Journal of Southeast University (English Edition) Vol. 33, No. 3, pp. 362 - 369 Sept. 2017 ISSN 1003—7985

Mathematical modeling for ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii

Dai Lin Zhang Yong Hu Chi Qian Hongliang Wang Zhixiang

(School of Engineering, China Pharmaceutical University, Nanjing 210009, China)

Abstract: A mathematical model based on Fick's first law was established to describe the process of ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii. Acid hydrolization with hydrochloric acid promotes the conversion of arctiin to arctigenin in the arctiin-rich active pharmaceutical ingredient, and the hydrolyzed products were further examined to investigate the process setup. By considering the mechanism of the extraction process and experimental data, the effects of parameters including solvent to solid ratio, particle size of hydrolyzed samples, ethanol volume fraction, ultrasound power, extraction temperature and extraction time on concentration of arctigenin were analyzed in detail. The model was suitable for simulating the process of ultrasonic-assisted extraction of arctigenin. The simulation results of the model agree well with experimental data with the deviation below 13%, indicating that the mathematical model can provide valuable guidance for the extraction of arctigenin from acid hydrolyzed FructusArctii.

Key words: FructusArctii; acid hydrolysis; ultrasonic-assisted extraction; arctigenin; mathematical model

DOI: 10.3969/j.issn.1003-7985.2017.03.017

FructusArctii (Niubangzi in Chinese), the dried fruits of *Arctiumlappa L.*, is one of the most popular traditional medicinal plants in China, which is widely used in Chinese prescriptions to treat inflammation and infection for centuries[1-3]. The major active chemical ingredients in the *Arctiumlappa L.* seeds are lignans and phenolic compounds[4-5]. A number of compounds have been separated and identified from FructusArctii, including arctiin, arctigenin, lappaol, matairesinol and diarctigenin[6]. Arctiin and arctigenin are the major lignan constituents[7-9]. Modern pharmacological studies have revealed that arctiin and arctigenin possess a variety of pharmacological properties and induce a number of important biological activities, such as anti-proliferative[10-11], anti-carcinogenesis[12], and anti-HIV properties[13-15]. So, in the process of chemical standardization of FructusArctii, the inherent-arctiin and arctigenin are usually chosen as "marker compounds"[16-17]. However, various studies have been conducted to identify the main active constituent of FructusArctii. These results indicated that arctiin was rapidly transformed to arctigenin in the rat gastrointestinal tract in vivo[18-19], and arctigenin rather than arctiin acted as the major effective ingredient[8, 14, 20-23]. Therefore, it is necessary to improve the extraction yield of arctigenin from *Arctiumlappa L.* seeds for food and the pharmaceutical industry. From a literature review in brief, studies on the analysis of FructusArctii extracts revealed that the level of arctiin was significantly higher than that of arctigenin[5, 16-17, 24]. To obtain high amounts of arctigenin, *Arctiumlappa L.* seeds were hydrolyzed by hydrochloric acid before extraction, which was a simple and efficient way to promote the conversion of arctiin to arctigenin.

The traditional methods used to extract bioactive constitutes from natural materials are heating reflux, soxhlet and solvent extraction. However, these methods have some critical disadvantages such as a long extraction time, large consumption of solvent, poor product quality, energy consumption and very few adjustable parameters. Since the solvent extraction requires a high temperature, it is not suitable for thermo labile compounds. In recent years, a number of new methods have been developed and applied to overcome these limitations, such as accelerated solvent extraction[25], supercritical fluid extraction[26], the microwave-assisted method[27] and ultrasonic-assisted extraction (UAE). Among them, UAE is reported to be a more economical and efficient method to isolate bioactive compounds[28-29] with minimal harm to their bioactivity[30]. The acoustic cavitation of ultrasound in extraction improves the interaction between targeted compounds and the solvent, causing destruction of the cellular wall and facilitating the mass transfer of contents[31-33]. From extensive literature research, there are no reports on mathematical models describing the kinetics process of the ultrasonic-assisted extraction of arctigenin from hydrolyzed FructusArctii.

In this paper, on the basis of single factor experimental data and Fick's first law, the corresponding solution to the mathematical model was established to simulate the process of ultrasonic-assisted extraction of arctigenin from hydrolyzed FructusArctii. The parameters including solvent to solid ratio, particle size of hydrolyzed samples, ethanol volume fraction, ultrasound power, extraction

Received 2016-11-14.

Biographies: Dai Lin (1981—), male, master, lecturer; Wang Zhixiang (corresponding author), male, doctor, professor, 1443590147@qq.com.

Foundation items: The National Natural Science Foundation of China (No. 21406272, 21676291), the Fundamental Research Funds for the Central Universities (No. 2632017ZD01), Jiangsu Planned Projects for Postdoctoral Research Funds (No. 1402060B).

Citation: Dai Lin, Zhang Yong, Hu Chi, et al. Mathematical modeling for ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii[J]. Journal of Southeast University (English Edition), 2017, 33(3): 362 - 369. DOI: 10.3969/j.issn.1003-7985.2017.03.017.

temperature and extraction time were taken into consideration in the model. The parameters of the model were estimated by single factor experiments.

1 Materials and Methods

1.1 Reagents and herbs

The fruits of *Arctiumlappa L.* were obtained from Nanjing Zelang Pharmaceutical Technology Co., Ltd., Jiangsu, China. *Arctiumlappa L.* seeds were ground to powder (mesh size 20-40, 40-60, 60-80, 80-100) using an electronic grinder and stored at 4 ℃ for use. The standard arctigenin was purchased from the National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China, see Fig. 1 for chemical structure). The methanol was chromatographically pure and all other reagents were analytically pure.

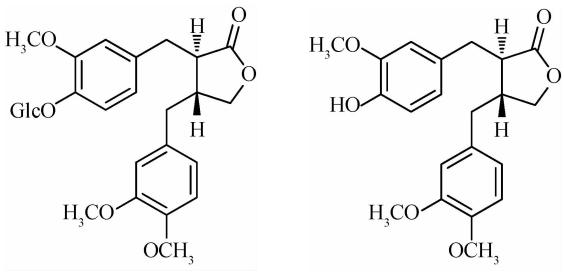

Fig. 1 Chemical structures. (a) Arctiin; (b) Arctigenin

1.2 Sample pre-treatment

In order to convert arctiin to arctigenin, the powder of FructusArctii was hydrolyzed in 3% (weight percentage) hydrochloric acid for 6 h, and the ratio of ground materials to hydrochloric acid solution was about 1∶6. After hydrolysis, the mixture was filtrated and the residues were washed with a large amount of distilled water until the pH of the washing liquid was 7. Then, the hydrolyzed materials were dried at temperature of 50 ℃ for 24 h. The dried materials were kept at 4 ℃ without light until use.

1.3 Apparatus and instruments

The ultrasonic bath (DCTZ-2000E type, 40.0 kHz, Hongxianglong Co., Ltd., Beijing, China) was equipped with a stainless extraction vessel of 500 mL and a ultrasonic generator (maximum power 1 200 W). Circulating water was used to keep the solution's temperature stable during the experiment. The analytical high-performance liquid chromatograph (10ATvp, Shimadzu, Japan) was equipped with a LC-10AT pump, a CTO-10AS column oven, a SCL-10A controller, a SPD-10A ultraviolet (UV) detector and a manual injector with a 20 μL sample loop. A CLASS-VP software package was used for data analysis.

1.4 Determination of arctigenin in the extract by HPLC

The concentration of arctigenin in the extracts was determined by HPLC. A ODS-2 Hypersil column (5 μm, 150 mm × 4.6 mm) operating at 25 ℃ was applied to separate the arctigenin by isocratic elution with a mobile phase consisting of methanol: water (50∶55 in volume percentage)[1] at a flow rate of 0.5 mL/min. The detector was employed at a wavelength of 280 nm and the injection volume of filtered sample was 20 μL. The identification of arctigenin was carried out by comparing the retention time with the reference standard of arctigenin. Standard calibration curves applied to calculate the concentrations of arctigenin were generated by using seven standard dilutions ranging from 0.022 to 1.386 mg/mL. The regression line for arctigenin was $y = 3.0 \times 10^7 x + 406\,489$ ($R^2 = 0.999\,7$), where y is the peak area (mAU) of arctigenin, and x is the concentration of standard solution (mg/mL).

1.5 Ultrasonic-assisted extraction

The extraction was performed in an ultrasound bath. A mixture of ethanol and water at different ratios was put into the stainless extraction vessel as the extraction solvent. When the temperature of the solvent reached a preset temperature and remained steady in the water bath, the dry hydrolyzed samples were macerated into the extraction vessel, following the immersion of an ultrasonic generator into the solvent at approximately 2 cm. Under the sets of designed ultrasonic conditions (ultrasonic power and time), the solvent-material slurry was extracted and then filtered. After each run, 1 mL of the extract solution was put into volumetric flask and diluted 10-fold with a mobile phase of high performance liquid chromatograph (HPLC). Then, the diluted solution was filtered through 0.22 μm nylon syringe membranes. 20 μL aliquot of filtrated solution was injected into the HPLC for analysis. The result was expressed as the extraction yield:

$$Y = \frac{C \times V \times 10}{M} \times 100\% \quad (1)$$

where Y is the extraction yield, %; C is the measured concentration of arctigenin in injections, mg/mL; V is the volume of extract solution, mL; M is the mass of dry hydrolyzed samples, mg.

1.6 Experimental design

The parameters of single factor experiments are as follows:

1) The effect of solvent to solid ratio on the concentration of arctigenin was experimentally studied at the extraction temperature 313 K, ethanol volume fraction 50%, ultrasound power 400 W, extraction time 20 min and particle size 20 to 40 mesh;

2) The effect of the particle size on the concentration of arctigenin was experimentally studied at an extraction temperature 313 K, solvent to solid ratio 20 mL/g, ultrasound power 400 W and extraction time 20 min and ethanol volume fraction 50%;

3) The effect of the ethanol volume fraction on the concentration of arctigenin was experimentally studied at an extraction temperature 313 K, solvent to solid ratio 20

mL/g, ultrasound power 400 W, extraction time 20 min and particle size 20 to 40 mesh;

4) The effect of the ultrasound power on the concentration of arctigenin was experimentally studied at extraction temperature 313 K, ethanol volume fraction 50%, solvent to solid ratio 20 mL/g, extraction time 20 min and particle size 20 to 40 mesh;

5) The effect of the extraction temperature on the concentration of arctigenin was experimentally studied at a solvent to solid ratio 20 mL/g, ethanol volume fraction 50%, ultrasound power 400 W, and extraction time 20 min and particle size 20 to 40 mesh;

6) The effect of the extraction time on the concentration of arctigenin was experimentally studied at an extraction temperature 313 K, ethanol volume fraction 50%, solvent to solid ratio 20 mL/g, and ultrasound power 400 W and particle size 20 to 40 mesh.

2 Theoretical Analysis

During the process of liquid-solid extraction, the solute transforms from the solid phase to the liquid phase. The process is comprised of three steps[34]:

1) Extraction solvent permeates into the solid matrix;

2) Solute dissolves into solvent and then diffuses to the solid-liquid interface;

3) Solute is transformed from the solid-liquid interface to the liquid phase. The schematic diagram of the extraction process and the variation of solute concentrations in the solid phase and the liquid phase are illustrated in Fig. 2.

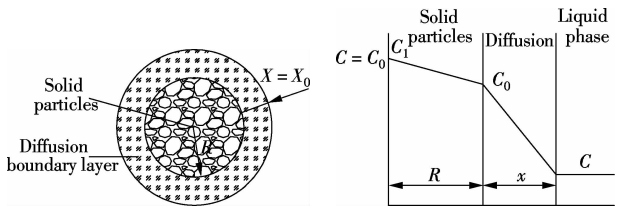

Fig. 2 Schematic diagram of solute concentrations variation in the process of liquid-solid extraction. (a) Schematic representation of liquid-solid interface; (b) Concentration variation as a function of the distance from the solid particle

By considering Fick's first law, the following equation can be obtained:

$$\frac{dW}{dt} = -DS\frac{dC}{dx} \tag{2}$$

where $\frac{dW}{dt}$ is the leaching rate of arctigenin, kg/s; D is the diffusion coefficient of arctigenin in the liquid phase, m^2/s; S is the diffusion area, m^2; $\frac{dC}{dx}$ is the concentration gradient of arctigenin from the surface of the hydrolyzed FructusArctii powder to the bulk of the solution, kg/m^4; a negative sign indicates that arctigenin diffuses in the opposite direction of the concentration gradient.

During the process of ultrasonic extraction, D is generally composed of the molecular diffusion coefficient and eddy diffusion coefficient; therefore, the diffusion coefficient can be proposed as follows:

$$D = D_M + D_E \tag{3}$$

where D_M is the molecular diffusion coefficient, m^2/s; D_E is the eddy diffusion coefficient, m^2/s;

The molecular diffusion coefficient D_M can be described by the Arrhenius equation:

$$D_M = Ae^{-E/(RT)} \tag{4}$$

where A is the transfer coefficient factor, m^2/s; E is the activation energy for the extraction, J/mol; R is the universal gas constant, 8.314 J/(mol · K); T is the extraction temperature, K.

During the process of extraction, A is a function of concentration for concentrated solution, the following equation can be proposed[35]:

$$A_M = D_0 C^n \tag{5}$$

where D_0 is the intrinsic diffusion coefficient, m^2/s; C is the mass concentration of arctigenin, kg/m^3; n is a constant. Since the diffusion coefficient decreases with the increase in distance, n is usually less than 0.

On the basis of predecessors' study[36], the eddy diffusion coefficient is a function of ultrasound power and extraction temperature, which can be defined as

$$D_E = k_3 e^{k_1 T} P^{k_2} D_M \tag{6}$$

where k_1, k_2 and k_3 are the influence parameters of the extraction temperature, ultrasound power and their interaction on the transfer coefficient, respectively; P is the ultrasound power, W.

As the turbulence degree of extraction solution is greatly enhanced by ultrasonic waves, the effect of eddy diffusion is much larger than that of molecular diffusion, which means $D \approx D_E$. According to Eqs. (3) to (6), the following equation can be obtained:

$$D = k_3 D_0 P^{k_2} C^n e^{k_1 T - E/(RT)} \tag{7}$$

In general, the process of extraction is usually unstable, thus the concentration gradient of the solute is usually a function of space and time. Since a larger concentration gradient leads to a faster diffusion and a greater variation of concentration gradient with time, the following equation is proposed; which assumes that the change of concentration gradient with time is proportional to the concentration gradient[35]:

$$\frac{d}{dt}\left(-\frac{dC}{dx}\right) = \alpha\left(-\frac{dC}{dx}\right) \tag{8}$$

where α is a proportionality constant. Since the concentration gradient decreases with the increase of solute concentration in solvent, α is usually less than 0. With the initial condition listed as follows, Eq. (8) can be integrated to obtain the following equation:

$$t = 0, \quad -\frac{dC}{dx} = C_0$$

$$-\frac{\mathrm{d}C}{\mathrm{d}x}=C_0\mathrm{e}^{\alpha t} \tag{9}$$

$$C_0=ac^b\mathrm{e}^{k_4T} \tag{10}$$

where C_0 is the arctigenin concentration on the solid-liquid interface, kg/m^3; c is the ethanol volume fraction, %; b, k_4 and a are the influence parameters of ethanol volume fraction, extraction temperature and their interaction on C_0, respectively

According to Eqs. (2), (7), (9) and (10) and defining $W=VC$ and $k=k_1+k_4$, the following equation can be obtained:

$$\frac{\mathrm{d}C}{\mathrm{d}t}=\frac{k_3aD_0P^{k_2}C^n\mathrm{e}^{kT-E/RT+\alpha t}c^bS}{V} \tag{11}$$

where W is the mass flux of arctigenin transferred across the diffusion layer, kg; V is the total volume of extracts, m^3.

During the process of ultrasonic-assisted extraction, the diffusion area S and the mass of hydrolyzed FructusArctii G can be proposed as follows:

$$S=k'\omega\sigma^2 \tag{12}$$

$$G=k''\omega\rho_s\sigma^3 \tag{13}$$

where ω is the granule number of granule number; σ is the particle size of sample powders, μm; G is the mass of hydrolyzed FructusArctii, g; ρ_s is the density of samples, g/m^3; k' and k'' are both the proportionality constants related to the shape of particles of hydrolyzed samples.

For a certain quality of hydrolyzed FructusArctii powder, the ratio of V to G is proportional to the solvent to solid ratio. According to Eqs. (12) and (13) and defining $k_1=\frac{k'}{k''\rho_s}$, the following equation can be obtained:

$$\frac{S}{V}=\frac{k_1\lambda}{q\sigma} \tag{14}$$

where λ is the proportionality constant.

According to Eq. (14) and the initial condition $t=0$, $C=0$, Eq. (11) can be integrated as

$$C^{1-n}=\frac{(1-n)k_1k_3\lambda aD_0P^{k_2}c^b\mathrm{e}^{KT-E/RT}(\mathrm{e}^{\alpha t}-1)}{\alpha q\sigma} \tag{15}$$

Eq. (15) is a mathematical model of ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii, which gives the relationship among the arctigenin concentration C and ultrasonic power P, extraction temperature T, solvent to solid ratio q, ethanol volume fraction c, particle size σ and extraction time t.

With the value of β defined, Eq. (15) can be transferred into the following equation:

$$\beta=\frac{1}{1-n}\ln\frac{(1-n)k_1k_3\lambda aD_0}{-\alpha} \tag{16}$$

$$\ln C=\beta-\frac{\ln\sigma}{1-n}-\frac{\ln q}{1-n}+\frac{k_2\ln P}{1-n}+\frac{b\ln c}{1-n}+\left[\frac{kT}{1-n}-\frac{E}{(1-n)RT}\right]+\frac{\ln(1-\mathrm{e}^{\alpha t})}{1-n} \tag{17}$$

In Eq. (17), n, k_1, k_2, k_3, k, λ, a, b, D_0, α, E and R are all constants. The parameters n, k_2, k, b, α and E can be determined by single factor experiments and Eq. (17) can be rewritten as

$$\ln C=\varphi_1-\frac{\ln q}{1-n} \tag{18}$$

$$\ln C=\varphi_2-\frac{\ln\sigma}{1-n} \tag{19}$$

$$\ln C=\varphi_3-\frac{b\ln c}{1-n} \tag{20}$$

$$\ln C=\varphi_4-\frac{k_2\ln P}{1-n} \tag{21}$$

$$\ln C=\varphi_5-\frac{kT}{1-n}-\frac{E}{(1-n)RT} \tag{22}$$

$$\ln C=\varphi_6-\frac{\ln(1-\mathrm{e}^{\alpha t})}{1-n} \tag{23}$$

where φ_1 to φ_6 are the constant terms when only one factor is considered in the model. Then, substituting n, k_2, k, b, α, E and φ_1 to φ_6 into Eq. (17) gives the corresponding values of β_1 to β_6 which are then averaged to obtain the value of β for the mathematical model. The mean value of $(1-n)k_1k_3\lambda aD_0/(-\alpha)$ can be determined by the value of β.

3 Results and Discussion

3.1 Solution of the model

3.1.1 Single factor experiment of solvent to solid ratio

To obtain the value of n, the values of all factors except the solvent to solid ratio are kept constant. Fig. 3 shows the relationship between arctigenin concentration and solvent to solid ratio. The linear regression equation is shown as follows:

$$\ln C=2.955\ 7-0.758\ 7\ln q \quad R^2_{\text{adjusted}}=0.989\ 0 \tag{24}$$

$$\frac{1}{1-n}=0.758\ 7 \tag{25}$$

$$\beta_1-\frac{\ln 594}{1-n}+\frac{k_2\ln 400}{1-n}+\frac{b\ln 0.5}{1-n}+\left[\frac{313k}{1-n}-\frac{E}{(1-n)R\times 313}\right]+\frac{\ln(1-\mathrm{e}^{20\alpha})}{1-n}=2.955\ 7 \tag{26}$$

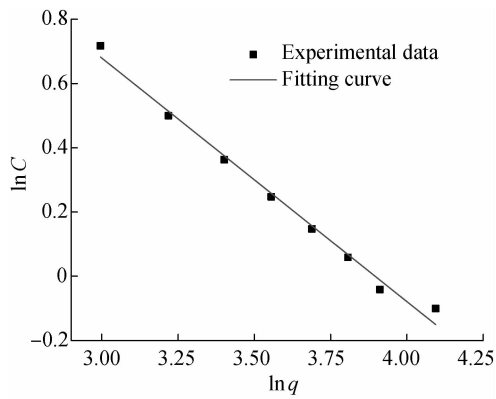

Fig. 3 Relationship between arctigenin concentration and solvent to solid ratio

3.1.2 Single factor experiment of particle size

To obtain the value of n, the values of all factors except particle size are kept constant. Fig. 4 shows the relationship between the arctigenin concentration and particle size. The linear regression equation is given as

$$\ln C = 5.426\ 6 - 0.743\ 5 \ln\sigma \quad R^2_{\text{adjusted}} = 0.998\ 5 \tag{27}$$

$$\frac{1}{1-n} = 0.743\ 5 \tag{28}$$

$$\beta_2 - \frac{\ln 20}{1-n} + \frac{k_2 \ln 400}{1-n} + \frac{b \ln 0.5}{1-n} + \left[\frac{313k}{1-n} - \frac{E}{(1-n)R \times 313}\right] + \frac{\ln(1-\mathrm{e}^{20\alpha})}{1-n} = 5.426\ 6 \tag{29}$$

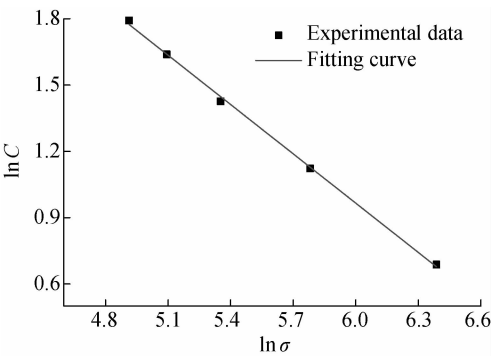

Fig. 4 Relationship between arctigenin concentration and particle size

3.1.3 Single factor experiment of ethanol volume fraction

To obtain the value of b, the values of all factors except ethanol volume fraction are kept constant. Fig. 5 shows the relationship between the arctigenin concentration and ethanol volume fraction. The linear regression equation is given as

$$\ln C = 1.852\ 1 - 1.773\ 0 \ln\sigma \quad R^2_{\text{adjusted}} = 0.995\ 0 \tag{30}$$

$$\frac{b}{1-n} = 1.773\ 0 \tag{31}$$

$$\beta_3 - \frac{\ln 594}{1-n} - \frac{\ln 20}{1-n} + \frac{b \ln 0.5}{1-n} + \left[\frac{313k}{1-n} - \frac{E}{(1-n)R \times 313}\right] + \frac{\ln(1-\mathrm{e}^{20\alpha})}{1-n} = 1.852\ 1 \tag{32}$$

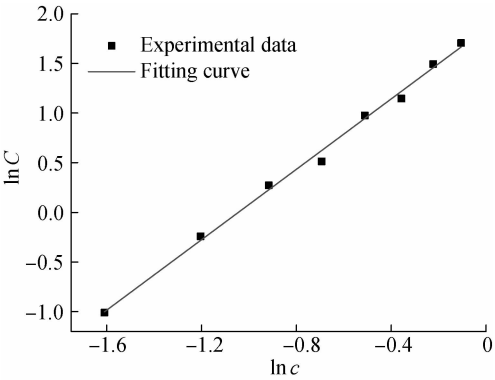

Fig. 5 Relationship between arctigenin concentration and ethanol volume fraction

3.1.4 Single factor experiment of ultrasound power

To obtain the value of k_2, the values of all factors except ultrasound power are kept constant. Fig. 6 shows the relationship between arctigenin concentration and ultrasound power. The linear regression equation is given as

$$\ln C = -0.541\ 0 - 0.195\ 3 \ln P \quad R^2_{\text{adjusted}} = 0.953\ 0 \tag{33}$$

$$\frac{k_2}{1-n} = 0.195\ 3 \tag{34}$$

$$\beta_4 - \frac{\ln 594}{1-n} - \frac{\ln 20}{1-n} + \frac{b \ln 0.5}{1-n} + \left[\frac{313k}{1-n} - \frac{E}{(1-n)R \times 313}\right] + \frac{\ln(1-\mathrm{e}^{20\alpha})}{1-n} = -0.514\ 0 \tag{35}$$

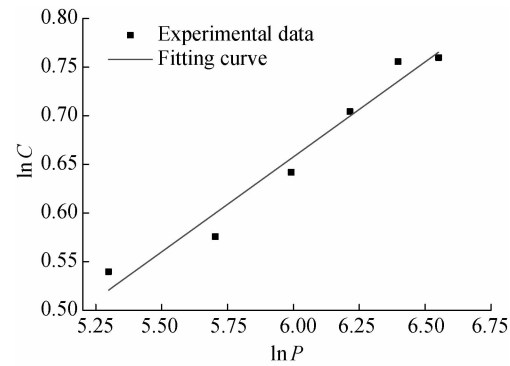

Fig. 6 Relationship between arctigenin concentration and ultrasound power

3.1.5 Single factor experiment of extraction temperature

To obtain the values of k and E, the values of all factors except extraction temperature are kept constant. Fig. 7 shows the relationship between the arctigenin concentration and extraction temperature. The linear regression equation is given as

$$\ln C = 516.975\ 9 - 0.815\ 9T - 8.170\ 7 \times 10^4 \frac{1}{T} \quad R^2_{\text{adjusted}} = 0.993\ 5 \tag{36}$$

$$\frac{k}{1-n} = 0.815\ 9 \tag{37}$$

$$\frac{E}{(1-n)R} = 8.170\ 7 \times 10^4 \tag{38}$$

$$\beta_5 - \frac{\ln 594}{1-n} - \frac{\ln 20}{1-n} + \frac{k_2 \ln 400}{1-n} + \frac{b \ln 0.5}{1-n} + \frac{\ln(1-\mathrm{e}^{20\alpha})}{1-n} = 516.975\ 9 \tag{39}$$

3.1.6 Single factor experiment of extraction time

To obtain the value of α, the values of all factors except extraction time are kept constant. Fig. 8 shows the relationship between the arctigenin concentration and extraction time. The linear regression equation is shown as follows:

$$\ln C = 0.754\ 8 + 0.751\ 1 \ln(1 - \mathrm{e}^{-0.120\ 7t}) \cdot \quad R^2_{\text{adjusted}} = 0.987\ 6 \tag{40}$$

$$\alpha = -0.120\ 7 \tag{41}$$

$$\beta_6 - \frac{\ln 594}{1-n} - \frac{\ln 20}{1-n} + \frac{k_2 \ln 400}{1-n} + \frac{b \ln 0.5}{1-n} +$$

$$\left[\frac{313k}{1-n}-\frac{E}{(1-n)R\times 313}\right]=0.754\ 8 \tag{42}$$

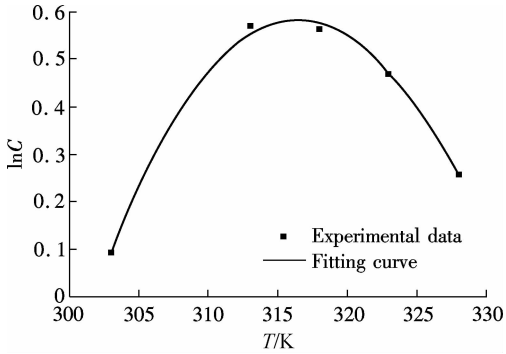

Fig. 7 Relationship between arctigenin concentration and extraction temperature

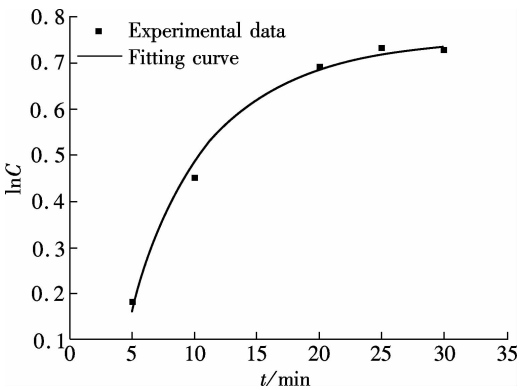

Fig. 8 Relationship between arctigenin concentration and extraction time

The values of n, b, k_2, k, E and α can be calculated by Eqs. (25), (28), (31), (34), (37), (38) and (41):

$$n=-0.331\ 4,\ b=2.360\ 6,\ k_2=0.260\ 0$$
$$k=-1.086\ 3,\ E=9.044\ 8\times 10^5,\ \alpha=-0.120\ 7 \tag{43}$$

Substituting Eq. (43) into Eqs. (26), (29), (32), (35), (39) and (42), respectively, the value of β can be obtained as 524.280 7, 524.227 3, 524.151 0, 524.195 7, 524.094 0 and 524.224 0. Substituting the mean value of β, n and α into Eq. (16), the following expression can be obtained:

$$k_1k_3\lambda aD_0=e^{695.594\ 7} \tag{44}$$

Combining Eqs. (43) and (44) with Eq. (15), the mathematical model of ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii is obtained:

$$C=\left[\frac{11.030\ 6P^{0.260\ 0}c^{2.360\ 6}e^{695.594\ 7-1.086\ 3T-1.087\ 8\times 10^5T^{-1}}}{q\sigma}\right]^{0.751\ 1} \tag{45}$$

where P is the ultrasound power, W; c is the ethanol volume fraction, dimensionless; T is the extraction temperature, K; t is the extraction time, min; q is the solvent to solid ratio, mL/g; σ is the particle size of material, μm; C is the arctigenin concentration in the extraction solvent, mg/mL.

3.2 Verification of the model

Further experiments are carried out under different conditions to verify the accuracy of the presented model (see Tab. 1). Each experiment was repeated three times and the average values were used to measure the accuracy of the model. Fig. 9 presents the resulting concentration level for arctigenin in the extract.

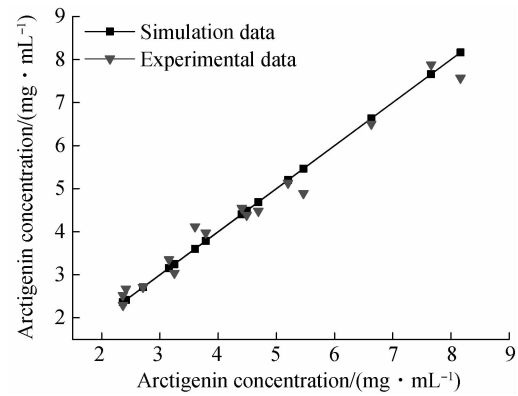

Fig. 9 Verification of the mathematical model for ultrasonic-assisted extraction

Tab. 1 Comparison between simulation and experimental data in verification experiment

Run	T/K	t/min	P/W	c	q/(mL · g^{-1})	σ/μm	Arctigenin concentration/(mg · mL^{-1})		
							Simulation data	Experimental data	Relative error/%
1	308	30	300	0.6	20	324	3.603 5	4.121 5	12.57
2	308	30	500	0.6	40	324	2.365 6	2.294 3	3.11
3	308	10	300	0.8	20	324	4.689 9	4.480 1	4.68
4	328	10	300	0.8	40	324	2.415 0	2.673 6	9.67
5	328	30	300	0.8	20	324	5.201 1	5.132 1	1.34
6	328	10	500	0.8	20	324	4.491 0	4.389 5	2.31
7	318	15	500	0.7	13	324	7.660 3	7.883 5	2.83
8	308	30	500	0.8	20	324	6.630 8	6.502 3	1.98
9	308	20	500	0.6	20	324	3.787 2	3.976 0	4.75
10	328	20	500	0.8	20	324	5.466 3	4.893 8	11.70
11	328	20	500	0.8	40	324	3.247 8	3.038 8	6.88
12	301	20	500	0.7	30	324	2.362 5	2.524 9	6.43
13	318	20	500	0.5	30	324	2.709 0	2.711 9	0.10
14	318	20	500	0.7	13	324	8.164 7	7.571 1	7.84
15	318	20	500	0.7	47	324	3.155 6	3.357 4	6.01
16	318	20	500	0.7	30	324	4.406 9	4.551 4	3.17

From Tab. 1, it can be seen that the relative error between the experimental data and simulation data is between 0.10% to 12.57%. Higher relative errors of above 10% are observed in Runs 1 and 10, most likely resulting from the inherent nonuniform character of FructusArctii as a natural product. Although there is still an error between simulating data and experimental data, the prediction tendency of the model shown in Fig. 9 basically matches the experimental data. So, the process of ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii can be described appropriately by the mathematical model.

4 Conclusion

A mathematical model of ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii is established based on Fick's first law and the model explains the relationship among arctigenin concentration and solvent to solid ratio, the particle size of samples, ethanol volume fraction, ultrasound power, extraction temperature and extraction time. The parameters of the model are estimated by single factor experiments. Although there is still an error between simulation data and experimental data, the prediction tendency of the mathematical model basically matches experimental data. The calculated data agrees well with the experimental data and the error is within an allowable range. Therefore, the process of ultrasonic-assisted extraction of arctigenin from acid hydrolyzed FructusArctii can be described appropriately by the model. Moreover, the mathematical model can also provide theoretical guidance for describing other similar extraction processes.

References

[1] Committee of National Pharmacopoeia. Pharmacopoeia of the People's Republic of China[S]. Beijing: China Medical Science Press, 2010: 66 - 67. (in Chinese)

[2] de Almeida A B A, Sánchez-Hidalgo M, Martín A R, et al. Anti-inflammatory intestinal activity of Arctium lappa L. (Asteraceae) in TNBS colitis model[J]. *J Ethnopharmacol*, 2013, **146**(1): 300 - 310. DOI: 10.1016/j.jep.2012.12.048.

[3] Wang G X, Han J, Feng T T, et al. Bioassay-guided isolation and identification of active compounds from Fructus Arctii against Dactylogyrus intermedius (Monogenea) in goldfish (Carassius auratus)[J]. *Parasitol Res*, 2009, **106**(1): 247 - 255. DOI: 10.1007/s00436-009-1659-7.

[4] Ferracane R, Graziani G, Gallo M, et al. Metabolic profile of the bioactive compounds of burdock (Arctium lappa) seeds, roots and leaves[J]. *J Pharm Biomed Anal*, 2010, **51**(2): 399 - 404. DOI: 10.1016/j.jpba.2009.03.018.

[5] Liu H, Zhang Y, Sun Y, et al. Determination of the major constituents in fruit of Arctium lappa L. by matrix solid-phase dispersion extraction coupled with HPLC separation and fluorescence detection[J]. *J Chromatogr B*, 2010, **878**(28): 2707 - 2711. DOI: 10.1016/j.jchromb.2010.08.007.

[6] Park S Y, Hong S S, Han X H, et al. Lignans from arctium lappa and their inhibition of LPS-induced nitric oxide production[J]. *Chem Pharm Bull*, 2007, **55**(1): 150 - 152. DOI: 10.1248/cpb.55.150.

[7] Byung Hoon H, Young Hwa K, Hyun Ok Y, et al. A butyrolactone lignan dimer from Arctium lappa[J]. *Phytochemistry*, 1994, **37**(4): 1161 - 1163. DOI: 10.1016/s0031-9422(00)89550-3.

[8] Umehara K, Nakamura M, Miyase T, et al. Studies on differentiation inducers. VI. Lignan derivatives from Arctium fructus. (2)[J]. *Chem Pharm Bull*, 1996, **44**(12): 2300 - 2304. DOI: 10.1248/cpb.44.2300.

[9] Ichihara A, Numata Y, Kanai S, et al. New sesquilignans from arctium lappa L. The structure of lappaol C, D and E[J]. *Agric Biol Chem*, 1977, **41**(9): 1813 - 1814. DOI: 10.1271/bbb1961.41.1813.

[10] Ryu S Y, Ahn J W, Kang Y H, et al. Antiproliferative effect of arctigenin and arctiin[J]. *Archives of Pharmacal Research*, 1995, **18**(6): 462 - 463. DOI: 10.1007/bf02976353.

[11] Moritani S, Nomura M, Takeda Y, et al. Cytotoxic components of bardanae fructus (Goboshi)[J]. *Biol Pharm Bull*, 1996, **19**(11): 1515 - 1517. DOI: 10.1248/bpb.19.1515.

[12] Hirose M, Yamaguchi T, Lin C, et al. Effects of arctiin on PhIP-induced mammary, colon and pancreatic carcinogenesis in female Sprague—Dawley rats and MeIQx-induced hepatocarcinogenesis in male F344 rats[J]. *Cancer Lett*, 2000, **155**(1): 79 - 88. DOI: 10.1016/s0304-3835(00)00411-0.

[13] Vlietinck A J, De Bruyne T, Apers S, et al. Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection[J]. *Planta Med*, 1998, **64**(2): 97 - 109. DOI: 10.1055/s-2006-957384.

[14] Eich E, Pertz H, Kaloga M, et al. (-)-Arctigenin as a lead structure for inhibitors of human immunodeficiency virus type-1 integrase[J]. *J Med Chem*, 1996, **39**(1): 86 - 95. DOI: 10.1021/jm950387u.

[15] Schröder H C, Merz H, Steffen R, et al. Differential in vitro anti-HIV activity of natural lignans[J]. *Z Naturforsch C*, 1990, **45**(11/12): 1215 - 1221. DOI: 10.1515/znc-1990-11-1222.

[16] Liu Q D, Qin K M, Shen B J, et al. Optimization of the processing technology of Fructus Arctii by response surface methodology[J]. *Chinese Journal of Natural Medicines*, 2015, **13**(3): 222 - 231. DOI: 10.1016/S1875-5364(15)30008-X.

[17] Lü W, Chen Y, Zhang Y, et al. Microemulsion electrokinetic chromatography for the separation of arctiin and arctigenin in Fructus Arctii and its herbal preparations[J]. *J Chromatogr B*, 2007, **860**(1): 127 - 133. DOI: 10.1016/j.jchromb.2007.10.017.

[18] Nose M, Fujimoto T, Takeda T, et al. Structural transformation of lignan compounds in rat gastrointestinal tract[J]. *Planta Med*, 1992, **58**(6): 520 - 523. DOI: 10.1055/s-2006-961540.

[19] Nose M, Fujimoto T, Nishibe S, et al. Structural transformation of lignan compounds in rat gastrointestinal tract; Ⅱ. Serum concentration of lignans and their metabolites[J]. *Planta Med*, 1993, **59**(2): 131 - 134. DOI: 10.1055/s-2006-959627.

[20] Toshihiko H, Manabu G, Kitaro O. Natural flavonoids and lignans are potent cytostatic agents against human leu-

kemic HL-60 cells[J]. *Life Sci*, 1994, **55**(13): 1061 - 1069. DOI: 10.1016/0024-3205(94)00641-5.
[21] Takasaki M, Konoshima T, Komatsu K, et al. Anti-tumor-promoting activity of lignans from the aerial part of Saussurea medusa[J]. *Cancer Lett*, 2000, **158**(1): 53 - 59. DOI: 10.1016/s0304-3835(00)00499-7.
[22] Ishihara K, Yamagishi N, Saito Y, et al. Arctigenin from Fructus Arctii is a novel suppressor of heat shock response in mammalian cells[J]. *Cell Stress Chaperones*, 2006, **11**(2): 154 - 161. DOI: 10.1379/csc-148r.1.
[23] Wu X, Yang Y, Dou Y, et al. Arctigenin but not arctiin acts as the major effective constituent of Arctium lappa L. fruit for attenuating colonic inflammatory response induced by dextran sulfate sodium in mice[J]. *Int Immunopharmacol*, 2014, **23**(2): 505 - 515. DOI: 10.1016/j.intimp.2014.09.026.
[24] MI J Y, Wang Z C, Song C Q. Quantitative analysis of arctiin and arctigenin of Arctium lappa L. from different areas by HPLC [J]. *LiShiZhen Medicine and Materia Medica Research*, 2004, **11**: 737 - 739. (in Chinese)
[25] Zaghdoudi K, Pontvianne S, Framboisier X, et al. Accelerated solvent extraction of carotenoids from: Tunisian Kaki (Diospyros kaki L.), peach (Prunus persica L.) and apricot (Prunus armeniaca L.)[J]. *Food Chem*, 2015, **184**: 131 - 139. DOI: 10.1016/j.foodchem.2015.03.072.
[26] Sharif K M, Rahman M M, Azmir J, et al. Ethanol modified supercritical carbon dioxide extraction of antioxidant rich extract from Pereskia bleo[J]. *Journal of Industrial and Engineering Chemistry*, 2015, **21**: 1314 - 1322. DOI: 10.1016/j.jiec.2014.05.047.
[27] Dahmoune F, Nayak B, Moussi K, et al. Optimization of microwave-assisted extraction of polyphenols from Myrtus communis L. leaves[J]. *Food Chem*, 2015, **166**: 585 - 595. DOI: 10.1016/j.foodchem.2014.06.066.
[28] Delgado-Povedano M M, Luque de Castro M D. Ultrasound-assisted extraction and in situ derivatization[J]. *J Chromatogr A*, 2013, **1296**: 226 - 234. DOI: 10.1016/j.chroma.2013.04.004.
[29] Wang L, Li D, Bao C, et al. Ultrasonic extraction and separation of anthraquinones from Rheum palmatum L [J]. *Ultrason Sonochem*, 2008, **15**(5): 738 - 746. DOI: 10.1016/j.ultsonch.2007.12.008.
[30] Peralta-Jiménez L, Cañizares-Macías M P. Ultrasound-assisted method for extraction of theobromine and caffeine from cacao seeds and chocolate products[J]. *Food and Bioprocess Technology*, 2013, **6**(12): 3522 - 3529. DOI: 10.1007/s11947-012-1014-3.
[31] Ebringerová A, Hromádková Z. An overview on the application of ultrasound in extraction, separation and purification of plant polysaccharides[J]. *Central European Journal of Chemistry*, 2010, **8**(2): 243 - 257. DOI: 10.2478/s11532-010-0006-2.
[32] Jalali-Heravi M, Parastar H, Ebrahimi-Najafabadi H. Characterization of volatile components of Iranian saffron using factorial-based response surface modeling of ultrasonic extraction combined with gas chromatography—mass spectrometry analysis[J]. *J Chromatogr A*, 2009, **1216**(33): 6088 - 6097. DOI: 10.1016/j.chroma.2009.06.067.
[33] Save S S, Pandit A B, Joshi J B. Use of hydrodynamic cavitation for large scale microbial cell disruption[J]. *Food and Bioproducts Processing*, 1997, **75**(1): 41 - 49. DOI: 10.1205/096030897531351.
[34] Chu M Q, Gu H C, Liu G J. Kinetic model on medicinal herb extraction process[J]. *Chinese Traditional and Herbal Drugs*, 2000, **31**(7): 504 - 506. (in Chinese)
[35] Lin Y P, Lu W L. A new dynamic model of release for not corroded drug system revision and use of Fick's first law[J]. *Acta Pharmaceutica Sinica*, 1997, **32**(11): 869 - 873. (in Chinese)
[36] Qin W, Zhang Y, Dai Y. Effect of ultrasound on diffusivities of electrolyte in a capillary[J]. *Journal of Tsinghua University* (*Science and Technology*), 2001, **41**(6): 41 - 43.

超声提取牛蒡子酸水解产物中牛蒡苷元的数学模型

戴 琳 张 勇 胡 驰 钱红亮 王志祥

(中国药科大学工学院, 南京 210009)

摘要: 基于 Fick 第一定律对超声提取牛蒡子酸水解产物中牛蒡苷元的过程建立了数学模型及其求解方法. 采用盐酸对牛蒡子原药材进行酸水解,促使药材中含量较高的牛蒡子苷转化为苷元,然后以酸水解产物为原料,研究超声提取牛蒡苷元的工艺条件. 在超声提取单元素实验中,着重考察了温度、时间、超声功率、乙醇浓度、液固比、原料粒径、占空比和提取溶剂 8 个因素对牛蒡苷元提取率及浸膏纯度的影响. 将模拟结果与实验值进行比较,结果表明模型的计算值与实验值之间存在一定的误差,误差低于 13%,但各因素对提取效果的影响规律与实验结果基本一致.

关键词: 牛蒡子;酸水解;超声提取;牛蒡苷元;数学模型
中图分类号: R93