Adsorption and desorption of berberine chloride on kaolinite material

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ABSTRACT

Berberine is a very popular drug in Vietnam for intestinal diseases. Research on improving berberine purification is of interest due to the high demand for berberine in current drug consumption. Instead of using extraction processes with the presence of sulfuric acid, berberine was extracted by berberine adsorption from diluted NaOH solution with pH = 11 on the surface of kaolinite material and desorption with dilute HCl solution containing 5% NaCl with pH = 5 at 50 ^{o}C. The adsorption and desorption efficiencies of berberine under optimal conditions reached 91% and 92%, respectively, when using kaolinite absorbent content at 2000 ppm for 1 hour. This purification method was successfully applied to the medicinal plant sample of Coscinium fenestratum (Vàng đắng in Vietnamese) with a berberine total recovery efficiency of 81% and berberine content of 94%. The NMR spectrum confirmed the molecular structure of berberine.

Keywords: Berberine; Absorption; Desorption; Kaolinite.

1. INTRODUCTION

Berberine has long been used in traditional medicine in many parts of the world and available in most Vietnamese family, which was mentioned as the treatments for inflammatory disorders, skin diseases, wound healing [1], fever reducing, eye diseases, tumors, [2] digestive and respiratory diseases, and bacterial diseases. [3] In addition, many clinical studies have shown that berberine has several valuable pharmacological properties, such as immunoregulation, anti-oxidation, cardioprotection, hepatoprotection, and nephroprotection. [4] With the characteristic of being a natural antibiotic, berberine is relatively safe for users, specially to treat intestinal diseases such as diarrhea, dysentery, and amoebic infection without affecting the balance of intestinal microflora. Berberine is combined with synthetic antibiotics to improve antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) [3].

Berberine can be found as yellow crystal, with a bitter taste, without asymetrial carbon in berberine molecules. Berberine is normally available in the base form $[C_{20}H_{18}O_4N]^+OH^-$ or chloride form $[C_{20}H_{18}NO_4]^+Cl^-$. In Vietnam, there are about 15 species belonging to 5 plant families containing berberine, including species with high berberine content such as *Berberis julianne* Schneid*, Berberis wallichiana* DC., *Coptis chinensis* Franch., *Coptis quinquesecta* W.T.Wang, *Coscinium fenestratum* Colebr., *Mahonia bealei* Carr*., Mahonia japonica* Thunb., *Mahonia nepalensis* DC., and *thalictrum foliolosum DC*. [5].

With great potential in treatment and research, the demand for berberine as an active ingredient is increasing. In the world, berberine is often produced by extraction from medicinal herbs which are cultivated through a combination of aeroponic technology, and chemical synthesis. In Vietnam, berberine is mainly produced by extraction from medicinal herbs [5, 6], and there have been initial studies on the synthesis of berberine on a laboratory scale from available raw commercial chemicals [7]. Classical extraction techniques such as water extraction, Soxhlet extraction, and cold or hot extraction use different solvent systems such as methanol, ethanol, chloroform, acid-

water mixtures, or acidification. The sensitivity of berberine to light and heat is a significant challenge for extracting this compound [1]. Therefore, developing simple and effective berberine purification methods is essential. Recently, some research groups have used alkaline solutions in the extraction process of berberine from Vietnamese native plants [8], which have berberine content of 87%. In this study, we screened some natural and synthetic materials, especially kaolinite [9], that have the ability to selectively and efficiently adsorb and desorb berberine through weak ionic strength adsorption. From there, berberine can be selectively purified by kaolinite, reducing the steps of traditional extraction methods and the purification time.

2. EXPERIMENT

2.1. Instrumentation

Chemicals: Berberine chloride (98%, Vietnam), methanol (HPLC ≥ 98%, Merck, sodium hydroxide (99%, Taiwan), sodium chloride (99%, China), kaolinite (K99-C, 2 µm, Australia), hydrotalcite (0.5 – 1.0 µm, China), talc (90%, 28 µm, China), bentonite (74 µm, India), vermiculite (1-3 mm, China), distilled water.

UV - Vis absorption spectrophotometer Jasco V630 (Japan), IRAffinity-1S SHIMADZU fourier shift infrared spectrometer, using KBr pellet method, Bruker Avance 500 MHz nuclear magnetic resonance instrument, Faculty of Chemistry, University of Science - Vietnam National University, Hanoi.

2.2. Experimental materials

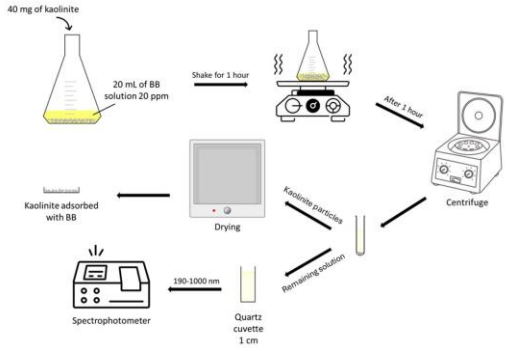

Figure 1. *The procedure of berberine absroption.*

Weigh 40 mg (error ±0.0001g) of kaolinite accurately, transfer it to a conical flask containing 20 ml of 20 ppm berberine aqueous solution, and put it in a shaker for 1 hour as mentioned in figure 1. After 1 hour, use a centrifuge to separate the kaolinite particles, dry them, and measure the remaining solution with a UV-Vis spectrum, measuring wavelength range 190-1000 nm, quartz cuvette with a thickness of 1 cm to evaluate the absorption yields.

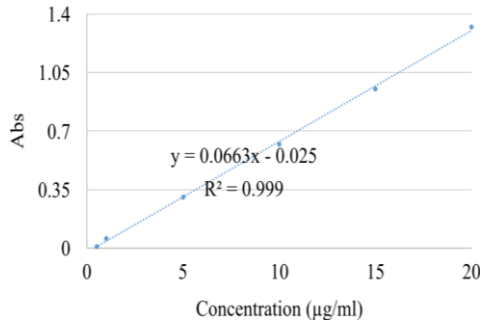

Figure 2. *Berberine standard curve in the range of 0.5- 20 ppm at pH = 7.*

The UV-Vis absorption spectra of berberine chloride is characterized by three peaks of wavelengths: 265 nm, 344 nm, and 423 nm. The signal survey results show no significant change in the optical absorption peak at 344 nm of berberine in water at different pHs. Therefore, Berberine chloride concentration in water at different pHs can be determined based on the 344 nm wavelength standard curve. The standard curve in figure 2 was based on the relationship between Abs values and the concentrations of 0.5; 1; 5; 10; 20 ppm to determine the concentration of berberine.

The H_A adsorption efficiency was calculated as follows:

$$\boldsymbol{H_A\% = \frac{C_i - C_f}{C_i} \times 100}$$

In which: H_A is the adsorption efficiency, the C_f is the concentration of berberine in the solution after the experiment when m_i is the concentration of berberine in the solution before the experiment

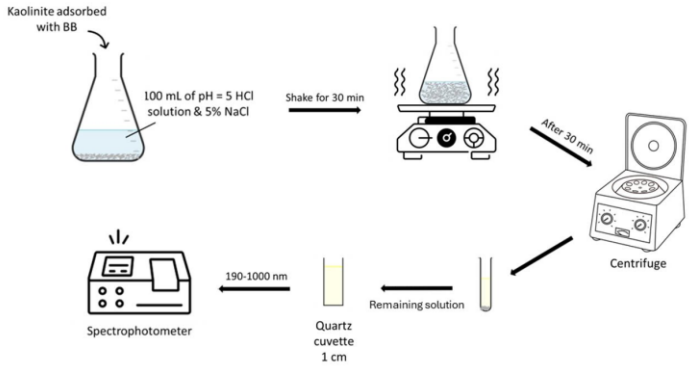

Figure 3. *The procedure of berberine desorption.*

To evaluate the desorption, the remaining berberine on the kaolinite was calculated from the H_A, adsorption efficiency, named as m_i. As in figure 3, transfer all the kaolinite adsorbed with berberine into a cup, add 100 ml of pH=5 HCl acid solution and 5% NaCl, put it in a shaker for 30 minutes, centrifuge to separate the solution, and measure the UV-Vis absorption signal to determine the concentration of berberine in solution, then the amount of berberine named m_f. The H_D desorption efficiency was calculated as follows:

$$\boldsymbol{H_D\% = \frac{m_f}{m_i} \times 100}$$

After reducing the solvent at low pressure and letting the product crystallize, filter to collect the solid and dry. The purity of the product was checked by thin-layer chromatography (TLC) together with standards and infrared and nuclear magnetic resonance spectroscopy. The factors of temperature, volume, solution pH, and absorbent loading were varied to determine the optimized conditions.

Coscinium fenestratum (Gaertn.) Colebr. was collected in Nam Dong, Thua Thien Hue, in January 2025 and identified by a plant expert at the Faculty of Biology, University of Science, Vietnam National University, Hanoi. *Coscinium fenestratum* samples were dried naturally and the berberine content was evaluated by HPLC before experiments. In addition, 1 g of *Coscinium fenestratum* was finely ground and soaked in 500 mL NaOH solution with pH = 11 at 4 ^oC for 48 h. The extract was filtered from the mixture and concentrated in a vacuum until the volume reached 100 mL. Then, the extract was treated according to the optimal purification conditions of absorption and desorption. The purified berberine solution was evaporated at low pressure, and HCl and NaCl were added, then crystallized in the refrigerator.

3. RESULTS AND DISCUSSION

3.1. Berberine adsorption and desorption capacity of some materials

In the initial study, the adsorption experiment conditions were carried out with a berberine content of 20 ppm and a content of various inorganic adsorbents of 2000 ppm in 20 mL of water with pH = 7 at room temperature (25 ^{o}C) in figure 4. The results showed that kaolinite material showed the best adsorption capacity with an adsorption yield of 78%. When evaluating the structural characteristics of the materials, kaolinite was found to be quite effective in adsorbing some cationic dyes [10] due to its mesopore properties and surface characteristics containing solid acid groups of Al^{3+} ions and self-helix structure [SiO_4]. Hydrotalcite also showed the ability to adsorb berberine as a cation, but with a lower yield, reaching 54%, while other materials, including talc, bentonite, and vermiculite, showed poor adsorption capacity.

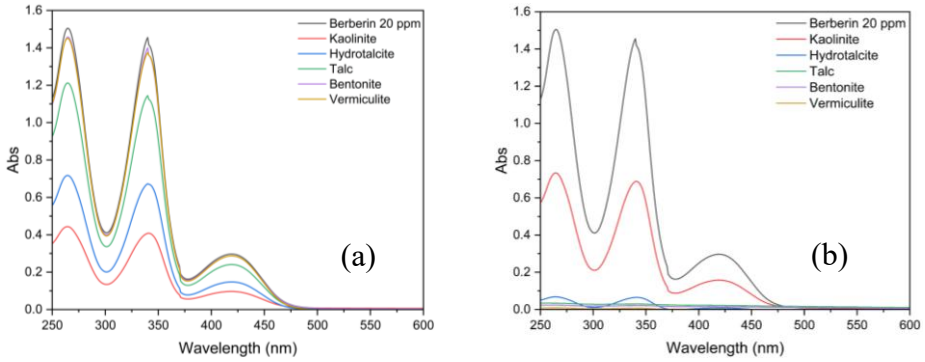

Figure 4. *UV-Vis spectra of berberine solution after adsorption (a) and desorption (b).*

The study on the desorption process of berberine on materials containing berberine after the adsorption process was carried out under the condition of inorganic adsorbent is content of 2000 ppm in 20 mL of water with pH = 7, at room temperature (25 ^{o}C). After the berberine adsorbed to saturation, the material will be centrifuged to collect the solid and transferred to a beaker containing 100 mL of dilute HCl acid solution. Desorption will be carried out for 60 minutes. After the desorption process, the solution is filtered, and the berberine content is evaluated through the UV-Vis spectrum in figure 4. The results show that kaolinite material desorbs 51% of the adsorbed berberine, and the total obtaining efficiency of berberine through the combined adsorption/desorption process is 40%. Hydrotalcite and talc materials show weak desorption ability, reaching only 12 and 4% of yield, respectively. Bentonite and vermiculite materials have poor berberine adsorption capacity, so the berberine recovering efficiency is too low, which is not of practical significance. Therefore, kaolinite was focused on studying and evaluating the factors affecting the berberine adsorption and desorption process in the following studies. In addition, the signals on the UV-Vis spectrum of berberine after desorption have completely similar shapes to the original berberine solution, which is of great significance in evaluating the adsorption and desorption capacity through the UV-Vis spectrum of the studied samples.

3.2. Factors affecting the absorption of berberine

The factors affecting the adsorption process of berberine on kaolinite materials are shown in figure 5, which optimizes the conditions for berberine adsorption. In the experiment evaluating the pH factor of the solution on the adsorption capacity of the material in figure 5a, the adsorption efficiency of berberine on kaolinite gradually increased when the pH value of the solution containing dissolved berberine rose from 2 to 11, reaching the highest value of 91%, however at pH = 13, the adsorption efficiency of kaolinite decreased slightly to 79%, which is explained by the fact that when the pH gradually increased to the value of 11, the surface of kaolinite was deprotonated by the OH^- ions of the solution, causing them to gradually shift to a negative charge,

then combining the cationic berberine effectively from the solution, consequently increasing the berberine adsorption material. However, at pH values from 13, due to the solubility of berberine in an alkaline environment, the interaction of berberine with the material surface is reduced, leading to a decrease in adsorption efficiency. Berberine was still stable even in the solution with pH = 13, confirmed by the quantitative analysis of berberine through UV-Vis spectra and crosschecked by TLC.

In figure 5b, the temperature factor has a significant influence on the adsorption capacity of berberine on the material surface; when the temperature is high, the adsorption capacity decreases, entirely consistent with the assumption that the adsorption process on kaolinite is based on electrostatic bonding. There is no apparent difference in adsorption efficiency between the working temperatures of 4 ºC and 25 ºC. The working conditions are determined at a room temperature of 25 ºC. In addition, the ratio of berberine concentration and material content reaching the value of 1:100 is the most optimal condition to apply for future studies.

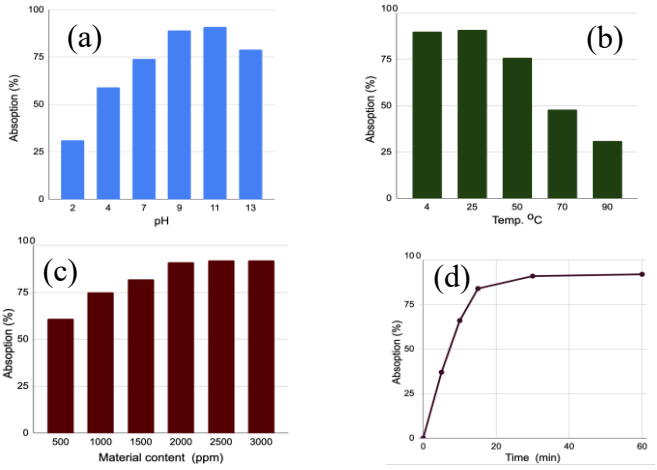

Figure 5. *Berberine adsorption efficiency at different conditions: pH (a), temperature (b), adsorbent content (c) and time (d). Condition: berberine 20 ppm, kaolinite 2000 ppm, adsorbed in 20 mL of dilute HCl or dilute NaOH solution.*

At higher material concentrations in figure 5c, there was no significant improvement in berberine adsorption efficiency. In addition, the adsorption time of berberine at a concentration of 20 ppm in 20 mL of solution in the presence of kaolinite with a content of 2000 ppm, after only 15 minutes, the material had adsorbed 84% of berberine in the solution. After only 30 minutes, the research system reached equilibrium. The adsorption efficiency at pH = 11 reached 92%. Based on the research results, with the initial berberine solution at 20 ppm, the amount of kaolinite material required at a ratio of 1:100 in a solution with pH = 11 for 1 hour and at 25 ºC is the optimal condition for berberine adsorption onto the material surface of kaolinite in figure 5d.

3.3. Factors affecting the desorption capacity of berberine

After the saturated adsorption of berberine in the previous experiment, the material was centrifuged at 4000 rpm and washed 3 times with ice water, then added to 100 mL of NaCl solution at several concentrations and pH values from 2 to 7 in figure 6. The research system was stirred at room temperature to ensure the material/berberine system reached equilibrium. The desorption yield was determined by the amount of berberine in the solution after desorption and the total amount of berberine in the material after adsorption.

The effect of pH on the desorption of berberine from the material surface in a solution without NaCl showed that at low pH, the material tended to release berberine more strongly, reaching 78%

at pH = 2. However, in practical conditions, low pH conditions will cause difficulties in designing equipment due to the corrosiveness of acid. Therefore, NaCl was added as an additive to create competition between ions Na^+ and cationic berberine ions adsorbed on the material's surface. The results showed that at pH = 4 and NaCl concentration of 5%, the desorption yield of berberine from the material reached 93%. After the adsorption/desorption system reached equilibrium, the solution was centrifuged to separate the solid for reuse experiments and the clear solution. The solution was filtered once through a filter paper with a pore size of 0.22 µm, evaporated at low pressure to 20 mL, and cooled to allow berberine chloride to crystallize.

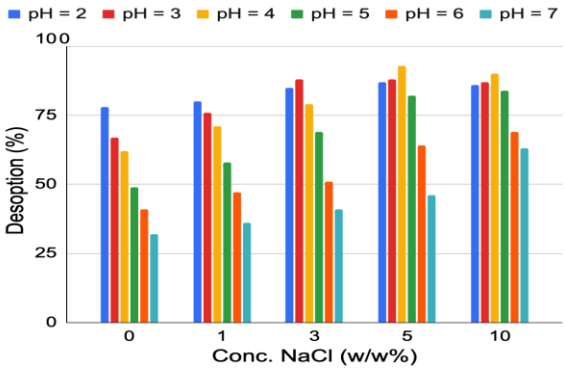

Figure 6. *Berberine desorption efficiency at different pH and concentrations of NaCl.*

Condition: berberine 20 ppm, kaolinite 2000 ppm, 100 mL of NaCl/HCl solution

Temperature also plays a vital role in the adsorption and desorption process. To focus on the temperature study, berberine solutions at pHs from 4 to 7 with 5% NaCl concentration were selected for study with temperature conditions from 4 °C to 70 °C. The results in figure 7a show that the desorption yield was better at higher temperatures. However, when evaluating the practical application, the temperature condition of 50 °C and pH = 5 gives a desorption efficiency of up to 92%. Under more stringent conditions with higher temperatures or pH values, the adsorption yield is not significantly improved (1-2% difference).

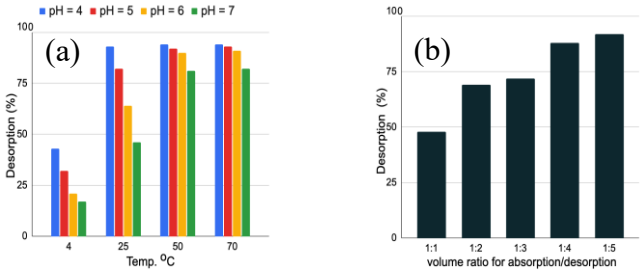

Figure 7. *Berberine desorption yield at different temperatures (a) and different volume ratios of adsorption and desorption solutions (b).*

Condition: berberine 20 ppm, kaolinite 2000 ppm, NaCl/HCl solution, pH = 5, 50 °C.

Berberine concentration in solutions greatly influences the desorption and adsorption processes. To optimize the research conditions in figure 7b, different volumes of 5% NaCl solution at pH = 5 were used with the same amount of kaolinite samples saturated with berberine. For 5% NaCl solution at pH = 5 being 5 times the amount of the initial berberine-containing solution, the desorption yield reached 92% after 90 minutes. At larger volume ratios, the desorption yield increased insignificantly.

3.4. Reusability of adsorbent material

After being used for both adsorption and desorption processes, the kaolinite material was

washed with distilled water and 5% NaOH solution and left to dry naturally for 24 hours. The activated material was then used for subsequent reuses. Figure 8a depicts the berberine recovery efficiency after each reuse, showing that in the first use of kaolinite, the berberine recovery efficiency from both adsorption and desorption processes reached 81%, and the first reuse still reached 70%. However, the efficiency gradually decreased to 61%, 53%, and 47% in subsequent material reuses. This is entirely consistent with the results of the X-ray diffraction pattern (figure 8b) and SEM images (figures 8c, and 8d) before and after reusing kaolinite 5 times. The material analysis results showed a slight decrease in the composition of crystalline structure of the kaolinite phase; however, the surface morphology of the materials did not show significant differences.

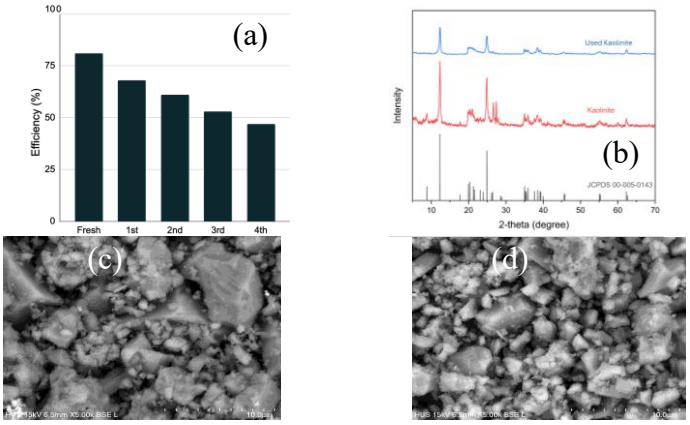

Figure 8. *Berberine recovery efficiency after each reuse (a) X-ray diffraction pattern of the material before and after the adsorption - desorption process (b), SEM image of the material before (c) and after (d) the adsorption - desorption process.*

3.5. Initial survey on the purification of berberine chloride from the *Coscinium fenestratum* (Vàng đắng in Vietnamese)

After applying the mentioned method, 22.4 mg of yellow solid berberine sample was obtained from the 1 g *Coscinium fenestratum*. Compared with the berberine content in *Coscinium fenestratum*, with a content of 2.74 ± 0.023% by mass, the berberine purification efficiency through kaolinite material reached 81% of yield. The structure of the berberine product was evaluated through the ^{1}H and ^{13}C nuclear magnetic resonance spectra.

^{1}H-NMR (500 MHz, DMSO-d_6) *δ (ppm)* 3,12 (2H, t, *J* = 6,5 Hz); 4,06 (3H, s); 4,10 (3H, s); 4,96 (2H, t, *J* = 6,5 Hz); 6,17 (2H, s); 7,08 (1H, s); 7,78 (1H, s); 8,01 (1H, d, *J* = 9,0 Hz); 8,18 (1H, d, *J* = 9,5 Hz); 8,97 (1H, s); 9,92 (1H, s)

^{13}C-NMR (125 MHz, DMSO-d_6) *δ (ppm),* 26,79; 55,63; 57,52; 62,42; 102,55; 105,91; 108,88; 120,67; 120,90; 121,85; 124,02; 127,13; 131,11; 133,44; 137,88; 144,10; 145,93; 148,11; 150,25; 150,85.

The ^{1}H-NMR spectral data showed that the total number of H in the measured sample was 18 H with multiple signals in multiplet form. In contrast, the ^{13}C-NMR spectrum showed that the number of signals of 20 carbon atoms recorded in the product was consistent with the expected structure of berberine chloride salt and was completely consistent with the NMR spectral data for berberine in the reference literature [7], the berberine content in the purified sample reached 94%.

4. CONCLUSIONS

Berberine can be purified through the adsorption and desorption process on natural kaolinite materials with a purification efficiency of 81% for the first time. The berberine adsorption and desorption processes were optimized with temperature, adsorbent content, solution pH, and NaCl

concentration. The selective adsorption process of berberine occurred in aqueous solution at pH = 11 for an adsorption efficiency of up to 91% with a kaolinite content of 2000 ppm. Berberine was desorbed from the surface of kaolinite materials with an efficiency of 92% in a dilute HCl solution containing 5% NaCl, pH = 5 at 50 ºC. The purification process of berberine chloride from the adsorption and desorption process on kaolinite materials successfully purified berberine from *coscinium fenestratum* with an efficiency of 81%, with purity reaching 94%.

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TÓM TẮT

Khả năng hấp phụ và giải hấp của berberine chloride trên vật liệu kaolinite

Berberine là một dược chất rất phổ biến tại Việt Nam cho các bệnh liên quan đến đường ruột. Nghiên cứu cải tiến các phương pháp tinh chế berberine đáng quan tâm do nhu cầu cao của berberine trong thực tế tiêu dùng thuốc hiện nay. Thay vì sử dụng các quy trình tách chiết với sự xuất hiện của axit sulfuric, berberine được tách chiết bằng hấp phụ berberine từ dung dịch NaOH pH = 11 trên bề mặt vật liệu kaolinite và giải hấp bằng dung dịch HCl loãng có chứa NaCl 5% với pH = 5 ở 50 ºC. Hiệu suất hấp phụ và giải hấp berberine ở điều kiện tối ưu lần lượt đạt 91% và 92% khi sử dụng hàm lượng chất hấp thụ kaolinite tại 2000 ppm. Thời gian hấp phụ và giải hấp lần lượt đều trong 1 giờ. Phương pháp tinh chế này đã được áp dụng thành công trên mẫu dược liệu cây vàng đắng với hiệu suất thu hồi berberine đạt 81% và berberine sản phẩm có hàm lượng đạt 94%. Cấu trúc phân tử của berberine được chứng minh lại bằng phổ NMR.

Keywords: Berberine; Hấp phụ; Giải hấp; Kaolinite.