Total uncertainty for bulk density	g/cm^3	±0.0705
Total uncertainty for solubility	%	±0.56
Total uncertainty for antioxidant capacity	%	±0.32

Table 2: Independent variables and their values tested in the experimental design.

Factor	Units	Type	Low actual	High actual	Low coded	High coded	Mean	Std. Dev.
Pressure	kPa	Numeric	20	40	-1	1	30	7.071
Temperature	°C	Numeric	55	75	-1	1	65	7.071
Concentration	%	Numeric	2	3	-1	1	2.5	0.354

of spray-dried extraction powder. In this work, 20 experimental runs were produced based on the corresponding rotatable and orthogonal central composite design (Table 2). It has to be noted that the experiments had a randomized design.

Statistical analysis

The multiple regression analysis of data was applied using the least-squares procedure. Second order polynomial equation was used to express the each response surface as a function of the independent variables. A quadratic model was employed to illustrate the responses as a function of independent variables, which is given by Eq. (7):

$$Y_i = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_{11} X_1^2 + \beta_{22} X_2^2 + \beta_{33} X_3^2 + \beta_{12} X_1 X_2 + \beta_{13} X_1 X_3 + \beta_{23} X_2 X_3 \quad (7)$$

Y_i: the response value predicted by the model,

β_0: constant,

β_1, β_2, and β_3: the regression coefficients for the linear effects,

β_{11}, β_{22}, and β_{33}: the regression coefficients for the quadratic effects

β_{12}, β_{13}, and β_{23}: the regression coefficients included in interaction effects.

x_1, x_2, and x_3: the independent variables of the model.

The significance of statistical test shows the total error criteria, with a confidence level of 95%. The significant phrases in the model were determined by analysis of variance (ANOVA) for each response. The efficiency of the model was investigated by calculating the coefficient of determination (R^2) and adjusted-R^2 coefficient. The R^2 indicates the appropriateness of variation in the response attributed to the model rather than to random error. It has been proposed that a good-fitting model should have R^2 value no less than 80%. When R^2 tends to 1, the empirical model is totally proper for fitting the actual data. A lower value of R^2 indicates that the model is inappropriate for explaining the relation among variables [26]. The numeral and graphical optimization techniques of the Design-Expert software were used simultaneously to optimize the multiple responses at a time. The desired goals for each variable and response were chosen. The analysis results show that all independent variables are within the determined range, while the responses are either maximized or minimized.

RESULTS AND DISCUSSION

Model fitting

The independent variables were tested at three levels in CCD-type experimental design and, finally, 20 experiments

Table 3: Matrix of the central composite design.

Run	x_1	x_2	x_3	Y_1	Y_2	Y_3	Y_4	Y_5
1	30.00	65.00	2.50	7.5	0.63	50	12.79	18.52
2	30.00	65.00	2.50	7.6	0.64	47.63	12.56	18.29
3	20.00	75.00	2.00	6.4	0.54	63.66	12.96	18.22
4	40.00	75.00	3.00	7	0.64	51	12.35	17.85
5	40.00	75.00	2.00	7.3	0.63	54.68	12.13	18
6	30.00	65.00	2.50	7.4	0.63	52.46	12.93	18.37
7	20.00	55.00	2.00	7.5	0.64	50.72	14.33	19.08
8	30.00	65.00	2.50	7.3	0.62	51.7	13.38	18.33
9	30.00	55.00	2.50	8.2	0.72	44.73	14.13	19
10	30.00	65.00	3.00	7.8	0.67	47.28	13.66	18.54
11	20.00	55.00	3.00	7.6	0.67	48.56	14.78	19.17
12	30.00	65.00	2.00	7.2	0.63	52.49	12.69	18.32
13	30.00	75.00	2.50	6.8	0.6	59.2	12.28	18.11
14	40.00	65.00	2.50	8	0.7	46.27	12.58	18.32
15	30.00	65.00	2.50	7.4	0.63	49.27	13.45	18.46
16	30.00	65.00	2.50	7.7	0.66	47.35	12.89	18.55
17	40.00	55.00	3.00	9	0.78	40.52	13.83	18.9
18	20.00	65.00	2.50	7	0.62	56.34	13.97	18.65
19	40.00	55.00	2.00	8.6	0.75	42.38	13.46	18.76
20	20.00	75.00	3.00	6.6	0.56	61.5	13.24	18.37

x_1, x_2 and x_3 are the independent variables including vacuum pressure (kPa), inlet temperature (℃) and concentration of the solution (%) respectively. Y_1 to Y_5 are the response variables of moisture content (%), bulk density (g/cm^3), solubility (%), total phenolic content (mg/g GAE) and antioxidant capacity (%), respectively.

including 6 replicates at the center point, were conducted (Table 3). The experimental data were employed to calculate the coefficients of the quadratic equation. The ANOVA results for the significance and regression coefficients of the models are summarized in Tables 4. For any of the terms in the model, a large regression coefficient and a great absolute F-value demonstrate a more significant effect on the related response variables. Based on ANOVA results, the R^2 of the resulting quadratic models are 0.9615, 0.9564, 0.9637, 0.9045 and 0.9639 for the responses of MC, solubility, bulk density, TPC and antioxidant capacity, respectively The results indicated that R^2 value was greater than 90% for all of the responses in this study, therefore the models are able to identify the optimum operating conditions of spray drying of artichoke leave extract.ANOVA also showed that the lack of fit was not significant for any response models at a 5% significance level and that model adequacieswere appropriate[36].

Analysis of moisture content

According to Table 3, variables with the most significant effect on the moisture content are a linear term of inlet temperature (A) ($p<0.0001$), the linear term of vacuum pressure (B) ($P<0.0001$), and the interaction term of A×B ($P< 0.05$). However, the term of the concentration of the solution (C) and the interaction effects of A×C and B×C and quadratic terms of A_2, B_2, and C_2 were found to be insignificant ($P> 0.05$). The R^2 of the predicted models for moisture content was 0.9615

Table 4: Analysis of variance using response surface quadratic model.

Source of variation	df [a]			F-value		
		Moisture content (%)	Bulk density (gr/cm^3)	Solubility(%)	Total phenolic content (mg/g GAE)	Antioxidant capacity (%)
Model	9	27.73**	29.51**	24.38**	10.53**	29.68**
Pressure (P)	1	79.22**	98.31**	71.31**	25.06**	32.29**
Temperature (T)	1	159.00**	154.91**	134.73**	59.09**	227.79**
Concentration (C)	1	3.44	7.52*	7.68*	5.41	2.37
P×T	1	6.19*	1.39	0.41	0.013	0.33
P×C	1	0.17	0.056	0.063	0.021	0.92
T×C	1	1.55	0.50	0.14	0.13	0.77
P^2	1	1.954×10^{-3}	0.65	0.63	0.89	0.36
T^2	1	1.954×10^{-3}	0.65	2.04	0.32	3.46
C^2	1	1.954×10^{-3}	0.091	0.33	0.17	0.15
Residual	10					
Lake of fit	5	1.68	1.37	0.36	0.61	0.52
Pure Error	5					
Correlation total	19					

*** Highly significant at 1% level, * Significant at 5% level, and [a] Degrees of freedom.*

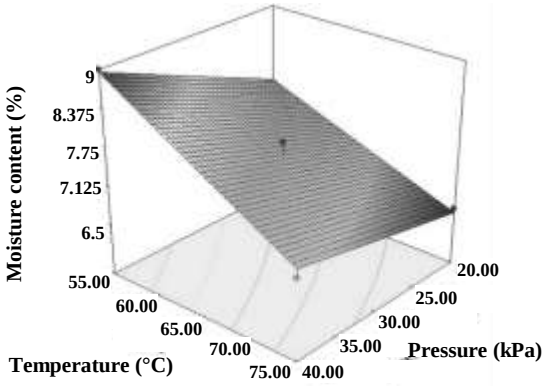

Fig. 2: The intraction effect of inlet temperature and vacuum pressure on moisture content.

indicating a good fit to the mathematical model in Eq. (8).

$$MC = 7.5 + 0.48A - 0.68B - 0.15A \times B \quad (8)$$

Fig. 2 is the response surface plot (three-dimensional) showing the interaction effect of A×B on the moisture content. The interaction term of A×B showed a negative significant effect on the response ($p< 0.05$). The values of this response varied from 6.4% to 9% (dry basis). Based on Fig. 2, the moisture content decreased with an increase in temperature and a decrease in vacuum pressure, indicating that higher temperatures accompanied with lower vacuum pressures are favorable to obtain low moisture content. However, higher levels of vacuum pressure and temperature resulted in the reduction in the moisture content as well probably due to the effect of temperature on the extract powder. At a higher inlet temperature and lower vacuum pressure, a greater thermal and pressure gradient are created between the atomized solution and inside the drying chamber, which promotes a higher rate of simultaneous heat and mass transfer and rate of water evaporation. Consequently, low-water powders are produced in accordance with the moisture content reduction under higher inlet temperature and lower vacuum pressure conditions. Therefore, higher inlet drying temperatures with lower vacuum pressures should be chosen as the optimum operation condition to achieve lower moisture content values. Fig. 2 demonstrated that the lowest moisture content (6.4%) was observed for the vacuum pressure of 20kPa and an air temperature of 75℃.These results are in good agreement with the previous studies [29, 37-39].

Analysis of solubility

Based on ANOVA analysis in Table 3, the relationship between the solubility and independent variables was quadratic, and had a good determination coefficient (R^2 =0.9564). Vacuum pressure and concentration of the extract solution were found to have a negative linear effect on the solubility ($p< 0.0001$) and ($p <0.05$), respectively. However, the inlet drying temperature had a positive linear effect on this response ($p< 0.0001$).The association between solubility and the independent variables of vacuum pressure (A), inlet temperature (B) and concentration of the solution (C) are shown in Eq. (9):

$$\text{Solubility} = 50.03 - 4.59A + 6.31B - 1.51C \quad (9)$$

Fig. 3a, 3b and 3c are the one factor plots demonstrating the effects of vacuum pressure, inlet temperature and concentration of solution on the solubility. The values of this response varied within the range of 40.52 to 63.66% (Fig. 3). Solubility showed an increase with rising inlet air temperature and a decrease in the vacuum pressure. The higher inlet air temperature and lower vacuum pressure may have resulted in the larger particles and faster dissolution. Large particles may immerge, whereas the small ones are dustier and generally float on water, leading to uneven wetting [29, 38]. A decrease in the concentration of extract solution or in the ratio extract/excipient is accompanied by a slight decrease in solubility. The explanation for this phenomenon is that due to the constant concentration of the additive when the concentration is reduced, the ratio of excipient to extraction and the solubilityboth have an increase probably because ofthe high solubility of excipient [38- 41].

Analysis of bulk density

The relationship between bulk density and independent variables was quadratic, with a coefficient of determination of R^2 =0.9637 (Table 3). The bulk density was influenced positively by the vacuum pressure ($p< 0.0001$) and negatively by the inlet temperature ($p<0.0001$). In addition, the concentration of extract solution had a positive linear effect on the response ($p<0.05$). Eq. (10) expresses the association between solubility and the independent variables as follows:

$$\text{Bulk density} = 0.64 + 0.045A - 0.059B + 0.013C \quad (10)$$

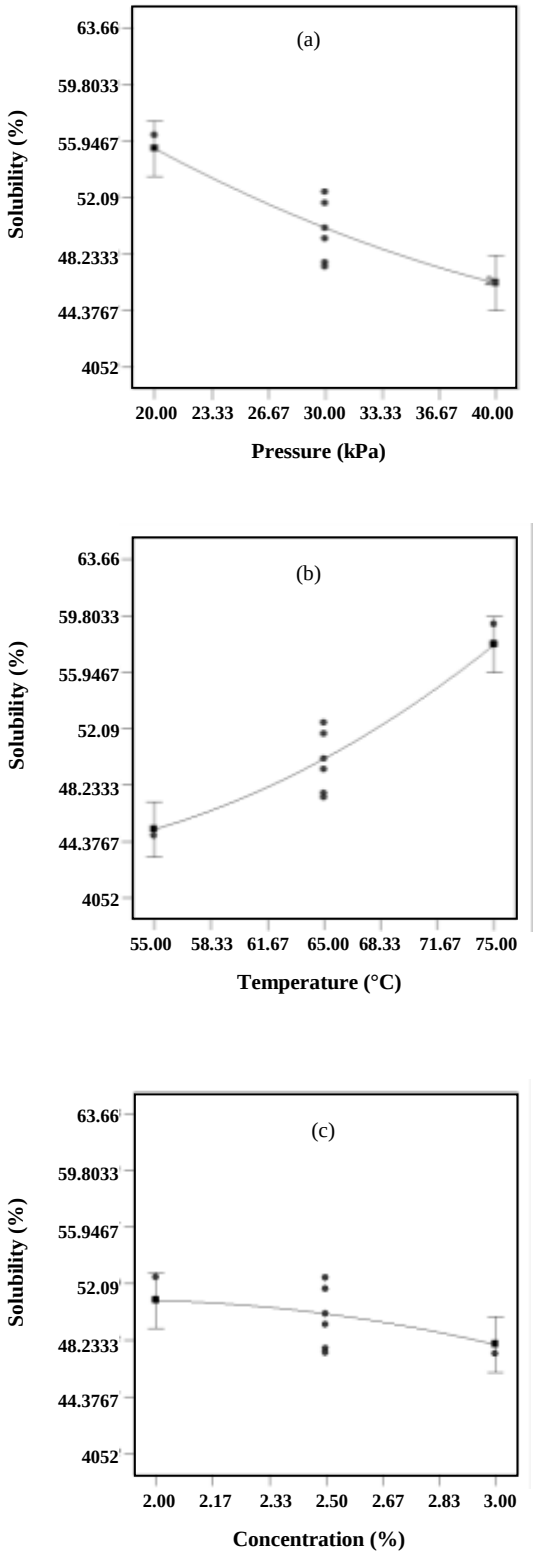

Fig. 3: One factor plots of solubility representing the effects of: (a) vacuum pressure, (b) inlet temperature and (c) concentration.

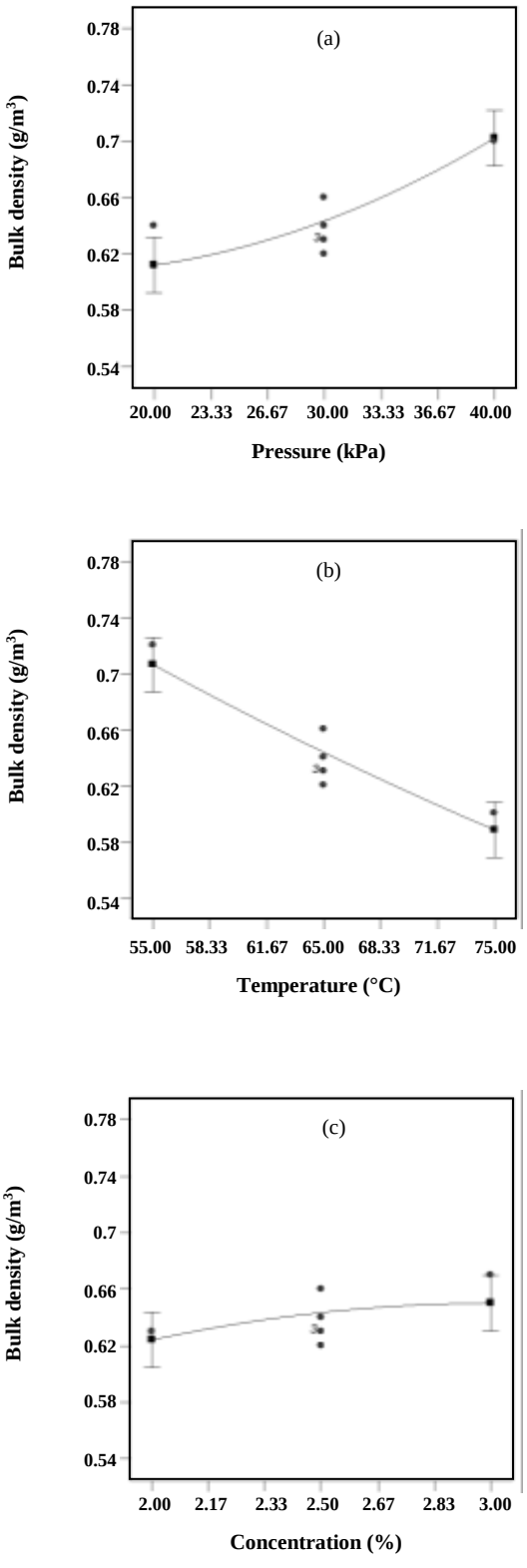

Fig. 4: One factor plots of bulk density representing the effects of: (a) vacuum pressure, (b) inlet temperature and (c) concentration.

Fig. 4a, b and c are the one factor plots describing the effects of vacuum pressure, inlet temperature and concentration of solution on the bulk density. The values of this response vary from 0.54 to 0.78 gcm^{-3}(Fig. 4). It was verified that the bulk density decreased with increasing inlet temperature and decrease in the vacuum pressure of the chamber. Under high temperature and low vacuum pressure conditions, the evaporation rates are faster, leading to a more porous structure in the dry product. Therefore, the formation of more hollow particles causes a decrease in the bulk density. The obtained results are similar to those of the previous studies [42-45]. However, at high concentrations of solution, there was an increase in the bulk density of the powder. In fact, an increase in the concentration of the solution is accompanied by a decrease in the amount of excipient in ratio extract/excipient. Thus a decrease in excipient concentration may cause a reduction in the volume of air trapped in the space between particles and excipient as a skin-forming material. Particles of skin-forming spray dried materials mostly contain air bubbles, which can occur as a result of desorption of air was initially present in the solution feed or was absorbed during atomization [29]. Generally, a decrease in the volume of the trapped air results in an increase in the apparent density of the particles and this increase primarily determines the powder bulk density [43].

Analysis of Total Phenol Content (TPC)

As shown in Table 3 , like other responses mentioned earlier, the relationship between the Total Phenol Content (TPC) and independent variables is quadratic with a relatively high coefficient of determination (R^2 =0.9045). The TPC was influenced negatively both by the vacuum pressure ($p< 0.001$) and the inlet temperature ($p< 0.0001$). Nevertheless, the concentration of the solution was found to have a positive linear effect on the response ($p <0.05$). Eq. (11) expresses the association between TPC and the independent variables as follows:

$$TPC = +13.04 - 0.49A - 0.76B + 0.23C \quad (11)$$

Figs.5a, 5b and 5c are the one-factor plots explaining the effects of vacuum pressure, inlet temperature and concentration of extract solution on the TPC, respectively. It is obvious from the figures that with increasing inlet temperature, the TPC of the powder

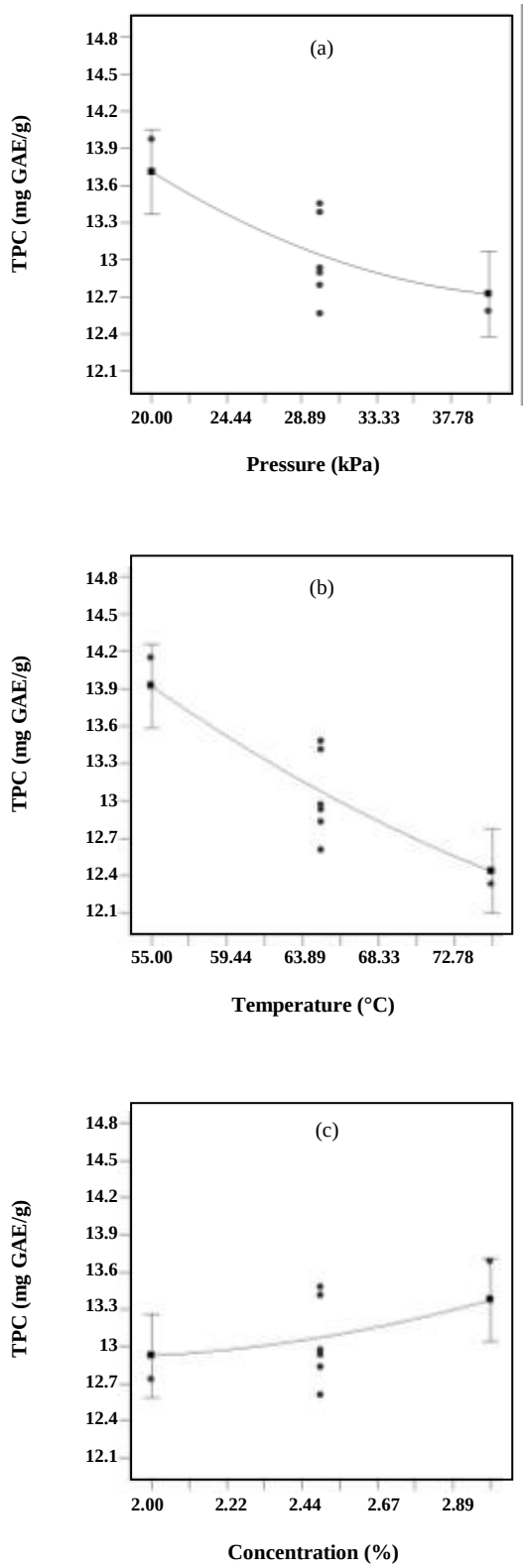

Fig. 5: One factor plots of total phenol content representing the effects of: (a) vacuum pressure, (b) inlet temperature and (c) concentration.

decreased as well. At high inlet temperature, more cynarine and phenolic compounds are destroyed leading to the degradation of TPC [27, 39]. With increasing the concentration of the solution, the TPC of the powder also increased. Therefore, under high concentration of the solution, the amount of extract in ratio extract/excipient increased, as well [15]. Another factor contributed to the TPC reduction was the increase in the vacuum pressure of drying chamber. It can be explained by the fact that less oxygen exists in the drying chamber under low pressure condition. As a result, less oxidation reaction occurs, which is the main cause of the TPC increase of the dried powders [46].

Analysis of DPPH scavenging capacity

Based on Table 3, a quadratic model with a high coefficient of determination (R^2 = 0.9639) was given to demonstrate the relationship between the free radical scavenging capacity (DPPH) and independent variables. It was found that inlet drying temperature ($p < 0.001$) and vacuum pressure ($p < 0.0001$) had a negative linear effect on the DPPH scavenging capacity. Meanwhile, the term concentration of the solution (C) was found to be insignificant. Eq. (12) shows the association between antioxidant capacity and independent variables as follows:

$$\text{Antioxidant capacity} = +18.43 - 0.17A - 0.44B \quad (12)$$

The effect of vacuum pressure and inlet drying temperature on the DPPH scavenging activity is depicted in Fig. 6a and b, respectively. According to these figures, DPPH scavenging activity decreased with increase in the inlet drying temperature. At higher inlet temperatures, antioxidant capacity decreased, due to the degradation and thermal decomposition of antioxidant compound [47-49]. On the other hand, when vacuum pressure decreased, the antioxidant capacity increased due to the decreased drying time and oxidation reaction [50].

Optimization of spray drying operating condition

The ultrasonic vacuum spray drying condition can be optimized if the DPPH scavenging activity, TPC and SI reached to their maximum values while moisture content and bulk density reached their minimum values. The values of all the responses at operating conditions were transformed into a desirability function. The desirability

Table 5: The combinations of variables that could give levels of responses with high desirability.

Number	Pressure	Temperature	Concentration	Moisture content	Solubility	Bulk density	TPC	DDPH capacity	Desirability
1	20.00	70.58	3	6.80615	57.5691	0.584628	13.614	18.44705	0.668

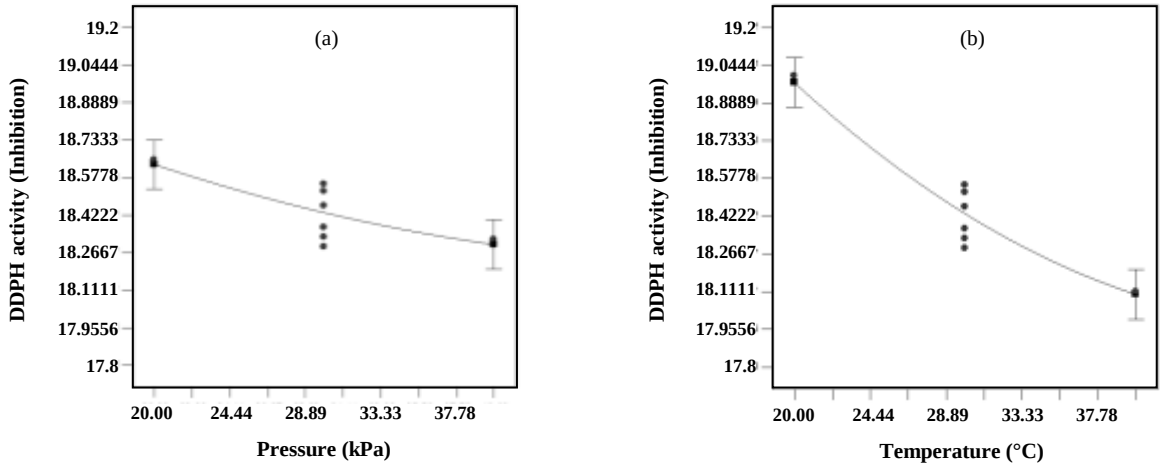

Fig. 6: One factor plots of DPPH scavenging activity representing the effects of: (a) vacuum pressure and (b) inlet temperature.

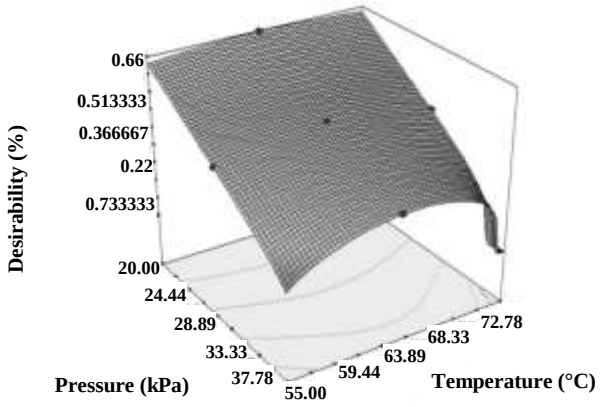

Fig. 7: Effect of vacuum pressure and inlet temperature on desirability.

values of the minimum and maximum were configured as 0 and 1, respectively. The optimum operating condition is determined based on the obtained maximum desirability function [51]. As illustrated in Table 5, several combinations were found to optimize these responses taking into consideration the desirability and feasibility of the experiments. The optimal conditions for desired moisture content, solubility, bulk density, TPC and DPPH scavenging activity corresponded to vacuum pressure of 20 kPa, the concentration of solution 3% and inlet temperature of 70.58°C with the desirability of 66% (Fig. 7). The experimental values of this optimum condition were 6.806%, 57.57%, 0.584 g/cm3, 13.614 mg of GAE/g of spray dying extract powder and 18.47 % of inhibition for five responses of moisture content, solubility, bulk density, TPC and DPPH scavenging capacity, respectively. Due to the high pressure and thermal gradients between the atomized solution and inside of the drying chamber under the vacuum pressure of 20 kPa and temperature of 70.58°C, the evaporation rate was found to be faster causes reduction in the moisture content and bulk density and increase in the solubility, which agreed with observations reported by *Mishra et al.* (2014), who found that an increase in drying temperature significantly affect the moisture content, bulk density and water solubility index [39]. In the vacuum pressure of 20 kPa, total phenol content and antioxidant capacity increased due to the lack of oxygen inside the chamber and oxidation reaction reduction of extract compounds. In accordance with the present study, *Vuong et al.* (2015) verified that*Vitex agnus-castus*leaves dried by freeze and vacuum drying at 65°C had higher levels of bioactive compounds as well as higher antioxidant capacity in comparison with other drying conditions [46]. Morever, in the concentration of 3%, the amount of extract in ratio

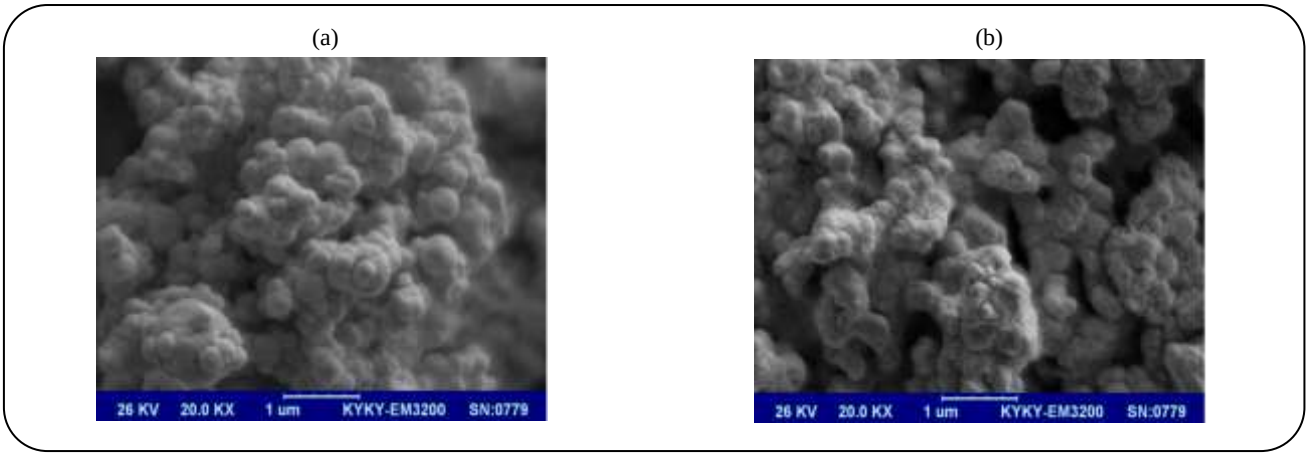

Fig. 8: SEM image samples of extract powders in (a) proposed optimized and (b) undesirable conditions.

extract/excipient increased and resulted in a subsequent increase in the total phenol content. According to the extract powder characteristics in optimum condition, Fig.8a offers the most optimal condition; however Fig. 8b is a demonstration of an undesirable process condition. According to *Tonon et al.* [52], at higher inlet temperature and lower vacuum pressure, water diffusion in the material is faster and allows the deformation process in the particles to be less pronounced. Accordingly, thegenerated larger particles are smoother and more spherical.

CONCLUSIONS

Experiments have been carried out on ultrasonic vacuum spray drying of *C. scolymus* L. leave aqueous extract for several operating conditions including inlet temperature (55–75°C) , vacuum pressure (20-40 kPa) and concentration of extract solution (2 to 3%). An experimental design was constructed as the response surface methodology (RSM) central composite design conditions to study the influence of the previously mentioned parameters on moisture content, solubility, bulk density, TPC and DPPH scavenging capacity. To determine the optimum zone within the experimental region, RSM and the conventional graphical and desirability function procedures were employed as effective tools. From the response surface quadratic model, it was found that the ultrasonic vacuum spray drying conditions were significantly affected by the inlet temperature, vacuum pressure and concentration of the solution. At optimum condition of vacuum spray drying: moisture content, solubility, bulk density, total phenolic content and DPPH scavenging capacity were found to be 6.824%, 57.33%, 0.59 g/cm^3, 13.63 mg of GAE/g of spray dying extract powder and 18.48 %, respectively. As a result, smoother and larger particles were produced. This study also revealed that *C. scolymus* L. leave aqueous extract powder is a good source of antioxidants and phenolic compounds.

Nomenclature

Symbols

M_{db}	Dry basis moisture content, %
M_0	Initial mass of the sample, g
M_t	The sample mass after drying in the oven, g
m_s	The mass obtained by drying of the supernatant, g
m_p	The mass of the powder, g
R^2	Coefficient of determination
v	The volume of graduated cylinder occopied by the powder, cm^3
w_i	The uncertainties in the independent variables
w_R	The uncertainty in the result
x_i, x_j	The levels of the independent variables
y_i	The i response

Greek Letters

β_o, β_i, β_{ii} and β_{ij}	The constant; linear coefficient, quadratic coefficient and cross-product coefficients, respectively
ρ	Bulk density, g/cm^3

Abbreviations

ALEs	Atichoke leaf extracts
CCD	Central Composite Design
DPPH	2; 2-diphenyl picryl hydrazyl

GAE	Gallic acid equivalent
MC	Moisture content
RSM	Responces surface methodology
SEM	Scanning electron microscopy
SI	Solubility index
TPC	Total phenol content
UVSD	Ultrasonic vacuum spray drying

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