ISSN 1807-1929
Revista Brasileira de Engenharia Agrícola e Ambiental
Brazilian Journal of Agricultural and Environmental Engineering
v.27, n.12, p.941-947, 2023
Campina Grande, PB – http://www.agriambi.com.br – http://www.scielo.br/rbeaa

DOI: http://dx.doi.org/10.1590/1807-1929/agriambi.v27n12p941-947

Extraction technology of flavonoids from *Angelica dahurica*[1]

Tecnologia de extração de flavonoides de *Angelica dahurica*

Fei Fan[2], Ning Lu[2], Shunchang Pu[2*] & Zhien Ding[3]

[1] Research developed at Bozhou University, Department of Biological and Food Engineering, Bozhou, China
[2] Bozhou University, Bozhou, China
[3] Anhui Agricultural University, Hefei, China

HIGHLIGHTS:
A response surface experimental design was used to optimize extraction conditions.
Ultrasonic extraction technology saves costs and is highly efficient.
The flavonoids in Angelica dahurica *function as potential antioxidants.*

ABSTRACT: As a traditional Chinese medicine, *Angelica dahurica* has significant medicinal and nutritional value. To optimize the extraction of flavonoids from *Angelica dahurica* and enhance its medicinal value, this study was conducted to optimize the process using response surface methodology and investigated the effects of ultrasonication time, ethanol concentration, and solid-liquid ratio on the extraction rate of flavonoids in *Angelica dahurica* based on single-factor tests. The ultrasound-assisted extraction process can significantly improve the extraction rate of flavonoids in *Angelica dahurica*, and the flavonoids exhibit antioxidant capacities, which provides a practical basis for the extraction of active ingredients from *Angelica dahurica*.

Key words: extraction technology, ultraviolet-visible spectrophotometry, response surface method, antioxidation

RESUMO: Como medicamento tradicional chinês, a *Angelica dahurica* tem um importante valor medicinal e nutricional. A fim de otimizar o efeito de extração de flavonoides em *Angelica dahurica* e melhorar o seu valor medicinal, este estudo foi realizado para otimizar o processo de flavonoides em *Angelica dahurica* usando a metodologia de superfície de resposta, e investigar os efeitos do tempo ultrassônico, concentração de etanol e concentração de solução de alimentação na taxa de extração de flavonoides em *Angelica dahurica* com base no teste de fator único. O processo de extração assistida por ultrassom pode melhorar significativamente a taxa de extração de flavonoides em *Angelica dahurica*, e os flavonoides têm certas capacidades antioxidante, o que fornece uma base teórica para a extração de ingredientes ativos em *Angelica dahurica*.

Palavras-chave: tecnologia de extração, espectrofotometria ultravioleta visível, método da superfície de resposta, antioxidação

• Ref. 272077 – Received 15 Feb, 2023
* Corresponding author - E-mail: 975803286@qq.com
• Accepted 20 Jul, 2023 • Published 25 Jul, 2023
Editors: Geovani Soares de Lima & Hans Raj Gheyi

Introduction

Angelica dahurica belongs to the Umbelliferae family of plants. Its roots have both medicinal and culinary properties and are used in traditional Chinese herbal medicine. Flavonoids are widely found in many plant species (Li et al., 2022; Yang et al., 2022; D'Arcy, 2022), most of which combine with sugars to form sugar or carbon sugar groups, and natural flavonoids are yellow in color (Petrotos et al., 2021). Flavonoids have numerous physiological and pharmacological functions (Hao et al., 2019; Kejík et al., 2021; Huynh et al., 2022).

Many methods have been proposed for flavonoid extraction, including thermal extraction, ultrasound-assisted ethanol extraction, and alkaline leaching. Certain vegetables and other natural products contain flavonoids. Tian et al. (2021) optimized the extraction of flavonoids from honeysuckles. The main beneficial components of *Angelica dahurica* are volatile oils, coumarins, and flavonoids, and studies on its chemical composition are dominated by volatile oils and coumarins (Hu et al., 2021; Dong et al., 2021).

Although some process experiments and studies on the extraction process of flavonoids from *Angelica dahurica* have been conducted in China, the extraction rate has not been optimized for the extraction process (Lee et al., 2011; Mei et al., 2016; Yang et al., 2017; Yang et al., 2022). A great deal of research has yet to be done on this process, and there is space for progress and exploration. In this study, the ultrasound-assisted extraction of flavonoids from *Angelica dahurica* was used to optimize the extraction process using response surface design experiments to investigate the effects of ultrasonication time, ethanol concentration, and material-to-liquid ratio on the extraction rate.

Materials and Methods

The experiments were conducted from March 2021 to May 2022 at the Experimental Center, Bozhou College, Bozhou City, Anhui Province, China, geographically located at 33.80° N and 115.77° E at an altitude of 39 m. The selected *Angelica dahurica* belonged to a local cultivar of Bozhou City; it was collected by hand locally in Bozhou City and harvested when the leaves of *Angelica dahurica* wilted. The laboratory environment was relatively constant (temperature 25 ± 2 °C, air humidity of 50 ± 5%).

Ultraviolet-visible (UV-vis) spectrophotometry is one of the most widely used and effective methods for research globally. It is used to determine the chemical fluorescence color reaction with a specific property that can be carried out in a light-emitting reaction mechanism, depending on the characteristics of the major components of the sample: the spectral wavelength of the maximum absorption or maximum emission of fluorescence can thus be determined at the appropriate time. A reference specific value is obtained by calculating the average fluorescence absorbance value of the measured substance at the maximum spectral absorption, or the maximum absorption wavelength. Furthermore, quantitative analysis of the content of the chemical components of each molecular chemical structure type or compounds with a common fluorescence characteristic can be conducted to achieve fluorescence quantification. In this analysis, the fluorescence content of total flavonoids was determined by the spectrophotometric method in the presence sodium nitrite and aluminum nitrate, the extraction rate of total flavonoids was calculated, and the absorbance at the optimal wavelength of 510 nm was measured (Zhao et al., 2019). The flavonoid extraction rates were estimated using the following Eq. (1):

$$\text{Flavonoid extraction rate}(\%) = \frac{C \times V_1 \times V_2}{M \times V_3} \times 100\% \quad (1)$$

where C is the gradient of the regression equation, the relative concentration of total flavonoids in the sample solution (mg mL^{-1}), V_1 is the total volume of extract (mL), V_2 is the constant volume of the color reaction (mL), V_3 is the sample volume (mL), and M is the sample size (g).

To produce standard curve for determining the total flavonoids content in samples, 10 mg of rutin was weighed, the appropriate amount of anhydrous ethanol was added, and the mixture was shaken well under ultrasonication until it was completely dissolved. The solution was then decanted into a 50 mL bottle, with a standard concentration of rutin of 0.2 mg mL^{-1}, for use in later experiments. To accurately measure the absorbance at 0, 1.0, 2.0, 4.0, 6.0, and 8.0 mL of the rutin standard solution, a 2 mL solution of 5% $NaNO_2$ was added to the bottle and shaken for 6 min after the solution was fully mixed. A 2 mL solution of 10% $Al(NO_3)_3$ was then added to the bottle and shaken for 6 min, after which 10 mL of 4% NaOH solution was added, and the volume was fixed to the scale with 60% ethanol. After standing for 15 min, the samples were analyzed using UV-vis spectrophotometry at 510 nm using a No. 1 volume bottle as a blank control. The average value was measured in triplicate. Considering the absorption rate (A) as the vertical axis, and the standard solution of rutin (C) as the horizontal axis, a standard curve was drawn, through which the regression equation was obtained (Zhou et al., 2021).

The appropriate amount of *Angelica dahurica* extract was quantitatively absorbed in 2 mL with a pipette and placed in a 25 mL volumetric bottle. The absorbance of the solution was determined at the optimum absorbance wavelength of 510 nm using a UV fluorescence chromogenic test method. After three consecutive groups of comparison experiments, the average value was obtained and the extraction rate of total flavonoids from *Angelica dahurica* was calculated.

In the single-factor test, the effect of ethanol concentration on flavonoid extraction was evaluated. Two grams of treated *Angelica dahurica* root powder was accurately weighed, a solid-liquid ratio of 1:20 (mass/volume) was selected, the extraction time was maintained at 2 hours, and the ultrasonication time was 50 min. After the two extraction processes, the volume fractions of ethanol were fixed at 40, 50, 60, 70, and 80%, and the total flavonoids in *Angelica dahurica* were extracted through filtration at a constant volume. Light absorption and extraction rates of the extracts were determined.

To evaluate the effect of the solid-liquid ratio on the extraction of flavonoids, 2 g of treated *Angelica dahurica* root powder was accurately weighed, and the extraction time was

2 hours with a 60% ethanol volume fraction. Two extractions were performed. The design of the solid-liquid ratio for the experiment was based on the study by Liu et al. (2022), with slight modifications, and the experiment was conducted in a solution with solid-liquid ratios of 1:10, 1:15, 1:20, 1:25, and 1:30 (mass/volume). The total flavonoid content in *Angelica dahurica* was determined by UV-Vis spectrophotometry, and the amount of flavonoids extracted was calculated.

Ultrasonication time is an important factor in ultrasound-assisted extraction. The treated *Angelica dahurica* root powder was accurately weighed (2 g), the solid-liquid ratio was set to 1:20, and the extraction time was 2 hours. The extraction was performed twice successively in a 60% ethanol solution, and the ultrasonication times were 30, 40, 50, 60, and 70 min. The absorbance of the total flavonoids in *Angelica dahurica* was obtained by further filtration at a constant volume. The extraction rate of the flavonoids was then calculated.

The response surface method applies a defined set of tests that use a polynomial function to infinitely approximate the limit state. Suitable test points and iterative methods are selected to ensure that the failure probability of the polynomial function converges to the failure probability of the true implicit limit state function and that the linear response surface of the method has good approximation accuracy if the actual limit state function has no associated linear relationship (Xue et al., 2021).

The results were obtained through a comprehensive analysis of three single-factor experimental parameters for the extraction of total flavonoids from *Angelica dahurica*. From the three factors of ethanol volume fraction (A), solid-liquid ratio (B), and ultrasonication time (C), three levels of ethanol volume fraction (50, 60, and 70%), solid-liquid ratio (1:15, 1:20, and 1:25), and ultrasonication time (40, 50, and 60 min) were selected as having the greatest positive influence on the total flavonoids extracted from *Angelica dahurica*. With the extraction amount of flavonoids as the objective of the investigation and evaluation, response surface analysis software was used to conduct the combined evaluation design of the response surface experimental results. Based on the Box-Behnken center combination evaluation design and the evaluation principle proposed, the response surface test scheme was determined and designed. A prediction model for the regression equation was obtained through a data analysis. From these results, the maximum predicted extraction amount of flavonoids and the optimal extraction parameters for *Angelica dahurica* were determined.

The response surface test analysis design is shown in Table 1. The ethanol concentration (X1), solid-liquid ratio (X2), and extraction time (X3) were independent variables, and the flavonoids extraction rate (Y) of each independent variable was the response value. The response surface analysis test with three factors and three levels was designed comprehensively based on the extraction conditions and experimental results of flavonoids extractions using a central rotation combination experimental design (Table 1).

Finally, the antioxidant capacity of total flavonoids was determined using the method described by Bottamedi et al. (2020) and Thitilertdecha et al. (2022), with slight modifications. DPPH (1,1-Diphenyl-2- picrylhydrazyl) free radical scavenging activity was estimated using the following Eq. (2):

Table 1. Three-factor and three-level response surface analysis for *Angelica dahurica* extraction

Level	Factor		
	Volume fraction of ethanol/% (A)	Solid-liquid ratio (B)	Ultrasonication time/min (C)
-1	50	1:15	40
0	60	1:20	50
1	70	1:25	60

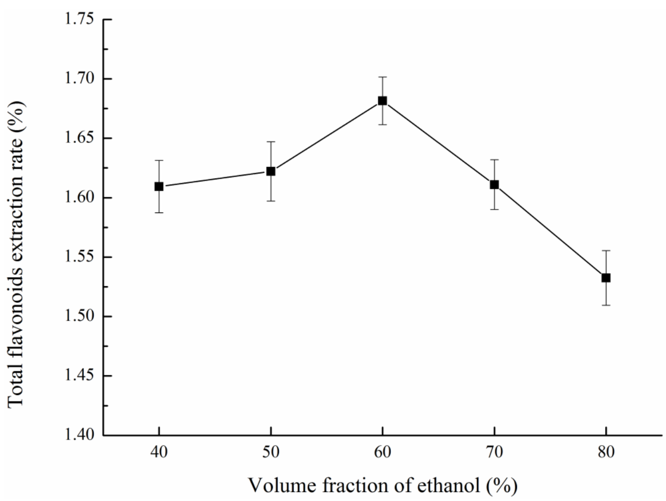
$$\text{DPPH free radical clearance rate}\left(\%\right)=\frac{1-A_1}{A_0}\times 100 \quad (2)$$

where A_1 is the absorbance value of sample mixed with DPPH and A_0 is the absorbance value of the DPPH solution.

Results and Discussion

As shown in Figure 1, with increasing ethanol concentration, the extraction rate of flavonoids increased continuously until it reached a peak and then decreased, showing an increasing and then decreasing trend. Based on the above preliminary analysis, the higher the ethanol concentration in the range of 40-60%, the stronger the solvent permeability and the more damaging to the cell membrane. The dissolution rate of flavonoids increased accordingly. With the increase of ethanol concentration, the extraction of flavonoids from *Angelica dahurica* showed a trend of first increase and then decrease; the trends in the current study are consistent with those of the study by Alara et al. (2020).

With a further increase in concentration, some alcohol-soluble pigments and impurities would precipitate in the solution, thus reducing the extraction efficiency of *Angelica dahurica* flavonoids. A 60% ethanol solution and ultrasonic extraction resulted in the maximum extraction efficiency of flavonoids. Further, the best extraction effect was achieved when the ethanol concentration was 60%; thus, the ethanol



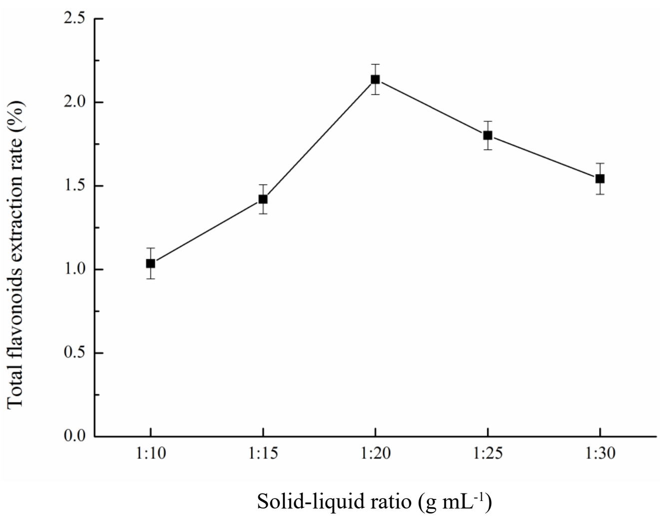
Vertical bars represent the standard deviation of the mean of three values

Figure 1. Effects of different ethanol concentrations on the extraction rate of flavonoids from *Angelica dahurica*

volume fractions of 50, 60, and 70% were selected for response surface optimization.

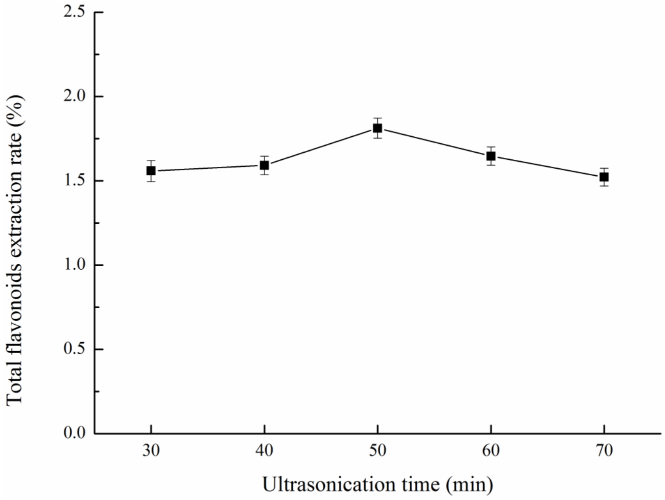
As shown in Figure 2, when the solid-liquid ratio was 1:10, the solvent volume was limiting, so the angelica samples could not be fully extracted in the solvent; thus, the total flavonoids could not be obtained. At a solid-liquid ratio of 1:30, an excessive amount of solvent would be used, which leads to an increase in the cost of extraction. Furthermore, the addition of excess solvent increases the difficulty of the subsequent filtration process, requiring more time and effort and incurring greater costs owing to the larger volumes to be processed. In addition, at that solid-liquid ratio, the extraction of flavonoids from *Angelica dahurica* was close to saturation, and some impurities in *Angelica dahurica* may compete with the flavonoid compounds as the solution precipitated, leading to a reduction in the flavonoid extraction rate (Noriega et al., 2022). The findings showed that the optimal extraction effect was obtained when the solid-to-liquid ratio was 1:20. Solid-to-liquid ratios of 1:15, 1:20, and 1:25 were thus selected for optimization.

As shown in Figure 3, the ultrasound-assisted extraction rate of flavonoids increased with increasing ultrasonication time, which was mainly due to the mechanical vibration, diffusion, mixing, and other effects of ultrasonication, which increased the moving speed and vibrational frequency of materials and accelerated the complete dissolution of flavonoids in *Angelica dahurica*. Therefore, the longer the duration of the effect of ultrasound, the higher the extraction rate of the flavonoids. However, a downward trend was observed at longer ultrasonication times. This is because although ultrasonic shock aids the extraction of flavonoids to a certain extent, prolonged shock causes the surface of the instrument, and thus the solution, to heat up, destroying or denaturing some flavonoids and reducing their activity (Kan et al., 2019). Therefore, extraction time should not be excessively long. If it is too short, however, the extraction rate is low owing to insufficient extraction. Through comprehensive analysis, it can be concluded that an extraction time of 50 min is most appropriate, and ultrasonication times of 40, 50, and 60 min were selected for optimization.



Vertical bars represent the standard deviation of the mean of three values

Figure 2. Effects of different solid-liquid ratios on the extraction rate of flavonoids from *Angelica dahurica*



Vertical bars represent the standard deviation of the mean of the three values

Figure 3. Effects of different ultrasonication times on the extraction rate of flavonoids from *Angelica dahurica*

The Box-Behnke mode provided in DesignExpert (version 8.0.6) was used to conduct the experimental analysis and design of the response surface for the volume fraction of ethanol, solid-liquid ratio, ultrasonication time, and other data. The experimental analysis and design were performed according to the values of the influencing factors in Table 1, and the experimental results in Table 2 were obtained.

Through multiple regression simulation numerical analysis, the predicted value of the extraction rate of flavonoids from *Angelica dahurica* root was determined as influenced by the independent variables of ethanol volume fraction (A), solid-liquid ratio (B), and ultrasonication time (C), which directly affected the quadratic multinomial regression equation model:

$$\begin{aligned} Y &= 0.55-0.036A-0.16B-0.001C+ \\ &+ 0.12AB-0.007AC+0.51BC+ \\ &+ 0.11A^2+0.16B^2-0.015C^2 \end{aligned} \tag{3}$$

Table 2. Design and results of response surface test for *Angelica dahurica* extraction (A - ethanol volume fraction, B - solid-liquid ratio, and C - ultrasonication time)

Test number	A	B	C	Extraction rate of total flavonoids (%)
1	-1	-1	0	0.7968
2	1	-1	0	1.1978
3	-1	1	0	1.7843
4	1	1	0	1.5860
5	-1	0	-1	1.7665
6	1	0	-1	1.6295
7	-1	0	1	1.4453
8	1	0	1	1.4081
9	0	-1	-1	1.1079
10	0	1	-1	1.6744
11	0	-1	1	1.4400
12	0	1	1	1.6877
13	0	0	0	1.6840
14	0	0	0	1.8035
15	0	0	0	1.7860
16	0	0	0	1.8729
17	0	0	0	1.9457

As can be seen from Table 3, the established regression model with F = 5.10 and P-value < 0.05, indicates that the difference in the regression model is significant; the P-value in the misfit term is 0.666 (p > 0.05), which shows that the model difference is not significant. The correlation coefficient of the model, R^2 = 0.8677, indicates that the predicted values correlate with the measured values. The order of the factors affecting the extraction rate of flavonoids obtained by the F-value and significance level was as follows: solid-liquid ratio > ultrasonication time > volume fraction of ethanol.

The interactions of ethanol concentration, solid-liquid ratio, and ultrasonication time on the extraction rate of flavonoids from *Angelica dahurica* are shown in Figure 4. The effect of these factors on the flavonoid extraction rate is greater when the slope of the response surface is steeper. The slope of the response surface of the liquid-solid ratio and ethanol concentration is steep, indicating that they have a significant interaction, which is corroborated by the analysis of variance. Further, the slope of the ultrasonication time and solid-liquid ratio is also steep, indicating that the interaction of these two factors greatly affected the extraction rate of *Angelica dahurica* flavonoids.

Design-Expert (version 8.0.6) software predicted the best model process parameters for the ultrasound-assisted extraction of flavonoids from *Angelica dahurica* at 60% ethanol concentration, 1:20 material-to-liquid ratio, and 50 min ultrasonication time. A maximum flavonoid extraction rate of 2.179% was predicted using this regression equation. They were experimentally verified to determine whether the model-predicted results were reliable. An average extraction rate of 2.162% was obtained from three parallel validation experiments using this process, which was very similar to the predicted result of 2.179%, indicating the good reliability of the model extraction results.

As shown in Figure 5, within the experimental concentration range, the rate of DPPH free radical scavenging increased with increasing flavonoid concentrations. The free radical scavenging ability of DPPH continued to increase when the total flavonoid concentration in *Angelica dahurica* is 0-120 μg mL^{-1}. At concentrations above 120 μg mL^{-1}, the DPPH free-radical-scavenging capacity tended to taper off. The *Angelica dahurica* flavonoids exhibit some antioxidant capacity, slightly inferior to that of vitamin C (Vc).

Table 3. Variance analysis of response surface experimental results

Variance source	Sum of squares	Mean squares	Value of F	Value of P
Model	1.27	0.14	5.10	0.0215
A	0.0001	0.0001	0.0037	0.9535
B	0.60	0.60	21.60	0.0023
C	0.0049	0.0049	0.18	0.6881
AB	0.090	0.090	3.24	0.1151
AC	0.0025	0.0025	0.090	0.7732
BC	0.025	0.025	0.92	0.3705
A^2	0.16	0.16	5.84	0.0463
B^2	0.33	0.33	11.98	0.0105
C^2	0.015	0.015	0.054	0.4846
Residual	0.19	0.028		
Misfit item	0.16	0.052	5.39	0.0686
Pure error	0.0039	0.010		
Total dispersion	1.47			

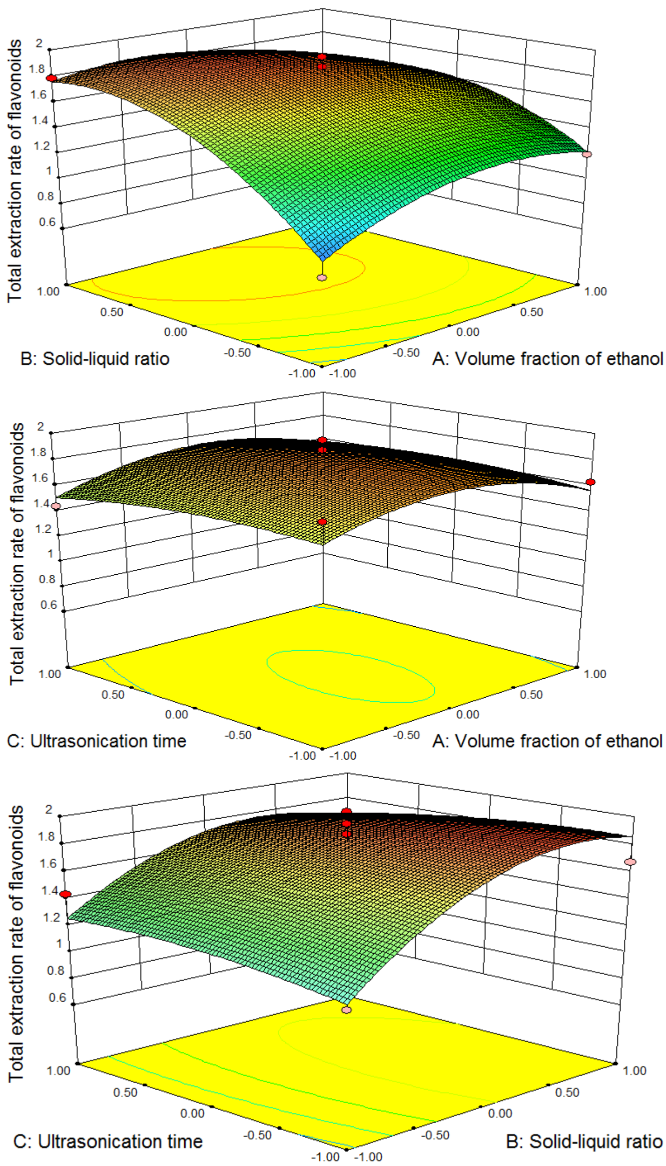
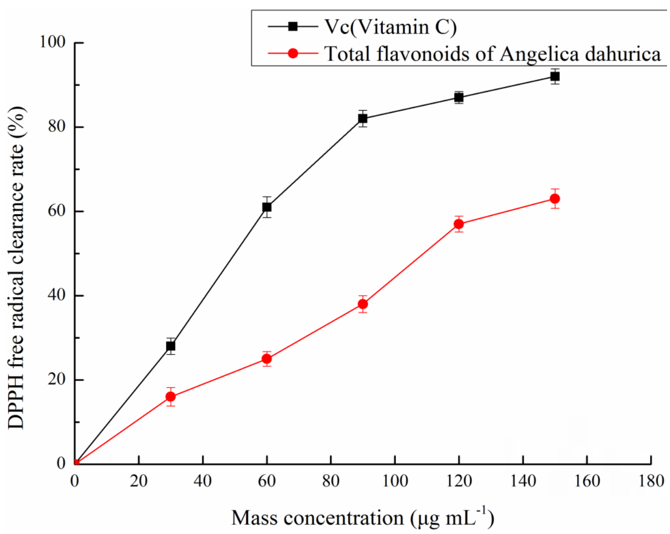


Figure 4. Response surface diagram of effects of interaction factors (A - solid-liquid ratio, B - ethanol volume fraction, and C - ultrasonication time) on flavonoid extraction rate of *Angelica dahurica*



Vertical bars represent the standard deviation of the mean of three values

Figure 5. DPPH (1,1-Diphenyl-2-picrylhydrazyl) free radical scavenging ability of total flavonoids of *Angelica dahurica*

Conclusions

1. Ultrasound-assisted extraction of flavonoids from *Angelica dahurica* was used, and response surface optimization design experiments effectively optimized the extraction rate with respect to solid-liquid ratio, ethanol volume fraction, and ultrasonication time.

2. The antioxidant capacity of the total flavonoids extracted were compared with that of vitamin C; the total flavonoids in *Angelica dahurica* exhibit antioxidant capacity and can be used as potential antioxidants.

Acknowledgements

The authors thank Bozhou University for providing the Bozhou Key Laboratory of Medicinal and Edible Homology Functional Food. This study was supported by the Research on the development of bacteriostatic and moisture resistant film of modified polyvinyl alcohol for traditional Chinese medicine beverage (bzzc2021026), a First-class discipline food science and engineering project (BYXKA202202), a grant from the Anhui University Natural Science Research Project (KJ2020a0769), and the Discipline team of food processing technology (BYZXKTD201802).

Literature Cited

Alara, O. R.; Abdurahman, N. H.; Olalere, O. A. Ethanolic extraction of flavonoids, phenolics and antioxidants from *Vernonia amygdalina* leaf using two-level factorial design. Journal of King Saud University - Science, v.32, p.7-16, 2020. https:// doi.org/10.1016/j.indcrop.2022.115422

Bottamedi, M.; Pereira, M. V.; Fratoni, E.; Jim, Y.; Mendes, B. G. Antioxidant and anti-inflammatory action (*in vivo* and *in vitro*) from the trunk barks of cabreúva (*Myrocarpus frondosus* Allemao, Fabaceae). Journal of Ethnopharmacology, v.267, p.1-11, 2020. https://doi.org/10.1016/j.jep.2020.113545

D'Arcy, M. S. A review of biologically active flavonoids as inducers of autophagy and apoptosis in neoplastic cells and as cytoprotective agents in non-neoplastic cells. Cell Biology International, v.8, p.1179-1195, 2022. https://doi.org/10.1002/cbin.11813

Dong, X. D.; Liu, Y. N.; Zhao, Y.; Liu, A. J.; Ji, H.Y.; Yu, J. Structural characterization of a water-soluble polysaccharide from *Angelica dahurica* and its antitumor activity in H22 tumor-bearing mice. International Journal of Biological Macromolecules, v.193, p.219-227, 2021. https://doi.org/10.1016/j.ijbiomac.2021.10.110

Hao, X.Q.; Wang, J.D.; Wei, G.; Yang, G. E.; Chan, Q. Determination of several compounds in *Rosa roxburghii* fruit extract. Journal of Shanxi Medical University, v.5, p.621-625, 2019. https://doi.org/10.13753/j.issn.1007-6611.2019.05.017

Hu, Y.; Lei, S.; Yan, Z.; Hu, Z.; Guo, J.; Guo, H.; Sun, B.; Pan, C. *Angelica dahurica* regulated the polarization of macrophages and accelerated wound healing in diabetes: A network pharmacology study and in vivo experimental validation. Frontiers in Pharmacology, v.12, p.1-11, 2021. https://doi.org/10.3389/phar.2021.678713

Huynh, K. D.; Pham, V. T.; Tran, V. K.; Pham, H. D.; Pham, T. N. Polyphenol, Flavonoid content and antioxidant activity of the garlic (*Allium sativum* L.) extract obtained by two different extraction processes. Materials Science Forum, v.1048, p.493-501, 2022. https://doi.org/10.4028/www.scientific.net/MSF.1048.493

Kan, X.; Yan, Y; Ran L.; Lu, L.; Cao, Y. Ultrasonic-assisted extraction and high-speed counter-current chromatography purification of zeaxanthin dipalmitate from the fruits of *Lycium barbarum* L. Food Chemistry, v.310, p.1-8, 2019. https://doi.org/10.1016/j.foodchem.2019.125854

Kejík, Z.; Kaplánek, R.; Masarik, M.; Babula, P.; Jakubek, M. Iron complexes of flavonoids-antioxidant capacity and beyond. International Journal of Molecular Sciences, v.2, p.1-20, 2021. https://doi.org/10.3390/ijms22020646

Lee, M. Y.; Ha, K.; Lee, H.; Son, J. K.; Shin.H. K. Anti-inflammatory activity of *Angelica dahurica* ethanolic extract on RAW264.7 cells via upregulation of heme oxygenase-1. Food & Chemical Toxicology, v.49, p.1047-1055, 2011. https://doi.org/10.1016/j.fct.2011.01.010

Li, T.; Zhao, M.; Yang, J.; Raza, A.; Yang, P.; Yu, M.; Hu, D.; Zou, T.; Song, H. Characterization of key aroma-active compounds in bobaizhi (*Angelica dahurica*) before and after boiling by sensomics approach. Journal of Food Composition and Analysis, v.105, p.1-10, 2022. https://doi.org/10.1016/j.jfca.2021.104247

Liu, Y.; Sun, Y.; Li, H.; Ren, P.; Inam, M.; Liu, S.; Liu, Y.; Li, W.; Niu, A.; Liu, S.; Li, Z.; Guan, L. Optimization of ultrasonic extraction of polysaccharides from *Flammulina velutipes* residue and its protective effect against heavy metal toxicity. Industrial Crops and Products, v.187, p.1-10, 2022. https://doi.org/10.1016/j.indcrop.2022.115422

Mei, Z. Y.; Shen, J. Z.; Wang, Y.; Lu, A.; Ho, W. S. Anti-oxidant and anti-cancer activities of *Angelica dahurica* extract via induction of apoptosis in colon cancer cells. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, v.23, p.1267-1274, 2016. https://doi.org/10.1016/j.phymed.2015.11.008

Noriega, M. A.; Figueroa, L. A.; Narváez, P. C. Fatty acid solvent extraction from palm oil using liquid-liquid film contactor: Mathematical model including mass transfer effects. Food and Bioproducts Processing, v.133, p.2-16 2022. https://doi.org/10.1016/j.fbp.2022.02.004

Petrotos, K.; Giavasis, I.; Gerasopoulos, K.; Mitsagga, C.; Gkoutsidis, P. Optimization of vacuum-microwave-assisted extraction of natural polyphenols and flavonoids from raw solid waste of the orange juice producing industry at industrial scale. Molecules, v.26, p.1-27, 2021. https://doi.org/10.3390/molecules26010246

Thitilertdecha, N. Storage effect on phenolic compounds and antioxidant activity of *Nephelium lappaceum* L. extract. Cosmetics, v.9, p.1-9, 2022. https://doi.org/10.3390/cosmetics9020033

Tian, S.; Sun, Y.; Chen, Z. Extraction of flavonoids from corn silk and biological activities in vitro. Journal of Food Quality, v.2021, p.1-9, 2021. https://doi.org/10.1155/2021/7390425

Xue, H.; Tan, J; Li, Q.; Cai, X.; Tang, J. Optimization ultrasound-assisted extraction of anthocyanins from cranberry using response surface methodology coupled with genetic algorithm and identification anthocyanins with HPLC-MS2. Journal of Food Processing and Preservation, v.45, p.14-9, 2021. https://doi.org/10.1111/jfpp.15378

Yang, H. S.; Tang, K. X.; Qin, H. Y.; Xu, X. X.; Liu, X. Y.; Zheng, Z. J. Optimization of supercritical CO_2 extraction process of total flavonoids from *Angelica dahurica* and study on its antibacterial and antioxidant activities in vitro. Specialty Research, v.4, p.126-131, 2022.

Yang, W. T.; Ke, C. Y.; Wu, W. T.; Harn, H. J.; Lee, R. P. Effects of *Angelica dahurica* and *Rheum officinale* extracts on excisional wound healing in rats. Evidence-Based Complementary and Alternative Medicine, v.2017, p.1-9, 2017. https://doi.org/10.1155/2017/1583031

Zhao, X.; Li, Y. J.; Han, W.; Zhang, M. Y.; Liu, S. J.; Li, Y. R. Study on the determination of total flavonoids in peanut shell by spectrophotometry. Food Industry Technology, v.40, p.269-273, 2019.

Zhou, X.; Qin, D.; Xiang, B.; Xi, J. Cyclodextrin-based liquid-phase pulsed discharge extraction of flavonoids from tangerine (*Citrus reticulata*) pericarp: Optimization, antioxidant activity and storage stability. Separation and Purification Technology, v.278, p.1-11, 2021. https://doi.org/10.1016/j.seppur.2021.119603