



HU000032129T2

(19) **HU****MAGYARORSZÁG****Szellemi Tulajdon Nemzeti Hivatala**(11) Lajstromszám: **E 032 129**(13) **T2**

EURÓPAI SZABADALOM SZÖVEGÉNEK FORDÍTÁSA

(21) Magyar ügyszám: **E 11 827788**(22) A bejelentés napja: **2011. 10. 12.**(51) Int. Cl.: **C01B 33/12** (2006.01)**A61K 47/02** (2006.01)**A61K 47/46** (2006.01)

(96) Az európai bejelentés bejelentési száma:

EP 20110827788

(97) Az európai bejelentés közzétételi adatai:

EP 2627606 A2 **2012. 04. 19.**

(86) A nemzetközi (PCT) bejelentési szám:

PCT/HU 11/000098

(97) Az európai szabadalom megadásának meghirdetési adatai:

EP 2627606 B1 **2016. 08. 31.**

(87) A nemzetközi közzétételi szám:

WO 12049527

(30) Elsőbbségi adatok:

P1000547 **2010. 10. 12.** **HU**

(73) Jogosult(ak):

Egis Gyógyszergyár Zrt., 1106 Budapest (HU)**ONP Holdings SE, 1065 Nicosia (CY)**

(72) Feltaláló(k):

MIKULÁSIK, Endre, H-9783 Egyházaskér (HU)**SPAITS, Tamás, Körmend (HU)****NAGY, Kálmán, H-1025 Budapest (HU)****LUKÁCS, Gyula, H-1163 Budapest (HU)****MARKOVITS, Imre, H-1051 Budapest (HU)****FODORNÉ KOCSMÁR, Krisztina, H-1173 Budapest (HU)****GREGORNÉ BOROS, Livia, H-2141 Csömör (HU)****MÓRÁSZ, Tamás, H-1163 Budapest (HU)****SZLÁVIK, László, H-1135 Budapest (HU)****HUDÁK, Máté, H-1074 Budapest (HU)****HERÉB, Gyöngyi, H-1106 Budapest (HU)****PUSKÁS, Réka, Eszter, H-3300 Eger (HU)****VARGA, Zoltán, H-1171 Budapest (HU)****KAPUI, Imre, H-2030 Érd (HU)****CLEMENTIS, György, H-8600 Siófok (HU)****BACHER, Gábor Attila, H-1203 Budapest (HU)****BÁNKÖVI, Beatrix, H-1039 Budapest (HU)****KISS, Gitta, H-1163 Budapest (HU)****ALBRECHT, Ottó, H-1148 Budapest (HU)**

(54)

Eljárás gyógyszerészeti célra alkalmazható diatómaföld tisztítására

Az európai szabadalom ellen, megadásának az Európai Szabadalmi Közlönyben való meghirdetésétől számított kilenc hónapon belül, felszólalást lehet benyújtani az Európai Szabadalmi Hivatalnál. (Európai Szabadalmi Egyezmény 99. cikk(1))

A fordítást a szabadalmat az 1995. évi XXXIII. törvény 84/H. §-a szerint nyújtotta be. A fordítás tartalmi helyességét a Szellemi Tulajdon Nemzeti Hivatala nem vizsgálta.

(19)



(11)

EP 2 627 606 B1

(12)

EUROPEAN PATENT SPECIFICATION

(45) Date of publication and mention
of the grant of the patent:
31.08.2016 Bulletin 2016/35

(51) Int Cl.:
C01B 33/12 ^(2006.01) **A61K 47/02** ^(2006.01)
A61K 47/46 ^(2006.01)

(21) Application number: **11827788.8**

(86) International application number:
PCT/HU2011/000098

(22) Date of filing: **12.10.2011**

(87) International publication number:
WO 2012/049527 (19.04.2012 Gazette 2012/16)

(54) METHOD FOR PURIFYING DIATOMACEOUS EARTH SUITABLE FOR PHARMACEUTICAL USE

VERFAHREN ZUR REINIGUNG VON ZUR PHARMAZEUTISCHEN ANWENDUNG GEEIGNETER
KIESELERDE

PROCÉDÉ DE PURIFICATION DE TERRE DE DIATOMÉE POUR UTILISATION
PHARMACEUTIQUE

(84) Designated Contracting States:
**AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO RS SE SI SK SM TR**
Designated Extension States:
BA ME

(30) Priority: **12.10.2010 HU P1000547**

(43) Date of publication of application:
21.08.2013 Bulletin 2013/34

(73) Proprietors:
• **Egis Gyógyszergyár Zrt.**
1106 Budapest (HU)
• **ONP Holdings SE**
1065 Nicosia (CY)

(72) Inventors:
• **MIKULÁSIK, Endre**
H-9783 Egyházaskörde (HU)
• **SPAIT, Tamás**
Körmend (HU)
• **NAGY, Kálmán**
H-1025 Budapest (HU)
• **LUKÁCS, Gyula**
H-1163 Budapest (HU)
• **MARKOVITS, Imre**
H-1051 Budapest (HU)
• **FODORNÉ KOCSMÁR, Krisztina**
H-1173 Budapest (HU)
• **GREGORNÉ BOROS, Livia**
H-2141 Csömör (HU)

- **MÓRÁSZ, Tamás**
H-1163 Budapest (HU)
- **SZLÁVIK, László**
H-1135 Budapest (HU)
- **HUDÁK, Máté**
H-1074 Budapest (HU)
- **HERÉB, Gyöngyi**
H-1106 Budapest (HU)
- **PUSKÁS, Réka, Eszter**
H-3300 Eger (HU)
- **VARGA, Zoltán**
H-1171 Budapest (HU)
- **KAPUI, Imre**
H-2030 Érd (HU)
- **CLEMENTIS, György**
H-8600 Siófok (HU)
- **BACHER, Gábor Attila**
H-1203 Budapest (HU)
- **BÁNKÖVI, Beatrix**
H-1039 Budapest (HU)
- **KISS, Gitta**
H-1163 Budapest (HU)
- **ALBRECHT, Ottó**
H-1148 Budapest (HU)

(74) Representative: **Stolmár & Partner**
Patentanwälte PartG mbB
Blumenstraße 17
80331 München (DE)

(56) References cited:
EP-A1- 0 758 560 GB-A- 1 299 798
JP-A- 11 000 554

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

EP 2 627 606 B1

- | | |
|---|---|
| <ul style="list-style-type: none"> • SAN O ET AL: "Purification of diatomite powder by acid leaching for use in fabrication of porous ceramics", INTERNATIONAL JOURNAL OF MINERAL PROCESSING 20090901 ELSEVIER NLD, vol. 93, no. 1, 1 September 2009 (2009-09-01), pages 6-10, XP002677357, DOI: DOI:10.1016/J.MINPRO.2009.04.007 • GOREN R ET AL: "A study on the purification of diatomite in hydrochloric acid", SCANDINAVIAN JOURNAL OF METALLURGY APRIL 2002 BLACKWELL MUNKSGAARD DK, vol. 31, no. 2, April 2002 (2002-04), pages 115-119, XP002677358, DOI: DOI:10.1034/J.1600-0692.2002.310205.X | <ul style="list-style-type: none"> • DATABASE WPI Week 200739 Thomson Scientific, London, GB; AN 2007-404423 XP002677359, & CN 1 883 739 A (LI Z) 27 December 2006 (2006-12-27) • DATABASE WPI Week 200568 Thomson Scientific, London, GB; AN 2005-659522 XP002677360, & CN 1 618 734 A (HU X) 25 May 2005 (2005-05-25) |
|---|---|

Description**Technical field of the invention**

5 **[0001]** The present invention is related to a method for the preparation of a pharmaceutical excipient, more specifically, the purification of diatomaceous earth suitable for use in the pharmaceutical industry. The principle of the present invention resides in that during the purification method according to the present invention, only such steps are employed wherein the natural colloidal structure of diatomaceous earth remains unchanged.

Background art

10 **[0002]** Diatomaceous earth (siliceous earth, diatomite) is a mineral mainly comprising of amorphous silicone dioxide having a natural colloidal structure and high specific surface area originating from the fossile frustules (the hard and porous cell wall or external layer) of diatomaceous algae (Diatoms). Besides the frustules of diatomaceous algae, diatomaceous earth contains further minerals in various amounts (e.g. montmorillonite, caolinite, quartz, feldspar, calcite). Diatomaceous earth is a loamy, earthy, soft, easily dispersible, fine-grained, usually light-coloured silicon-containing sedimentary mineral. It is of natural origin formed from the bulk deposition of the frustules of fossile Diatoms in salty and freshwater lakes and seas of the early Jurassic period. Many occurrences of the diatomaceous earth are known worldwide.

20 **[0003]** Diatomaceous earth is used in various fields of the industry. It has been used for a long time in the chemical, cosmetical and pharmaceutical industry as a general auxiliary agent having high sorption capacity and relative lack of chemical reactivity.

[0004] During the use in the chemical industry, high specific surface area of diatomaceous earth particles is exploited. Although specific surface area of artificial amorphous silicone dioxide derivatives (e.g. Aerosil) is similarly high, diatomaceous earth exhibit far more advantageous properties during pharmaceutical formulation methods involving compression than said artificial siliceous products. Diatomaceous earth has a favourable pore structure comprising macro-meso- and micropores, which provides advantageous wetting and adsorption properties during the formulation of hydrophilic and hydrophobic materials or mixtures including emulsions or colloidal systems.

30 **[0005]** Since diatomaceous earth is a naturally occurring material of organic origin, a critical characteristic of the product is its purity. Diatomaceous earth is produced by mining the natural deposit, separating, calcining and chemically purifying the mineral. (Lloyd de Antonides 1998, Diatomite U.S. Geological Survey Mineral Commodity Summaries 1998; Tasnády Kubacska András: Ásványok). A common feature of silicon-containing preparations used in the pharmaceutical industry is that these materials are purified by calcination. Calcined diatomaceous earth has been admitted into the United States Pharmacopoeia. The principle of the manufacturing method disclosed in the pharmacopoeial monograph resides in separating crude diatomaceous earth in an air jet mill or by sieving, separating silicon-containing part from carbonates by acidic treatment and heat-treating (calcining) the resulting material at a high temperature (calcination at 900-1100 °C). During the heat treatment, volatile impurities are vaporized and thereby removed and the solid material partially melts, thus forming beads. The treated material is milled and the acidic treatment is optionally repeated in order to remove acid-soluble components. The diatomaceous earth powder is dried and sized. While this method yields a product having adequate chemical purity, the natural structure of diatomaceous earth originating from diatomaceous algae is broken, thus destroying the greater part of macro- and mesoporous structure.

[0006] There are no known purification methods in the prior art which are devoid of calcination step. For example, in published US Patent No. 2164500, the calcining step is essential. Published US Patent No. 4325844 discloses an energy-efficient method for calcination, which involves the treatment of diatomaceous earth at a temperature which is significantly higher than that applied in the method of the present invention.

45 **[0007]** Chinese Patent Application No. 100346858 is related to a method for purification of diatomaceous earth and a process for removing lubricant oil therefrom, which comprises wetting of diatomaceous earth, treating the wetted solid with an acid, preferably using sulfuric acid and filtering, neutralizing and dehydrating the solids.

[0008] Chinese Patent Application No. 1401567 is related to the purification of diatomaceous earth by acidic treatment using oxalate or phosphate, thereafter thoroughly stirring, ultrasonically treating or boiling the mixture. Subsequently the solids are allowed to settle and the iron- containing sediment is removed magnetically.

50 **[0009]** Chinese Patent Application No. 1322673 is related to a two-step method for the purification of diatomaceous earth. In the first step, the structure of the inorganic impurities is transformed by heat-treatment. Subsequently, in the second step, the material is treated with sulfuric acid while heating at low temperature until a purified silicone dioxide product is obtained.

55 **[0010]** Published Japanese Patent Application No. 200109771 1 discloses a method for purification of diatomaceous earth free of boron impurity and suitable for manufacturing silicone semiconductors, which comprises the steps of acidic treatment optionally followed by neutralization with a basic reagent; heating and separating diatomaceous earth at a suitable pH and optionally treating diatomaceous earth with a suitable salt, for example, aluminium nitrate.

[0011] San et al. (Purification of diatomite powder by acid leaching for use in fabrication of porous ceramics; Int. J. Miner. Process, vol. 93, no. 1) discloses an investigation of the purification of a raw diatomite by acid leaching conducted in hot solution for up to 240 hours.

[0012] Goren et al. (A study on the purification of diatomite in hydrochloric acid; Scandinavian Journal of Metallurgy, vol. 31, no. 2) discloses the purification of diatomaceous earth by two different processing routes.

[0013] GB 1 299 798 discloses a process for treating contaminated water by the use of chemically treated diatomaceous earth of perlite. EP 0 758 560 A1 discloses purified calcined and non-calcined diatomite products and methods for their preparation.

Summary of the invention

[0014] The disadvantage of the methods according to the prior art resides in that these methods involve one or more steps which damage or destroy the natural physical structure of diatomaceous earth, which results in a chemically purified product having a structure that differs from the natural structure of diatomaceous earth. Such products lack the superior compressibility properties of diatomaceous earth having the natural structure. At the same time, however, providing diatomaceous earth in suitable chemical purity is essential since impurities present therein can interact with the active ingredient of the formulation and such interactions may affect bioavailability or stability of the active ingredient.

[0015] The objective of the present invention is providing a new method for preparing diatomaceous earth in a chemically purified form wherein the valuable natural structure of raw diatomaceous earth is retained since the original boat-, cylinder-, comb-, box-like structures of the outer wall or layer (frustules) of Diatom algae with micro- meso- and macro-porous structure are preserved essentially unchanged. Obtaining a diatomaceous earth product with the structure of natural diatomaceous earth provides for the exploitation of advantages thereof in the pharmaceutical technology.

[0016] The principle of the present invention resides in that during the purification method according to the present invention, only such steps are employed wherein the natural colloidal structure of diatomaceous earth remains unchanged.

[0017] The method according to the present invention comprises exclusively simple physical or chemical steps (acidic or oxidative treatment, separation, drying) thus preserving the natural structure of diatomaceous earth. At the same time, it was surprisingly observed that the chemical purity of the product obtained by the method according to the present invention is better than that of the products obtained according to the methods known from the prior art.

Detailed description of the invention

[0018] According to the first aspect of the present invention, there is provided a method for the preparation of diatomaceous earth suitable for use in the pharmaceutical industry, wherein the natural structure of diatomaceous earth is retained, which comprises providing a suspension of raw diatomaceous earth in a liquid wherein diatomaceous earth is not soluble; separating diatomaceous earth from said suspension optionally by applying ultrasonic irradiation; treating the separated diatomaceous earth with an organic or inorganic acid optionally by applying simultaneous ultrasonic irradiation; heating the thus obtained diatomaceous earth at a temperature not higher than 300°C; purifying the heat-treated diatomaceous earth by oxidative treatment optionally applying simultaneous ultrasonic irradiation and drying the purified diatomaceous earth product.

[0019] According to the present invention, in the first step of the purification method, any polar or apolar organic solvents which do not dissolve the diatomaceous earth can be used for the preparation of the suspension. Preferably water is used.

[0020] Separation in the second step is preferably carried out by sieving using a suitable mesh size. Suitable mesh sizes are 0.5 mm or smaller which are suitable for retaining particles of impurities and accompanying materials to diatomaceous earth, e.g. calcite. Preferably, a sieve having 0.25 mm or smaller mesh size is used. If desired, ultrasonic irradiation can be applied during the processing of diatomaceous earth having a predetermined radiation profile and radiation power. The frequency range suitable for ultrasonic treatment (sonication) is between 16 and 42 kHz while the continuous or pulse ultrasonic power is 0.1 to 10 kW. The most advantageous frequency range is between 20 and 42 kHz with 0.5 to 2 kW ultrasonic power.

[0021] In the third step of the purification process comprising an acidic treatment of the separated diatomaceous earth, an inorganic or an organic acid is used. Preferable acids for such treatment include but are not limited to the inorganic acids such as hydrochloric acid, sulfuric acid, sulfurous acid, nitric acid, nitrous acid, phosphorous-containing acids such as hypophosphorous acid, phosphoric acid, hypophosphoric acid, orthophosphoric acid, pyrophosphoric acid, metaphosphoric acid, boron-containing acids e.g. orthoboric acid, metaboric acid, pyroboric acid, chlorine-containing oxoacids such as hypochlorous acid, hypochloric acid, chlorous acid, chloric acid, perchloric acid, bromine-containing oxoacids e.g. hypobromous acid, hypobromic acid, bromous acid, bromic acid, perbromic acid; less concentrated hydrogen fluoride and the like. Suitable organic acids include but are not limited to acetic acid, citric acid, formic acid, carbonic

acid, butyric acid, phthalic acid, tartaric acid and the like. Inorganic mineral acids, such as hydrochloric acid, nitric acid and sulfuric acid are preferred.

[0022] In most cases, the acid can be used as a concentrated acid or an aqueous solution thereof. When hydrochloric acid is used, the method is most efficient if hydrochloric acid solution having 6 to 12 % by weight concentration, preferably concentrated hydrochloric acid solution diluted at least with threefold volume of water is used. Water is preferred for the dilution of an acid, but any polar or apolar liquid can be used wherein the solubility of diatomaceous earth is less than 500 g/dm³ and which is miscible with the acid.

[0023] During the acidic treatment, acid-soluble impurities of diatomaceous earth are dissolved. The temperature of the acidic treatment is between the melting point and the boiling point of the acid or the diluted solution of the acid at atmospheric pressure. Preferably, the temperature of the acidic treatment is close the boiling point of the acidic reagent. It is especially advantageous to carry out the acidic treatment at the boiling point of the acidic reagent mixture. If desired, ultrasonic irradiation having a predetermined radiation profile and radiation power can be applied during the acidic treatment. The frequency range suitable for ultrasonic treatment is between 16 and 42 kHz while the continuous or pulse ultrasonic power is 0.1 to 10 kW. The most advantageous frequency range is between 20 and 42 kHz with 0.5 to 2 kW ultrasonic power.

[0024] The efficiency of the treatment can be improved by using oxidizing reagents e.g. hydrogen peroxide, simultaneously. However, any oxidizing agent mentioned below in connection with the oxidation step of the method can be used in this phase of purification as well.

[0025] In the fourth step of the process, diatomaceous earth subjected to acidic treatment is heat-treated in a furnace. The temperature of heat treatment according to the present invention is 300 °C or lower, preferably 250±25°C. The duration of the heat treatment is between 10 minutes and 24 hours, preferably 6 hours.

[0026] In the fifth step, the heat-treated product is subjected to a further purification by an oxidative treatment. During this step, the heat-treated diatomaceous earth is stirred in a solution of an oxidizing agent having appropriate pH at a predetermined temperature for a sufficient period, optionally simultaneously subjecting the suspension of diatomaceous earth and oxidizing agent to ultrasonic irradiation.

[0027] The scope of oxidizing agents is not limited to any particular reagent. Inorganic or organic oxidizing reagents can be used. Particularly suitable oxidizing agents are hydrogen peroxide, organic peroxides (e.g. peroxodisulfuric acid, peroxosulfuric acid), permanganic acid (HMnO₄) and salts thereof (e.g. potassium permanganate, KMnO₄) dichromic acid (H₂Cr₂O₇) and salts thereof (e.g. potassium dichromate, K₂Cr₂O₇), chromic acid or salts thereof, aqueous chlorine solution, mixtures of hydrochloric acid and hydrogen peroxide, mixtures of aqueous ammonia solution and hydrogen peroxide, oxidizing gases (e.g. oxygen, ozone, fluorine, chlorine, bromine). Particularly advantageous oxidants are hydrogen peroxide, peroxosulfuric acid and peroxodisulfuric acid or solutions thereof.

[0028] According to the method of the present invention, the oxidizing agent can be used in the form of a saturated or a diluted solution. Practically, a solution of the oxidizing reagent having 0 to 50 % by weight concentration is used. Preferably, the concentration of the oxidizing reagent can be set to 0.05 to 50, preferably 1 to 40 % by weight. During the oxidative treatment, the pH of the liquid phase has to be selected according to the oxidizing agent. In the case when hydrogen peroxide solution is used, alkaline pH is especially advantageous.

[0029] The temperature of the oxidative treatment is depending on the quality of the oxidizing agent. For example, in case of hydrogen peroxide, room temperature is preferable. The duration of the oxidative treatment is at least 1 minute, however, it is advantageous to contact the diatomaceous earth with the oxidating reagent for a longer period. Suitable period of oxidative treatment is approx. 25 minutes but depending on the composition of the diatomaceous earth to be purified and the oxidizing reactant, the duration of the treatment can be increased up to 1-3 days.

[0030] If desired, during the oxidative treatment, ultrasonic irradiation having a predetermined radiation profile and radiation power can be applied. The frequency range suitable for ultrasonic treatment is between 16 and 42 kHz while the continuous or pulse ultrasonic power is 0.1 to 10 kW. The most advantageous frequency range is between 20 and 42 kHz with 0.5 to 2 kW ultrasonic power.

[0031] The product obtained from the oxidative treatment is subsequently dried. The drying operation is carried out in a drying cabinet or in a fluid-bed dryer at atmospheric pressure or in vacuo. During the drying, the wet product is treated for a predetermined period of time at a predetermined temperature and pressure optionally using a drying fluid.

[0032] The minimum drying temperature is 50° C. It is advantageous to carry out the drying process at a temperature close to the boiling point of the solvent used in the oxidizing step. In most cases, it is especially preferable to perform the drying process at 90°C.

[0033] The drying can be carried out at atmospheric pressure or in vacuo. Preferable pressure for drying is less than 15 kPa. Using vacuum is advantageous, it is especially preferable to carry out the drying at the pressure of 20±10 torr.

[0034] The length of the drying period is at least 1 hour but, depending on the drying temperature and the solvent to be dried, it can be increased up to several days. Drying is carried out preferably for 20±0.5 hours. When drying is carried out by applying a drying fluid, the process is carried out in a fluid-bed dryer. Advantageous drying fluids are inert gases, e.g. air, nitrogen, noble gases etc.

[0035] By carrying out the method according to the present invention, a diatomaceous earth product can be obtained wherein the natural colloidal structure of diatomaceous earth is retained and which has suitable purity for use in the pharmaceutical industry. The retention of said natural colloidal structure can be assessed by imaging or surface analytical methods including but not limited to optical or electron microscopy.

[0036] The quality of diatomaceous earth produced according to the present invention can be tested and controlled using methods known in the art. As an example, methods of the corresponding pharmacopoeial monographs can be used. Silicon dioxide content can be determined on the basis of the loss of weight upon reacting diatomaceous earth with hydrogen fluoride. Metal impurities, such as arsenic and especially the heavy metals cadmium, lead and mercury can be assayed by atomic absorption spectroscopy (AAS) or by X-ray fluorescence spectroscopy (XRF). As a guidance, an XRF assay disclosed in EPA6200 method is suitable for the assay of metal impurities. Amorphous or crystalline phases can be studied by X-ray diffraction analysis.

[0037] According to a further aspect of the present invention, there is provided a purified diatomaceous earth wherein the natural colloidal structure of the material is retained, obtainable by preparing a suspension of diatomaceous earth in a liquid wherein diatomaceous earth is insoluble, separating diatomaceous earth from the suspension, treating diatomaceous earth with an inorganic or organic acid, heat-treating the thus obtained product at a temperature not higher than 300°C, subjecting the product obtained to oxidizing treatment and drying the purified product.

[0038] The method according to the present invention is demonstrated by the following examples without limiting said method to the examples only.

Examples

Example 1

Analysis results of the impurities in commercially available diatomaceous earth preparation and in diatomaceous earth purified according to the present invention

[0039] Table 1 exhibits the most important impurities of diatomaceous earth. In Table 1, the concentrations of the individual impurities (expressed in % by weight) are compared for the diatomaceous earth purified according to the method of the present invention and commercially available diatomaceous earth purified by calcination. Assays were carried out by X-ray fluorescence analysis (XRF) using a Spectro Xepos energy-dispersive X-ray fluorescence spectrometer.

[0040] Measurements were carried out using approx. 3 g sample, a 32-mm sample vial and using ProleneFilm. During the measurements, He flushing was applied. The following three targets were used:

Target:	Energy	Measurement time
1., Mo	25 keV	300 s
2., Al ₂ O ₃	50 keV	300 s
3. Bragg crystal, HOPG	12.5 keV range	300 s

[0041] During the measurements, samples are irradiated by X-ray radiation and analysis was carried out by an energy-dispersive measurement method. Calibration is carried out empirically using a normalization method.

Table 1

	Na	Mg	Al	S	Ca	Fe	P	K	Ti
Diatomaceous earth purified according to the invention	0.112	0	0.373	0.023	0.154	0.080	0.019	0.068	0.030
Celpure C1000	0.249	0	1.817	0.022	0.166	0.713	0.021	0.026	0.091
Celpure C300	0.157	0.042	0.509	0.028	0.096	0.846	0.036	0.097	0.080
Celite 535 NF	0.162	0.191	1.702	0.027	0.375	1.427	0.055	0.322	0.145
Celite 545 NF	0.154	0.187	1.622	0.020	0.372	1.432	0.049	0.319	0.145
Celite Hyflo	0.301	0.170	1.608	0.028	0.430	1.645	0.047	0.409	0.192

[0042] From the data of Table 1 it is apparent that diatomaceous earth purified according to the method of the present

invention has higher purity (i.e. the concentration of the particular impurity is lower) with regard to almost all impurities listed in Table 1 than that in case of commercially available diatomaceous earth preparations. Consequently, it can be concluded that according to the method of the present invention, the diatomaceous earth excipient having high degree of purity exceeding that of the commercially available similar products can be produced while retaining the natural colloidal structure of diatomaceous fustules.

Example 2

1. Suspending and separating

[0043] Wet raw diatomaceous earth was dispersed in a reaction vessel using 7.5 kg of water and was subsequently sieved using a 0.25-mm mesh sieve.

[0044] The purity of the product was analyzed by XRF. According to the measurements, the product contained 35 % by weight Si, 8 % by weight Ca. Loss of ignition, 16 %. Assay (expressed as silicon dioxide, SiO_2): 68 % by weight.

2. Acidic treatment

[0045] The sieved fraction wherein the size of the suspended particles is smaller than 0.25 mm, obtained in 1 was used.

[0046] Into the suspension, 2.875 kg (2.5 l) of concentrated hydrochloric acid were added in 15 ± 5 minutes while removing the evolved hydrogen sulfide containing gases by suction. After the evolution of gases subsided, the suspension was stirred at 25°C for 30 minutes. The mixture was heated until reflux temperature and kept under reflux for 24 hours. Subsequently the suspension was filtered while hot, suspended in the vessel with 7.5 kg hot water and filtered while hot. The last suspending step was repeated five times with the same amount of hot water.

[0047] The product was analyzed by XRF. Analysis: Si 50 % by weight, Ca 0.1 % by weight. Loss of ignition: 9 % by weight. Assay (expressed as silicone dioxide, SiO_2): 99 % by weight.

3. Heat treatment

[0048] The wet material was subjected to heat treatment for 6.5 ± 0.5 hours at 250°C in a furnace. The heat-treated product was subjected to XRF analysis. Analysis: Si 54 % by weight, Ca 0.1 % by weight. Loss of ignition, 3 % by weight. Assay (expressed as silicone dioxide, SiO_2), 99 % by weight.

4. Oxidative treatment

[0049] The heat-treated product was transferred into a vessel and 8.325 kg (7.5 l) of 35 % hydrogen peroxide solution and 0.5 kg of 10 % by weight sodium hydroxide solution were added. The mixture was treated by sonication for 25 minutes using an ultrasonic probe while care was exercised to prevent foaming. Subsequently, the suspension was filtered and the product was washed with 1.25 kg of water.

5. Drying

[0050] The product was dried in a drying cabinet at a temperature of 90°C spread out in a thin layer for 20 ± 0.5 hours, allowed to cool at atmospheric pressure and packaged.

[0051] The product is analyzed by XRF. Analysis: Si, 53 % by weight; Ca, 0.1 % by weight. Loss of ignition, 3 % by weight. Assay (expressed as silicone dioxide, SiO_2): 99 % by weight.

Claims

1. Method for purifying diatomaceous earth wherein the natural colloidal structure of the material is retained, which comprises preparing a suspension of raw diatomaceous earth in liquid wherein diatomaceous earth is insoluble, separating diatomaceous earth from the suspension, treating diatomaceous earth with an inorganic or organic acid, whereby a mineral acid, preferably hydrochloric acid, sulfuric acid or nitric acid, an inorganic acid such as phosphoric acid, an organic acid such as acetic acid and citric acid is used heat-treating the thus obtained product at a temperature not higher than 300°C , subjecting the product obtained to oxidative treatment, whereby an organic or inorganic oxidizing agent, preferably hydrogen peroxide, peroxosulfuric acid or peroxodisulfuric acid is used.

2. Method according to claim 1, wherein simultaneously to any of the steps of purification according to claim 1, ultrasonic

irradiation is applied.

3. Method according to claim 1, wherein the liquid used for preparing the suspension is water.

4. Method according to any of claims 1 to 3, **characterized in that** the diatomaceous earth is separated from the suspension by sieving.

5. Method according to claim 4, **characterized in that** sieving is carried out using a sieve with a mesh size of 0.5 mm or smaller, preferably using a sieve with a mesh size of 0.25 mm or smaller.

6. Method according to claim 1, **characterized in that** during the separation step, ultrasonic irradiation is applied.

7. Method according to any of claims 1 to 6, wherein during the acidic treatment step, water is used as diluent.

8. Method according to any of claims 1 to 6, **characterized in that** the concentration of the acidic solution is 6 to 12 % by weight, preferably using the diluent in threefold amount to the amount of the concentrated acid.

9. Method according to claim 1, **characterized in that** the efficacy of the acidic treatment is enhanced by using an oxidizing reagent.

10. Method according to any of claims 1 to 6, wherein simultaneously to the acidic treatment, ultrasonic irradiation is applied.

11. Method according to any of claims 1 to 10, **characterized in that** the heat treatment is carried out at a temperature lower than 300°C.

12. Method according to any of claims 1 to 9, wherein the heat treatment is carried out at a temperature of $250 \pm 25^\circ\text{C}$.

13. Method according to any of claims 1 to 9, **characterized in that** the diatomaceous earth is subjected to heat treatment for a period between 10 minutes and 25 hours, preferably for 6 hours.

14. Method according to any of claims 1 to 13, **characterized in that** the pH of the liquid phase is selected according to the oxidizing agent.

15. Method according to any of claims 1 to 13, **characterized in that** during the oxidizing step, 0-50 % by weight hydrogen peroxide solution is used.

16. Method according to any of claims 1 to 13, **characterized in that** the duration of the oxidizing treatment is between 1 minute and 3 days, preferably 25 minutes.

17. Method according to any of claims 1 to 13, wherein simultaneously to the oxidizing treatment, ultrasonic irradiation is applied.

18. Method according to any of claims 1 to 17, **characterized in that** the drying is carried out at a temperature between 50 and 90°C.

19. Method according to any of claims 1 to 17, wherein the drying is carried out at atmospheric pressure or in vacuo, preferably at a pressure lower than 15 kPa.

20. Method according to any of claims 1 to 17, **characterized in that** drying is carried out at 20 ± 10 Torr pressure.

21. Method according to any of claims 1 to 17, **characterized in that** the length of the drying period is between 1 hour and 3 days, preferably 20 ± 0.5 hours.

22. Method according to any of claims 1 to 21, **characterized in that** the frequency and power of the ultrasonic treatment is between 16 and 42 kHz and between 0.1 and 10 kW, preferably 20-42 kHz and 0.5-2 kW, respectively.

Patentansprüche

1. Verfahren zur Aufreinigung von kieselalgenhaltiger Erde, wobei die natürliche kolloidale Struktur des Materials beibehalten wird, welches umfasst Herstellen einer Suspension von roher kieselalgenhaltiger Erde in einer Flüssigkeit, wobei die kieselalgenhaltige Erde unlöslich ist, Trennen der kieselalgenhaltigen Erde von der Suspension, Behandeln der kieselalgenhaltigen Erde mit einer anorganischen oder organischen Säure, wobei eine Mineralsäure, vorzugsweise Salzsäure, Schwefelsäure oder Salpetersäure, einer anorganischen Säure wie Phosphorsäure, eine organischen Säure wie Ameisensäure und Zitronensäure verwendet wird, Hitzebehandeln des so erhaltenen Produkts bei einer Temperatur nicht höher als 300°, Unterziehen des erhaltenen Produkts einer oxidativen Behandlung, wobei ein organisches oder anorganisches Oxidationsmittel, vorzugsweise Wasserstoffperoxid, Peroxoschwefelsäure oder Peroxodischwefelsäure verwendet wird.
2. Verfahren gemäß Anspruch 1, wobei gleichzeitig mit irgendeinem der Aufreinigungsschritte Ultraschallbestrahlung angewendet wird.
3. Verfahren gemäß Anspruch 1, wobei die Flüssigkeit, die für die Herstellung der Suspension verwendet wird, Wasser ist.
4. Verfahren gemäß einem der Ansprüche 1 bis 3, **dadurch gekennzeichnet, dass** die kieselalgenhaltige Erde von der Suspension durch Sieben getrennt wird.
5. Verfahren gemäß Anspruch 4, **dadurch gekennzeichnet, dass** das Sieben mit einem Sieb mit einer Maschengröße von 0,5 mm oder kleiner, vorzugsweise mit einem Sieb mit einer Maschengröße von 0,25 mm oder kleiner, durchgeführt wird.
6. Verfahren gemäß Anspruch 1, **dadurch gekennzeichnet, dass** während des Trennschritts Ultraschallbestrahlung angewendet wird.
7. Verfahren gemäß einem der Ansprüche 1 bis 6, wobei während des Säurebehandlungsschritts Wasser als Verdünnungsmittel verwendet wird.
8. Verfahren gemäß einem der Ansprüche 1 bis 6, **dadurch gekennzeichnet, dass** die Konzentration der sauren Lösung 6-12 Gewichtsprozent ist, wobei vorzugsweise das Verdünnungsmittel in dreifacher Menge der Menge der konzentrierten Säuren verwendet wird.
9. Verfahren gemäß Anspruch 1, **dadurch gekennzeichnet, dass** die Effizienz der Säurebehandlung durch Verwenden eines Oxidationsmittels verbessert wird.
10. Verfahren gemäß einem der Ansprüche 1 bis 6, wobei gleichzeitig mit der Säurebehandlung Ultraschallbestrahlung angewendet wird.
11. Verfahren gemäß einem der Ansprüche 1 bis 10, **dadurch gekennzeichnet, dass** die Hitzebehandlung bei einer Temperatur niedriger als 300 °C durchgeführt wird.
12. Verfahren gemäß einem der Ansprüche 1 bis 9, wobei die Hitzebehandlung bei einer Temperatur von 250 ± 25 °C durchgeführt wird.
13. Verfahren gemäß einem der Ansprüche 1 bis 9, **dadurch gekennzeichnet, dass** die kieselalgenhaltige Erde einer Hitzebehandlung unterworfen wird für eine Dauer zwischen 10 Minuten und 25 Stunden, vorzugsweise für 6 Stunden.
14. Verfahren gemäß einem der Ansprüche 1 bis 13, **dadurch gekennzeichnet, dass** der pH der flüssigen Phase gemäß dem Oxidationsmittel ausgewählt wird.
15. Verfahren gemäß einem der Ansprüche 1 bis 13, **dadurch gekennzeichnet, dass** während des Oxidationsschrittes 0-50 Gewichtsprozent WasserstoffperoxidLösung verwendet wird.
16. Verfahren gemäß einem der Ansprüche 1 bis 13, **dadurch gekennzeichnet, dass** die Dauer der Oxidationsbehandlung zwischen 1 Minute und 3 Tagen beträgt, vorzugsweise 25 Minuten.

17. Verfahren gemäß einem der Ansprüche 1 bis 13, wobei gleichzeitig mit der Oxidationsbehandlung Ultraschallbestrahlung angewendet wird.
18. Verfahren gemäß einem der Ansprüche 1 bis 17, **dadurch gekennzeichnet** das die Trocknung bei einer Temperatur zwischen 50 und 90° durchgeführt wird.
19. Verfahren gemäß einem der Ansprüche 1 bis 17, wobei die Trocknung bei atmosphärischem Druck oder im Vakuum durchgeführt wird, vorzugsweise bei einem Druck niedriger als 15 kPa.
20. Verfahren gemäß einem der Ansprüche 1 bis 17, **dadurch gekennzeichnet, dass** die Trocknung bei 20 ± 10 Torr Druck durchgeführt wird
21. Verfahren gemäß einem der Ansprüche 1 bis 17, **dadurch gekennzeichnet, dass** die Länge der Trocknungsdauer zwischen 1 Stunde und 3 Tagen beträgt, vorzugsweise $20 \pm 0,5$ Stunden.
22. Verfahren gemäß einem der Ansprüche 1 bis 21, **dadurch gekennzeichnet, dass** die Frequenz und Leistung der Ultraschallbehandlung zwischen 16 und 42 kHz und zwischen 0,1 und 10 kW ist, vorzugsweise 20-42 kHz und 0,5-2 kW ist.

Revendications

1. Procédé de purification de terre de diatomées, dans lequel la structure colloïdale naturelle du matériau est conservée, qui comprend préparer une suspension de terre de diatomées brute dans du liquide dans lequel la terre de diatomées est insoluble, séparer la terre de diatomées de la suspension, traiter la terre de diatomées avec un acide inorganique ou organique, moyennant quoi un acide minéral, de préférence l'acide chlorhydrique, l'acide sulfurique ou l'acide nitrique, un acide inorganique tel que l'acide phosphorique, un acide organique tel que l'acide acétique et l'acide citrique est utilisé, traiter thermiquement le produit ainsi obtenu à une température ne dépassant pas 300°C, soumettre le produit obtenu à un traitement oxydatif, moyennant quoi un agent d'oxydation organique ou inorganique, de préférence du peroxyde d'hydrogène, de l'acide peroxosulfurique ou de l'acide peroxodisulfurique est utilisé.
2. Procédé selon la revendication 1, dans lequel simultanément à l'une quelconque des étapes de purification selon la revendication 1, une irradiation ultrasonique est appliquée.
3. Procédé selon la revendication 1, dans lequel le liquide utilisé pour préparer la suspension est de l'eau.
4. Procédé selon l'une quelconque des revendications 1 à 3, **caractérisé en ce que** la terre de diatomées est séparée de la suspension par tamisage.
5. Procédé selon la revendication 4, **caractérisé en ce que** le tamisage est effectué en utilisant un tamis avec une largeur de maille de 0,5 mm ou inférieure, de préférence en utilisant un tamis avec une largeur de maille de 0,25 mm ou inférieure.
6. Procédé selon la revendication 1, **caractérisé en ce qu'**au cours de l'étape de séparation, une irradiation ultrasonique est appliquée.
7. Procédé selon l'une quelconque des revendications 1 à 6, dans lequel au cours de l'étape de traitement acide, de l'eau est utilisée comme diluant.
8. Procédé selon l'une quelconque des revendications 1 à 6, **caractérisé en ce que** la concentration de la solution acide est de 6 à 12 % en poids, de préférence en utilisant le diluant en une quantité triple de la quantité de l'acide concentré.
9. Procédé selon la revendication 1, **caractérisé en ce que** l'efficacité du traitement acide est amplifiée en utilisant un réactif d'oxydation.
10. Procédé selon l'une quelconque des revendications 1 à 6, dans lequel simultanément au traitement acide, une irradiation ultrasonique est appliquée.

EP 2 627 606 B1

11. Procédé selon l'une quelconque des revendications 1 à 10, **caractérisé en ce que** le traitement thermique est effectué à une température inférieure à 300 °C.
- 5 12. Procédé selon l'une quelconque des revendications 1 à 9, dans lequel le traitement thermique est effectué à une température de 250+/-25°C.
- 10 13. Procédé selon l'une quelconque des revendications 1 à 9, **caractérisé en ce que** la terre de diatomées est soumise à un traitement thermique pendant une période comprise entre 10 minutes et 25 heures, de préférence pendant 6 heures.
14. Procédé selon l'une quelconque des revendications 1 à 13, **caractérisé en ce que** le pH de la phase liquide est sélectionné en fonction de l'agent d'oxydation.
- 15 15. Procédé selon l'une quelconque des revendications 1 à 13, **caractérisé en ce qu'**au cours de l'étape d'oxydation, 0 à 50 % en poids de solution de peroxyde d'hydrogène sont utilisés.
16. Procédé selon l'une quelconque des revendications 1 à 13, **caractérisé en ce que** la durée du traitement d'oxydation est comprise entre 1 minute et 3 jours, de préférence 25 minutes.
- 20 17. Procédé selon l'une quelconque des revendications 1 à 13, dans lequel simultanément au traitement d'oxydation, une irradiation ultrasonique est appliquée.
- 25 18. Procédé selon l'une quelconque des revendications 1 à 17, **caractérisé en ce que** le séchage est effectué à une température comprise entre 50 et 90°C.
- 30 19. Procédé selon l'une quelconque des revendications 1 à 17, dans lequel le séchage est effectué à pression atmosphérique ou sous vide, de préférence à une pression inférieure à 15 kPa.
20. Procédé selon l'une quelconque des revendications 1 à 17, **caractérisé en ce que** le séchage est effectué à une pression de 20+/-10 Torr.
- 35 21. Procédé selon l'une quelconque des revendications 1 à 17, **caractérisé en ce que** la durée de la période de séchage est comprise entre 1 heure et 3 jours, de préférence 20+/-0,5 heures.
- 40 22. Procédé selon l'une quelconque des revendications 1 à 21, **caractérisé en ce que** les fréquence et puissance du traitement ultrasonique sont comprises entre 16 et 42 kHz et entre 0,1 et 10 kW, de préférence 20 et 42 kHz et 0,5 et 2 kW, respectivement.
- 45
- 50
- 55

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 2164500 A [0006]
- US 4325844 A [0006]
- CN 100346858 [0007]
- CN 1401567 [0008]
- CN 1322673 [0009]
- JP 2001097711 B [0010]
- GB 1299798 A [0013]
- EP 0758560 A [0013]

Non-patent literature cited in the description

- **SAN et al.** Purification of diatomite powder by acid leaching for use in fabrication of porous ceramics. *Int. J. Miner. Process*, vol. 93 (1 [0011]
- **GOREN et al.** A study on the purification of diatomite in hydrochloric acid. *Scandinavian Journal of Metallurgy*, vol. 31 (2 [0012]



EP 2 627 606 (bejelentési szám: 11827788.8)

1. Eljárás diatómaföld természetes kolloid szerkezetét megtartó módon történő tisztítására azzal jellemezve, hogy a nyers diatómaföldet a diatómaföldet nem oldó folyadékban szuszpendáljuk, a diatómaföldet a szuszpenzióból elválasztjuk, szervesen vagy szerves savval kezeljük, amelyhez mint ásványi savat előnyösen sósavat, kénsavat, salétromsavat, mint szervesen savat foszforsavat, vagy szerves savat, például ecetsavat és citromsavat használunk; az ilyen módon előállított terméket 300 °C-t meg nem haladó hőmérsékleten hőkezeljük, a nyert terméket oxidatív kezelésnek vetjük alá, amelyben szerves vagy szerves oxidálószerrel, előnyösen hidrogén-peroxidot, peroxo-kénsavat vagy peroxo-dikénsavat használunk.
2. Az 1. igénypont szerinti eljárás azzal jellemezve, hogy valamely tisztítási lépéssel egyidejűleg ultrahangos besugárzást használunk.
3. Az 1. igénypont szerinti eljárás azzal jellemezve, hogy a szuszpendáláshoz vizet alkalmazunk.
4. Az 1-3. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a diatómaföld szuszpenzióból történő elválasztása szűréssel végezzük.
5. A 4. igénypont szerinti eljárás azzal jellemezve, hogy a szűrést 0.5 mm-nél kisebb, előnyösen 0.25 mm-nél kisebb szítaméretű szűrővel végezzük.
6. Az 1. igénypont szerinti eljárás azzal jellemezve, hogy az elválasztási lépés során ultrahangos besugárzást alkalmazunk.
7. Az 1-6. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a savas kezelés során hígítószerként vizet alkalmazunk.
8. Az 1-6. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a sav oldat koncentrációja 6-12 tömegszázalék közötti, előnyösen a hígítószerrel a tömény sav mennyiségére számolva háromszoros mennyiségben használjuk.
9. Az 1. igénypont szerinti eljárás azzal jellemezve, hogy a savas kezelés hatékonyságát oxidálószerrel növeljük.
10. Az 1-6. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a savas kezeléssel egyidejűleg ultrahangos besugárzást alkalmazunk.
11. Az 1-10. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a hőkezelést 300 °C-t meg nem haladó hőmérsékleten végezzük.
12. Az 1-10. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a hőkezelést 250±25 °C hőmérsékleten végezzük.
13. Az 1-9. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a diatómaföld hőkezelésének időtartama 10 perc és 25 óra közötti, előnyösen 6 óra.

14. Az 1-13. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a folyadék fázis pH értékét az oxidálószernek megfelelően választjuk meg.
15. Az 1-13. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy az oxidatív kezelés során 0-50 tömegszázalékos hidrogén-peroxid oldatot alkalmazunk.
16. Az 1-13. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy az oxidatív kezelés időtartama 1 perc és 3 nap közötti, előnyösen 25 perc.
17. Az 1-13. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy az oxidatív kezeléssel egyidejűleg ultrahangos besugárzást végzünk.
18. Az 1-17. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a szárítást 50 és 90 °C közötti hőmérsékleten végezzük.
19. Az 1-17. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a szárítást légköri nyomáson vagy vákuumban, előnyösen 15 kPa-t meg nem haladó nyomáson végezzük.
20. Az 1-17. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a szárítást 20 ± 10 torr nyomáson végezzük.
21. Az 1-17. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy a szárítási időtartam hossza 1 óra és 3 nap közötti, előnyösen 20 ± 0.5 óra.
22. Az 1-21. igénypontok bármelyike szerinti eljárás azzal jellemezve, hogy az ultrahangos besugárzás frekvenciája 16 és 42 kHz közötti, előnyösen 20-42 kHz, energiája 0.1-10 kW közötti, előnyösen 0.5-2 kW.

