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Prediction of the extraction yield using artificial neural network and response surface methodology: ultrasound-assisted extraction from *Achillea berbresteinii* L.

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RESEARCH ARTICLE

Abstract

This study investigates the extraction efficiency of phenolic compounds from *Achillea berbresteinii* by ultrasound-assisted extraction (UAE) method. Meanwhile, to predict the phenolic compound extraction yield, artificial neural network-genetic algorithm (ANN-GA) and response surface methodology (RSM) were compared. The results indicated that UAE method could significantly improve the extraction yield in comparison to conventional method. Optimised processing conditions were 35 °C, 6.3, 20% and 35 min as temperature, pH, solvent to sample ratio and extraction time, respectively. On the other hand, hybrid ANN-GA was employed to estimate the phenolic compound extraction yield. The results revealed the better capability of this method in comparison to RSM. Optimised network contained 8 and 3 neurons in first and second hidden layers, respectively. This configuration could estimate phenolic compound extraction yield with high correlation coefficient (0.94). Finally, *A. berbresteinii* can be considered as an excellent potential source of phenolic compounds and ANN-GA as a successful applied method for the prediction of the phenolic compound extraction yield.

Keywords: *Achillea* L., artificial neural network-genetic algorithm, phenolic compounds, response surface methodology

1. Introduction

Achillea L. is a new genus of the *Asteraceae* family while *Achillea berbresteinii* is an important species which can be found in Asia abundantly. It has numerous medicinal applications such as spasmolytic, choleretic, treatment for wounds and an anti-inflammatory, stomatiche and antihemorrhoidal agent (Candan *et al.*, 2003; Rahimmalek *et al.*, 2009). This plant also contains considerable amounts of phenolic compounds (Konyalioglu and Karamenderes, 2005; Salarbashi *et al.*, 2014; Stojanovic *et al.*, 2005). Phenolic compounds are characterised by their significant antioxidant capacity (Spigno and Marco de Faveri, 2007; Valant-Vetscheraa and Wollenweberb, 1996). Recently, consumer demand is toward natural additives, therefore *A. berbresteinii* can be considered as an excellent potential source for food applications.

The extraction method has a strong effect on the yield of phenolic compound. Numerous investigations have been conducted on the extraction of phenolic compound from agriculture products dealing with the influence of the process variables on the extraction operation (e.g. pH, kind of solvent and extraction temperature) (Dimitrios, 2006; Heydari Majd *et al.*, 2014; Hu *et al.*, 2007; Lapornik *et al.*, 2005). Although the conventional extraction method suffers from long extraction time and low extraction yield, ultrasound-assisted extraction method can be considered as a novel, inexpensive, rapid and efficient alternative to conventional extraction technique. Ultrasound form the

micro channels in the plant tissue due to cavitation. Hence it increases the diffusion of extractable compounds (Rostagno *et al.*, 2008; Wang *et al.*, 2008).

Mathematical modelling provides insights concerning the process under investigation and avoids excessive experimentation. Response surface methodology (RSM) is a combination of statistical and mathematical techniques, which has been successfully applied for optimising many processes. There are a few studies on mathematical modelling of mass transfer during extraction of phenolic compounds. Garcia-Perez *et al.* (2010) applied classical models to gain an insight into the mass transfer process occurred in the extraction of antioxidants from grape stalk. However, due to the complexity of mass transfer during extraction process, application of empirical models has some limitations. Artificial neural networks (ANN), which is inspired on biological nervous system process information, have emerged as one of the powerful heuristic artificial intelligence modelling concepts that could be used for various modelling applications in food science. ANNs can deal with non-linear phenomena due to their massive parallel structure, insensitivity to noisy data and adaptive learning capability. In spite of different advantages of ANN, there are some limitations relating to this modelling system (e.g. the lack of a precise method to choose the most appropriate network topology and parameters of the training algorithm). Therefore, determination of ANN architectures such as the number of hidden neurons and learning parameters carries out by trial and error method, which is time consuming and has insufficient accuracy. Use of an optimisation technique such as genetic algorithm (GA) is a useful solution for overcoming of these inherent shortcomings associated with ANN. GA, which is a global search procedure, mimics the mechanism of the biological evolution process based on genetic operators without facing local minima. Unlike other optimisation techniques such as linear programming, GAs require little knowledge of the process itself (Aghajani *et al.*, 2012; Kashiri *et al.*, 2012; Mohebbi *et al.*, 2008b; Morimoto, 2006).

To the best of our knowledge, there is no published data relating to the investigation of phenolic compounds of *Achillea*. Therefore, the aim of this study is investigating the efficiency of ultrasound-assisted extraction of phenolic compounds from *Achillea Berbresteinii* and possibility of application of ANN-GA and RSM to predict phenolic compounds extraction yield.

2. Materials and methods

Materials

Methanol, sodium carbonate, NH_3, HCl and gallic acid were purchased from Sigma-Aldrich Co. (St. Louis, MO, USA), Folin-Ciocalteu reagent from Merck Co. (Darmstadt, Germany).

Sample preparation

Astane Qods-e-Razavi farm in Toroq, Mashhad, Iran is the place where *A. beibrestinii* was collected from. All samples were dried at room temperature and ground using an electrical mill (CH820; Kenwood, Havant, UK) at low temperature. The remained powder was passed through a 149 micron (no. 100) sieve (Damavand Sieve Ind., Tehran, Iran) and stored in a dark and dry place until the test time.

Extraction of plant materials

Both conventional and ultrasound-assisted extraction (UAE) methods were employed to obtain leaf and flower extracts using 80% methanol as solvent.

Conventional extraction

5 g of ground sample was soaked and mixed with 100 ml methanol (80%). After 24 h, the solution was filtered using Whatman paper no. 1 (GE Healthcare, Little Chalfont, UK) and stored in a refrigerator. The residue was scratched, added to the methanol (1:20 w/v), shaken for 24 h again, filtrated and mixed with the first extraction solution. Methanol was evaporated at 35 °C using a rotary condenser (Laborota 4001; Heidolph, Schwabach, Germany). Final removing of the solvent was accomplished in a vacuum oven at 35 °C, under partial vacuum of 60 cm Hg until a fixed weight was achieved. The dried sample was scraped and stored in a desiccator until the test time.

Ultrasound-assisted extraction

In order to optimise the extraction condition, different factors affecting the extraction procedure, including temperature, time, pH and sample to solvent ratio, were considered as the operation variables. The ultrasound treatments were performed in a bath (model S2; Hielscher GmbH, Teltow, Germany) with internal dimensions of 280×195×135 mm, frequency of 24 kHz and acoustic power of 0.171402 W. It should be mentioned that sonication could lead to an increase of 3.3 °C. Therefore, temperature of the water bath should be set at 11.7, 21.7 and 26.7 °C to achieve experimental temperatures of 15, 25 and 30 °C, respectively. The sample to liquid ratio was kept constant (20, 35 and 50% w/v). Then the extracts were filtered through Whatman paper (no. 1) and dried exactly the same as the conventional extraction.

pH adjustment

Our pre-tests indicated that adding just 1 g of extracted powder into the solvent lead to a pH increase from 5.3 to 6.3. On the other hand, mixing the extracted powder and solvent will result in an alkaline pH more than 6.3 and raising pH to more than 6.9 will have led to a decrease in the

extraction yield of phenolic compounds. Therefore, pH of the solvent was decreased using HCl and NH_3. Briefly, 100 µl HCl (1 N) and 110 µl NH_3 (1 N) were used for adjusting the pH to 5.7 and 6.9, respectively. NH_3 was applied due to its ability to produce less sedimentation. At the end, pH of 6.9, 6.3 and 5.7 were assigned as upper, central and lower thresholds, respectively.

Total phenolic content

Total phenolic contents for both conventional and UAE methods were determined spectrophotometrically (at wavelength of 760 nm) according to Folin-Ciocalteu method (Hayouni *et al.*, 2007). For this purpose, an aliquot of diluted extracts (100 µl) was added to 500 µl of the Folin-Ciocalteu reagent and 6 ml of distilled water. Then, 2 ml of 15% (w/v) sodium carbonate was added to the mixture and shook vigorously. Finally, the solution was brought up to 10 ml by adding distilled water. After 1 h of reaction at ambient temperature in a dark place, the absorbance was determined. Total amount of phenolic compounds were expressed as gallic acid (at concentrations of 0, 30, 70, 110, 150, 190 and 220 mg/kg in 80% methanol) equivalent (mg gallic acid/g sample). All tests were carried out in triplicate.

Prediction using response surface methodology

RSM is an empirical statistical modelling approach, which permit us to determine the input combination of factors. However, this optimisation method is suitable for only quantitative factors. The second order polynomial regression models can be developed to predict the optimal point as follows:

$$Y = \beta_0 + \sum_{i=1}^{k} \beta_i X_i + \sum_{i=1}^{k} \beta_{ii} X_i^2 + \sum_{\substack{i=1 \\ (i<j)}}^{k-1} \sum_{j=2}^{k} \beta_{ji} X_i X_j \quad (1)$$

Where, Y denotes the predicted response, β_0, β_i, β_{ii} and β_{ij} are the regression coefficients for intercept, linear, quadratic and interaction terms, respectively. X_i, and X_j are the independent variables. In this study the Design Expert statistical package (version 7.0.2.0; Stat-Ease Inc., Minneapolis, MN, USA) was employed to generate response surface optimisation. Determination of significant differences of means was carried out by Duncan's test applying MSTAT (version C; Michigan State University, East Lansing, MI, USA).

Prediction using hybrid artificial neural network-genetic algorithm

ANN is considered as a powerful parallel distributed data process system for prediction of material properties. The main advantages of the ANN models are: (1) no particular knowledge is required for the system being modelled; (2) noisy data is acceptable; and (3) very efficient for complex non-linear systems. ANN consists of a series of processing elements (neurons) containing complicated equations for the calculation of outputs based on a given series of input values. Each neuron consists of a transfer function, which performs mathematical computations and convey a signal (weight) from an input neuron to output neuron. Hidden layer connects input (independent) variables into output (dependent). The neurons in this layer are computational processing units, which receive weighted output from the preceding layer as input for computation and send the processed data to output layer. Each neuron in hidden and output layers receives information from several neurons through connections in proportion to their weights, sums them up, adds a constant value (b) to improve convergence and puts the sum in a non-linear or in some cases linear function, called transfer function (f) before passing the signal to other neurons. The mathematical operation of a neuron can be expressed as:

$$Y_i = \sum_{i=1}^{n} f(w_{ij} x_i) + b_j \quad (2)$$

Where, x and y are input and output of neuron, respectively, n is number of inputs to the neuron, w_{ij} is the weight of the connection between neuron i and neuron j and b_j is the bias associated with j^{th} neuron.

In this study, a multilayer feed forward (perceptron) ANN based on back propagation algorithm was developed to estimate phenolic compound yield of *A. berbresteinii*. The input layer consists of four variables in the process (temperature (°C), pH, sample to solvent ratio (%) and time (min)) and the output layer contains phenolic compounds yield (mg/g dry plant) neuron. Hyperbolic tangent function (Equation 3) was used in first and second hidden layers, while a linear function was applied in the output layer. The number of hidden neurons varied from 1 to 20 and was optimised using GA.

$$\tanh(x) = \frac{(e^x - e^{-x})}{(e^x + e^{-x})} \quad (3)$$

In total, 81 data were experimentally collected and divided into three partitions for training (40% of data), validating (30% of data) and testing (30% of data) randomly. Training process was carried in for 1000 epochs or until the cross-validation data's mean-squared error (MSE) (Equation 4), did not improve for 100 epochs (to avoid over-fitting of the network).

Back propagation algorithm was applied as the learning algorithm of ANN. In this method, the error of the output back propagated from the output layer to the hidden layer, and finally to the input layer to modify the weights. Evaluation of the performance of the trained network was based on the accuracy of the network in the test partition. The test data's errors were calculated by means of the MSE,

normalised mean square error (NMSE) and mean absolute error (MAE) as defined in Equation 4-6:

$$MSE = \frac{\sum_{i=1}^{N} (O_i - T_i)^2}{N} \quad (4)$$

$$NMSE = \frac{1}{\sigma^2} \frac{1}{N} \sum_{i=1}^{N} (O_i - T_i)^2 \quad (5)$$

$$MAE = \frac{1}{N} \sum_{i=1}^{N} |O_i - T_i| \quad (6)$$

Where O_i is the i^{th} actual value, T_i is the i^{th} predicted value, N is the number of data and σ^2 is the variance. Sensitivity analysis was carried out to find the most sensitive processing variable affecting the phenolic compounds extraction yield. This analysis was performed by varying the first input between the mean ± standard deviation, while all other inputs were fixed at their respective means and then the phenolic compounds extraction yield was computed for 50 steps above and below the mean. This process was repeated for each input again. Finally, the standard deviation of output with respect to the variation of each input was calculated and the values were used to identify the most important input, which is more effective on the phenolic compounds extraction yield of *A. berbresteinii*.

GA which is based on the principle of a Darwinian-type survival of the fittest in natural evolution, is an adaptive heuristics and parallel global search algorithm that has a high ability to find optimal or near optimal value of a complex objective function, without falling into local optima (Morimoto, 2006). This algorithm is carried out based on three operators namely selection, crossover and mutation, in order to optimise the process. This operator chooses the individuals based on their fitness functions. The chromosomes with higher values of fitness functions will be selected with higher probability. The crossover operator chooses genes from parent chromosomes and creates a new offspring. The mutation operation changes randomly the new offspring according to the mutation probability to introduce new information into the population. This operator has an extremely effect to prevent falling into a local optimum. Aforementioned cycle is repeated until desired convergence on optimal or semi-optimal of the solutions is achieved.

The neural network structure and training parameters were represented by haploid chromosomes consisting of four genes of binary codes. The first two genes corresponds to the number of neurons in the first and second hidden layers (varying from 1 to 20) and third and fourth genes represent the learning rate and momentum of network (varying from 0 to 1), respectively. An initial population of 60 chromosomes was randomly generated. According to the literature (Heckerling *et al.*, 2004; Izadifar and Jahromi, 2007; Mohebbi *et al.*, 2008a; Mokhtarian *et al.*, 2014; Shahabi Ghahfarrokhi *et al.*, 2013) the best generation number is set of 50. Therefore, the termination criterion of 60 was applied. The selection operator was performed applying roulette wheel selection based on ranking algorithm. Uniform crossover and mutation operators with mixing ratio of 0.5 were used and the probabilities of the crossover and mutation operators were adjusted on 0.9 and 0.01, respectively. In this work, the ANN modelling and GA optimisation were performed by Neurosolution software (version 5.0; NeuroDimension Inc., Gainesville, FL, USA).

3. Results and discussion

Extraction yields of phenolic compounds using UAE method are depicted in Table 1. The results indicated that yields of total phenolic compounds of UAE method (2.02 mg/g dry plant) were significantly higher than conventional method while using some specific operation conditions, the extraction yield could increase up to 490.23%. Similar results were reported by Jacques *et al.* (2007) for *Ilex paraguariensis*. It is due to creation of bubbles in the liquid and production of negative pressure. These bubbles then collapse and produce high-speed jets of liquid. The liquid jets have strong impact on the solid surface and enhancement of extraction yield (Luque-Garcia and Luque de Castro, 2003).

Response surface methodology

Response surface methodology was employed to predict the extraction yield of phenolic compounds. Independent variables, their codes and actual values used for optimisation are given in Table 2. Second order polynomial coefficients for each term of the equation are determined through multiple regression analysis using Design Expert statistical package (version 7.0.2.0; Stat-Ease Inc., Minneapolis, MN, USA). Estimated effects of each variable as well as their interactions on phenolic compound extraction yield, are shown in Table 3.

Furthermore, analysis of variance of the independent variables for quadratic polynomial model of UAE are shown in Table 4. Three operation parameters, i.e. temperature, pH and time, showed significant effects on the extraction yield, whereas the effect of solvent to sample ratio wasn't significant ($P<0.05$). The regression model for total phenolic compounds extraction yield is represented in Equation 7. The correlation coefficient for prediction of yield of phenolic compounds using RSM was 0.91, while MSE, NMSE and MAE of this model was 0.10, 0.22 and 0.26, respectively.

Table 1. Average values and standard deviation of phenolic compounds extraction yield using ultrasound-assisted extraction method.

Temperature (°C)	pH	Sample to solvent ratio (%)	Time (min)	Phenolic compounds (mg/g dry plant)
15	6.3	35	35	10.14±0.04
	5.7	35	20	8.96±0.02
	6.3	35	5	8.06±0.07
	6.3	50	20	9.86±0.08
	6.3	20	20	9.31±0.02
	6.9	35	20	8.54±0.03
25	6.3	20	35	10.75±0.03
	6.3	35	20	8.96±0.05
	6.3	50	35	10.26±0.08
	6.3	50	5	10.13±0.07
	6.3	35	20	8.63±0.04
	5.7	35	5	9.10±0.02
	5.7	50	20	9.01±0.05
	5.7	35	35	9.20±0.05
	6.9	35	35	10.48±0.07
	5.7	20	20	9.14±0.06
	6.3	20	5	9.35±0.05
	6.9	50	20	10.33±0.07
	6.9	20	20	10.06±0.04
	6.3	35	20	8.78±0.04
	6.9	35	5	9.72±0.06
35	6.3	35	35	11.79±0.11
	6.3	20	20	10.00±0.08
	5.7	35	20	9.42±0.06
	6.9	35	20	10.71±0.04
	6.3	50	20	10.25±0.12
	6.3	35	5	9.59±0.10

Table 2. Independent variables and coded values employed for optimisation of the extraction procedure.

Independent variable	Symbol	Coded level		
		-1	0	+1
Temperature (°C)	X_1	15	25	35
pH	X_2	5.7	6.3	6.9
Solvent to sample ratio (%)	X_3	20	35	50
Time (min)	X_4	5	20	35

Table 3. Regression coefficients of predicted quadratic polynomial models using response surface methodology.[1]

Coefficient	UAE	Coefficient	UAE
β_0	8.79***	Cross-product	
Linear		β_{12}	0.43***
β_1	0.57***	β_{13}	-0.076^{ns}
β_2	0.41***	β_{14}	0.030^{ns}
β_3	0.10^{ns}	β_{23}	0.10^{ns}
β_4	0.56***	β_{24}	0.20^{ns}
Quadratic		β_{34}	-0.32**
β_{11}	0.43***		
β_{22}	0.18*	R	0.92
β_{33}	0.66***	CV%	4.75
β_{44}	0.66***		

[1] Coefficient of multiple determination, significant at: *5%; **1%; ***0.1%. UAE = ultrasound-assisted extraction; ns = not statistically significant; R = correlation coefficient; CV% = coefficient of variation

Table 4. Analysis of variance of independent variables for the quadratic polynomial model.[1]

Source	Sum of squares	DF	Mean square	*F*-value	*P*-value
Model	15.05	14	1.08	5.12	0.0001
X_1	11.86	1	11.86	98.17	0.0001
X_2	6.20	1	6.20	51.30	0.077
X_3	0.39	1	0.39	3.22	0.0001
X_4	11.23	1	11.23	92.91	0.001
X_1X_2	2.21	1	2.21	18.30	0.0001
X_1X_3	0.069	1	0.069	0.57	0.45
X_1X_4	0.011	1	0.011	0.091	0.76
X_2X_3	0.122	1	0.122	1.01	0.32
X_2X_4	0.35	1	0.35	2.93	0.092
X_3X_4	1.20	1	1.20	9.97	0.0023
X_1X_1	2.92	1	2.92	24.13	0.0001
X_2X_2	0.50	1	0.50	4.2	0.044
X_3X_3	6.9	1	6.9	57.2	0.0001
X_4X_4	7.10	1	7.10	58.76	0.0001
Residual					
Pure error	7.98	66	0.12		
Lack of fit	7.6	10	0.76	116.55	0.0001

[1] X_1 = temperature; X_2 = pH; X_3 = solvent to sample ratio; X_4 = time. DF = degree of freedom.

$$\text{Total phenolic compounds (mg/g)} = 8.79 + \\ + 0.57X_1 + 0.41X_2 + 0.1X_3 + 0.57X_4 + \\ + 0.43X_1X_1 + 0.18X_2X_2 + 0.66X_3X_3 + 0.66X_4X_4 + \\ + 0.43X_1X_2 - 0.32X_3X_4 \quad (7)$$

The results indicated that both linear (except X_3) and quadratic parameters were significant (P<0.05) for UAE method. However, interactions parameters of X_1X_2 and X_3X_4 only produce a significant effect. Thus, linear and

quadratic effects of independent variables were primary determining terms that may cause significant effects in the response while the interaction terms were insignificant (except X_1X_2 and X_3X_4). The positive coefficients for X_1, X_2, X_3 and X_4 indicated that linear effects may increase the responses (Table 4). The quadratic effects of independent variables demonstrated the positive effects. Also the interaction of X_1X_2 indicated positive effect while X_3X_4 showed negative effect. The highest extraction yield was achieved at the processing conditions of temperature of 35 °C, pH=6.3, a solvent to sample ratio of 20% and an extraction time of 35 min.

Hybrid artificial neural network-genetic algorithm

ANNs with 1 to 20 neurons and learning rate and momentum values ranging from 0 to 1 were trained using GA to find out the optimal network configuration and learning parameters for estimation of phenolic compound extraction yield. Neural network properties of optimal configuration were tabulated in Table 5. The prediction errors (MSE, NMSE and MAE) of ANN-GA model were lower than RSM model. The best network included 8 and 3 neurons in first and second hidden layers respectively. The best fitness (lowest MSE) attained during each generation of GA optimisation decreased crosswise generations until it became relatively constant after 47 generations (Figure 1). The ultimate aim of an ANN modelling is calculation of connecting weights and bias of each neuron. The corresponding weight and bias values between input and first hidden neurons (W_1 and B_1), first and second hidden neurons (W_2 and B_2) and second hidden and output neurons (W_{Out} and B_{Out}) are represented in the following matrices:

Table 5. Neural network parameters of optimised configuration.

		Network properties
First hidden layer	Learning rate	0.8271
	Momentum	0.7325
Second hidden layer	Learning rate	0.6343
	Momentum	0.1231
Output layer	Learning rate	0.2426
	Momentum	0.1346
Predicted error	MSE	0.054
	NMSE	0.12
	MAE	0.2

MSE = mean square error; NMSE = normalised mean square error; MAE = mean absolute error.

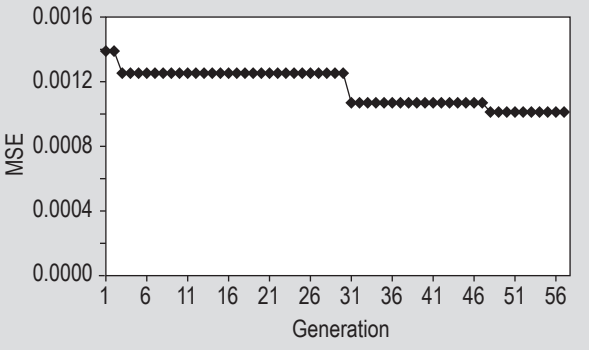

Figure 1. Best fitness (lowest mean square error (MSE) value) versus generation during the optimisation procedure of the artificial neural networks-genetic algorithm system.

$$W_1 = \begin{bmatrix} 2.02\times10^{-4} & 2.86\times10^{-4} & 1.40\times10^{-5} & -5.52\times10^{-4} \\ -4.44\times10^{-4} & 6.41\times10^{-4} & -8.64\times10^{-4} & 2.79\times10^{-4} \\ -1.99\times10^{-5} & -1.08\times10^{-4} & 7.95\times10^{-5} & -2.35\times10^{-4} \\ -3.87\times10^{-4} & -7.47\times10^{-4} & -1.82\times10^{-4} & -1.08\times10^{-5} \\ 7.01\times10^{-6} & -1.09\times10^{-5} & -3.47\times10^{-5} & 2.10\times10^{-4} \\ 4.15\times10^{-4} & -6.20\times10^{-4} & -1.88\times10^{-4} & -6.95\times10^{-4} \\ 2.08\times10^{-4} & -5.71\times10^{-4} & -1.23\times10^{-3} & -4.67\times10^{-4} \\ -8.87\times10^{-4} & -1.52\times10^{-4} & 3.77\times10^{-4} & 1.87\times10^{-4} \end{bmatrix}; \; B_1 = \begin{bmatrix} -1.95\times10^{-3} \\ -5.78\times10^{-3} \\ -5.74\times10^{-4} \\ 5.19\times10^{-4} \\ -5.44\times10^{-4} \\ 6.18\times10^{-3} \\ -4.51\times10^{-3} \\ 2.56\times10^{-3} \end{bmatrix}$$

$$W_2 = \begin{bmatrix} 7.4\times10^{-5} & 3.78\times10^{-5} & 7.08\times10^{-5} & 6.48\times10^{-4} & -1.26\times10^{-4} & -3.14\times10^{-4} & 6.51\times10^{-4} & -5.82\times10^{-4} \\ -2.92\times10^{-4} & 8.06\times10^{-5} & -2.21\times10^{-5} & -7.93\times10^{-4} & 9.70\times10^{-5} & 3.93\times10^{-4} & -2.44\times10^{-4} & 4.93\times10^{-4} \\ -1.35\times10^{-4} & 1.15\times10^{-4} & -1.12\times10^{-5} & 1.40\times10^{-4} & -1.32\times10^{-4} & 4.32\times10^{-5} & 1.68\times10^{-4} & -9.06\times10^{-5} \end{bmatrix}$$

$$B_2 = \begin{bmatrix} -8.75\times10^{-03} \\ 7.99\times10^{-03} \\ -4.48\times10^{-03} \end{bmatrix}$$

$$W_{Out} = \begin{bmatrix} 2.76\times10^{-03} & -3.50\times10^{-03} & 6.56\times10^{-03} \end{bmatrix}; \; B_{Out} = \begin{bmatrix} -3.99\times10^{-3} \end{bmatrix}$$

The values in columns of matrix of W_1 representing the weights of the connections between first hidden neurons and extraction temperature, pH, sample to solvent ratio and extraction time neurons in input layer, respectively. The sensitivity of each variable in the proposed model is shown in Figure 2. Among the input variables, pH was the most sensitive compared to other variables and therefore special care must be taken on this parameter. On the other hand, sample to solvent ratio showed to be the less important factor in extraction yield. This result was also approved by RSM. Plot of experimental values of phenolic compound extraction yield versus predicted data of neural network-GA model was traced in Figure 3. High correlation coefficient reveals good agreement between predicted and experimental data (correlation coefficient of 0.94) and potential application of developed ANN-GA model for estimation of phenolic compound yield. The results of the current study showed that hybrid ANN-GA modelling system was more efficient in comparison to RSM in case of higher correlation coefficient and lower MSE, NMSE and MAE for prediction of phenolic compounds extraction yield.

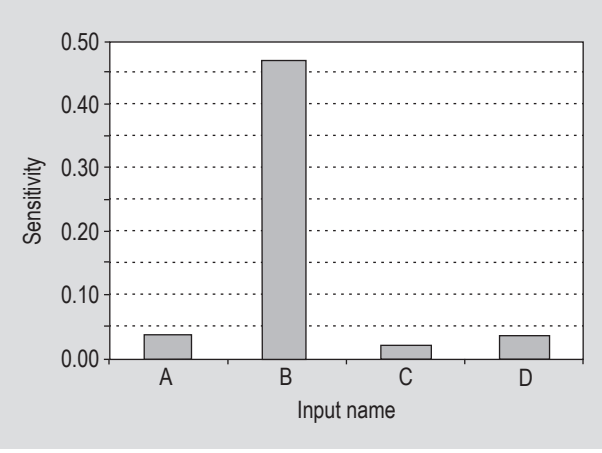

Figure 2. Sensitivity analysis of the optimised network configuration (A = temperature; B = pH; C = sample to solvent ratio; D = extraction time).

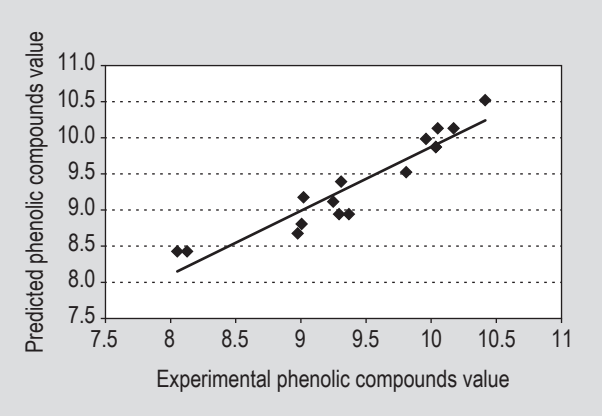

Figure 3. Experimental phenolic compound values versus predicted values applying artificial neural networks-genetic algorithm (diamonds = experimental data; solid line = predicted data; R=0.94).

4. Conclusions

In the current study, the potential application of *A. berbresteinii* as a neutral source of phenolic compounds and the effect of different processing conditions (i.e. pH, temperature, sample to solvent ratio and time) were studied. On the other hand, the capabilities of hybrid ANN-GA and response surface methodology for prediction of phenolic compounds extraction yields were compared. The highest extraction yield was achieved at the processing conditions of 35 °C, pH=6.3, a solvent to sample ratio of 20% and an extraction time of 35 min. The optimised network (with MSE, NMSE and MAE of 0.054, 0.12 and 0.20, respectively), which contains 8 and 3 neurons in first and second hidden layers could predict output neuron with correlation coefficient of 0.94. Sensitivity analysis indicated that pH is the most important parameter affecting phenolic compounds extraction yield. The results of this paper show that the applied intelligent model had a higher capability for prediction of phenolic compounds extraction yield in comparison to RSM.

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