

35

CAVELIER

ABOGADOS

WEB SITE: www.cavelier.com
E-MAIL: cavelier@cavelier.com

EDIFICIO SISKI
CARRERA 4 No. 72 - 35
BOGOTA 8, COLOMBIA

TELEFONO: (57) (1) 7-3611

SUPERINDUSTRIA Y COMERCIO

Folios: 31

Radicacion : 01101335 00000002

Fecha (AMD): 2002-03-21 16:54:26

Tramite : 002 PATENTES D 1 REGISTRO/ 329 COMPLEME

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Señora Jefe de la
DIVISION DE NUEVAS CREACIONES
SUPERINTENDENCIA DE INDUSTRIA Y COM
E. S. D.

Referencia : Expediente No. 01.101.335

Solicitante : BOMSUND GRUPO ASESOR, S.L.

Asunto : Solicitud de patente para: "PROCEDIMIENTO
PARA PREPARAR EXTRACTOS ACUOSOS DE PLANTAS
Y EXTRACTOS OBTENIDOS DE ESTE MODO"

Fecha de solicitud : 26 de noviembre de 2001.

TRAMITE: 002 - EVENTO: 001 - ACTUACIÓN: 329

1. Yo, Emilio FERRERO, obrando como apoderado de la solicitante en referencia, atentamente presento con este escrito la copia certificada de la solicitud de patente PCT No. PCT/IB00/01947 del 27 de noviembre de 2000, junto con su respectiva traducción de sus reivindicaciones y carátula, de la cual se reclama prioridad en esta solicitud de patente.

2. Ruego a la Señora Jefe se sirva aceptar este escrito con sus anexos, y se continúe con el trámite de la solicitud.

Bogotá, 21 MAR. 2002
Señora Jefe,



EMILIO FERRERO

T.P.A. No. 31.929

COLO 13059-801-002-8

MRE-7



**WORLD INTELLECTUAL PROPERTY ORGANIZATION
ORGANISATION MONDIALE DE LA PROPRIÉTÉ INTELLECTUELLE**

34, chemin des Colombettes, Case postale 18, CH-1211 Genève 20 (Suisse)
Téléphone: (41 22) 338 91 11 - e-mail: wipo.mail @ wipo.int. - Fac-similé: (41 22) 733 54 28

**PATENT COOPERATION TREATY (PCT)
TRAITÉ DE COOPÉRATION EN MATIÈRE DE BREVETS (PCT)**

**CERTIFIED COPY OF THE INTERNATIONAL APPLICATION AS FILED
AND OF ANY CORRECTIONS THERETO**

**COPIE CERTIFIÉE CONFORME DE LA DEMANDE INTERNATIONALE, TELLE QU'ELLE
A ÉTÉ DÉPOSÉE, AINSI QUE DE TOUTES CORRECTIONS Y RELATIVES**

International Application No. } PCT / IB 00 / 0 1 9 4 7 International Filing Date } 27 NOVEMBER 2000
Demande internationale n° } Date du dépôt international } (27. 11. 00)

Geneva/Genève,

11 DECEMBER 2001
(11. 12. 01)

**International Bureau of the
World Intellectual Property Organization (WIPO)**

**Bureau International de l'Organisation Mondiale
de la Propriété Intellectuelle (OMPI)**



J.-L. Baron

Head, PCT Receiving Office Section
Chef de la section "office récepteur du PCT"

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

PCT / IB. 0 0 / 0 1 9 4 7
International Application No.

27 NOVEMBER 2000

International Filing Date

(27. 11. 00)

INTERNATIONAL BUREAU OF WIPO
Name of receiving Office and "PCT International Application"Applicant's or agent's file reference
(if desired) (12 characters maximum) 2000411

Box No. I TITLE OF INVENTION

PROCESS FOR PREPARING AQUEOUS EXTRACTS OF PLANTS AND EXTRACTS SO OBTAINED

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

BOMSUND GRUPO ASESOR, S.L.
C/Mallorca 235, pp1c. 1º
08008 BARCELONA
SPAIN

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (that is, country) of nationality:
ESState (that is, country) of residence:
ESThis person is applicant
for the purposes of:☐ all designated
States☒ all designated States except
the United States of America☐ the United States
of America only☐ the States indicated in
the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

FRIAS PEÑA, José Manuel
C/Mallorca 235, pp1c. 1º
08008 BARCELONA
SPAIN

This person is:

☐ applicant only☒ applicant and inventor☐ inventor only (If this check-box
is marked, do not fill in below.)State (that is, country) of nationality:
ESState (that is, country) of residence:
ESThis person is applicant
for the purposes of:☐ all designated
States☐ all designated States except
the United States of America☒ the United States
of America only☐ the States indicated in
the Supplemental Box☐ Further applicants and or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf
of the applicant(s) before the competent International Authorities as:

☒ agent☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

CARPINTERO LÓPEZ, Francisco
Herrero & Asociados, S.L.
C/Alcalá, 35
28014 MADRID
SPAIN

Telephone No.

+34915227420

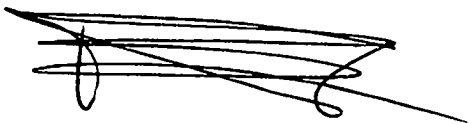
Facsimile No.

+34915226249

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No.V DESIGNATION OF STATES	
The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):	
Regional Patent	
☒ AP	ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
☒ EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
☒ EP	European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
☒ OA	OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)
National Patent (if other kind of protection or treatment desired, specify on dotted line):	
☒ AE	United Arab Emirates
☒ AG	Antigua and Barbuda
☒ AL	Albania
☒ AM	Armenia
☒ AT	Austria
☒ AU	Australia
☒ AZ	Azerbaijan
☒ BA	Bosnia and Herzegovina
☒ BB	Barbados
☒ BG	Bulgaria
☒ BR	Brazil
☒ BY	Belarus
☒ BZ	Belize
☒ CA	Canada
☒ CH and LI	Switzerland and Liechtenstein
☒ CN	China
☒ CR	Costa Rica
☒ CU	Cuba
☒ CZ	Czech Republic
☒ DE	Germany
☒ DK	Denmark
☒ DM	Dominica
☒ DZ	Algeria
☒ EE	Estonia
☒ ES	Spain
☒ FI	Finland
☒ GB	United Kingdom
☒ GD	Grenada
☒ GE	Georgia
☒ GH	Ghana
☒ GM	Gambia
☒ HR	Croatia
☒ HU	Hungary
☒ ID	Indonesia
☒ IL	Israel
☒ IN	India
☒ IS	Iceland
☒ JP	Japan
☒ KE	Kenya
☒ KG	Kyrgyzstan
☒ KP	Democratic People's Republic of Korea
☒ KR	Republic of Korea
☒ KZ	Kazakhstan
☒ LC	Saint Lucia
☒ LK	Sri Lanka
☒ LR	Liberia
☒ LS	Lesotho
☒ LT	Lithuania
☒ LU	Luxembourg
☒ LV	Latvia
☒ MA	Morocco
☒ MD	Republic of Moldova
☒ MG	Madagascar
☒ MK	The former Yugoslav Republic of Macedonia
☒ MN	Mongolia
☒ MW	Malawi
☒ MX	Mexico
☒ MZ	Mozambique
☒ NO	Norway
☒ NZ	New Zealand
☒ PL	Poland
☒ PT	Portugal
☒ RO	Romania
☒ RU	Russian Federation
☒ SD	Sudan
☒ SE	Sweden
☒ SG	Singapore
☒ SI	Slovenia
☒ SK	Slovakia
☒ SL	Sierra Leone
☒ TJ	Tajikistan
☒ TM	Turkmenistan
☒ TR	Turkey
☒ TT	Trinidad and Tobago
☒ TZ	United Republic of Tanzania
☒ UA	Ukraine
☒ UG	Uganda
☒ US	United States of America
☒ UZ	Uzbekistan
☒ VN	Viet Nam
☒ YU	Yugoslavia
☒ ZA	South Africa
☒ ZW	Zimbabwe
☐	Check-box reserved for designating States which have become party to the PCT after issuance of this sheet:
Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)	

Box No. VI PRIORITY CLAIM		☐ Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1)				
item (2)				
item (3)				
☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s):				
* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.				
Box No. VII INTERNATIONAL SEARCHING AUTHORITY				
Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):		Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):		
ISA / EP		Date (day/month/year)	Number	Country (or regional Office)
Box No. VIII CHECK LIST; LANGUAGE OF FILING				
This international application contains the following number of sheets: request : 3 description (excluding sequence listing part) : 11 claims : 5 abstract : 1 drawings : sequence listing part of description : Total number of sheets : 20		This international application is accompanied by the item(s) marked below: 1. ☒ fee calculation sheet 2. ☐ separate signed power of attorney 3. ☐ copy of general power of attorney; reference number, if any: 4. ☐ statement explaining lack of signature 5. ☐ priority document(s) identified in Box No. VI as item(s): 6. ☐ translation of international application into (language): 7. ☐ separate indications concerning deposited microorganism or other biological material 8. ☐ nucleotide and/or amino acid sequence listing in computer readable form 9. ☐ other (specify):		
Figure of the drawings which should accompany the abstract:		Language of filing of the international application: ENGLISH		
Box No. IX SIGNATURE OF APPLICANT OR AGENT				
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).				
				
FRANCISCO CARPINTERO LOPEZ				

1. Date of actual receipt of the purported international application: 27 NOV 2000		2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): ISA / EP		6. ☒ Transmittal of search copy delayed until search fee is paid.

Date of receipt of the record copy
by the International Bureau:

For International Bureau use only

PROCESS FOR PREPARING AQUEOUS EXTRACTS OF PLANTS AND EXTRACTS SO OBTAINED

FIELD OF THE INVENTION

The present invention relates to a process for preparing aqueous extracts of plants and to the aqueous extracts thus obtained, some of which find application in medicine, particularly in the treatment of immune suppressant diseases or in the treatment of viral diseases.

BACKGROUND OF THE INVENTION

Plants and, in general, vegetals are still an important source of active compositions and compounds employed in medicine. New plants, new compounds present in plants or even modifications of compounds present in plants are of potential interest to the phitochemical industry.

The methods employed in the extraction of the components of vegetals and plants are of great importance regarding not only the yields of the compounds to be obtained, but also the chemical nature of the compounds which can in fact be gained.

The usual methods employed in the phitochemical industry are based on the extraction of the comminuted plant or vegetal with water or steam, with organic solvents, or with mixtures of water and organic solvents such as water and alcohols. The inclusion of a maceration step is also well known in the art. Finally, the separation of the aqueous extract from the solid phase can be effected by conventional methods such as decantation, centrifugation or filtration. Additional chemical treatments to modify the structure of the compounds present in the plants can also be effected. For more information on the subject, see Dr. Pio Font Quer, "Medicinal Plants. The updated Discorides" Ed. Labor, S.A., 12th Edition, 1990.

The French patent FR 2733419 describes the preparation of extracts of a mixture of at least three different plants selected from the genus *Geranium*, *Plantago* and *Calendula* by steeping 300-400 g of fresh *Geranium robertianum* leaves, 10-50 g of dried *Plantago lanceolata* leaves and 10-50 g dried *Calendula officinalis* leaves in 3 l. of water at 15-30 °C for 3-15 days. According to FR 2733419, the composition thus obtained finds application in the treatment of cancer. However, a non-

satisfactory activity has been showed by these extracts, as reflected in the examples below.

The European patent application EP 0 934 746 A discloses the preparation of an aqueous extract of plants from the genus *Geranium* and *Plantago* as well as from the species *Calendula officinalis*, wherein said extracts are obtained from the following amounts in grams of said plants in water: 10 to 60 of dried *Geranium sibiricum* or 300 to 360 of fresh *Geranium sibiricum*, 10 to 60 of dried *Plantago lanceolata*, and 10 to 60 of dried *Calendula Officinalis* in 300 grams of water. The method for producing said aqueous extracts comprises macerating the comminuted plants in water before press-filtering the mixture and submitting it to a centrifugal treatment. According to EP 0 934 746 A, this extract may be used in oncological practice as part of a cancer therapeutic program. However, non-satisfactory activity has been showed by these extracts as reflected in the examples below.

There is, thus, a need in the art for methods for preparing alternative extracts of plants which can be used as therapeutic agents, and which eventually can provide access to new compounds.

SUMMARY OF THE INVENTION

The present invention provides a method for preparing aqueous extracts of vegetals, particularly of plants, as well as the compositions obtained by this method, some of which find application in medicine, particularly in the treatment of immune-suppressant diseases such as cancer, tuberculosis, influenza, common cold, allergies, lupus erythematosus, psoriasis and AIDS, or in the treatment of viral diseases such as hepatitis.

An aspect of the invention relates thus to a method for preparing aqueous extracts of vegetals, particularly of plants, which comprises the following steps:

- a) Decontamination of the plant
- b) Comminuting the plant.
- c) Treatment of the comminuted plant with a laser radiation.
- d) Suspension of the mixture obtained in step c) in water.
- e) Maceration of the suspension obtained in step d).

f) Separation of the resulting liquid.

A second aspect of the invention relates to the compositions or aqueous extracts (hydrolates) obtained by the present method.

A further aspect of the invention relates to the use of the present composition as therapeutic agent in the treatment of immune suppressant diseases such as cancer, tuberculosis, influenza, common cold, allergies, lupus erythematosus, psoriasis and AIDS; or in the treatment of viral diseases such as hepatitis.

A further aspect of the invention relates to pharmaceutical compositions comprising the aqueous extracts obtained by the present method.

The method of the invention differs from those of the cited prior art in the fact that the comminuted plant is treated with a laser radiation.

As demonstrated in the examples below, the treatment of the comminuted plants with the laser results in either the presence of new activities or in unexpectedly high increments of the activities of the extracts. Therefore, the extracts thus obtained have necessarily to be different from those obtained by methods which do not effect the laser treatment.

DETAILED DESCRIPTION OF THE INVENTION

As mentioned above, the first aspect of the invention relates to a method for preparing aqueous extracts of vegetals, particularly of plants, which comprises the steps of:

- a) Decontamination of the plant
- b) Comminuting the plant.
- c) Treatment of the comminuted plant with a laser radiation.
- d) Suspension of the mixture obtained in step c) in water.
- e) Maceration of the suspension obtained in step d).
- f) Separation of the resulting liquid.

By the term "plant" it is understood either a unit or several units of the same species, or several units of different species, or part or parts of a plant such as stems, leaves, flowers, etc.

5 The decontamination (step a) is effected by washing the plant with water. The amount of water employed in this step is not determinant, and can be varied depending on the contamination state of the plant. Although higher and lower temperatures are not discarded, the water temperature should be between 10 and 40 °C, preferably between 20 and 35°C, and most preferably 28°C. A washing tunnel
10 can be employed to facilitate this step. Both the amount of water and the residence time of the plant in the washing tunnel are not determinant, and can therefore be varied depending on the contamination state of the plant. The washing step can be carried out several times, with a drying step in between. This drying step is preferably effected by placing the plant in the sun.

15 Once the plant has been thoroughly decontaminated, it is comminuted (step b) by conventional methods such as a comminuting machine or even manually. Although higher and lower temperatures are not discarded, the temperature at which the plant is comminuted should be between 10 and 40 °C.

20 The comminuted plant is next subjected to a treatment with laser radiation (step c). As source of the laser radiation, a red linear laser diode with a capability of harmonic generation in wavelengths within the range of 150 to 810 nm is preferably employed. The wavelength of the laser radiation is more preferably of 200 to 400
25 nm and most preferably of 250 nm. The power of the laser radiation is preferably of 1 to 60 watts, more preferably of 10 to 30 watts and most preferably of 20 watts. The spot is preferably of 1 to 6 mm, more preferably of 2 to 5 mm and most preferably of 4 mm of diameter. The comminuted plant is exposed to the laser radiation so that the whole or most of the mixture is irradiated. This is achieved either by displacing
30 manually the laser generator through the comminuted plant, or by passing the comminuted matter on a conveyor belt through a set of several laser generators. Preferably each kilogram of the comminuted matter is treated with the laser radiation for a period of 3 to 10 minutes, more preferably for a period of 5 minutes. Although higher and lower temperatures are not discarded, the temperature at which the
35 comminuted plant is treated with the laser radiation should be between 10 and 40 °C.

The laser treated matter is next suspended in water (step d). Any commercial mineral water can be employed in this step. The suspension is effected so that 50 to 300, preferably 100 to 250, grams of the laser treated matter are present per litre of water. Although higher and lower temperatures are not discarded, the temperature at which the comminuted plant is suspended in water should be between 10 and 40 °C.

The suspension is then kept for a period of between 5 to 20 days, preferably of 7 to 15 days, at a temperature of 2 to 10 °C, preferably of 4 to 8°C, so that maceration of the mixture takes place (step e).

Finally, after the maceration step, a separation of the liquid phase from the solid phase is effected (step f). The solids can be pressed to facilitate the separation. The separation can be achieved by decantation alone or, preferably, by decantation followed by filtration. The filtration is preferably effected under pressure. Most preferably three consecutive press-filtrations are effected with filters of 5 µm, 1 µm and 0.22 µm. Although higher and lower temperatures are not discarded, the temperature at which the separation is effected should be between 10 and 40 °C.

The process of the invention can be applied to any kind of plants, both monocotyledonae and dicotyledonae. It can be applied to mixtures of different plants. The whole plant can be submitted to the method of the invention, although leaves and flowers are preferred.

Non limitative examples of families of plants to which the method of the invention can be applied are: *Asteraceae*, *Rosaceae*, *Crucifrae*, *Labiatae*, *Equisetaceae*, *Saxifraganceae*, *Compositae*, *Araliaceae* and *Umbeliferae*. Non limitative examples of species of plants to which the present method can be applied are: *Mentha sativa*, *Pimpinella anisum*, *Eleutherococcus senticosus*, *Equinacea angustifolia*, *Symphytum officinalis* and *Equisetum arvense*. The preferred species to which the method of the invention can be applied are *Calendula officinalis*, *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album*.

The aqueous extracts (hydrolates or compositions) obtained by the method of the invention constitute the second aspect of the invention. Thus, compositions resulting from the application of the present method to the non limitative examples: *Mentha sativa*, *Pimpinella anisum*, *Eleutherococcus senticosus*, *Equinacea*

angustifolia, *Symphytum officinalis* and *Equisetum arvense* fall within the scope of the invention. Of special interest are the aqueous extracts obtained by applying the method of the invention to *Calendula officinalis* and to the mixture of *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album*, which also fall within the scope of the invention.

It has been found that some of the aqueous extracts obtained according to the method of the invention find application in medicine. This constitutes, as mentioned above, the third aspect of the invention.

The aqueous extract obtained by applying the method of the invention to *Calendula officinalis*, and, especially, the aqueous extract obtained by applying the method of the invention to the flowers of this plant presents activity as immune stimulator. This activity being unexpectedly extremely high, as demonstrated in the examples showed below. It is believed, without wanting to be bound to this theory, that the present extract acts stimulating the lymphocyte transformation activity of the lymphocytes T, B and macrophages. The extract obtained by applying the method of the invention to *Calendula officinalis* finds, thus, application in the treatment of immune-suppressant diseases. Non limitative examples of these diseases are cancers such as hepatic carcinoma, lung cancer, kidney cancer, colon cancer, breast cancer, prostate cancer or prostatic adenocarcinoma; brain cancers such as astrocytoma and glioblastoma; cervix cancer and blade cancer; tuberculosis, influenza, common cold, allergies, lupus erythematosus psoriasis and AIDS.

Moreover, the aqueous extract obtained by applying the method of the invention to the mixture of the plants *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album* and, especially, the aqueous extract obtained by applying the method of the invention to the mixture of the leaves of the plants *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album* unexpectedly presents antiviral activity. More specifically, this extract is especially active against the virus of hepatitis A, B, C, D and E. This activity being extremely high as demonstrated in the examples showed below. Furthermore, this extract also presents a high regulatory activity of the metabolism of transaminases and bilirrubine, as well as activity as stimulator of the hepatocytic regeneration. Therefore, the extract obtained by applying the method of the invention to *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album* finds application in the treatment of viral diseases. Non limitative examples of these diseases are hepatitis A, B, C, D and E. This extract finds also application in the

treatment of liver pathologies related to high levels of transaminases and bilirrubine. Non limitative examples of such diseases are hepatitis A, B, C, D and E; hepatic cirrhosis and hepatic carcinoma.

5 According to the studies and experiments made by the inventor, it is believed, without wanting to be bound to this theory, that the laser treatment catalyses reactions between certain compounds of the plants and/or facilitates the extraction of certain compounds of the plants, so that the presence of these compounds in the extracts results in the unexpected activities referred above.

10 A further aspect of the invention relates to pharmaceutical compositions comprising the aqueous extracts obtained by the present method.

15 The aqueous extracts according to the present invention can be employed either as such or lyophilised for preparing the pharmaceutical compositions. It can be administrated either separately, as aqueous extract or lyophilised, or in the form of pharmaceutical preparations. The drug combination is in the form of a formulation which (1) contains the extract according to the invention alone; (2) contains one or more appropriate binders, carriers and/or further auxiliary materials, and (3) may
20 further contain additional therapeutically active substances.

25 The carrier materials, binders and/or auxiliary materials must be pharmaceutically and pharmacologically tolerable, so that they can be combined with the other components of the formulation or preparation and do not exert adverse effects on the organism treated .

30 The formulations include those which are suitable for oral or parenteral (including subcutaneous, intradermal, intramuscular and intravenous) administration, even though the best route of administration is dependent on the patient's status.

35 The formulations can be in the form of single doses. The formulations are prepared according to methods known in the field of pharmacology. The appropriate quantities of active substances suitable for administration may vary as a function of the particularly field therapy. In general, the active substance concentration in a single-dose formulation is 5% to 95% of the total formulation.

The invention provided by the application is illustrated by the examples presented hereinbelow.

Example 1: Preparation of an aqueous extract of flowers of *Calendula officinalis* according to a standard method (comparative example).

500 g. of flowers of *Calendula officinalis* are placed in a wash tunnel and subjected to a thorough wash with water at about 28°C. The flowers are next comminuted with a comminuting machine. The resultant 500 g of comminuted matter are next suspended in 2 litres of water at a temperature of about 20 °C. The suspension is then kept for 12 days at a temperature of 4 °C. Finally, the separation of the liquid and the solid phase is effected, first by decantation of the liquid (the solids are pressed to facilitate the separation), and then, by three consecutive press-filtrations with filters of 5, 1 and 0.22 µm at a temperature of about 20 °C. The process yields approximately 1.7 litres of a solution (aqueous extract) of an ochre colour.

Example 2: Preparation of an aqueous extract of flowers of *Calendula officinalis* according to the method of the invention.

500 g. of flowers of *Calendula officinalis* are placed in a wash tunnel and subjected to a thorough wash with water at about 28°C. The flowers are next comminuted with a comminuting machine. The resultant 500 g of comminuted matter are subjected to a treatment with a red linear laser diode with a capability of harmonic generation in a wavelength of 250 nm, a power of 20 watts and a spot of 4 mm of diameter. The treatment is effected by manually displacing the laser generator through the comminuted matter during 2.5 minutes, so that the whole or most of the mixture is irradiated. The laser treated matter is next suspended in 2 litres of water at a temperature of about 20 °C. The suspension is then kept for 12 days at a temperature of 4 °C. Finally, the separation of the liquid and the solid phase is effected, first by decantation of the liquid (the solids are pressed to facilitate the separation), and then, by three consecutive press-filtrations with filters of 5, 1 and 0.22 µm at a temperature of about 20 °C. The process yields approximately 1.7 litres of a solution (aqueous extract) of an ochre colour.

Examples 3-14:

The aqueous extracts of the plants listed below were prepared according to the procedures of examples 1 and 2. The parts of the plants which were subjected to the processes mentioned above are indicated in brackets. *Equisetum arvense* (stems),

Symphytum officinalis (leaves), *Equinacea angustifolia* (leaves and flowers), *Eleutherococcus senticosus* (leaves), *Pimpinella anisum* (leaves and flowers), and *Mentha sativa* (leaves).

The aqueous extracts obtained in the examples 1-14 were tested in order to establish their activity as immune stimulator by quantifying the lymphocyte transformation activity (LTA). By lymphocyte transformation activity it is meant the fact that the lymphocytes are transformed from a dormant to an active state, which is necessary to fight diseases through an immunological mechanism, or to restore the immune system, which might be weakened by different factors. These tests were performed in vitro by adding the extracts to lymphocytes isolated from mice according to the literature reference Max, W. et al., *Journal of Natural Products*, vol. 54, no. 6, pp. 1531-1542 (1991). The incorporation of thymidine, which means replication of DNA, was monitored. This incorporation is indicative both of an increase in lymphocyte number and an increase in lymphocyte activity. The results are summarised in table 1.

Table 1

Examples	Plant	Increase LTA (%) (Standard method)	Increase LTA (%) (Method including laser treatment)
1/2	<i>Calendula officinalis</i>	+ 277	+ 1204
3/4	<i>Equisetum arvense</i>	+ 26	+ 123
5/6	<i>Symphytum officinalis</i>	+ 43	+ 211
7/8	<i>Echinacea angustifolia</i>	+ 98	+ 270
9/10	<i>Eleutherococcus senticosus</i>	+ 106	+ 280
11/12	<i>Pimpinella anisum</i>	+ 11	+ 26
13/14	<i>Mentha sativa</i>	+ 12	+ 28

From the results showed in table 1, it is clear how the aqueous extracts prepared according to the method of the invention present higher increases in the lymphocyte transformation activity values than the aqueous extracts obtained according to the standard methods, i.e., extraction without laser treatment. Furthermore, it is really surprising the extremely high increase in the lymphocyte

transformation activity value showed by the extract of *Calendula officinalis* obtained according to the method of the invention.

5 **Example 15:** Preparation of an aqueous extract of the leaves of the plants *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album* according to a standard method (comparative example).

250 g. of leaves of *Agrimonia eupatoria*, 250 g. of leaves of *Lepidium latifolium* and 250 g. of leaves of *Lamium album*, are placed in a wash tunnel and subjected to a thorough wash with water at about 28°C. The leaves were next
10 comminuted with a comminuting machine. The resultant 750 g of comminuted matter are next suspended in 3 litres of water at a temperature of about 20 °C. The suspension is then kept for 12 days at a temperature of 4 °C. Finally, the separation of the liquid and the solid phase is effected, first by decantation of the liquid (the solids are pressed to facilitate the separation), and then, by three consecutive press-
15 filtrations with filters of 5, 1 and 0.22 µm at a temperature of about 20 °C. The process yields approximately 2.7 litres of a solution (aqueous extract) of an dark green colour.

20 **Example 16:** Preparation of an aqueous extract of the leaves of the plants *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album* according to the method of the invention.

250 g. of leaves of *Agrimonia eupatoria*, 250 g. of leaves of *Lepidium latifolium* and 250 g. of leaves of *Lamium album*, are placed in a wash tunnel and subjected to a thorough wash with water at about 28°C. The leaves were next
25 comminuted with a comminuting machine. The resultant 750 g of comminuted matter are submitted to a treatment with a red linear laser diode with a capability of harmonic generation in a wavelength of 250 nm, a power of 20 watts and a spot of 4 mm of diameter. The treatment is effected by manually displacing the laser generator through the comminuted matter during 4 minutes, so that the whole or most of the
30 mixture is irradiated. The laser treated matter is next suspended in 3 litres of water at a temperature of about 20 °C. The suspension is then kept for 12 days at a temperature of 4 °C. Finally, the separation of the liquid and the solid phase is effected, first by decantation of the liquid (the solids are pressed to facilitate the separation), and then, by three consecutive press-filtrations with filters of 5, 1 and
35 0.22 µm at a temperature of about 20 °C. The process yields approximately 2.7 litres of a solution (aqueous extract) of an dark green colour.

The aqueous extracts obtained in the examples 15 and 16 were employed in clinical tests on 28 human beings suffering from different hepatic diseases and, consequently, presenting high values of transaminases (GOT, GPT, GGT), bilirrubine and high viral charges. Those patients treated with the extract obtained in example 15 presented, after three months of treatment, a slight decrease in the transaminases and no variation of the viral charges. However, those patients treated with the extract obtained in example 16 surprisingly presented, after two months of treatment, a symptomatic recovery, normal values of transaminases and bilirrubine, as well as an important decrease of the viral charges, even in the case of hepatitis C of strain 1-B and mutated virus.

CLAIMS

1. Method for preparing aqueous extracts of plants which comprises the following steps:
 - a) Decontamination of the plant
 - b) Comminuting the plant.
 - c) Treatment of the comminuted plant with a laser radiation.
 - d) Suspension of the mixture obtained in step c) in water.
 - e) Maceration of the suspension obtained in step d).
 - f) Separation of the resulting liquid.
2. Method according to claim 1, wherein the method is applied to a plant unit, to several plant units of the same species or to several plant units of different species.
3. Method according to any precedent claim, wherein the method is applied to a part or parts of a plant such as stems, leaves or flowers.
4. Method according to any precedent claim, wherein the decontamination is effected with water, preferably in a washing tunnel.
5. Method according to any precedent claim, wherein the comminuting is effected manually or with a comminuting machine.
6. Method according to any precedent claim, wherein the treatment with the laser radiation is effected with a red linear laser diode with a capability of harmonic generation in wavelengths within the range of 150 to 810 nm, a power of 1 to 60 watts and a spot of 1 to 6 mm of diameter.
7. Method according to claim 6, wherein the wavelength is within the range of 200 to 400 nm, preferably 250 nm, the power of 20 watts and the spot of 4 mm of diameter.
8. Method according to any precedent claim, wherein each Kilogram of the comminuted matter is treated with the laser radiation for a period of 3 to 10 minutes, preferably for a period of 5 minutes.

9. Method according to any precedent claim, wherein the suspension is effected so that 50 to 300, preferably 100 to 250 grams of the laser treated matter are present per litre of water.
10. Method according to any precedent claim, wherein the suspension is kept for a period of between 5 to 20 days, preferably 7 to 15 days, at a temperature of 2 to 10 °C, preferably 4 to 8 °C, so that maceration takes place.
11. Method according to any precedent claim, wherein the liquid phase separated from the solid phase by effecting a decantation followed by a filtration consisting of three consecutive press-filtrations with filters of 5, 1 and 0.22 µm.
12. Method according to any precedent claim wherein the method is applied to monocotyledonae or dicotyledonae plants.
13. Method according to any precedent claim, wherein the plant belongs to the following families: *Asteraceae*, *Rosaceae*, *Crucifrae*, *Labiatae*, *Equisetaceae*, *Saxifraganceae*, *Compositae*, *Araliceae* and *Umbeliferae*.
14. Method according to any precedent claim, wherein the plant is chosen from the following species: *Mentha sativa*, *Pimpinella anisum*, *Eleutherococcus senticosus*, *Equinacea angustifolia*, *Symphytum officinalis*, *Equisetum arvense*, *Calendula officinalis*, *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album*.
15. Method according to any precedent claim, wherein the plant is *Calendula officinalis*.
16. Method according to claim 15, wherein, the method is applied to the flowers of *Calendula officinalis*.
17. Method according to claims 1-14, wherein the method is applied to a mixture of *Agrimonia eupatoria*, *Lepidium latifolium* and *Lamium album*.
18. Method according to claim 17, wherein the method is applied to the leaves of

Agrimonia eupatoria, Lepidium latifolium and Lamium album.

19. Aqueous extracts obtainable according to any of the methods defined in claims 1-14.
20. Lyophilised aqueous extracts according to claim 19.
21. Aqueous extracts obtainable according to any of the methods defined in claims 15 and 16.
22. Lyophilised aqueous extracts according to claim 21.
23. Aqueous extracts obtainable according to any of the methods defined in claims 17 and 18.
24. Lyophilised aqueous extracts according to claim 23.
25. Aqueous extracts or lyophilised aqueous extracts according to claims 19-24 for use as therapeutic agents.
26. Aqueous extracts or lyophilised aqueous extracts according to claims 21-22 for use in the treatment of immune suppressant diseases.
27. Aqueous extracts or lyophilised aqueous extracts according to claims 21-22 for use in the treatment of cancer, tuberculosis, influenza, common cold, allergies, lupus erythematosus, psoriasis and AIDS.
28. Aqueous extracts or lyophilised aqueous extracts according to claims 21-22 for use in the treatment of hepatic carcinoma, lung cancer, kidney cancer, colon cancer, breast cancer, prostate cancer or prostatic adenocarcinoma; brain cancers such as astrocytoma and glioblastoma; cervix cancer and bladder cancer.
29. Aqueous extracts or lyophilised aqueous extracts according to claims 23, 24 for use in the treatment of viral diseases.
30. Aqueous extracts or lyophilised aqueous extracts according to claims 23, 24 for use as stimulators for the regeneration of hepatocytes.

31. Aqueous extracts according to claims 23, 24 for use in the treatment of pathologies related to high levels of transaminases and bilirrubine.
32. Aqueous extracts according to claims 23 and 24 for use in the treatment of hepatitis A, B, C, D and E; hepatic cirrhosis and hepatic carcinoma.
33. Use of the aqueous extracts or lyophilised aqueous extracts according to claims 19-24 for the manufacture of a medicament.
34. Use of the aqueous extracts or lyophilised aqueous extracts according to claims 21-24 for the manufacture of a medicament for treating immune suppressant diseases.
35. Use according to claim 34 for the manufacture of a medicament for treating cancer, tuberculosis, influenza, common cold, allergies, lupus erythematosus, psoriasis and AIDS.
36. Use according to claim 35 for the manufacture of a medicament for treating hepatic carcinoma, lung cancer, kidney cancer, colon cancer, breast cancer, prostate cancer or prostatic adenocarcinoma; brain cancers such as strocytoma and glioblastoma; cervix cancer and blade cancer.
37. Use of the aqueous extracts or lyophilised extracts according to claims 23-24 for the manufacture of a medicament for treating viral diseases.
38. Use according to claim 37 for the treatment of hepatitis A, B, C, D and E.
39. Use of the aqueous extracts or lyophilised aqueous extracts according to claims 23-24 for the manufacture of a medicament for the treatment of pathologies related to high levels of transaminases and bilirrubine.
40. Use according to claim 39 for the treatment of hepatic cirrhosis and hepatic carcinoma.
41. Use of the aqueous extracts or lyophilised aqueous extracts according to claims 23-24 for the manufacture of a medicament for use in the stimulation of hepatocytic regeneration

of hepatocytes

42. A pharmaceutical preparation comprising an aqueous extract according to claims 19-24.

5

43. The pharmaceutical preparation according to claim 42 further including a pharmaceutically acceptable vehicle.

44. The pharmaceutical preparation of claims 41 and 42 further including at least one other pharmaceutically active compound.

10

15

20

25

30

35

**PROCESS FOR PREPARING AQUEOUS EXTRACTS OF PLANTS AND
EXTRACT SO OBTAINED**

ABSTRACT

The present invention provides a method for preparing aqueous extracts of vegetals, particularly of plants, which comprises the steps of a) decontamination of the plant, b) comminuting the plant, c) treatment of the comminuted plant with a laser radiation, d) suspension of the mixture obtained in step c) in water, e) maceration of the suspension obtained in step d), and f) separation of the resulting liquid. The invention also provides the compositions obtained by the present method, some of which find application in medicine, particularly in the treatment of immune-suppressant diseases such as cancer, tuberculosis, influenza, common cold and AIDS, or in the treatment of viral diseases such as hepatitis.

56-51

ORGANIZACIÓN MUNDIAL DE LA PROPIEDAD INTELECTUAL
34, chemin des Colombettes, Apartado postal 18, CH-1211
Ginebra 20 (Suiza)
Teléfono: (4122)338 91 11 e-mail: wipo.mail@wipo.int. -
Facsimil: (4122)733 54 28

TRATADO DE COOPERACIÓN EN MATERIA DE PATENTES (PCT)

COPIA CERTIFICADA DE LA SOLICITUD INTERNACIONAL COMO FUE
PRESENTADA Y DE CUALQUIER CORRECCION EN LA MISMA

Solicitud Internacional No. PCT/IB00/01947

Fecha de presentación internacional 27 de noviembre de 2000
(27.11.00)

Ginebra,
Diciembre 11 de 2001
(11.12.01)

Oficina Internacional de la
Organización Mundial de la
Propiedad Intelectual
(OMPI)

J.-L. Baron
Jefe de Sección de la oficina
receptora PCT

REIVINDICACIONES

1. Un procedimiento para preparar extractos acuosos de plantas que comprende las siguientes etapas:
- 5 a) Descontaminación de la planta
 b) Trituración de la planta.
 c) Tratamiento de la planta triturada con una radiación láser.
 d) Suspensión de la mezcla obtenida en la etapa c)
10 en agua.
 e) Maceración de la suspensión obtenida en la etapa d).
 f) Separación del líquido resultante.
- 15 2. El procedimiento de acuerdo con la reivindicación 1, aplicándose el procedimiento a una unidad vegetal, a diversas unidades vegetales de la misma especie o a diversas unidades vegetales de diferentes especies.
- 20 3. El procedimiento de acuerdo con cualquier reivindicación anterior, aplicándose el procedimiento a una parte o a varias partes de una planta tales como tallos, hojas o flores.
- 25 4. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que la descontaminación se lleva a cabo con agua, preferiblemente en un túnel de lavado.
- 30 5. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que la trituración se

lleva a cabo manualmente o usando una máquina de trituración.

6. El procedimiento de acuerdo con cualquier
5 reivindicación anterior, en el que el tratamiento con la radiación láser se lleva a cabo con un láser diódico lineal rojo que tiene una capacidad de generación de armónicos con longitudes de onda en el intervalo de 150 a 810 nm, una potencia de 1 a 60 vatios y una mancha focal
10 de 1 a 6 mm de diámetro.

7. El procedimiento de acuerdo con la reivindicación 6, en el que la longitud de onda está en el intervalo de 200 a 400 nm, siendo preferiblemente de 250 nm, la potencia
15 es de 20 vatios y la mancha focal es de 4 mm de diámetro.

8. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que se trata cada kilogramo de materia triturada con la radiación láser
20 durante un periodo de 3 a 10 minutos, preferiblemente durante un periodo de 5 minutos.

9. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que la suspensión se lleva
25 a cabo de modo que haya de 50 a 300 gramos, preferiblemente de 100 a 250 gramos, de la materia tratada con láser por litro de agua.

10. El procedimiento de acuerdo con cualquier
30 reivindicación anterior, en el que la suspensión se deja en reposo durante un periodo de entre 5 a 20 días,

preferiblemente de 7 a 15 días, a una temperatura de 2 °C a 10 °C, preferiblemente de 4 °C a 8 °C, de modo que se produzca la maceración.

- 3 11. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que la fase líquida se separa de la fase sólida mediante una decantación seguida de una filtración que consiste en tres filtraciones a presión consecutivas con filtros de 5 µm, 1 µm y 0,22 µm.
- 10 12. El procedimiento de acuerdo con cualquier reivindicación anterior, aplicándose el procedimiento a plantas monocotiledóneas o dicotiledóneas.
- 15 13. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que la planta pertenece a las siguientes familias: *Asteraceae*, *Rosaceae*, *Cruciferae*, *Labiatae*, *Equisetaceae*, *Saxifragaceae*, *Compositae*, *Araliaceae* y *Umbeliferae*.
- 20 14. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que la planta se elige entre las siguientes especies: *Mentha sativa*, *Pimpinella anisum*, *Eleutherococcus senticosus*, *Equinacea angustifolia*, *Symphytum officinalis*, *Equisetum arvense*, *Calendula officinalis*, *Agrimonia eupatoria*, *Lepidium latifolium* y *Lamium album*.
- 25 15. El procedimiento de acuerdo con cualquier reivindicación anterior, en el que la planta es *Calendula officinalis*.
- 30

61...
60

16. El procedimiento de acuerdo con la reivindicación 15, aplicándose el procedimiento a flores de *Calendula officinalis*.

5

17. El procedimiento de acuerdo con las reivindicaciones 1-14, aplicándose el procedimiento a una mezcla de *Agrimonia eupatoria*, *Lepidium latifolium* y *Lamium album*.

10 18. El procedimiento de acuerdo con la reivindicación 17, aplicándose el procedimiento a hojas de *Agrimonia eupatoria*, *Lepidium latifolium* y *Lamium album*.

15 19. Extractos acuosos que pueden obtenerse de acuerdo con cualquiera de los procedimientos definidos en las reivindicaciones 1-14.

20 20. Los extractos acuosos liofilizados de acuerdo con la reivindicación 19.

20

21. Los extractos acuosos que pueden obtenerse de acuerdo con cualquiera de los procedimientos definidos en las reivindicaciones 15 y 16.

25 22. Los extractos acuosos liofilizados de acuerdo con la reivindicación 21.

30 23. Los extractos acuosos que pueden obtenerse de acuerdo con cualquiera de los procedimientos definidos en las reivindicaciones 17 y 18.

24. Los extractos acuosos liofilizados de acuerdo con la reivindicación 23.

25. Los extractos acuosos o los extractos acuosos liofilizados de acuerdo con las reivindicaciones 19-24 para su uso como agentes terapéuticos.

26. Los extractos acuosos o los extractos acuosos liofilizados de acuerdo con las reivindicaciones 21-22 para su uso en el tratamiento de enfermedades inmunosupresoras.

27. Los extractos acuosos o los extractos acuosos liofilizados de acuerdo con las reivindicaciones 21-22 para su uso en el tratamiento de: cáncer, tuberculosis, gripe, resfriado común, alergias, lupus eritematoso, psoriasis y SIDA.

28. Los extractos acuosos o los extractos acuosos liofilizados de acuerdo con las reivindicaciones 21-22 para su uso en el tratamiento de: carcinoma hepático, cáncer de pulmón, cáncer de riñón, cáncer de colon, cáncer de mama, cáncer de próstata o adenocarcinoma prostático; cánceres de cerebro tales como astrocitoma y glioblastoma; cáncer de cuello uterino y cáncer de vejiga.

29. Los extractos acuosos o los extractos acuosos liofilizados de acuerdo con las reivindicaciones 23 y 24 para su uso en el tratamiento de enfermedades virales.

30. Los extractos acuosos o los extractos acuosos liofilizados de acuerdo con las reivindicaciones 23 y 24 para su uso como estimuladores de la regeneración de hepatocitos.

5

31. Los extractos acuosos de acuerdo con las reivindicaciones 23 y 24 para su uso en el tratamiento de patologías relacionadas con niveles elevados de las transaminasas y la bilirrubina.

10

32. Los extractos acuosos de acuerdo con las reivindicaciones 23 y 24 para su uso en el tratamiento de: hepatitis A, B, C, D y E; cirrosis hepática y carcinoma hepático.

15

33. El uso de los extractos acuosos o de los extractos acuosos liofilizados de acuerdo con las reivindicaciones 19-24 para la fabricación de un medicamento.

20 34. El uso de los extractos acuosos o de los extractos acuosos liofilizados de acuerdo con las reivindicaciones 21-14 para la fabricación de un medicamento destinado al tratamiento de enfermedades inmunosupresoras.

25 35. El uso de acuerdo con la reivindicación 34 para la fabricación de un medicamento destinado al tratamiento de: cáncer, tuberculosis, gripe, resfriado común, alergias, lupus eritematoso, psoriasis y SIDA.

30 36. El uso de acuerdo con la reivindicación 35 para la fabricación de un medicamento destinado al tratamiento

de: carcinoma hepático, cáncer de pulmón, cáncer de riñón, cáncer de colon, cáncer de mama, cáncer de próstata o adenocarcinoma prostático; cánceres de cerebro tales como astrocitoma y glioblastoma; cáncer de cuello
5 uterino y cáncer de vejiga.

37. El uso de los extractos acuosos o los extractos liofilizados de acuerdo con las reivindicaciones 23-24 para la fabricación de un medicamento destinado al
10 tratamiento de enfermedades virales.

38. El uso de acuerdo con la reivindicación 37 para el tratamiento de la hepatitis A, B, C, D y E.

15 39. El uso de los extractos acuosos o los extractos acuosos liofilizados de acuerdo con las reivindicaciones 23-24 para la fabricación de un medicamento para el tratamiento de patologías relacionadas con niveles elevados de las transaminasas y la bilirrubina.

20

40. El uso de acuerdo con la reivindicación 39 para el tratamiento de: cirrosis hepática y carcinoma hepático.

41. El uso de los extractos acuosos o los extractos
25 acuosos liofilizados de acuerdo con las reivindicaciones 23-24 para la fabricación de un medicamento para su uso en la estimulación de la regeneración de hepatocitos.

42. Una preparación farmacéutica que incluyen un extracto
30 acuoso de acuerdo con las reivindicaciones 19-24.

65-64

43. La preparación farmacéutica de acuerdo con la reivindicación 42 que incluye además un vehículo farmacéuticamente aceptable.

5 44. La preparación farmacéutica de las reivindicaciones 41 y 42 que incluye además al menos otro compuesto farmacéuticamente activo.