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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 October 2016 (06.10.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/157029 A1

(51) International Patent Classification:
A61K 36/87 (2006.01) *A61K 36/185* (2006.01)
A61K 8/97 (2006.01) *A61K 36/63* (2006.01)
A61K 9/14 (2006.01) *A61K 36/73* (2006.01)

(21) International Application Number:
PCT/IB2016/051607

(22) International Filing Date:
22 March 2016 (22.03.2016)

(25) Filing Language: Italian

(26) Publication Language: English

(30) Priority Data:
102015000010139 27 March 2015 (27.03.2015) IT

(71) Applicant: **LEVIUS VITA FOODS S.R.L.** [IT/IT]; Via Enrico Magnani 16/4, 51016 Montecatini Terme PT (IT).

(72) Inventor: **MELE, Antonio**; Via Enrico Magnani 16/4, 51016 Montecatini Terme PT (IT).

(74) Agents: **BORRINI, Stefano** et al.; c/o Societa' Italiana BrevettI S.p.A., Piazza di Pietra, 39, 00186 Rome (IT).

(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, BN, 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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, 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,

[Continued on next page]

WO 2016/157029 A1

(54) Title: A PROCESS FOR THE PRODUCTION OF A PHYTODERIVATIVE

(57) Abstract: The present invention relates to a process for the preparation of a stable phytoderivative or phytocomplex, comprising active antioxidant molecules. In particular, the process comprises schematically a micronization step and a dehydration one of the starting plant material in order to obtain a stable phytoderivative in form of powder. Furthermore, the present invention also relates to the phytoderivative which can be obtained by means of such process and to the uses thereof. At last, the invention also provides a plant for implementing the process for preparing the phytoderivative itself.

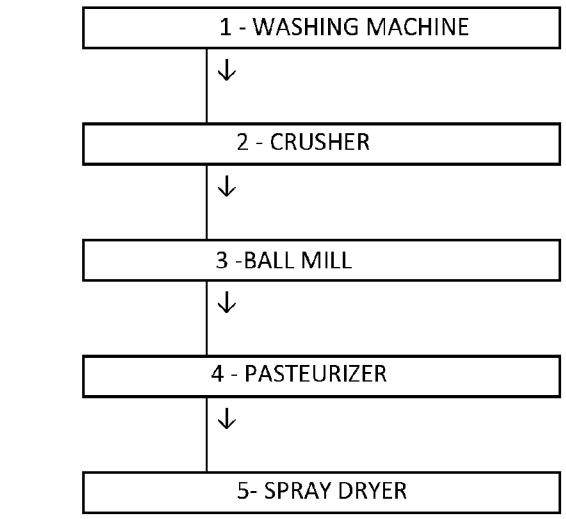

FIGURE 1

SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

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

PROCESS FOR THE PREPARATION OF PHYTODERIVATIVES

DESCRIPTION

The present invention relates to a process for the preparation of a stable phytoderivative, comprising active antioxidant molecules. In particular, the process comprises schematically a micronization step and a dehydration one of the starting plant material in order to obtain a stable phytoderivative in form of powder including the whole natural antioxidant molecular mixture of the starting matrix. Furthermore, the present invention also relates to the phytoderivative which can be obtained by means of such process and uses thereof. At last, the invention even provides a plant for implementing the process for preparing the phytoderivative itself.

STATE OF PRIOR ART

In the last years a more and more interest has been directed by operators in different industrial fields to the development of products mainly or wholly constituted by components of plant origin. For example, one can think about the replacement of chemical synthesis dyes with plant natural dyes.

Among the different molecules of plant origin particular attention was given to and it is given, in the specific case, to the antioxydant molecules.

In fact, innumerable studies were performed, both in the human field and in the animal field, demonstrating the the effectiveness of the natural antioxidant molecules, such as for example flavonoids and polyphenols, in the prevention and treatment of different pathological conditions.

As it is known, the free radicals, as they have an odd electron on the outest orbit, are highly instable and particularly reactive molecules. The free radicals react easily with any molecule lying near them (carbohydrates, lipids, proteins, nucleic acids) by damaging it and often by compromising the function thereof. Furthermore, the reaction of the same with other molecules determine the transformation of the molecular targets, in turn, into free radicals, by causing auto-propagation chain reactions which, in turn, can cause large damages in the cell.

The beneficial action associated to the antioxidant substances is then to prevent, limit or lock the antioxidant action exerted by the free radicals on the different biological components and, then, in the molecular processes, involved in the occurrence and/or consolidation of pathological conditions such as, for example, ageing.

Even the action of the antioxidant substances, added to the foods and beverages such as aromas, ingredients and additives, is very important in contrasting phenomena of food rancidity and deterioration.

The possibility of having available antioxidant molecules of plant origin such as flavonoids and polyphenols first of all raises the problem of the extraction thereof from the plant material and subsequently of the stabilization thereof, by considering indeed that these molecules are highly instable which then react easily by loosing quickly the oxidant action thereof.

In particular, water plays an important role in the destabilization of such molecules as it constitutes the most abundant component of most part of the materials of plant origin and the one which more than any other one favours the propagation of the radical chain reactions. Furthermore, it has to be added that the presence of water in the plant material, especially when such material is moved away from the natural environment thereof, is essential for the growth of microrganisms which can generate processes for decomposing and putrefying the plant material itself. A strategy used for limiting the above mentioned damages due to the presence of water consists in freezing the included plant material at low temperatures. However, such approach has different disadvantages, for example, it results to be difficult to be implemented when considerable material volumes are involved, requesting a huge energy expenditure during the freezing step and transportation costs. In other words, the freezing in order to guarantee the preservation of the plant material as well as of the molecules/components existing therein remains an approach which actually is difficult to be implemented. The lyophilisation, another technique for removing water from solid matrixes, has disadvantages too, linked to the process length and to the connected high costs.

As far as the isolation of the antioxidant molecules from the plant material is concerned instead, the generally used approach is that of the extraction thereof. The extraction usually is performed by using: a) aqueous solutions with various pH which then involve the addition of acids or bases; b) hydroalcoholic solutions generally based upon methyl and/or ethyl alcohol; c) various organic solvents (ethyacetate, propan-2-ol, acetone); d) enzymatic preparations apt to degrade the plant material; e) supercritical fluids such as liquid carbon dioxide under supercritical conditions; f) physical media such as microwaves and ultrasounds to destructure the plant material; g) methods for crushing and remove the different structural components of the plant matrix such as lignin, cellulose and pectine by means of using centrifugation and/or filtering on various types of polymeric and/or ceramic membranes; h) chromatographic methods for separating antioxidants from other unwished molecules; i) addition of acids and/or stabilizing and/or antimicrobic agents (citric, acetic and ascorbic acids, sodium benzoate).

One will understood that such methods do not allow the 100% recovery of the different antioxidant molecules existing in the starting plant material since in the different steps provided by the extraction inevitably the different chemical or physical selectivity of the various techniques for the different antioxidant molecules would lead to the loss of a portion thereof. Then the correspondence between the "natural composition" of the starting matrix and that of the phytoderivative is lost and therewith the health effectiveness undoubtedly brought by the phytocomplex in the fresh vegetable; effectiveness which is often associated to the presence of quantitatively "lower" components, sometimes even difficult to be identified at analytical level and which can show action synergism with the quantitatively more present antioxidants and thereon all the extracting strategy is concentrated.

It is also important the fact that often the concentrated extracts of antioxidant molecules themselves are very unstable and a way to guarantee their duration compatible with the industrial uses is the transformation thereof in powders. An often found limit is the impossibility of obtaining directly the passage of these molecules from the step of solution to solid in powder, and the remedy consists in additioning to the extract hydrosoluble complex carbohydrates such as for example the maltodextrines as supporting material, therefore the "naturalness" of the phytoderivative is lost, often the adsorbption of the antioxidants to the polysaccharide reduces considerably the bioavailability thereof and at last they increase the production costs.

Furthermore, some of the above shown methods, such as for example the extraction by means of chromatography, however request the presence of means and specialized technical personnel which not always is always present, for example, in the sites for collecting the plant material itself.

To the above illustrated problems one has to add the fact that the seasonability in the maturity and collection of the plant material imposes the adoption of technical solutions of quick processing coherent with the easy perishability of the plant material itself. Furthermore, the collection and processing of the plant material, such as fruits, flowers, etc, even imposes the need for having available valid strategies for disposing the residues and the waste of the plant material transformation usually not used and then intended to be however removed in some way. Last but not least in case of considerable amounts of waste material, even the transfer to sites or seats, different from those wherein the plant material was treated or processed, results to be a problem.

The object of the present invention is to develop a strategy allowing to overcome the disadvantages associated to the fact of obtaining natural molecules such as

antioxidants starting from plant material, at the same time allowing to dispose vegetable waste deriving from the processing procedures of the plant material.

SUMMARY OF THE INVENTION

The present invention is based upon the observation that antioxidant molecules of plant origin are currently obtained, as above illustrated, by means of extraction of the same from plant material with a whole series of disadvantages which is reflected in the stability of the same and then in the capability thereof of acting as effective antioxidants.

The approach underlying the process for the production of phytoderivatives comprising antioxidant molecules according to the present invention consists in preserving such molecules inside the same starting natural plant matrix by guaranteeing apart from stability even the complete presence of the molecular pool thereof which expresses the whole effectiveness of the natural phytocomplex which inevitably would be lost after steps such as crushing and extraction.

The process of the invention first of all provides a mechanical treatment for reducing the sizes of the plant material which is to be followed by a dehydration step without using solvents or other chemical-physical methods aimed at separating and/or extracting the antioxidants from the remaining plant components.

An advantageous aspect of the present invention, differently from the extractive methods in general, is the fact that one does not run the risk of obtaining a phytoderivative wherein there are only some of the antioxidant molecules of the specific plant matrix. Such aspect results to be particularly important as the cooperation between different antioxidant molecules determines a more effective protection against the free radicals than that determined by each single antioxidant alone. An example of this synergism between antioxidants is to be found in the series polyphenols – ascorbic acid - Vitamin E, wherein the possible oxidation of the latter is restored to the form reduced by the action of the ascorbate in turn regenerated by the presence of polyphenols. This capability is due to the potential redox of the antioxidants therefore antioxidants with lower (reducing) redox potential are able to regenerate (reduce) other antioxidants in turn oxidized in radical reactions (ISTISAN Reports 05/40 pg 112). Therefore, the action synergism played by quantitatively “lower” components, sometimes even difficult to be identified, but fundamental in the redox scale of the pool of antioxidants of a given phytoderivative, is lost when the extracting process which focalizes on the recovery of a single antioxidant looses several other ones thereof on the way.

Consequently, the pool of antioxidants of the natural phytoderivative is potentially more stable on itself than the single antioxidant extracted from the plant

matrix.

The operating simplicity characterizing the process of the invention and in particular, the removal at economically compatible conditions of the water from the plant matrix puts then the herein described process as alternative strategy substantially viable for stabilizing the substances, in particular antioxidants, present in the plant matrix. Additional advantage of the present invention is the fact that the process, in an economic and effective way, allows transforming the vegetable waste of the processing in a product that is a phytoderivative in extremely versatile powder and usable in different types of industries. In particular, the transformation of the waste in powder allows reducing weight and volume of the plant material with consequent advantages for the storage and transportation.

Therefore a subject of the present invention is:

- a process for the preparation of a stable phytoderivative comprising antioxidant molecules comprising the following steps:
  - preparation of the plant material;
  - crushing
  - water addition
  - micronization of said plant material by means of means with mechanical action; and
  - dehydration of said micronized material so as to obtain said phytoderivative in form of powder;
- a phytoderivative in form of powder which can be obtained by means of the above process, comprising antioxidant molecules;
- the use of a phytoderivative as designate above for the preparation of foods, feeds, drugs, cosmetics, dyes or pigments for textile, furnishing products, for components of means of transport;
- a plant for the preparation of a phytoderivative as defined above.

Additional advantages and features of the present invention will result evident from the following detailed description.

BRIEF DESCRIPTION OF THE FIGURES

Three drawing tables are enclosed to the present description, showing:

Figure 1 the plant for the preparation of a phytoderivative according to the invention; The Washer, The Crusher and the Pasteurizer are optional machines to be used in case depending upon the different structure of the plant matrix itself and of the market destination of the phytoderivative.

Figure 2 the measurement in time from the moment of the preparation of the quantity of total polyphenols in mg/g of powder of phytoderivative from olive leave.

The total polyphenols were determined with HPLC method. The quantity of total polyphenols is determined with calibration against standards of most representative biophenols existing in the olive leaf.

Figure 3 the measurement in time from the moment of the preparation of the quantity of the total polyphenols in mg/g of powder of the phytoderivative from defatted olive pulp. The total polyphenols were determined with HPLC method. The quantity of total polyphenols was determined with calibration against standards of the most representative biophenols existing in the olive pulp.

DESCRIPTION OF THE INVENTION

A detailed description of the different subject of the present invention is reported hereinafter.

Process for the preparation of a stable phytoderivative in form of powder

A process for the preparation of a phytoderivative is herein described.

Under phytoderivative in the present description a plant derivative, that is a set of components of plant origin obtained starting from a plant/trees or portions thereof. In particular, the phytoderivative prepared with the process detailed hereinafter is a stable set of plant components comprising all active antioxidant molecules included in said plant materials detailed better hereinafter.

In particular, the process of the invention comprises operatively simple steps which can be generalized in destructuring of the starting plant material by means of using mechanical methods and subsequently removing water.

Under plant material in the present case any material of plant origin is meant. By way of example, the plant material can be selected in the group comprising: a whole plant, fruits, leaves, flowers, roots, branches, stems, buds, shoots, seeds, grass, but even by-products and processing vegetable waste.

In particular, the by-products and the processing waste, for example, of the agro-feeding industry, can include olive pomace, fruit peels, tomato skins, peels of vegetables, grape pomace, bran and however even any material derived from processing of plant products and which would be intended to be remove and not re-used in some type of industry. It is important underlying that the process according to the present invention can be re-used, without modifications, for all types of plant materials. Generally water is added in a quantity so as to obtain, before drying, a percentage of 4 - 12% of solid, preferably of 10%.

Step for preparing the material

In a first step the process according to the invention, the plant material as defined above is prepared, therefrom the phytocomplex is to be obtained.

The process according to the invention even provides a step for crushing the plant material before the micronization step, for example, when the preparation of the phytoderivative is made starting from roots, structurally compact whole fruits, bark and, then, under those conditions wherein the material micronization can be eased by a pre-reduction of the initial sizes. The crushing can be performed both manually and by using suitable machines or tools such as for example, impact millers, jaw millers, crushers, hammer crushers, disk crushers, knife crushers.

Preferably the crushing of shells and seeds is performed with disk and hammer crushers, even in sequence. The crushing of more structured plant material such as carrots or red beets, kiwi, garlic or onions is performed with knife crushers. These crushing procedures are performed at temperatures between 4°C and 35°C, preferably at room temperature with possible cooling of the mixture in outer loop if the crushing procedure is associated to heat development. The processing time is dictated by the specific type of apparatus and by the size thereof; usually by considering that one refers to plant material with big volumes (olives, grapes, tomatoes, fruits and vegetables in general) the output rates per hour are 10Kg/hour to 60 ton/hour, preferably 5-8 ton/hour.

Furthermore, even a step for washing the plant material can be provided before the micronization step and, in case a crushing is performed, preferably, before the latter. For the washing, for example, an inert solvent liquid can be used, that is which does not react and does not alter the composition of the starting plant material, or with a "wind" simply constituted by air and nitrogen. Preferably, said solvent liquid is water. In an embodiment, the washing step is performed by using water deionised at room temperature. Concretely the washing can be performed by dipping the material into the used liquid for a time variable depending upon the type and conditions thereunder the starting material is. Then one will understand that, for example, the washing of buds or flowers will request different time and modes from the ones requested for example for roots and barks. Since one speak about plant material, this is usually accompanied by powder or earth. It is also necessary to assume the possible presence of residues of phytodrugs or pesticides and then each time, and for each specific plant material, it is necessary to define the washing modes and time.

Micronization step

In the specific case, the micronization, herein designated even as destructuring, consists in reducing the plant material in particles with micrometric sizes. Preferably, the plant material is reduced to particles with sizes comprised between 1 μm and 1000 μm, on the average between 10 μm and 600 μm still more preferably between

20 µm and 250 µm. In the micronization step water is added. Advantageously, such addition is implemented so as to obtain a solution with solid content between 4 and 12% by weight, preferably of 10% by weight.

The micronization of the plant material is performed by means of using any means with mechanical action known to the person skilled in the art. By way of example and for limitative purpose, such means can be selected in the group comprising: marble millers (even known as sphere millers and ball millers), disk crushers, hammer crushers, knife crushers, pan crushers. In a preferred embodiment of the invention, the micronization of the plant material is performed by means of marble mills. The means for the above mechanical micronization are widely known and therefore it does not required further examinations (see for example: C. Ceschel, L. Fabris G., E. Lencioni, A. Rigamonti Impianti per l'industria farmaceutica Soc. Ed. Esculapio, Bologna).

The micronization can be performed at room temperature and for a time suitable to obtain the above mentioned sizes. Generally, the duration of the mechanical action will depend upon the type of the used mechanical means or a combination of two or more thereof, as well as upon the nature of the material and in particular upon its own humidity content and it can vary from 10-15 seconds to 4 hours.

Generally, the ball mill is able to micronize any plant matrix, but the micronization time could be comprised between 20 minutes and 4 hours, preferably between 40 minutes and 180 minutes.

The micronization step has the purpose, apart from that of reducing the plant material to the above mentioned sizes, of fluidizing the starting material in order to make it suitable to the subsequent dehydration step. In particular, the fluidisation is made possible thanks to the presence of water and, in general, of liquids made of the same plant material which usually fruits and vegetable include by over 85% of their own weight.

The fluidisation in case can be promoted even by the water addition, preferably water deionised before or even during the micronization step. During the micronization step water is added, advantageously deionised water having a temperature between 60° and 80°C. The addition of deionised water is also aimed at the optimum implementation of the subsequent process steps. It is to highlight that in the state of art for analogous processes water is removed - rather than in case of the invention – rather than added.

According to what shown above, then, the micronization step leads to an aqueous fluid suspension wherein there are particles in the order of micron of the plant

material. Such suspension, in case of need, can even be stored and thus not subjected, soon after having obtained it, to the dehydration step. In this regard, the suspension can be brought to a pH comprised between 2.0 and 4.5, preferably 3.0-3.5, and stored for a long time period. For example the defatted olive pulp brought to a pH<3.5 and micronized can be stored for about 12 months, on the average 8 months, preferably 6 months. In particular, the suspension can be brought to a pH 2.0-4.5 by adding any other food acid, such for example, lemon juice and/or wine vinegar and/or citric acid and/or acetic acid. Preferably such procedure is performed in absence of oxygen, in inert atmosphere and in absence of light. The temperature for storing the suspension can be comprised between 0°C and 35°C, preferably 4°C.

To the above described suspension additional components can even be added in order to obtain, ultimately, a phytoderivative enriched with particular components. By pure way of example and not for limitative purpose a solution comprising natural oxidants can be added to the micronized plant material. In particular, such antioxidants could be, for example, polyphenols of olives, ascorbic acid, Vitamin E.

Dehydration step

The micronized material as described above is subsequently dehydrated so as to obtain a stable phytoderivative in form of powder. The dehydration step then has the purpose of promoting the removal or however the significant reduction of the water content from the micronized material. Said even in other terms, the dehydration step leads to the reduction of the percentage of residual humidity in the phytoderivative.

The dehydration is a process widely known to the person skilled in the art described in many laboratory manuals or, as shown in www.niro.com, which then does not need herein additional explanations.

According to the invention, the dehydration is performed by using a spray dryer. However, the dehydration can be performed by using apparatuses which contemporary and in association to the dehydration allow the transformation of the above-described aqueous suspension into powder. Thereamong flash dryer, fluid-bed dryer, spray dryer, microwave oven in case associated to a micronizer of solids can be mentioned.

The conditions for the dehydration, analogously to what previously illustrated for the other steps,, could request different time and modes depending upon both the type of the starting material and the type of the used apparatus. Generally, however, it is preferred using a temperature comprised between 120°C and 250°C. In an exemplifying manner, in case a flash dryer is used, the temperature can be

comprised between 150°C and 230°C. In case a fluid-bed dryer is used, the temperature can be about 150°C. In case a spray dryer is used, the temperature can be between 180°C and 250°C, the dehydration time is in the order of 10-20 milliseconds.

In order to obtain the phytoderivative in form of powder not only only one of the above mentioned apparatuses can be used, but even two or more thereof in sequence. Therefore, for example, a first dehydration of the micronized material with a flash dryer or a spray dryer could be performed, which could be followed by a second dehydration step by using a fluid bed dryer.

The dehydration step leads then to a phytoderivative in powder wherein the percentage of residual humidity is very low. In an embodiment the content of residual humidity in the phytoderivative is comprised between 1% and 10% by weight (w/w), preferably between 2% and 8% by weight of said powder. Even powders with a humidity content between 0.5%-1.0% by weight of the powder can be obtained. An additional water removal can be obtained even by coupling to the mentioned devices a fluid-bed one.

As it will be better described subsequently, the phytoderivative in powder obtained with the process of the invention can have different uses and in particular, for example, t can be prepared for the preparation of foods and drugs. In this regard, it can be advantageous to provide a sterilization or pasteurisation step in order to obtain a phytoderivative in form of powder useful for applications wherein it is convenient to minimize the risks for the health due to the presence of pathogen microrganisms. Technical information related to the sterilization and pasteurisation procedures can be recovered in any laboratory manual, widely known in the art. Preferably, the pasteurisation or sterilization step is performed after the micronization step on the fluidized material but before the dehydration. The pasteurisation can be performed at a temperature comprised between 60°C and 100°C for a time interval comprised between 10-30 seconds. By way of example and not for limitative purpose, in case the phytoderivative in powder is intended to the preparation of beverages such as beer or wine, a pasteurisation can be performed at temperatures comprised between 60-65°C for 30 minutes. In case, instead, the phytoderivative in powder is intended to food products such as milk derivatives, oven products, meats, the pasteurisation can be performed at temperatures comprised between 75-85°C for 10-15 seconds.

As far as the sterilization is concerned, preferably it can be performed when the phytoderivative, for example, is intended to the preparation of products wherein the

sterility requirement results to be important. Such products are for example, but not only, pharmaceutical formulations such as those for parenteral administration.

Stable phytoderivative comprising active antioxidant molecules

A subject of the present invention is also a stable phytoderivative, defined obtained by the process according to the present invention, in form of powder and comprising, in the specific case, active antioxidant molecules that is capable of neutralizing the free radicals. The herein described phytoderivative comprises in particular, plant components associated to the type of starting plant material. For plant components one refers to any known plant molecule such as proteins, cellulose, starch, pectin, lignin, resins, nucleic acids, etc. The phytoderivative in form of powder as indicated above is characterized by the fact of being stable and representative of all the mixture of antioxidant molecules of the natural phytocomplex. In particular, the stability of the phytoderivative lies in the fact that it is not subjected to chemical/physical variations in time compatible with the use destination thereof. In other terms this means that the components existing therein are not subjected to alterations so as to compromise the properties thereby the phytoderivative is characterized at the time of its obtaining. For example, the phytoderivative in powder comprising antioxidant molecules has the property of being able to neutralize the free radicals. In this regard, the phytoderivative stability consists in keeping such capability in time, that is to be able however to be used as antioxidant even after the preparation thereof.

The phytoderivative of the present invention, as already mentioned, comprises active antioxidant molecules. Such molecules for example are: flavonoids, polyphenols not flavonoids, carotenoids, phenolic acids. In an embodiment the antioxidant molecules are comprised in the phytoderivative in form of powder at a concentration higher than 0.1% and lower than 8%, preferably between 0.1% and 5.0% by weight of the phytoderivative itself. The antioxidant capability usually expresses with the ORAC (Oxygen Radical Absorbance Capacity) value in micromols of Trolox Equivalent for gram of product (µmols TE/g). In an embodiment the ORAC of the phytoderivative in powder is higher than 2100 µmols TE/100g of powder, preferably between 2.100 and 135.000 µmols TE/100g by weight of the phytoderivative. Obviously as the phytoderivative is in reality the plant matrix as a whole, therefrom one intended to remove water only, the concentration of the antioxidant molecules will vary coherently to the presence of the same in the specific natural plant matrix and thus consequently even the corresponding ORAC. By way of example: the case of the olive biophenols can be taken. The use of the concentrated extracts of the olive polyphenols in the food field is demonstrating that

levels of such antioxidants of the order of 300 ppm are effective in lengthening the shelf life and compatible with keeping the organolectic features. Obtaining a liquid extract with a percentage of polyphenols of 5-6% is a demanding target as, even if it can rise, this then becomes a little compatible with the prices which the food market can accept, a liquid concentrate of such polyphenols, if it has to be brought to powder (suitable procedure in case of using for example in sausages), is subjected to a dilution due to the effect of the addition of the maltodextrins, although then water is removed. In other terms, the % on dry product passes to 3.5%-4,0%. In case of the present invention directly the defatted olive pulp is brought to powder after having micronized it. The percentage in polyphenols in such powder is 30-38 g/Kg then in line with the needs of the market with the important added value represented by the certainty that the whole pool of olive antioxidant molecules was kept in the phytoderivative.

Furthermore, as shown above, the phytoderivative is obtained by means of the process described above in form of powder. In particular, the particles of plant material comprised in such powder have an average size < a 200 μm, preferably <150 μm. In an embodiment of the invention, the average size of the particles is lower or equal to 40 μm

Uses of the phytoderivative

The phytoderivative in powder as described above can be used in several industrial fields. In particular, it can be used for the preparation of extremely heterogeneous products both from the structural and functional point of view. By way of example, the phytoderivative in powder can be used in the food industry as ingredient or additive for the preparation both of solid or half-solid food products for the human and animal consumption (such as oven products, sausages, yogurts, feeds for animals, etc) and liquid products (such as milk, beer, wine, juices, etc). The phytoderivative of the invention can even be used in the cosmetic or pharmaceutical industry for the development, for example and without limiting thereto, of products such as creams, lotions, integrators with antioxidant action, antimicrobics, anti-inflammatory substances and others.

Still, the phytoderivative can be used for the production of pigments or dyes, preferably 100% natural, to be destined to the colouration of textile products, furnishing products and components of means of transport.

Generally, then, the phytoderivative which can be obtained by means of the herein described process results to be extremely versatile in terms of industrial use, therefore the above shown uses are to be meant as exemplifying and absolutely not limiting.

Plant

A subject of the present invention is also a plant for implementing the above-described process. In particular, such plant comprises as essential components both means with mechanical action apt to the micronization of plant material and means apt to the dehydration of the micronized material.

The means with mechanical action which can be included in the plant, in general, are the means which is able to determine the reduction in the plant material in particles in the order of micrometres. By way of not limiting example, the means with mechanical action can be selected in the group comprising: marble mills (also known as sphere mills and ball mills), disk crushers, hammer crushers, knife crushers, pan crushers. In an embodiment of the invention, the plant includes marble mills.

As to the means apt to the dehydration which can be included in the plant, it can be selected among any device/apparatus considered suitable by the person skilled in the art to favour both the dehydration and the spraying of the micronized material. By way of not limiting example, such means can be selected among: flash dryer, fluid-bed dryer, microwave oven in case associated to a micronizer for solids, spray dryer.

In a preferred embodiment, the plant comprises a spray dryer.

The plant of the present description can comprise one or more of the means with mechanical action as well as one or more of the dehydration means shown above.

For example, the plant can include a marble mill and a spray dryer. Alternatively, a marble mill coupled to a flash dryer and to a fluid-bed dryer.

A preferred embodiment of the plant, as it is even simple, easy to be handled, with continuous operation and which can be wholly automated, comprises a marble mill and a spray dryer only. The only interventions left to the operator are the preparation of the plant material and the loading thereof in the mill and the transfer of the powder bags from the spray dryer to the storing warehouse. This plant allows obtaining phytoderivatives in micrometric powder with granulometry < 40 μm and a residual humidity < 1%. If this plant is destined to the production of a phytoderivative for human or animal food use, it is necessary to provide a washing machine and a pasteuriser/sterilizer upstream and downstream of the marble mill, respectively.

EXAMPLES

The following examples are shown by way of example and they are not intended to limit the invention as otherwise described in the present case.

EXAMPLE 1: ***phytoderivative obtained from the peels, core and pulp of apple (domestic Malus) or other fruit of the Rose family.***

The apple peels and the cores, or the whole apple are loaded inside the marble mill at first without water. The mill is started and after 10'-15' the consistence of the fluidized mass is observed. If the destructuring and fluidization of the plant matrix has not reached micrometric sizes, cold deionised water, acidified with food acid, preferably lemon concentrated juice, is added into the chamber of the marble mill. The pH is brought to values < 3.5 and the disgregation process is continued.

When the plant mass has adopted the consistency of a liquid, this is pasteurized/sterilized continuously and transferred directly to the spray dryer with T operating between 180°C and 250°C. A fine powder with granulometry ≥ 10 micrometres and residual humidity $1\%<U_r<8\%$ is obtained.

EXAMPLE 2: ***phytoderivative obtained from olive leaves (Olea europaea L.)***

Olive leaves derived from pruning or associated to the collection of olives are accurately washed with simple mains water to remove earth and/or powder or residues of possibly present copper Salts.

The leaves are loaded inside the marble mill at first without water. The mill is started and after 20'-25' the consistency of the fluidized mass is observed.

If the destructuring and fluidization of the plant matrix has not reached micrometric sizes, hot (60-80 °C) deionised water is added into the chamber of the marble mill in quantities from 1 to 4 times the weight of the leaves and the disgregation process is continued.

When the plant mass has adopted the consistency of an easily pumpable liquid, this is pasteurised/sterilized continuously and it is transferred directly to the spray dryer with T comprised between 180°C and 250°C. A fine powder is obtained with granulometry ≥ 20 micrometres and residual humidity $1\%<U_r<8\%$

An important feature of the product in powder is the fact of keeping the green colour, an index of the fact that chlorophyll has not degraded, to demonstrate that the process, even under the operating conditions experimenting temperatures higher than 180°C, is able to keep even the molecular components more sensible both to light and heat.

EXAMPLE 3: ***Agro-industrial transformation by-product; phytoderivative derived by grape skins, vitis vinifera and vitis labrusca.***

The grape skins are loaded inside the marble mill at first without water. The mill is started and after 10'-15' the consistency of the fluidized mass is observed.

If the destructuring and fluidization of the plant matrix has not reached micrometric sizes, an equal volume of cold deionised water is added into the chamber of the marble mill and the disgregation process is continued.

When the plant mass has adopted the consistency of a liquid, this is transferred directly to the spray dryer with T operating between 120°C and 250°C and a fine powder with granulometry ≥ 10 micrometres and residual humidity 1%<U_r<8% is obtained.

EXAMPLE 4: ***Phytoderivative obtained from the flowers of hop Humulus lupulus L 1753 of the Cannabacee family***

Hop male and female, preferably female, flowers are loaded inside the marble mill at first without water. The mill is started and after 30'-35' the consistency of the fluidized mass is observed.

If the destructuring and fluidization of the plant matrix has not reached micrometric sizes, an equal volume of cold deionised water is added into the chamber of the marble mill and the disgregation process is continued.

When the plant mass has adopted the consistency of a liquid, this is transferred directly to the spray dryer with T operating between 180°C and 250°C and a fine powder with granulometry ≥ 10 micrometres and residual humidity 1%<U_r<8% is obtained.

EXAMPLE 5: ***phytoderivative obtained from defatted olive pulp (Olea europaea L.)***

Defatted olive pulp, obtained downstream of crushing process and oil extraction and removal of the entire stone or possible wood fragments of stone, is loaded inside the marble mill at first without water. The mill is started and after 15'-20' the consistency of the fluidized mass is observed.

If the destructuring and fluidization of the plant matrix has not reached micrometric sizes, cold deionised water in quantities from 2 to 3 times the weight of the pulp, acidified with food acid, preferably lemon concentrated juice, is added into the chamber of the marble mill. The pH is brought to values < 3.5 and the disgregation process is continued.

When the plant mass has adopted the consistency of an easily pumpable liquid, this is pasteurized/sterilized continuously and it is transferred directly to the spray dryer with T comprised between 180°C and 250°C. A fine powder with granulometry ≥ 20 micrometres and residual humidity 1%<U_r<8% is obtained.

The invention has been described sofar with reference to the embodiments. As it will be evident to the person skilled in the art from what detailed, additional embodiments could be provided belonging to the same inventive core which, then, will be to be means as included in the protective scope defined by the claims of the present application.

CLAIMS

1. A process for the preparation of a stable phytocomplex comprising active antioxidant molecules starting from plant material, said process comprising the following steps:
    a. preparation of plant material
    b. crushing of said material
    c. water addition and mechanical micronization of said plant material until obtaining an aqueous suspension of particles with average size comprised between 20 and 600 μm and
    d. dehydration of said suspension by using a spray dryer at a temperature comprised between 180°C and 250°C so as to obtain a residual moisture content between 0.5% and 8% w/w, therefore a complete preservation of all said active antioxidant molecules, contained in said plant material, is obtained.
2. The process according to claim 1, wherein after said step b) a pasteurization/sterilization step is provided, which is carried out at a temperature comprised between 60°C and 100°C for a time interval comprised between 10-30 seconds, or between 80°C and 130°C for a time comprised between 2-4 seconds, or between 140°C and 150°C for a time comprised between 1-2 seconds.
3. The process according to at least one of the previous claims, wherein said plant material comprises: whole plants, fruits, leaves, flowers, roots, branches, stems, buds, shoots, grass and by-products and/or processing vegetable waste.
4. The process according to claim 3, wherein said by-products and/or vegetable waste include olive pomace, fruit peels, tomato skins and seeds, peels of vegetables, grape pomace, bran.
5. The process according to one of the previous claims, wherein said micronization is performed by using marble mills, disk crushers, hammer crushers, knife crushers and pan crushers.
6. The process according to anyone of the previous claims, wherein said micronization step is instantaneous or it is performed for 10 - 40 minutes at room temperature.
7. The process according to anyone of the previous claims, wherein during micronization said added water is deionised water at T between 60 and 80° C.

8. A stable phytocomplex in form of powder which can be obtained by means of the process according to anyone of claims 1 to 7, comprising active antioxidant molecules belonging to the class formed by flavonoids, carotenoids and phenolic acids and wherein said powder has particles with an average size of <200 μm, preferably <150 μm and wherein said antioxidant molecules are present in a concentration comprised between 0.1% and 8.0% by weight of said phytoderivative and they express a ORAC comprised between 2100 and 135.000 μmols TE/100g by weight of the phytocomplex.
9. The use of a phytocomplex according to claim 8 for the preparation of foods, feeds, drugs, cosmetics, dyes or pigments for textile, furnishing products, for components of means of transport .

Plant for the preparation of a phytoderivative

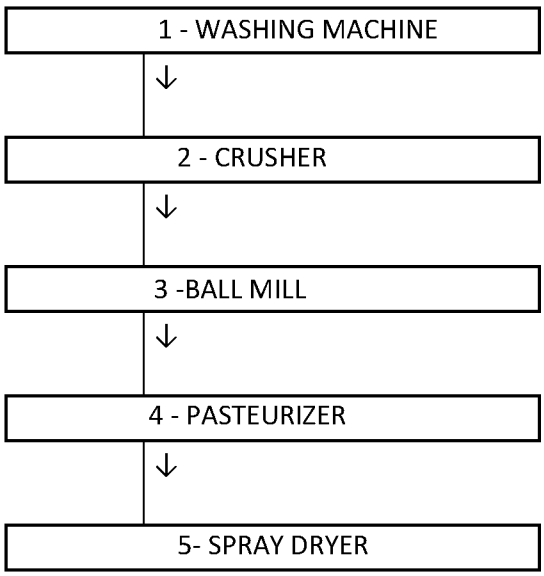

FIGURE 1

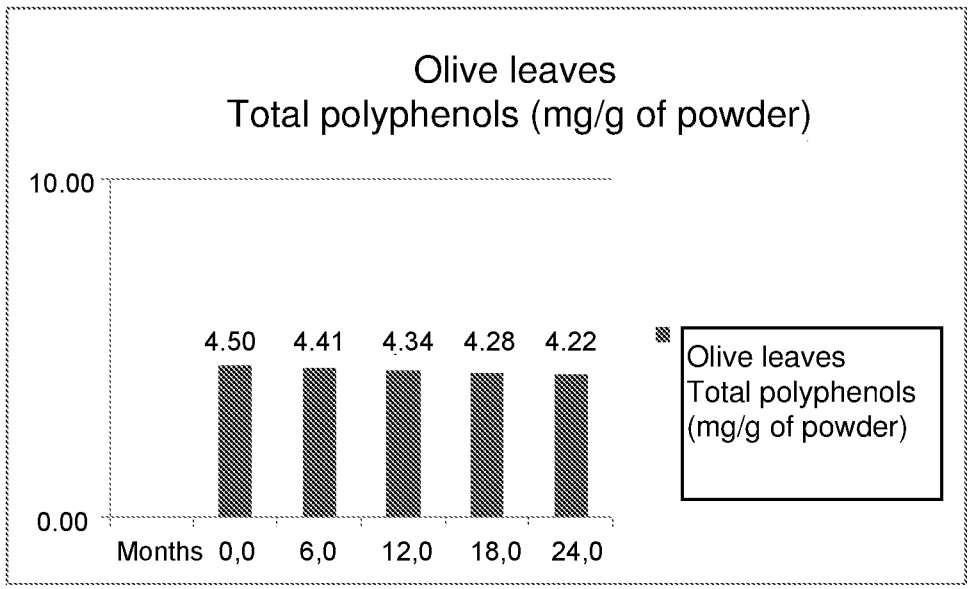
Olive leaves
Total polyphenols (mg/g of powder)
10.00
0.00
4.50
4.41
4.34
4.28
4.22
Months 0,0 6,0 12,0 18,0 24,0
Olive leaves
Total polyphenols
(mg/g of powder)

FIGURE 2

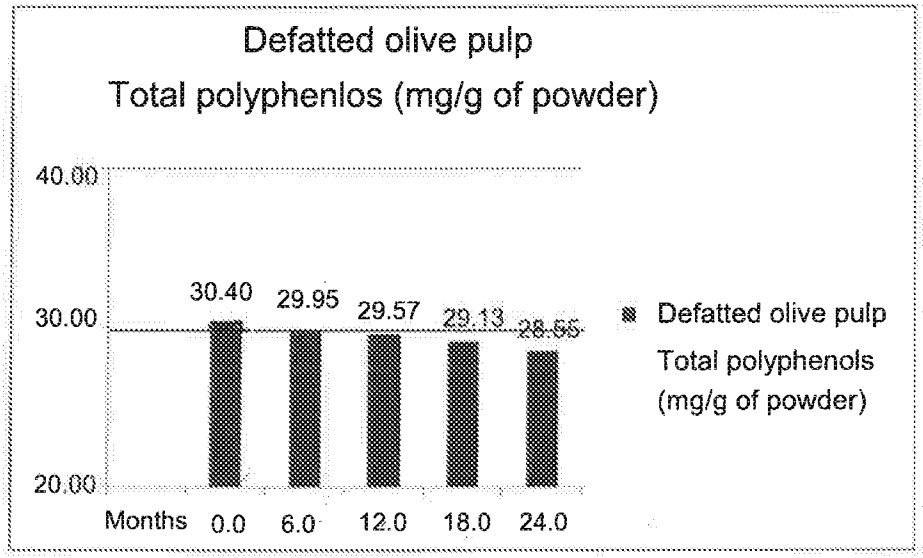
Defatted olive pulp
Total polyphenlos (mg/g of powder)
40.00
30.00
20.00
30.40
29.95
29.57
29.13
28.65
Months
0.0
6.0
12.0
18.0
24.0
Defatted olive pulp
Total polyphenols
(mg/g of powder)

FIGURE 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/051607

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K36/87 A61K8/97 A61K9/14 A61K36/185 A61K36/63 A61K36/73
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)
A61K

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 practicable, search terms used)
EPO-Internal, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/070237 A1 (COUNCIL SCIENT IND RES [IN]; JAYAPRAKASHA GUDDADARANGAVVANA [IN]; RAO) 4 August 2005 (2005-08-04)	8,9
Y	page 3, line 15 - page 5, line 11; claims -----	1-9
X	WO 2004/110171 A2 (NATRACEUTICAL SA [ES]; ZUMBE ALBERT [CH]) 23 December 2004 (2004-12-23)	8,9
Y	page 1, line 7 - line 25; claims; example 4 page 11, line 23 - line 29 ----- -/--	1-9

[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 application or patent 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
27 June 2016	08/07/2016

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	Langer, Astrid

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/051607

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	COUTO RENE O ET AL: "Processing of Apeiba tibourbou Aubl. Extract Via Spray Drying", LATIN AMERICAN JOURNAL OF PHARMACY, vol. 31, no. 1, February 2012 (2012-02), pages 104-111, XP009187338, ISSN: 0326-2383	8,9
Y	abstract; figures; tables	1-9
X	GB 2 415 136 A (NATRACEUTICAL SA [ES]) 21 December 2005 (2005-12-21)	8,9
Y	example 2	1-9
Y	WO 2005/037200 A2 (PACIFIC ARROW LTD [CN]; CHAN PUI-KWONG [US]; MAK MAY SUNG [CN]; WANG Y) 28 April 2005 (2005-04-28) page 7, line 13 - line 17 page 42, line 35 - page 43, line 10	1-9
X,P	WO 2015/066339 A1 (UNIV RUTGERS [US]) 7 May 2015 (2015-05-07) paragraph [0099]; claims	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2016/051607

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005070237 A1	04-08-2005	AU 2003290382 A1	11-08-2005
		EP 1708581 A1	11-10-2006
		US 2005158436 A1	21-07-2005
		WO 2005070237 A1	04-08-2005
WO 2004110171 A2	23-12-2004	AT 349914 T	15-01-2007
		DE 602004004121 T2	11-10-2007
		EP 1633204 A2	15-03-2006
		ES 2280029 T3	01-09-2007
		PT 1633204 E	30-04-2007
		WO 2004110171 A2	23-12-2004
GB 2415136 A	21-12-2005	EP 1755412 A1	28-02-2007
		GB 2415136 A	21-12-2005
		JP 2008502339 A	31-01-2008
		US 2008014322 A1	17-01-2008
		WO 2006005986 A1	19-01-2006
WO 2005037200 A2	28-04-2005	AU 2004281707 A1	28-04-2005
		CA 2541425 A1	28-04-2005
		CN 101242850 A	13-08-2008
		EP 1670491 A2	21-06-2006
		HK 1090303 A1	18-12-2015
		JP 4815558 B2	16-11-2011
		JP 2007508317 A	05-04-2007
		KR 20060109893 A	23-10-2006
		NZ 546138 A	24-12-2009
		US 2009041877 A1	12-02-2009
		WO 2005037200 A2	28-04-2005
WO 2015066339 A1	07-05-2015	AU 2014342214 A1	21-04-2016
		CA 2928752 A1	07-05-2015
		US 2015209395 A1	30-07-2015
		WO 2015066339 A1	07-05-2015