Process for extracting materials from biological material

Van Spronsen, J.; Witkamp, G.; Hollmann, F.; Choi, Y.H.; Verpoorte, R.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 December 2011 (15.12.2011)

PCT

(10) International Publication Number
WO 2011/155829 A1

(51) International Patent Classification:
B01D 11/02 (2006.01) *C07F 9/54* (2006.01)
A61K 31/14 (2006.01)

(21) International Application Number:
PCT/NL2011/050407

(22) International Filing Date:
7 June 2011 (07.06.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2004835 7 June 2010 (07.06.2010) NL

(71) Applicant *(for all designated States except US)*: **UNIVERSITEIT LEIDEN** [NL/NL]; Rapenburg 70, NL-2311 EZ Leiden (NL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **VAN SPRONSEN, Jacob** [NL/NL]; Spoelhoren 1, NL-2201 VW Noordwijk (NL). **WITKAMP, Geert-Jan** [NL/NL]; Leeghwaterweg 22, NL-2661 TV Bergschenhoek (NL). **HOLLMAN, Frank** [DE/NL]; Jan ten Brinkstraat 141, NL-2522 HX Den Haag (NL). **CHOI, Young Hae** [KR/NL]; Nieuwstraat 29, NL-2312 KA Leiden (NL). **VERPOORTE, Robert** [NL/NL]; Spanjaardslaan 7, NL-2352 AK Leiden (NL).

(74) Agent: **JANSEN, C., M.**; Vereenigde, Johan de Wittlaan 7, NL-2517 JR Den Haag (NL).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

WO 2011/155829 A1

(54) **Title**: PROCESS FOR EXTRACTING MATERIALS FROM BIOLOGICAL MATERIAL

(57) **Abstract**: The invention is directed to a process for extracting materials from biological material, which process is characterized in that the naturally occurring biological material is treated with an extractant consisting of a deep eutectic solvent of natural origin or a an ionic liquid of natural origin to produce a biological extract of natural origin dissolved in the said solvent or ionic liquid.

Title: Process for extracting materials from biological material

The present invention is directed to a process for extracting materials from biological materials.

Drugs, flavors, fragrances, agrochemicals, dyes etc., both from synthetic and natural sources are often poorly soluble in water. Therefore extraction, purification, administration requires the use of less polar solvents, such as alcohols, acetone, ethyl acetate, chloroform etc. Such solvents present several problems such as: toxicity for the producer/patient/consumer, environmental problems, explosions and the like.

Ionic liquids can be environmentally benign and safe replacements for the traditional volatile organic solvents in various chemical processes. The reason that ionic liquids are considered to be 'green' solvents is their negligible vapor pressure. However, ionic liquids can have a hidden environmental cost because they are synthesized from petrochemical resources. In a lot of synthesis routes halogen atoms are involved. Halogen materials in ionic liquids are undesirable, because of the low hydrolysis stability, the high toxicity, the low biodegradability and the high disposal cost. For example, fluorinated anions such as PF_6^- and BF_4^- are sensitive to water and may release the corrosive and toxic hydrogen fluoride. Moreover, the alkyl halides used in the syntheses of many ionic liquids are greenhouse gases and ozone-depleting materials.

The reason that ionic liquids are also considered to be safe solvents is because their lack of volatility greatly reduces any chance of exposure other than by direct physical contact with skin or by ingestion. However, most conventional ionic liquids are irritating and have a toxicity comparable to common organic solvents. From biological tests it appeared that the toxicity of ionic liquids is mainly determined by the type of cation and that ionic liquids with short alkyl substituents in the cation usually have a lower toxicity.

A solution to the problems mentioned above is the development of halogen-free ionic liquids, such as ionic liquids with the alkyl sulfate, the alkyl carbonate and the sulfonate anion. It was also found that some ionic liquids with ester

groups in their alkyl side chains are biodegradable. However, these ionic liquids are still synthesized using petrochemical resources.

In WO2006/116126 a process is described for extracting biopolymers from biomass, using ionic liquids. Generally the ionic liquids described therein are of petrochemical nature. The biopolymers extracted are chitin, chitosan, collagen and keratin. Polyhydroxyalkanoate is extracted from genetically engineered plants.

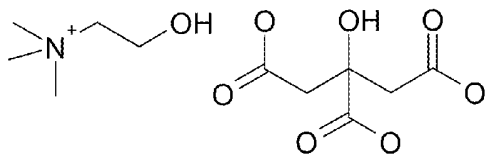
As indicated above, there is a need for an improved process for extracting organic compounds from natural sources, without the need for the use of organic solvents or other synthetic materials.

Further, there is a need for a process that can truly be considered ' green', i.e. using only natural compounds.

The invention is based on the surprising fact that some specific naturally occurring materials can suitably be used for extracting materials from biological sources. These materials are deep eutectic solvents (or mixtures) of natural origin or ionic liquids of natural origin.

Deep eutectic solvents are liquids having a melting point that is much lower than the melting points of the two compounds that form the eutectic mixture. Generally, they are formed between a variety of quaternary ammonium salts and carboxylic acids. The deep eutectic phenomenon was first described in 2003 for a mixture of choline chloride and urea in a 1:2 mole ratio, respectively. Other deep eutectic solvents of choline chloride are formed with phenol and glycerol. Deep eutectic solvents are able to dissolve many metal salts like lithium chloride and copper(II)oxide. Also, organic compounds such as benzoic acid and cellulose have great solubility in deep eutectic solvents. Compared to ordinary solvents, eutectic solvents have a very low volatility and are non-flammable. They share a lot of characteristics with ionic liquids, but they are ionic mixtures and not ionic compounds.

Instead, choline citrate is a real ionic liquid. This compound was formed by dissolving citric acid in water, followed by addition of choline hydroxide (in the ratio 2:1) dissolved in methanol. The solvent (water and methanol) was evaporated. The product choline citrate was a slightly yellow viscous liquid, and not a solid. This is probably the first naturally occurring ionic liquid found.



choline citrate

In addition to the ions, sugar-based liquids can be deep eutectic solvents.

According to the invention a process for extracting materials from biological material is provided, which process is characterized in that the naturally occurring biological material is treated with an extractant consisting of a deep eutectic solvent of natural origin or a an ionic liquid of natural origin to produce a biological extract of natural origin dissolved in the said solvent or ionic liquid.

Surprisingly it has been found that deep eutectic solvents of natural origin, as defined herein, and natural ionic liquids are suitable extractants for biological materials. These extractants are very efficient and selective, and as they are of natural origin, they are extremely efficient and suitable for extracting components from biological materials, resulting in an efficient process, providing a good yield. The melting points of the deep eutectic mixtures and ionic liquids is preferable below 25°C. The materials are thus preferably liquid at ambient temperatures.

Suitable deep eutectic solvents to be used in the present invention, i.e. mixtures of materials of natural origin, are based on mixtures of at least two compounds, substantially without chemical or ionic bonding. The first component of the solvents is preferably selected from at least one naturally occurring organic acid or an inorganic compound, such as a salt.

The second component is preferably selected from at least one naturally occurring mono- or dimeric sugar, sugar alcohol, amino acid, di or tri alkanol or choline derivatives, such as choline or phosphatidyl choline.

Said sugar or sugar alcohol may be selected from the group of sucrose, glucose, fructose, lactose, maltose, cellobiose, arabinose, ribose, ribulose, galactose, rhamnose, raffinose, xylose, sucrose, mannose, trehalose, mannitol,

sorbitol, inositol, ribitol, galactitol, erythritol, xyletol and adonitol, and, as well as their phosphates.

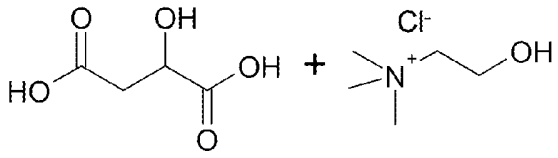
The said organic acid may be selected from malic acid, maleic acid, citric acid, lactic acid, pyruvic acid, fumaric acid, succinic acid, lactic acid, acetic acid, aconitic acid, tartaric acid, malonic acid, ascorbic acid, glucuronic acid, oxalic acid, neuraminic acid and sialic acids.

In general it is preferred that the ionic liquid or deep eutectic solvent is free of chlorine/chloride.

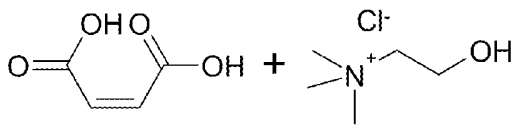
In certain solvents additionally further components may be present, such as water, phenolics, etc. These additional compounds are generally present in minor amounts, such as below 5 wt.%.

Suitable examples of inorganic compounds are the phosphates, sulfates, sulfites and halogenides, such as NaH_2PO_4, Na_2HPO_4, $NaHSO_3$, Na_2SO_4, $CaCl_2$, $MgCl_2$, KCl, NaCl and KI.

Specific examples of deep eutectic solvents are given in the table below, but also honey, maple syrup, and nectar are examples of deep eutectic solvents that can be used as extraction solvent (which are based on sugar, and small amounts of phenolics and amino acids).



Deep eutectic mixture of malic acid with choline chloride



Deep eutectic mixture of maleic acid with choline chloride

Suitable ionic liquids are based on naturally occurring anions selected from the group of malic acid, maleic acid, citric acid, lactic acid, tartaric acid glucosamine, glucuronic acid, neuraminic acid and sialic acids.

The said ionic liquid is further based on naturally occurring cations selected from the group of choline, betaine, betanine, gamma-amino butyric acid, betalaine, acetylcholine, glucosamine, glutamine, glutamate, asparagine, aspartic acid, alanine, lysine, arginine, proline, threonine, putrescine, cadaverine and choline derivatives.

In a more preferred embodiment the said ionic liquid is choline citrate.

The ratio of the components of the deep eutectic solvents and ionic liquids depends on the structure of the two or more constituents of the solvent or liquid.

For deep eutectic solvents quite often the two components are present in an equimolar ratio, although other ratio's have also been observed. Generally however, the molar ratio can be expressed in whole numbers. These ratio's generally vary from 1:1 to 4:1.

Ionic liquids are by definition salts anions and cations and accordingly the ratio is determined by the valence of the ions.

In the following tables 1 and 2 the composition and properties of deep eutectic solvent (des), as well as some solubility data have been given.

Table 1 : The composition and properties of deep eutectic solvent (des)

No.	Composition (molar ratio)	H_2O w %	water activity (40°C)	density(40°C) g/cm3	viscosity (40°C) mm2/s	E_T(NR)	T_{decom}/°C	T_g/°C
MCH	Ma:Ch:H_2O(1:1:2)	11,62%	0,195	1,246	445,9	44,81	201	-71,32
GlyCH	Gly:Ch:H_2O(2:1:1)	5,26%	0,126	1,1742	51,3	49,55	187	-101,59
MAH	Ma:ß-Ala:H_2O (1:1:3)	19,48%	0,573	1,352	174,6	48,05	164	-70,88
PMH	Pro:Ma:H_2O(1:1:3)	17,81%	0,591	1,3184	251	48,3	156	-61,29
CaGH8	CaCl2:Glc:H_2O(5/4:1:8)	31,11%	0,331	1,4904	720	54,56	137	-61,39
FCH	Fru: Ch:H_2O (1:2.5:2.5)	7,84%	0,151	1,2078	280,8	49,81	160	-84,58
XCH	Xyl: Ch:H_2O (1:2:2)	7,74%	0,141	1,2095	308,3	49,81	178	-81,8
SCH	Suc: Ch:H_2O (1:4:4)	7,40%	0,182	1,2269	581	49,72	>200	-82,96
FGSH	Fru:Glc:Suc: H_2O (1:1:1:11)	18,70%	0,662	1,3657	720	48,21	138	-50,77
GCH	Glc:Ch: H_2O (1:2,5:2,5)	7,84%	0,162	1,197	397,4	49,72	170	-83,86
PdCH	1,2Prop:Ch:H20 (1:1:1)	7,70%	0,242	1,0833	33.0	50,07	162	-109,55
LGH	Lac:Glc:H_2O(5:1:2)	7,89%	0,496	1,2495	37,0	44,81	135	-77,06
SoCH	So:Ch:H_2O(1:2,5;3)	11,17%	0,12	1,185385	138,4	49,98	>200	-89,62
XoCH	Xo:Ch:H_2O(1:2:3	11,17%	0,116	1,17841	86,1	49,72	>200	-93,33
M2	Ma:Pro:Xo:Ch:H2O(1:1:1:2,5:6)	12,58%	0,218	1,24729		49.13		-84,4
M3	Ma:Pro:Ch:H_2O(1:1:1:4)	15,62%	0,213	1,18469		49.21		-72,96

Ala = alanine
Ch = choline
Fru = fructose
Glc = glucose
Gly = glycerol
Lact - lactose
Ma = malic acid
1,2Pro = 1,2-propanediol
Pro = proline
So = sorbitol
Suc = sucrose
Xo = xylitol
Xyl = xylose

Table 2 Summary of some solubility data in some typical Des at 40 ℃ (mg/ml) (n=3)

Des	rutin	quercetin	cinnamic acid	carthamin	1, 8-dihy droxyanthraquinone	paclitaxel	ginkgolide B
LGH	8.14±0.79	1.72±0.09	13.11±0.38	1.24±0.21	0.20±0.01	5.39±0.55	1.93±0.31
GCH	121.63±1.45	20.06±0.41	8.64±0.46	27.20±0.39	0.20±0.04	0.83±0.16	5.85±0.42
PdCH	352.90±31.19	205.17±7.31	58.29±2.79	22.47±1.00	0.17±0.00	11.71±0.68	78.42±14.45
SoCH	149.21±2.61	145.84±2.82	4.50±0.21	14.05±0.66	0.08±0.01	0.59±0.01	1.70±0.01
H_2O	0.028±0.00	0.035±0.003	0.57±0.01	1.43±0.01	0.00±0.00	0.01±0.00	0.15±0.00

WO 2011/155829 PCT/NL2011/050407

The present invention deals with extracting materials from biological products. In the most general scope, all materials of biological origin may be used. Suitable examples are plants, insects, animals or micro-organisms.

From these materials a great variety of products can be isolated using the process of the present invention. More in particular the extracted or dissolved material is a flavonoid (e.g. rutin and quercetin), an anthocyanin, a colorant, an alkaloid, a terpenoid, a phenylpropanoid a glycoside, a phenolic compound, such as cinnamic acid, a ginkgolide, carthamin, an anthraquinone, paclitaxel, taxoid , a lignan, a coumarin, a cinnamic acid derivative, , azadirachtin, artimisinin, a hop bitter acid, a cannabinoid, vanillin, a polyketide, a colorant, a flavor, a fragrance, a dye, a biocide or a mixture of any of these compounds. Also proteins (enzymes), toxins, vaccins, DNA, RNA and polysaccharides may be extracted from suitable sources.

In particular, the invention is directed to extracting natural materials from natural sources, i.e. not genetically engineered. In a further preferred embodiment, valuable materials are thus extracted or dissolved, such as non-polymeric compounds, as listed above. Non-polymeric compounds are defined as those compounds that do not consist of three or more repeating units of the same moiety (monomer) or of the same type of monomers, such as amino acids or sugars.

These non-polymeric materials are, for example, suitable intermediates or products suitable in food, pharma, cosmetics and agrochemicals. More in particular it is preferred to extract flavors and fragrance from plant, vanillin from vanilla, capsaicin from *Capsicum*, hop bitter acids from hops, cannabinoids from cannabis, azadirachtin from neem plant material, paclitaxel from *Taxus* plant material, artimisinin from *Artemisia* plant material, alkaloids from *Catharanthus*, morphine and codeine from *Papaver* plant material, atropine and hyoscyamine from Solanacea plant material, galanthamine from Amaryllidaceae plants, antixoxidants from plant material, antibiotics from microorganisms,

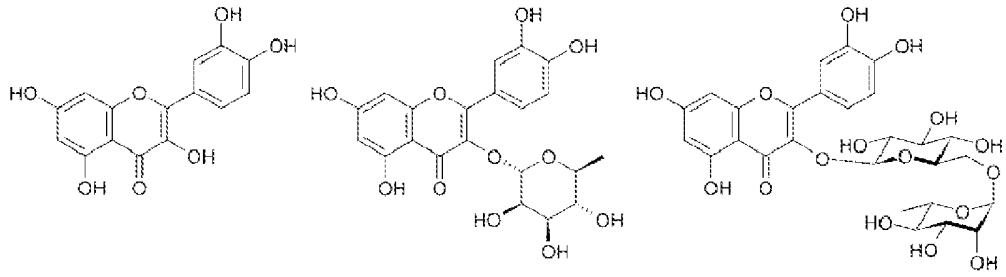
colorants from plants and microorganisms, flavonoids from plant materials, anthocyanins and carotenoids from flowers, an essential oil from a plant.

In another embodiment, specific polymeric compounds are extracted or dissolved, such as RNA, DNA, proteinic materials such as enzymes, toxins, vaccines, but excluding keratin, elastin and collagen, or polysaccharides, excluding chitin and chitosan. Preferred polysaccharides to be extracted or dissolved are lentinan, heparin, hyaluronan, alginate, agar, starch and inulineThe extracted materials can subsequently be isolated from the ionic liquid or deep eutectic solvent. It is also possible to use the solution as such for further processes. An example thereof of is the use of extracted enzymes, dissolved in the ionic liquid or eutectic solvent in enzymatic reactions. These reactions are then carried out in the said solvent or liquid. An example is the laccase reaction.

The invention is now elucidated on the basis of the following examples.

Examples

First the solubility of natural products, which are not soluble in water, was evaluated in a few selected natural deep eutectic solvents. Several flavonoids were chosen as the natural water-insoluble products, because they are one of the most abundant water-insoluble plant secondary metabolites. Up to now more than 500 flavonoids have been known. Most of these flavonoids occur in their glycosides forms (bounded to a sugar molecule) in plants. In spite of large abundance of flavonoids in plants, both the glycoside and the aglycone (non-sugar) part are not soluble in water. Thus, as a model research, the solubility of typical flavonoids including quercetin (aglycone), quercitrin (quercetin-3-O-rhamnoside) and rutin (quercetin-3-O-rhanmoglucoside), which have a very low water solubility, were tested in the naturally occurring deep eutectic solvents. The structure of these flavonoids are shown below.



Structures of quercetin, quercitrin and rutin (left to right)

As shown in the table below the three flavonoids were found to be well dissolved in the natural deep eutectic solvents, with solubilities that are 2 to 4 orders of magnitude higher as compared to their solubilities in water.

Table 3: Solubility of flavonoids in several naturally occurring deep eutectic solvents

Deep eutectic solvent	Solubility (mg/ml)		
	Quercetin	Quercitrin	Rutin
Sucrose + Choline chloride	15.63 ± 0.57	12.68 ± 0.38	2.41 ± 0.18
Glucose + Choline chloride	21.56 ± 0.94	7.81 ± 0.20	4.78 ± 0.84
Fructose + Choline chloride	23.34 ± 2.54	11.25 ± 0.64	10.94 ± 1.70
Water	0.300 ± 0.002	0.159 ± 0.001	<0.001

In order to confirm the solubility of flavonoids and the related anthocyanins, the flowers of red rose were extracted in the naturally occurring ionic liquids. It was observed that the red color metabolites are localized in the epidermis cells.

Extraction with the deep eutectic solvent fructose/glucose/malic acid (1:1:1 molar ratio) resulted in color removal from the flowers into the

deep eutectic solvent phase. The structure of the flowers remained intact, with no breakdown of the natural structure.

Claims

1. Process for extracting materials from biological material, which process is characterized in that the naturally occurring biological material is treated with an extractant consisting of a deep eutectic solvent of natural origin or a an ionic liquid of natural origin to produce a biological extract of natural origin dissolved in the said solvent or ionic liquid.

2. Process according to claim 1, wherein the said biological extract of natural origin is a non-polymeric compound, which may be used as intermediate or product in food, pharmaceutic, cosmetic or agrochemical applications.

3. Process according to claim 1, wherein the said biological extract of natural origin is a polymeric compound selected from the group of RNA, DNA, proteins, toxins, vaccins and polysaccharides, with the proviso that keratin, elastin, collagen, chitin and chitosan are excluded.

4. Process according to claim 1-3, wherein the deep eutectic solvent is based on a combination of at least one naturally occurring organic acid and at least one naturally occurring mono- or dimeric sugar, sugar alcohol, amino acid, di or tri alkanol or choline or choline derivatives, such as phosphatidyl choline.

5. Process according to claim 4, wherein the said sugar or sugar alcohol is selected from the group of sucrose, glucose, fructose, lactose, maltose, cellobiose, arabinose, ribose, ribulose, galactose, rhamnose, raffinose, xylose, sucrose, mannose, trehalose, mannitol, sorbitol, inositol, xylitol, ribitol, galactitol, erythritol and adonitol, and, as well as their phosphates.

6. Process according to claim 4 or 5, wherein the said organic acid is selected from malic acid, maleic acid, citric acid, lactic acid, pyruvic acid, fumaric acid, succinic acid, lactic acid, acetic acid, aconitic acid, tartaric

acid, ascorbic acid, malonic acid, oxalic acid, glucuronic acid, neuraminic acid and sialic acids.

7. Process according to claim 6, wherein further water is present.

8. Process according to claim 1-7, wherein the deep eutectic solvent is based on a combination of at least one inorganic compound and at least one sugar.

9. Process according to claim 8, wherein the inorganic compound is selected from phosphates, sulfates, sulfites and halogenides, such as NaH_2PO_4, Na_2HPO_4, $NaHSO_3$, Na_2SO_4, $MgCl_2$, $CaCl_2$, KCl, NaCl and KI.

10. Process according to claim 1-3, wherein the said ionic liquid is based on naturally occurring anions selected from the group of malic acid, maleic acid, citric acid, lactic acid, pyruvic acid, fumaric acid, succinic acid, lactic acid, acetic acid, aconitic acid, tartaric acid, ascorbic acid, malonic acid, glucuronic acid, oxalic acid neuraminic acid and sialic acids.

11. Process according to claim 1-3 or 10, wherein the said ionic liquid is based on naturally occurring cations selected from the group of choline, betaine, betanine, γ-amino butyric acid, ß-alaine, acetylcholine, glucosamine, alanine, glutamic acid, glutamate, asparagine, aspartic acid, lysine, arginine, proline, threonine, putrescine, cadaverine and choline and their derivatives, preferably choline citrate.

12. Process according to claim 1-11, wherein the said deep eutectic solvent of natural origin or an ionic liquid of natural origin, has a melting point below 25°C.

13. Process according to claim 1-12, wherein the extracted material is recovered from the said solvent or ionic liquid.

14. Process according to claim 1-13, wherein the said biological material is based on plants, insects, animals or micro-organisms.

15. Process according to claim 14, wherein the extracted material is a flavonoid (e.g. rutin and quercetin), an anthocyanin, a colorant, an alkaloid, a terpenoid, a phenylpropanoid a glycoside, a phenolic compound, such as cinnamic acid, a ginkgolide, carthamine, an anthraquinone, paclitaxel, a taxoid, a lignan, a coumarin, a cinnamic acid

derivative, , azadirachtin, artimisinin, a hop bitter acid, a cannabinoid, vanillin, a polyketide, a colorant, a flavor, a fragrance, a dye, a biocide or a mixture of any of these compounds.

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2011/050407

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01D11/02 A61K31/14 C07F9/54
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B01D A61K C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/116126 A2 (PROCTER & GAMBLE [US]; HECHT STACIE ELLEN [US]; NIEHOFF RAYMOND LOUIS) 2 November 2006 (2006-11-02)	1-15
Y	page 3, lines 15-31 page 6, lines 22-26 page 9, lines 5-13; examples 1-3 & US 2004/097755 A1 (ABBOTT ANDREW P [GB] ET AL ABBOTT ANDREW P [GB] ET AL) 20 May 2004 (2004-05-20) table 1A	2

A	US 2004/262578 A1 (WASSERSCHEID PETER [DE] ET AL WASSERSCHEID PETER [DE] ET AL) 30 December 2004 (2004-12-30) paragraphs [0014], [0015]; claims	1

	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 August 2011	09/08/2011

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Haderlein, Andreas

1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2011/050407

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2007/215300 A1 (UPFAL JONATHAN [AU] ET AL) 20 September 2007 (2007-09-20) paragraph [0072]; claims ----	1
A	CHIAPPE, C.: "The possibility to obtain a new geneartion of ionic liquids starting from natural compounds", GREEN CHEMICAL REACTIONS NATO SCIENCE FOR PEACE AND SECURITY SERIES, vol. 2008, 31 December 2008 (2008-12-31), pages 13-35, XP009144245, pages 19,20,25 ----	1-14
Y	WANG, ZHANG, HUANG, YIN, LI, WANG, ZENG, XIE: "New progress in ciocatalysis and biotransformation o f flavonoids", JOURNAL OF MEDICINAL PLANTS RESEARCH, vol. 4, no. 10, 18 May 2010 (2010-05-18), pages 847-856, XP002621197, Section Medium Engineering ----	2

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/NL2011/050407

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006116126 A2	02-11-2006	CA 2602145 A1	02-11-2006
		EP 1874996 A2	09-01-2008
		JP 2008535483 A	04-09-2008
US 2004262578 A1	30-12-2004	AT 387427 T	15-03-2008
		DE 10145747 A1	03-04-2003
		WO 03022812 A1	20-03-2003
		EP 1425268 A1	09-06-2004
		JP 4698945 B2	08-06-2011
		JP 2005515168 A	26-05-2005
		US 2008033178 A1	07-02-2008
US 2007215300 A1	20-09-2007	WO 2005017252 A1	24-02-2005
		BR PI0413559 A	17-10-2006
		CA 2534619 A1	24-02-2005
		CN 1836068 A	20-09-2006
		EP 1654415 A1	10-05-2006