**Bai Xian Pi = Dictamnus** rhizome of Dictammnus dasycarpus Turcz

**How to Get Healthy Skin with Bai Xian Pi**

Chinees de wortel (bast):   

westers kijken we naar de bovenkant 

It is a little more challenging to answer the question of how to get healthy skin as clinically there are a lot of different skin conditions such as rashes, eczema, acne, sores, and ringworm involved. In west medicine system, the treatments vary from condition to condition.

It would be all right if inflammation isn’t accompanied in mild skin problems. Unfortunately, inflammation, more often than not, is always there. In this case, chances are scars or dark marks would be left after healing as the inflammation leads to destruction of the surrounding tissue, in which main symptoms are redness, swelling, fever, pain, itch, ooze and pus. To prevent scarring and reverse the damaged skin, it need to reduce inflammation, remove pus, and kill germs at the same time.

Is there such a thing that is capable of completing the above-mentioned tasks once for all? The answer will be yes if you know something about Chinese medicine. And Bai Xian Pi (Burning Bush Root), one of common Chinese herbs for skin, may be the solution you have been looking for.

**What is Bai Xian Pi?**

Actually it refers to the rhizome of Dictammnus dasycarpus Turcz, which has a variety of other names such as Dictamnus albus., Fraxinella, Adiptam, Herba Dictamni Herba., Gas Plant, and Dittany. Burning Bush is a perennial herbaceous plant and with peculiar irritant odor. It has yellowish white ligneous roots in tight clusters. Stems are erect, 50 to 65cm high. Alternate pinnately compound leaves are oval or oblong elliptic in shape, 3.5 to 9cm long, and 2 to 4cm long. And it has racemose flowers, rachis and pedicel mixed white pubescence and black glandular hair, and pink with purple red lines. The fruit is capsule, densely covered with glandular hairs, splitting into 5 segments at maturity, one prickle at the end of each segment, and 2 to 3 round black seeds inside. Flower season is April and May. Fruiting time is May to June. It grows in hillside or woods.

As a frequently used herb for healthy skin in TCM remedies, its medicinal part is dictamnus root bark, which is collected in spring and autumn in the North and summer in the East in China. The process is to dig it out, remove fibril and tertia, split lengthways when it is still fresh, take out the woodent heart, and dry in the sun.

The dried rhizome presents coiling block or double barrels in shape, 7 to 12cm long, 1 to 2 in diameter, 2 to 5mm thick, yellowish white to light brown surface, slightly smooth, and with vertical wrinkles and lateral root scars. Internal surface is light yellow, smooth, and with round holes caused by branch roots. It is crisp and easy to break, with ivory and layered cross section. Put under the sunlight or lamp, small white sparkling crystals is seen. It smells like mutton and tastes slightly bitter. Medicinally the preferred one is in coiling block, without woodent heart, thick bark, and large in size. And it is mainly produced by provinces of Liaoning, Hebei, Sichuan, Jiangsu, Zhejiang, and Anhui.

**Why it treats skin problems?**

According to theory of Traditional Chinese Medicine (TCM), it is bitter and cold in nature. And it covers a few meridians of spleen, stomach and urinary bladder.

Main functions are to clear heat and dry damp, expel wind and stop itch, and detoxify. Main clinical usage and indications are measles due to the accumulation of wind, heat, and damp, eczema, scabies, ringworm, jaundice, and pain or numbness caused by damp and heat (arthritis). According modern researches, it is also capable of killing bacterium, diminishing inflammation, benefiting heart, fighting cancer, and contracting uterine smooth muscle. In terms of getting healthy skin naturally, it can remove dark spots, moisten skin and release toxins efficiently.

Regular dosage is 6 to 15 grams in decoction and more used externally.

In TCM practice, Ben Cao Jing Shu (Classic Theory of Materia Medica) said it should not be used in people suffering from cold and deficiency in Lower Jiao although dampness was there. Else, according to Ben Cao Jing Ji Zhu (Collected Annotation of Herbalism), it is incompatible with herbs like Sang Piao Xiao (Ootheca Mantidis), Jie Geng (Balloon Flower Rhizome), Fu Ling (Poria), and Bi Xie (Yam Rhizome).

**How to get healthy skin with herbal formulas?**

(1). Bai Xian Pi San, from Sheng Ji Zhong Lu (The Complete Record of Holy Benevolence), treats wind-heat hidden in lung, itch due to toxicity attack, discomfort in chest diaphragm, and fidget from time to time. Other individual herbs are Fang Feng (Ledebouriella), Ren Shen (Ginseng), Zhi Mu (Anemarrhena Rhizome), Sha Shen (Glehnia), and Huang Ling (Scutellaria Baicalensis).

(2). The Clinical Handbook of Chinese Medicinals in Qingdao said that it works with Ku Shen (Sophora) treated eczema and pruritus. And it would be better to apply its tinctures externally.

(3). For external treatment for wart and chloasma in face, it needs to combine with Ban Lan Gen (Isatis indigotica), Ku Shen, Hong Hua (Safflower Flower), Di Fu Zi (Broom Cyprus Fruit), Fan Shi (Alum), and Chan Tui (Cicada Moulting).

(4). For treating fungal infection of the hand externally, it needs to work with She Chuang Zi (Cnidium Seeds), Ku Shen, Bai Bu (Stemona), and Dang Gui (Dong Quai).

Just like love, healthy skin is always the eternal topic for women. But smooth, clear, young and beautiful look doesn’t come easy. From TCM’s point of view, the culprit of quite a big part of skin problems comes from the accumulated toxicity by wind, damp, and heat. In this case, the priority is to get rid of them all, which is exactly where Bai Xian Pi comes in. However, please note that the above are some proven remedies just for your reference, to name but a few.

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**ARTIGO**

**Extraction and isolation of dictamnine, obacunone and fraxinellone from *Dictamnus dasycarpus* Turcz. by supercritical fluid extraction and high-speed counter-current chromatography**

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**ABSTRACT**

Supercritical fluid extraction was used to extract active compounds from the Chinese traditional medicinal *D. dasycarpus* under the pressure of 30 MPa and temperature of 45 ºC. Further separation and purification was established by high-speed counter-current chromatography (HSCCC) with a two-phase solvent system composed of *n*-hexane-ethyl acetate-methanol-water (1:0.8:1.3:0.9, volume ratio). The separation yielded a total of 47 mg of dictamnine, 24 mg of obacunone and 83 mg of fraxinellone from 1.0 g of the crude extract in one step separation with the purity of 99.2, 98.4 and 99.0%, respectively, as determined by HPLC. The chemical structures of these compounds were identified by ESI-MS, IR, 1H-NMR and 13C-NMR.

**Keywords:** *Dictamnus dasycarpus*; dictamnine; obacunone.

**INTRODUCTION**

*D. dasycarpus* (Baixian-pi in Chinese, Rutaceae plants) is one of the most popular Chinese traditional medicines and has been used for the treatment of jaundice, rheumatism, cough, headache, colds, and other diseases.1 Modern pharmacological studies showed that its extract has anti-allergic effect, anti-fungal activity and appetite depressant.2-4 Numerous constituents were found including limonoids, furoquinoline alkaloids, flavonoids and sesquiterpenes.5-8 Among them, dictamnine, obacunone and fraxinellone are the most demonstrated representative. Dictamnine has the activity against fungi, cytotoxic effect, anti-platelet aggregation and vasorelaxing effect.9-11 Obacunone possesses the ability against aberrant crypt foci and carcinoma formation.12,13 Faxinellone has significant anti-inflammatory, hepatoprotective action and against colon carcinogenesis.13,14 Their chemical structures of these compounds are shown in [Figure 1](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#f1).



The preparative separation and purification of those compounds from the root bark of *D. dasycarpus* by traditional column methods are tedious and usually require multiple chromatographic steps.15 Therefore, it is important to develop an efficient method to extract, separate and purify them. Supercritical fluid extraction, for its low solvent consumption and mild conditions, has been used to extract the thermally labile components.16,17 High-speed counter-current chromatography (HSCCC) is a support free liquid-liquid partition chromatographic technique which eliminates the irreversible adsorptive loss of samples onto the solid support matrix used in the conventional chromatographic column. With a large volume of sample injection, multifarious relatively pure substances can be obtained at one step in large amount. It is especially suitable for separation and purification of active components from natural products.18-20 However, there are no reports of using SFE to extract and HSCCC to isolate chemical compounds from *D. dasycarpus*. The aim of this paper was to develop an efficient method for the preparative extraction, separation and purification of dictamnine, obacunone and fraxinellone with high purity from *D. dasycarpus* by SFE and HSCCC.

**EXPERIMENTAL**

**Apparatus**

HSCCC was carried out using a Model GS10A-2 commercial instrument (Beijing Institute of New Technology Application, China), with a multilayer PTFE coil of 1.6 mm i.d. and 110 m in length with a total capacity of 230 mL. The β values of this preparative column range from 0.5 at the internal to 0.8 at the external (β *= r/R*, where *r* is the rotation radius or the distance from the coil to the holder shaft, and *R* (*R* = 8 cm) is the revolution radius or the distances between the holder axis and central axis of the centrifuge). The solvent was pumped into the column with a Model NS-1007 constant-flow pump (Beijing Institute of New Technology Application, China). Continuous monitoring of the effluent was carried out with a Model 8823A-UV detector (Beijing Institute of New Technology Application, China) and a Model 320 pH meter (Mettler Toledo Instruments, China). A manual sample injection valve with 20 mL loop (Tianjin High New Science Technology Company, China) was used to introduce the sample into the column. A Model 3057 portable recorder (Yokogawa, Sichuan Instrument Factory, China) was used to draw the chromatogram.

The high-performance liquid chromatography (HPLC) used throughout this study consisted of a Waters 996 photodiode array detection (PDA), a Waters 600 Multisolvent Delivery, a Waters 600 system controller, a Waters 600 pump, and a Millennium32 workstation (Waters, Milford, USA).

The *Spe-ed*TM supercritical fluid extraction (SFE) system (Applied Separations, Inc., Allentown, PA, USA) was used for extracting the crude extract from the material.

**Materials**

Carbon dioxide (99.9%) was purchased from Yaotian Gas Company, Jinan, China. petroleum ether (60-90 °C), *n*-Hexane, methanol, ethanol, ethyl acetate were analytical grade (Juye Chemical Factory, Jinan, China). Methanol used for HPLC analysis was of chromatographic grade (Yuwang Special Reagent Factory, Dezhou, China). Reverse osmosis Milli-Q water (Millipore, USA) was used for all solutions and dilutions.

The root bark of *D. dasycarpus* was obtained from a local drug store and identified by Dr. L. Jia (College of Pharmacy, Shandong University of Traditional Chinese Medicine, China). The voucher specimen of this plant (KL 1012) is deposited in the Process Control Research Center of TCM, Shandong Academy of Sciences, Shandong Analysis and Test Center, Jinan, China.

**Sample preparation**

Air-dried and ground root bark (500 g) was placed into a 1 L extraction vessel and extracted statically for 1 h followed by further 6.5 h of dynamic extraction under the pressure of 30 MPa with a temperature of 45 °C. The flow-rate of carbon dioxide supercritical fluid was set at 2 L/min, and the extract in the supercritical fluid was depressed directly into a separation vessel which yielded 17.3 g of crude extract for further isolation and purification.

**Selection of two-phase solvent system**

The composition of the two-phase solvent system was selected according to the partition coefficient (*K*D) of the target compounds of the samples. The partition coefficient was determined by HPLC as follows: 10 mg of the crude extract was added to a test tube, to which 2 mL of each phase of the two-phase solvent system was added. The test tube was shaken violently for several minutes. Equal volumes of each phase were then analyzed by HPLC to obtain the partition coefficients (*K*D). The *K*D-value was defined as the peak area of compound in the upper phase divided by the peak area of compound in the lower phase.21

**Preparation of the two-phase solvent system and sample solution**

The HSCCC experiments were performed with a two-phase solvent system composed of *n*-hexane-ethyl acetate-methanol-water (1:0.8:1.3:0.9, volume ratio, the same as follows). The solvent system was equilibrated in a separation funnel, and the two phases were separated before use. The upper organic was used as stationary phase and the lower as mobile. The sample solution was prepared by dissolving the crude sample in the mixture solution of organic phase and aqueous phase (1:1) of the solvent system used for HSCCC separation.

**HSCCC separation**

The multilayer coiled column was first entirely filled with the upper phase, and then the lower phase was pumped into the column at 2.0 mL/min while the column was rotated at 800 rpm in the head to tail elution mode. After hydrodynamic equilibrium was reached as indicated by a clear mobile phase eluting from the tail outlet, the solution of the sample was injected through the injection valve. The effluent from the outlet of the column was continuously monitored by UV detector at 254 nm, and the peak fractions were collected according to the chromatogram. The retention of the stationary phase relative to the total column capacity was computed from the volume of the stationary phase collected from the column after the separation was completed.

**Separation and purification by silica gel column**

The SFE extract (10 g) was subjected to column chromatography on silica gel, elution with petroleum ether-ethyl acetate (petroleum ether, 5: 1, 4: 1, 3: 1, 2: 1, 3: 2, 1: 1, 1: 2), afforded eight fractions according to TLC and HPLC results. Fraction 2 (5: 1, containing fraxinellone) was repeatedly chromatographed on silica gel with the same solvent to afford fraxinellone. Fraction 5 (2: 1) and 8 (1: 2) afforded dictamnine and obacunone with the same method.

**Analysis and identification of HSCCC peak fractions**

The crude sample and each purified fraction from the HSCCC were analyzed by HPLC with a Shim-pack VP-ODS column (250 x 4.6 mm, i.d., 5 µm) and column temperature of 25 °C. The mobile phase, a solution of methanol and water (75:25), was set at a flow-rate of 1.0 mL/min. The effluent was monitored by PDA at 240 nm.

The identification of HSCCC peak fractions were performed by mass spectrometry (ESI-MS) with an Agilent 1100/MSD (California, USA), IR spectra with a Bruker Vertex 70 spectrometer and NMR spectra with a Varian-600 spectrometer (Varian, Palo Alto, CA, USA) with CDCl3 as solvent and tetramethylsilane (TMS) as internal standard.

**RESULTS AND DISCUSSION**

**Optimization of HSCCC conditions**

Partition coefficient (*K*D) is the most important parameter in solvent system selection. Successful separation by HSCCC needs a suitable *K*D-value. Large *K*D-value usually tends to produce excessive sample band broadening, while small *K*D-value results in a poor peak resolution.22,23 In this experiment, the solvent system based on *n*-hexane-ethyl acetate-methanol-water at different volume ratios were tested ([Table 1](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#t1)). As shown in [Table 1](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#t1), the *K*D-value of the compound 2 in the solvent system of *n*-hexane-ethyl acetate-methanol-water (1:0.5:1:0.5) was too small, while it was difficult to separate compound 1 and 3 for the close *K*D-value. The *K*D-value of *n*-hexane-ethyl acetate-methanol-water (1:1:1:1) was too big and would result in a long separation time. Among these solvents, *n*-hexane-ethyl acetate-methanol-water (1:0.2:1:0.2) and (1:0.8:1.3:0.9) have suitable *K*D-value. After trying all the above solvent systems, the solvent system *n*-hexane-ethyl acetate-methanol-water (1:0.8:1.3:0.9) was found to be the best. [Figure 3](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#f3) shows the separation of HSCCC using this solvent system.







The SFE extract (1.0 g) from the root bark of *D. dascarpus* was purified under the optimum HSCCC conditions. The upper phase was used as the stationary phase while the lower phase was used as the mobile phase in the head to tail elution mode. The retention of the stationary phase was 44.6%, and the total separation time was about 8 h. The HSCCC fractions were analyzed by HPLC, and their absorbance was measured at 254 nm to draw the elution curve ([Figure 3](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#f3)). Based on the HPLC analysis, three compounds were obtained in one step separation and yielded 47 mg of dictamnine (peak I in [Figure 3](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#f3)), 24 mg of obacunone (peak II in [Figure 3](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#f3)) and 83 mg of fraxinellone (peak III in [Figure 3](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#f3)) with the purity of 99.2, 98.4 and 99.0%, respectively ([Figure 2](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422012000200020#f2)).

**Separation with conventional silica gel column**

The SFE extract (10 g) was separated and purified by conventional silica gel column and 310 mg of fraxinellone, 153 mg of dictamnine and 68 mg of obacunone were obtained after several separation steps about 80 h. The recovery of fraxinellone, dictamnine and obacunone is about 35, 30 and 27%. However, HSCCC could purify the crude extract in one-step separation with more than 90% recovery. The separation time was only 8 h in each separation run. In comparison with open-column silica gel, HSCCC represents very low solvent consumption for a sample of the size and short separation time used in this experiment.

**The structural identification**

The structural identification of the three compounds was performed with ESI-MS, IR, 1H and 13C-NMR spectra.

Compound corresponding peak I: ESI-MS (positive mode), *m/z* 200.0 [M+H]+. IRνcmm ax-1: 3432, 3002, 1579, 1368, 1121, 1085, 980, 757, 721, 636, 575. Comparing the data of 1H and 13C-NMR with references, the obtained compound was identified as dictamnine.15,24

Compound corresponding peak II: ESI-MS (positive mode), *m/z* 454.2 [M+H]+. IRνcmm ax-1: 2988, 2947, 1736, 1708, 1281, 1029, 988, 802. Comparing the data of 1H and 13C-NMR with references, the obtained compound was identified as obacunone.15,24

Compound corresponding peak III: ESI-MS (positive mode), *m/z* 255.2 [M+Na]+. IRνcmm ax-1: 2932, 1743, 1672, 1204, 1161, 1135, 1023, 977, 950, 871, 814, 747, 607. Comparing the data of 1H and 13C-NMR with references, the obtained compound was identified as fraxinellone.15,24

**CONCLUSION**

Three main compounds including dictamnine, obacunone and fraxinellone from the root bark of *D. dasycarpus* were extracted and purified by SFE and HSCCC. With a two-phase solvent system composed of *n*-hexane-ethyl acetate-methanol-water (1:0.8:1.3:0.9), 47 mg of dictamnine, 24 mg of obacunone and 83 mg of fraxinellone were obtained from 1.0 g of SFE extract with the purity of 99.2, 98.4 and 99.0%, respectively. The recovery of this separation is over 90%, compared with the conventional silica gel column (less than 35%). The present study demonstrates that SFE and HSCCC are very useful techniques for the extraction, isolation and purification of bioactive natural components.

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# Identification of antioxidant activity of two new aromatic ring butyrolactone derivatives from Dictamnus dasycarpus Turcz.

[Guo LN](https://www.ncbi.nlm.nih.gov/pubmed/?term=Guo%20LN%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Pei YH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Pei%20YH%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)2, [Xie FX](https://www.ncbi.nlm.nih.gov/pubmed/?term=Xie%20FX%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Liu L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Liu%20L%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Cong H](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cong%20H%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Cui HX](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cui%20HX%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Wang XL](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wang%20XL%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Li WJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Li%20WJ%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Jian BY](https://www.ncbi.nlm.nih.gov/pubmed/?term=Jian%20BY%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)1, [Liu JC](https://www.ncbi.nlm.nih.gov/pubmed/?term=Liu%20JC%5BAuthor%5D&cauthor=true&cauthor_uid=27914532)3.

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### Abstract

The present study carried out a phytochemical investigation on the root barks of Dictamnus dasycarpus Turcz, leading to the isolation and characterization of two new aromatic ring butyrolactone derivatives, dasycarpusphenol acid A (1) and dasycarpusphenol acid B (2). Their structures were elucidated by using spectroscopic techniques and HR-FAB-MS. Compounds 1 and 2 exhibited antioxidant activity, with their IC50 values being 28.95 and 41.76 mg·mL-1, respectively.

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#### KEYWORDS:

Antioxidant activity; Dasycarpusphenol acid A; Dasycarpusphenol acid B; Dictamnus dasycarpus

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[Arch Toxicol.](https://www.ncbi.nlm.nih.gov/pubmed/27519711) 2016 Aug 12. [Epub ahead of print]

# Hepatotoxicity by combination treatment of temozolomide, artesunate and Chinese herbs in a glioblastoma multiforme patient: case report review of the literature.

[Efferth T](https://www.ncbi.nlm.nih.gov/pubmed/?term=Efferth%20T%5BAuthor%5D&cauthor=true&cauthor_uid=27519711)1, [Schöttler U](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sch%C3%B6ttler%20U%5BAuthor%5D&cauthor=true&cauthor_uid=27519711)2, [Krishna S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Krishna%20S%5BAuthor%5D&cauthor=true&cauthor_uid=27519711)3, [Schmiedek P](https://www.ncbi.nlm.nih.gov/pubmed/?term=Schmiedek%20P%5BAuthor%5D&cauthor=true&cauthor_uid=27519711)4, [Wenz F](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wenz%20F%5BAuthor%5D&cauthor=true&cauthor_uid=27519711)4, [Giordano FA](https://www.ncbi.nlm.nih.gov/pubmed/?term=Giordano%20FA%5BAuthor%5D&cauthor=true&cauthor_uid=27519711)4.

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### Abstract

Glioblastoma multiforme (GBM) represents an aggressive tumor type with poor prognosis. The majority of GBM patients cannot be cured. There is high willingness among patients for the compassionate use of non-approved medications, which might occasionally lead to profound toxicity. A 65-year-old patient with glioblastoma multiforme (GBM) has been treated with radiochemotherapy including temozolomide (TMZ) after surgery. The treatment outcome was evaluated as stable disease with a tendency to slow tumor progression. In addition to standard medication (ondansetron, valproic acid, levetiracetam, lorazepam, clobazam), the patient took the antimalarial drug artesunate (ART) and a decoction of Chinese herbs (Coptis chinensis, Siegesbeckia orientalis, Artemisia scoparia, Dictamnus dasycarpus). In consequence, the clinical status deteriorated. Elevated liver enzymes were noted with peak values of 238 U/L (GPT/ALAT), 226 U/L (GOT/ASAT), and 347 U/L (γ-GT), respectively. After cessation of ART and Chinese herbs, the values returned back to normal and the patient felt well again. In the literature, hepatotoxicity is well documented for TMZ, but is very rare for ART. Among the Chinese herbs used, Dictamnus dasycarpus has been reported to induce liver injury. Additional medication included valproic acid and levetiracetam, which are also reported to exert hepatotoxicity. While all drugs alone may bear a minor risk for hepatotoxicity, the combination treatment might have caused increased liver enzyme activities. It can be speculated that the combination of these drugs caused liver injury. We conclude that the compassionate use of ART and Chinese herbs is not recommended during standard radiochemotherapy with TMZ for GBM.

#### KEYWORDS:

Adverse side effects; Asteraceae; Cancer; Chemotherapy; Toxicity; Traditional Chinese medicine

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Onderzoek naar werking

[Molecules.](https://www.ncbi.nlm.nih.gov/pubmed/26690397) 2015 Dec 10;20(12):22128-36. doi: 10.3390/molecules201219840.

# Limonin, a Component of Dictamni Radicis Cortex, Inhibits Eugenol-Induced Calcium and cAMP Levels and PKA/CREB Signaling Pathway in Non-Neuronal 3T3-L1 Cells.

[Yoon YC](https://www.ncbi.nlm.nih.gov/pubmed/?term=Yoon%20YC%5BAuthor%5D&cauthor=true&cauthor_uid=26690397)1, [Kim SH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kim%20SH%5BAuthor%5D&cauthor=true&cauthor_uid=26690397)2, [Kim MJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kim%20MJ%5BAuthor%5D&cauthor=true&cauthor_uid=26690397)3, [Yang HJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=Yang%20HJ%5BAuthor%5D&cauthor=true&cauthor_uid=26690397)4, [Rhyu MR](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rhyu%20MR%5BAuthor%5D&cauthor=true&cauthor_uid=26690397)5, [Park JH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Park%20JH%5BAuthor%5D&cauthor=true&cauthor_uid=26690397)6,7.

### [Author information](https://www.ncbi.nlm.nih.gov/pubmed/26690397)

### Abstract

Limonin, one of the major components in dictamni radicis cortex (DRC), has been shown to play various biological roles in cancer, inflammation, and obesity in many different cell types and tissues. Recently, the odorant-induced signal transduction pathway (OST) has gained attention not only because of its function in the perception of smell but also because of its numerous physiological functions in non-neuronal cells. However, little is known about the effects of limonin and DRC on the OST pathway in non-neuronal cells. We investigated odorant-stimulated increases in Ca(2+) and cAMP, major second messengers in the OST pathway, in non-neuronal 3T3-L1 cells pretreated with limonin and ethanol extracts of DRC. Limonin and the extracts significantly decreased eugenol-induced Ca(2+) and cAMP levels and upregulated phosphorylation of CREB and PKA. Our results demonstrated that limonin and DRC extract inhibit the OST pathway in non-neuronal cells by modulating Ca(2+) and cAMP levels and phosphorylation of CREB.

#### KEYWORDS:

cAMP; calcium; dictamni radices cortex; furanolactone; limonin; olfactory

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////////////////////////////////////////////////meer onderzoek naar het moleculaire mechanisme

[J Ethnopharmacol.](https://www.ncbi.nlm.nih.gov/pubmed/26656538) 2016 Feb 3;178:13-6. doi: 10.1016/j.jep.2015.10.043. Epub 2015 Dec 3.

# Glabretal-type triterpenoid from the root bark of Dictamnus dasycarpus ameliorates collagen-induced arthritis by inhibiting Erk-dependent lymphocyte proliferation.

[Choi SP](https://www.ncbi.nlm.nih.gov/pubmed/?term=Choi%20SP%5BAuthor%5D&cauthor=true&cauthor_uid=26656538)1, [Choi CY](https://www.ncbi.nlm.nih.gov/pubmed/?term=Choi%20CY%5BAuthor%5D&cauthor=true&cauthor_uid=26656538)1, [Park K](https://www.ncbi.nlm.nih.gov/pubmed/?term=Park%20K%5BAuthor%5D&cauthor=true&cauthor_uid=26656538)1, [Kim N](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kim%20N%5BAuthor%5D&cauthor=true&cauthor_uid=26656538)1, [Moon HS](https://www.ncbi.nlm.nih.gov/pubmed/?term=Moon%20HS%5BAuthor%5D&cauthor=true&cauthor_uid=26656538)1, [Lee D](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lee%20D%5BAuthor%5D&cauthor=true&cauthor_uid=26656538)2, [Chun T](https://www.ncbi.nlm.nih.gov/pubmed/?term=Chun%20T%5BAuthor%5D&cauthor=true&cauthor_uid=26656538)3.

### [Author information](https://www.ncbi.nlm.nih.gov/pubmed/26656538)

### Abstract

#### ETHNOPHARMACOLOGICAL RELEVANCE:

The root bark of Dictamnus dasycarpus Turcz. (Rutaceae) has been used as a traditional herbal medicine to treat various inflammatory diseases in East Asia. We have showed previously that a glabretal type triterpenoid (dictabretol A) from D. dasycarpus root bark has immunosuppressive activity.

#### AIM OF THE STUDY:

This study was conducted to define the molecular mechanism of how dictabretol A inhibits lymphocyte proliferation and to evaluate the therapeutic efficacy of dictabretol A in an animal model of rheumatoid arthritis.

#### MATERIALS AND METHODS:

Various murine immune cells (T cells, B cells, and macrophages) and splenocytes were used to study the anti-proliferative effect of dictabretol A in vitro. A collagen-induced arthritis model was also used to examine the therapeutic effect of dictabretol A in vivo.

#### RESULTS:

Dictabretol A specifically inhibited lymphocyte proliferation by blocking the cell cycle transition from the G1 to the S phase. This effect was achieved by blocking Erk1/2, nuclear factor kappa B, and the C-myc axis of cell cycle progression. Further dictabretol A treatment alleviated the severity of collagen-induced arthritis.

#### CONCLUSION:

Our results reveal the molecular mechanism for the anti-lymphoproliferative effect of dictabretol A and show the therapeutic efficacy of dictabretol A for rheumatoid arthritis.

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#### KEYWORDS:

Cell cycle; Collagen induced arthritis; Dictabretol A; Lymphocyte; Signal transduction

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[PubMed - indexed for MEDLINE]

/////////////////////////////////// westerse visie op andere dictamnus soorten

[J Ethnopharmacol.](https://www.ncbi.nlm.nih.gov/pubmed/26387739) 2015 Dec 4;175:390-406. doi: 10.1016/j.jep.2015.09.011. Epub 2015 Sep 24.

# An ethnopharmacological and historical analysis of "Dictamnus", a European traditional herbal medicine.

[Martínez-Francés V](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mart%C3%ADnez-Franc%C3%A9s%20V%5BAuthor%5D&cauthor=true&cauthor_uid=26387739)1, [Rivera D](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rivera%20D%5BAuthor%5D&cauthor=true&cauthor_uid=26387739)2, [Heinrich M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Heinrich%20M%5BAuthor%5D&cauthor=true&cauthor_uid=26387739)3, [Obón C](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ob%C3%B3n%20C%5BAuthor%5D&cauthor=true&cauthor_uid=26387739)4, [Ríos S](https://www.ncbi.nlm.nih.gov/pubmed/?term=R%C3%ADos%20S%5BAuthor%5D&cauthor=true&cauthor_uid=26387739)5.

### [Author information](https://www.ncbi.nlm.nih.gov/pubmed/26387739)

### Abstract

#### ETHNOPHARMACOLOGICAL RELEVANCE AND BACKGROUND:

"Dictamnus" was a popular name for a group of medicinal herbaceous plant species of the Rutaceae and Lamiaceae, which since the 4th century have been used for gynaecological problems and other illnesses BCE and still appear in numerous ethnobotanical records.

#### AIMS:

This research has as four overarching aims: Determining the historical evolution of medical preparations labelled "Dictamnus" and the different factors affecting this long-standing herbal tradition. Deciphering and differentiating those medicinal uses of "Dictamnus" which strictly correspond to Dictamnus (Rutaceae), from those of Origanum dictamnus and other Lamiaceae species. Quantitatively assessing the dependence from herbal books, and pharmaceutical tradition, of modern Dictamnus ethnobotanical records. Determining whether differences between Western and Eastern Europe exist with regards to the Dictamnus albus uses in ethnopharmacology and ethnomedicine.

#### METHODS:

An exhaustive review of herbals, classical pharmacopoeias, ethnobotanical and ethnopharmacological literature was conducted. Systematic analysis of uses reported which were standardized according to International Classification of Diseases - 10 and multivariate analysis using factorial, hierarchical and neighbour joining methods was undertaken.

#### RESULTS AND DISCUSSION:

The popular concept "Dictamnus" includes Origanum dictamnus L., Ballota pseudodictamnus (L.) Benth. and B. acetabulosa (L.) Benth. (Lamiaceae), as well as Dictamnus albus L. and D. hispanicus Webb ex Willk. (Rutaceae), with 86 different types of uses. Between 1000 and 1700 CE numerous complex preparations with "Dictamnus" were used in the treatment of 35 different pathologies. On biogeographical grounds the widespread D. albus is a far more likely prototypical "Dictamnus" than the Cretan endemic Origanum dictamnus. However both form integral parts of the "Dictamnus" complex. Evidence exists for a sufficiently long and coherent tradition for D. albus and D. hispanicus, use to treat 47 different categories of diseases.

#### CONCLUSIONS:

This approach is a model for understanding the cultural history of plants and their role as resources for health care. "Dictamnus" shows how transmission of traditional knowledge about materia medica, over 26 centuries, represents remarkable levels of development and innovation. All this lead us to call attention to D. albus and D. hispanicus which are highly promising as potential herbal drug leads. The next steps of research should be to systematically analyse phytochemical, pharmacological and clinical evidence and to develop safety, pharmacology and toxicology profiles of the traditional preparations.

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#### KEYWORDS:

Dictamnus; Ethnobotany; Ethnomedicine; European herbal medicine; History of pharmacy; Western Mediterranean

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///////////////////// ze willen er medicijnen van maken op zijn westers

[J Ethnopharmacol.](https://www.ncbi.nlm.nih.gov/pubmed/26068434) 2015 Aug 2;171:247-63. doi: 10.1016/j.jep.2015.05.053. Epub 2015 Jun 9.

# Medicinal uses, phytochemistry and pharmacology of the genus Dictamnus (Rutaceae).

[Lv M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lv%20M%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)1, [Xu P](https://www.ncbi.nlm.nih.gov/pubmed/?term=Xu%20P%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)2, [Tian Y](https://www.ncbi.nlm.nih.gov/pubmed/?term=Tian%20Y%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)1, [Liang J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Liang%20J%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)3, [Gao Y](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gao%20Y%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)1, [Xu F](https://www.ncbi.nlm.nih.gov/pubmed/?term=Xu%20F%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)1, [Zhang Z](https://www.ncbi.nlm.nih.gov/pubmed/?term=Zhang%20Z%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)4, [Sun J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sun%20J%5BAuthor%5D&cauthor=true&cauthor_uid=26068434)5.

### [Author information](https://www.ncbi.nlm.nih.gov/pubmed/26068434)

### Abstract

#### ETHNOPHARMACOLOGICAL RELEVANCE:

Seven species from the genus Dictamnus are distributed throughout Europe and North Asia and only two species grow in China. One is Dictamnus dasycarpus Turcz., which could be found in many areas of China and has been recorded in Chinese Pharmacopoeia. The other is Dictamnus angustifolius G. Don ex Sweet, which is only present in Xinjiang province and has been used as an alternative for Dictamnus dasycarpus in the local for the treatment of rheumatism, bleeding, itching, jaundice, chronic hepatitis and skin diseases. The present paper reviewed the traditional uses, phytochemistry, pharmacology and toxicology of the genus Dictamnus.

#### MATERIALS AND METHODS:

Information on the Dictamnus species was collected from classic books about Chinese herbal medicine and globally accepted scientific databases including PubMed, Elsevier, ASC, Scopus, Google Scholar, Web of Science, CNKI and others.

#### RESULTS:

About 170 chemical compounds, which include quinoline alkaloids, limonoids, sesquiterpenes, coumarins, flavonoids and steroids, have been isolated from the genus Dictamnus. The characteristic and active constituents of Dictamnus species are considered to be quinoline alkaloids and limonoids, which exhibited a broad spectrum of biological activities such as anti-cancer, anti-inflammation, anti-microbe, anti-platelet-aggregation, vascular-relaxation, anti-insect, anti-HIV, anti-allergy and neuroprotection. Moreover, quinoline alkaloids and limonoids could be used as quality control markers to distinguish different species from the genus Dictamnus. However, there were also some reports on the toxic hepatitis and phototoxic effect of Dictamnus species, and the related research needs to be further studied.

#### CONCLUSION:

In this review, we summarized the chemical constituents, pharmacology, quality control and toxicology of the species from genus Dictamnus. Phytochemical investigations indicated that quinoline alkaloids and limonoids were the major bioactive components with potential cytotoxic, neuroprotective, anti-inflammatory, antimicrobial, anti-platelet-aggregation and vascular relaxing activities. These two kinds of compounds have attracted great interests in the past few years and may have great potential to be new drug lead compounds.

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#### KEYWORDS:

Dictamnus; Pharmacology; Phytochemistry; Toxicology

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