Patents

Scopolamine production

Abstract

The invention provides an improved method for the production of Scopolamine by extraction.

Classifications

C07D451/10 Oxygen atoms acylated by aliphatic or araliphatic carboxylic acids, e.g. atropine, scopolamine

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WO2020097635A1

WIPO (PCT)

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Other languages: French

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Worldwide applications

2019 EP *WO* ~~AU~~ ~~US~~ 2021 *ZA* *CL*

Application PCT/ZA2019/050069 events

2019-11-06	Application filed by The University Of Johannesburg
2019-11-06	Priority to AU2019374917A
2019-11-06	Priority to US17/291,688
2019-11-06	Priority to EP19845755.8A
2020-05-14	Publication of WO2020097635A1
2021-05-05	Priority to ZA2021/03033A

Info: Patent citations (3), Non-patent citations (2) , Legal events, Similar documents, Priority and Related Applications

External links: Espacenet, Global Dossier, PatentScope, Discuss

Claims

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1. A method for the production of Scopolamine, which method includes the steps of:

grinding plant material which contains Scopolamine;

adding the grinded plant material to a Sulfuric acid solution and allowing to stand in the solution for 1 to 4 days,

filtration separation of the acid solution from the plant material;

repeating the previous steps with the residue plant material and combining the acidic filtrates;

neutralising with a alkaline solution to a pH of between 7.5 and 9.5;

addition of dichloromethane for the extraction of the alkaloids in the neutralised solution to the organic layer and allowing to stand for 1 to 4 days; separation of the bottom organic layer from the upper aqueous layer;

evaporation of the dichloromethane solvent to obtain the coloured scopolamine rich extract;

adding the scopolamine rich extract to dichloromethane solvent and mixing with a NaOH solution and separating the layers; and

evaporation of the dichloromethane solvent to obtain the less coloured scopolamine rich extract.

2. A method for the production of Scopolamine as claimed in Claim 1 , wherein the Sulfuric acid solution is 1 %.

3. A method for the production of Scopolamine as claimed in Claim 1 or Claim 2, wherein the Sulfuric acid solution is allowed to stand for 2 to 3 days.

4. A method for the production of Scopolamine as claimed in any one of the previous claims, wherein the alkaline solution is a sodium bicarbonate solution at a pH of between 8 and 9.

5. A method for the production of Scopolamine as claimed in any one of the previous claims, wherein the Dichloromethane is added immediately.

6. A method for the production of Scopolamine as claimed in any one of the previous claims, wherein the organic layer is allowed to stand for 2 to 3 days.

7. A method for the production of Scopolamine as claimed in any one of the previous claims, wherein the NaOH solution is 1 %.

8. A method for the production of Scopolamine as claimed in any one of the previous claims, wherein the less coloured scopolamine rich extract is added to dichloromethane solvent and mixed with a 1 % sodium bicarbonate solution and the layers separated and the dichloromethane solvent evaporated to obtain the final scopolamine rich extract.

Description

Title: Scopolamine Production

Technical field of the invention

This invention relates to the production of Scopolamine. More particularly it relates to the production of Scopolamine by means of extraction from plant material.

Background to the invention

Scopolamine, also known as Hyoscine, is a well-known drug used inter alia for motion sickness and nausea. It is also a precursor to a number of other drugs. Scopolamine is expensive to synthesize and it is therefore economically viable to be extracted from plants of the Solanaceae family.

Previously, the applicant invented an extraction and purification method of scopolamine in flos daturae. The method included the following steps: firstly obtaining extract liquid of flos daturae; filtering the extract liquid by means of a ceramic membrane, concentrating by means of a nanofiltration membrane, recovering ethanol, and obtaining a mixture; dissolving the mixture by using diluted hydrochloric acid, carrying out suction filtering, and obtaining filtrate; extracting the filtrate, and reserving the aqueous solution; adjusting the pH value by using a water phase, re-extracting four times, and collecting a chloroformic solution; drying the chloroformic solution, recovering chloroform, and obtaining total alkaloids; and separating the total alkaloids by using alkaline aluminum oxide column chromatography, recovering chloroform, and obtaining scopolamine.

The applicant wishes to improve the yield and the scalability of the above method. It is an object of the invention to provide a simplified method to produce Scopolamine which is well suited for scale up to process 45 000kg or more of plant material per year.

General description of the invention

According to the invention there is provided a method for the production of Scopolamine, which method includes the steps of:

grinding plant material which contains Scopolamine;

adding the grinded plant material to a Sulfuric acid solution, preferably 1 %, and allowing to stand in the solution for 1 to 4, preferably 2 to 3 days;

filtration separation of the acid solution from the plant material;

repeating the previous steps with the residue plant material and combining the acidic filtrates;

neutralising with sodium bicarbonate to a pH of between 7.5 and 9.5, preferably between 8 and 9;

addition, preferably immediate, of dichloromethane for the extraction of the alkaloids in the neutralised solution to the organic layer and allowing to stand for 1 to 4 days, preferably 2 to 3 days;

separation of the bottom organic layer from the upper aqueous layer;

evaporation of the dichloromethane solvent to obtain the coloured scopolamine rich extract;

adding the scopolamine rich extract to dichloromethane solvent and mixing with a NaOH, preferably 1 %, solution and separating the layers;

evaporation of the dichloromethane solvent to obtain the less coloured scopolamine rich extract;

optionally, adding the less coloured scopolamine rich extract to dichloromethane solvent and mixing with a sodium bicarbonate, preferably 1 %, solution and separating the layers; and

evaporation of the dichloromethane solvent to obtain the final scopolamine rich extract.

The second last optional step improves the purity of the final product. The plant material may preferably be the seeds of Flos Daturae. It is to be appreciated that the seeds have less chlorophyll, which follows the extraction process to some extent.

The extraction method described is significantly less complex than known methods, does not need special equipment like columns and separation membranes, uses only one low cost solvent and produces a high yield with high purity. The method can also be economically scaled up as required to process 45 tons or more of plant material per year. The extraction method is also tuned to focus on scopolamine from a mixture of alkaloids contained in Flos Daturae.

Detailed description of the invention

The invention is now described by way of example.

500 Grams of Flos Daturae seeds were grinded and added to 1 500 ml of a 1 % Sulfuric acid solution and allowed to stand in the solution for 2 days. The mixture was filtered and 700 ml of the acid solution was recovered. This step can preferably be repeated to increase the yield. The filtrate was neutralised with sodium bicarbonate to a pH of 9. A 1000 ml of dichloromethane was mixed with the filtrate and allowed to stand for 2 days. The bottom organic layer was separated from the upper aqueous layer and the dichloromethane solvent was evaporated using a roto evaporator to obtain the coloured scopolamine rich extract. Once off, adding the scopolamine rich extract to 1000ml dichloromethane solvent and mixing with a 1 % NaOH 1000ml, solution and separating the layers. The dichloromethane solvent was again removed in a roto evaporator to obtain the less coloured scopolamine rich extract. The less coloured scopolamine rich extract was added to 1000ml dichloromethane solvent and mixed with a 1000ml 1 % sodium bicarbonate solution and the layers were separated. This step is also once off. The dichloromethane solvent was evaporated to obtain 12 grams of the final scopolamine rich extract, which contains 70% scopolamine in a pharmaceutically acceptable mixture. The use of sulphuric acid in the first step removes fat soluble impurities. The long extraction time of 2 days improves the yield significantly and it appears that the conversion from organic acid to salt is relatively slow. The selective neutralisation to pH of 8 to 9 avoided neutralising other compounds and their subsequent extraction to yield a purer product. Again, longer than normal extraction time improved the yield and the further steps improved the purity compared to known extraction methods.

It shall be understood that the example is provided for illustrating the invention further and to assist a person skilled in the art with understanding the invention and is not meant to be construed as unduly limiting the reasonable scope of the invention.

Patent Citations (3)

Publication number	Priority date	Publication date	Assignee	Title
FR2405947A1 *	1977-10-11	1979-05-11	Nativelle Sa Ets	Prepn. of scopolamine and hyoscyamine hydro:bromide(s) - by alcohol extraction of alkaloid(s), and separation of the hydro:bromide(s) in chloroform
CN108164523A *	2017-12-08	2018-06-15	大兴安岭林格贝寒带生物科技股份有限公司	A kind of preparation process that hyoscyamine is extracted from belladonna
CN108610339A *	2018-04-19	2018-10-02	安徽德信佳生物医药有限公司	The technique of extraction separation hyoscine in a kind of datura flower from low content
Family To Family Citations				

* Cited by examiner, † Cited by third party

Non-Patent Citations (2)

Title
DATABASE WPI Week 201847, Derwent World Patents Index; AN 2018-49462W *
DATABASE WPI Week 201880, Derwent World Patents Index; AN 2018-80416A *

* Cited by examiner, † Cited by third party

Similar Documents

Publication	Publication Date	Title
CA2467001A1	2004-12-05	Extraction process for removal of impurities from mother liquor in the synthesis of carboxylic acid
US4952603A	1990-08-28	Method for the isolation of artemisinin from Artemisia annua
CN102408314B	2013-10-30	Method for preparing high-purity magnolol and magnolol
CN104086425A	2014-10-08	Method for simultaneously extracting and separating chlorogenic acid, solanesol, alkaloid and rutin in tobacco
JP2013537888A	2013-10-07	Method for preparing Centella asiatica extract
CN102964408A	2013-03-13	Method for extracting naringin from red tangerine peel
CN102351939A	2012-02-15	Method for preparing high-purity ursolic acid and oleanolic acid from ligustrum lucidum ait
US6218541B1	2001-04-17	Method for extracting bisbenzylisoquinolines
CN102675910A	2012-09-19	Preparation method of high-color-value beet root red color
EP3877386B1	2022-06-29	Scopolamine production
US8765196B2	2014-07-01	Method for separating and purifying Ginkgolide C from root bark of ginkgo
JP6768970B2	2020-10-14	How to prepare rubusoside
JP7083920B2	2022-06-13	Cytisinicline isolation method
CN104262362B	2017-02-15	Vinblastine extraction and purification method
CN102464666A	2012-05-23	A kind of preparation method of ginkgolide C
CN101085780B	2011-06-08	Preparation method for ginkgolide
CN105481809B	2018-01-05	A kind of isolation and purification method of tanshin polyphenolic acid B and the preparation method of B magnesium tanphenolate
CN104356140A	2015-02-18	Method for separating and preparing high-purity Moxidectin membrane
WO2007083908A1	2007-07-26	A method for preparing decursinol from angelica gigas with high yield
CN113698334A	2021-11-26	Method for separating and purifying sojanine monomer from alkaloid extract
CN102911033A	2013-02-06	Method for preparing xanthohumol from European hop spike
CN109265428A	2019-01-25	A kind of extraction preparation method of tasselled phenanthrene
CN102675328B	2014-11-26	Method for extracting betulinic acid and camptothecin from camptotheca acuminate fruits
CN109761838B	2024-12-31	A method for preparing pregabalin intermediate and recovering resolving agent
SU449725A1	1974-11-15	The method of obtaining strophanthin-k

Priority And Related Applications

Priority Applications (4)

Application	Priority date	Filing date	Title
AU2019374917A	2018-11-07	2019-11-06	Scopolamine production
US17/291,688	2018-11-07	2019-11-06	Scopolamine Production
EP19845755.8A	2018-11-07	2019-11-06	Scopolamine production
ZA2021/03033A	2018-11-07	2021-05-05	Scopolamine production

Applications Claiming Priority (2)

Application	Filing date	Title
ZA201807451	2018-11-07	
ZA2018/07451	2018-11-07	

Legal Events

Date	Code	Title	Description
2020-06-24	121	Ep: the epo has been informed by wipo that ep was designated in this application	**Ref document number**: 19845755 **Country of ref document**: EP **Kind code of ref document**: A1
2021-05-08	NENP	Non-entry into the national phase	**Ref country code**: DE
2021-05-27	ENP	Entry into the national phase	**Ref document number**: 2019374917 **Country of ref document**: AU **Date of ref document**: 20191106 **Kind code of ref document**: A
2021-06-11	ENP	Entry into the national phase	**Ref document number**: 2019845755 **Country of ref document**: EP **Effective date**: 20210607

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