Separation and Purification Technology 183 (2017) 73–82

Contents lists available at ScienceDirect

Separation and Purification Technology

journal homepage: www.elsevier.com/locate/seppur

A novel approach for distillation of paeonol and simultaneous extraction of paeoniflorin by microwave irradiation using an ionic liquid solution as the reaction medium

Fengli Chen [a], Kailin Mo [b], Qiang Zhang [c], Shimin Fei [b], Yuangang Zu [a], Lei Yang [a,*]

[a] Key Laboratory of Forest Plant Ecology, Ministry of Education, Northeast Forestry University, Harbin 150040, China
[b] Sichuan Academy of Forestry, Chengdu 610081, China
[c] School of Forestry, Northeast Forestry University, Harbin 150040, China

ARTICLE INFO

Article history:
Received 14 December 2016
Received in revised form 15 March 2017
Accepted 30 March 2017
Available online 5 April 2017

Keywords:
Paeoniflorin
Paeonol
Ionic liquid
Microwave irradiation
Distillation and simultaneous extraction

ABSTRACT

In the present work, a simple and efficient method for steam distillation of paeonol and simultaneous extraction of paeoniflorin from the root bark of *Paeonia suffruticosa* Andr. (Cortex Moutan) was developed using an ionic liquid as the reaction medium and microwave irradiation. A series of 1-alkyl-3-methylimidazolium ionic liquids with different anions and alkyl chain lengths were evaluated for this method. The optimum conditions were 1.25 M 1-butyl-3-methylimidazolium bromine as the extraction solvent, 20 mL/g liquid–solid ratio, 25 min microwave irradiation time, 700 W microwave irradiation power, and 60–80 mesh particle size. Under these conditions, satisfactory yields of paeoniflorin (80.49 ± 2.58 mg/g) and paeonol (10.52 ± 0.36 mg/g) were obtained. The initial purity of paeonol was 84.95%, and this increased to >99% with simple recrystallization. The ionic liquid extraction solution, either with or without trace paeonol, was passed through HPD100B macroporous resin for enrichment and separation of paeoniflorin and recycling of the ionic liquid used. Recycling and reuse of the ionic liquid were achieved successfully, which could reduce ionic liquid requirements and the process cost. The method was validated using stability, recovery, and repeatability experiments. The proposed method is very promising for separation of natural compounds, especially for small molecules that can be isolated by steam distillation.

1. Introduction

Recently, microwave-assisted extraction (MAE) with an ionic liquid as the medium has been used as a powerful alternative to traditional extraction methods to isolate active ingredients from medicinal plants [1,2]. MAE is faster and uses less solvent, and provides equivalent or higher extraction yields for the target analytes than conventional techniques. Ionic liquids are composed of bulky organic cations and inorganic or organic anions, and are liquid at temperatures close to room temperature. Ionic liquids have recently attracted interest for a variety of applications because of their unique properties, including negligible vapor pressure, good miscibility in water and organic solvents, tunable viscosity, good extractability for various analytes, and ease of recycling and manipulation [3,4]. Because ionic liquids can efficiently absorb and transfer microwave energy, they have been used in various applications, including distillation of volatile essential oils and extraction of non-volatile active ingredients from *Schisandra chinensis* [5], *Rosmarinus officinalis* [6], Cortex cinnamomi [7], and *Eucalyptus camaldulensis* [8]. However, the target analytes separated in these studies are water-insoluble essential oils and fat-soluble ingredients.

Cortex Moutan (Mu Dan Pi in Chinese) is the root bark of *Paeonia suffruticosa* Andr., which belongs to the Paeoniaceae family and has been widely used as a traditional Chinese medicine. Cortex Moutan is well-known for its anti-inflammatory [9,10], antibiotic, anti-allergic [11] and anti-diabetic activity [12], ability to promote blood circulation [13], and neuroprotective effects [14]. The main active components in Cortex Moutan are paeonol and paeoniflorin. Paeonol (Fig. 1) is a simple phenolic compound, containing a phenolic hydroxyl group and a methoxy group. Paeonol easily dissolves in hot water and polar organic solvents, such as methanol and ethanol, but its solubility in cold water is very low. Paeonol is volatile and can be isolated by steam distillation. Paeonol has various important pharmacological and physiological effects,

* Corresponding author.
E-mail address: ylchennefu@163.com (L. Yang).

http://dx.doi.org/10.1016/j.seppur.2017.03.069
1383-5866/

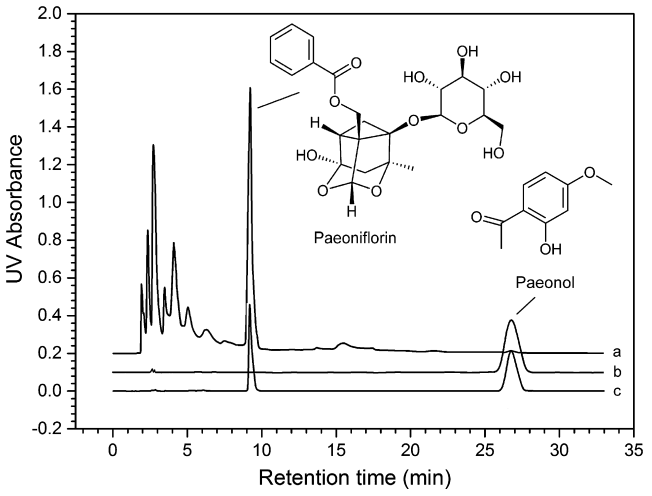

Fig. 1. HPLC results for paeoniflorin in the ionic liquid extraction solution (a), paeonol in the distillate (b), and standard solutions of paeoniflorin and paeonol (c). Inset: chemical structures of paeoniflorin and paeonol.

including anti-inflammatory [15], anti-tumor [16], anti-allergic [17], antidiabetic [12], inhibition of platelet aggregation [18], anti-atherosclerosis [19], and cardiovascular protective activity [20]. Paeoniflorin, a monoterpene glycoside (Fig. 1), is insoluble in water but soluble in ethanol and other organic solvents. However, it cannot be isolated by steam distillation because of its size. Paeoniflorin has been reported to have antioxidant [21], anti-inflammatory [22], immunoregulation [23], and anti-proliferative [24] effects, and protection against brain injury [25]. Paeoniflorin also has important cardiovascular effects, and it can lower cholesterol levels [26], reduce myocardial damage [27], and improve heart function [28]. In view of the beneficial pharmacological activities and the broad application range of these compounds, it is important to develop an efficient technique for isolation of paeonol and paeoniflorin.

Conventionally, paeonol and paeoniflorin have been extracted using organic solvents, such as methanol [29], ethanol [30], and some solvent mixtures [31]. Because paeonol and paeoniflorin have similar polarity, they tend to be extracted simultaneously. Consequently, subsequent separation and purification processes by complex column chromatography are required for paeonol and paeoniflorin, which increases the difficulty and expense of their extraction and limits their application.

The objective of this work was to develop an effective and simple method for distillation of paeonol and simultaneous extraction of paeoniflorin from Cortex Moutan using an ionic liquid as the extraction solvent and microwave irradiation (ILMDSE). Paeonol crystals were obtained by direct congelation or rapid cooling of the distillate to induce crystallization. The ionic liquid extraction solution containing paeoniflorin was treated by a dynamic macroporous resin column chromatography process for enrichment and separation of paeoniflorin, and recycling of the ionic liquid. Nine ionic liquids with different cations and anions were evaluated, and the concentration of ionic liquid, liquid–solid ratio, particle size, and microwave irradiation power and time were optimized systematically.

2. Experimental

2.1. Materials and chemicals

The dried sample of Cortex Moutan was purchased from Anguo Medicinal Materials Market (Hebei, China). The origin of the Cortex Moutan sample was Heze (Shandong, China). The materials were crushed using a pulverizer and sieved before distillation and extraction. The sample powders were stored in sealed desiccators at room temperature before use. The same batch of sample was used in all the tests. Reference compounds of paeoniflorin (purity $\geq$ 98%) and paeonol (purity $\geq$ 99%) were purchased from Sigma–Aldrich Inc. (St. Louis, MO, USA). The following ionic liquids containing 1-ethyl-3-methylimidazolium (Emim), 1-butyl-3-methylimidazolium (Bmim), 1-hexyl-3-methylimidazolium (Hmim), 1-octyl-3-methylimidazolium (Omim), and 1-decyl-3-methylimidazolium (Dmim) were purchased from Chengjie Chemical Co., Ltd. (Shanghai, China) and used without further purification: [Emim]Br, [Bmim]Br, [Hmim]Br, [Omim]Br, [Dmim]Br, [Bmim]BF_4, [Bmim]Cl, [Bmim]HSO_4 and [Bmim]NO_3. Chromatographic grade methanol and phosphoric acid were purchased from J & K Chemical Ltd. (Beijing, China). All the other reagents were of analytical grade and purchased from Aladdin Reagents Co. (Shanghai, China). Deionized water was purified by a Milli-Q system (Millipore, Billerica, MA, USA). A 0.45-μm microporous nylon membrane was used for filtering all solutions and samples before use.

HPD100B macroporous resin (surface area of 500–580 m^2/g, average pore diameter of 120–160 nm, particle diameter of 0.3–1.25 mm, non-polar) was purchased from Cangzhou Bon Adsorber Technology Co., Ltd. (Hebei, China). Because some monomers and porogenic agents were trapped inside the pores during the synthesis, the resins were pretreated directly before use. Briefly, the resins were firstly soaked in ethanol for 24 h, and then washed with a stream of deionized water until the ethanol was completely replaced by deionized water [32]. The treated resin was stored in a desiccator with deionized water to maintain constant moisture content. The moisture content of the HPD100B macroporous resin was tested to be 45.42%.

2.2. Apparatus and procedure for distillation of paeonol and simultaneous extraction of paeoniflorin

The procedure for distillation of paeonol and simultaneous extraction of paeoniflorin was carried out using microwave extraction equipment (UWave-1000, XTrust, Shanghai, China) with a microwave irradiation frequency of 2.45 GHz. As shown in Fig. 2, a round-bottom flask containing the materials for extraction and the extraction solvent was placed in the microwave, and then connected to a triple valve. The other two ends of the triple valve were connected to a condenser and a constant pressure charging hopper (250 mL). The lower end of the condenser was connected to a receiver with glass filter, and the outer jacket of the receiver was kept cool with circulated ice water, with the low temperature promoting precipitation of paeonol. Steam containing paeonol was condensed by the condenser to form distillate, which was collected in the receiver (200 mL). Paeonol crystals were precipitated after rapidly cooling the distillate using ice water and stirring. After the volume of distillate collected in the receiver reached 100 mL, the vacuum was opened to filter the liquid and the paeonol crystals accumulated on the glass filter. After turning off the vacuum, the filtrate was pumped into the constant pressure charging hopper by a peristaltic pump, and finally returned to the round-bottom flask. In the present study, five microwave power levels, 100% (700 W), 77% (540 W), 55% (385 W), 33% (230 W), and 17% (120 W) were used to investigate the influence of microwave irradiation power.

A 30 g Cortex Moutan sample powder was weighed accurately and placed into a round-bottom flask containing one of the nine ionic liquids. Then, the flask was placed in the microwave oven for irradiation. The temperature and pressure used was 100 °C and atmospheric pressure. The effects of the ionic liquid