PROCESSES FOR MAKING CARALLUMA EXTRACTS AND USES

BACKGROUND TO THE INVENTION

This invention refers to Caralluma plant extracts, their uses and applications and to processes for making the same.

The Caralluma group of plants belong to the Asclepiadaceae family and comprises over two hundred species that are distributed throughout the world. Some of these species investigated by these inventors are: c. indica, c.fimbriata, c.attenuata, c. tuberculata, c. edulis, c. adscendens, c. stalagmifera, c. umbellata, c. arabica, c.penicillata, c. retrospiciens, c. russeliana and c.lasiantha. Some of said species are found in India.

Caralluma plants are small, erect and fleshy. They have 4-grooved stems that are almost round. They are generally devoid of leaves and form small flowers in a variety of dark colours. Their pods are erect, linear and about 2.5 cms. in length and are velvety to touch. The thorns of caralluma are soft. The species of caralluma found in India are edible and form part of the traditional medicine system of the country.

Caralluma plants are reported to possess medicinal properties. The medicinal properties of caralluma have been attributed to the glycosides contained therein. A glycoside is a condensation product obtained from a sugar and non-sugar compound and may have further components such as for example, ring structures that are substituted or non-substituted. The glycosides contained in caralluma belong to the pregnane group of glycosides. Some of said pregnane group of glycosides found in caralluma plants are:

i. caratuberside A,
ii. caratuberside B,
iii. bouceroside I,
iv. bouceroside II,
v. bouceroside III,
vi. bouceroside IV,
vii. bouceroside V,
viii. bouceroside VI,

ix. bouceroside VII,
x. bouceroside VIII,
xi. bouceroside IX,
xii. bouceroside X,

Said curative/medicinal properties reported in literature and/or observed by these inventors are:

i. carminative,
ii. febrifugal,
iii. anthelmintic,
iv. anti-rheumatic,
v. anti-diabetic and anti-hyperglycaemic,
vi. anti-pyretic,
vii. anti-inflammatory,
viii. anti-nociceptive and
ix. anti-oxidant,
x. anti-hypertensive,
xi. anti-obesity and others.

Another important property of caralluma glycosides is their surprising synergy. This synergy was apparently first observed by these inventors. Said synergy is exhibited by pairs of caralluma glycosides and by higher order combinations, although the synergy contributed by said higher order combinations is not of much significance, in view of the fact that the content of glycosides other than the abovementioned two, namely, caratubersides and boucerosides in caralluma is extremely small. The caratuberside-bouceroside synergy is therefore, of most significance and includes the synergy arising out of isomer-isomer interactions in the said two glycosides. Said synergy is particularly strong with respect to the following three physiological effects of said glycosides: reduction of body weight and treatment of obesity in subjects; the reduction of blood glucose in subjects and the reduction or elimination of arthritic and other joint pains in subjects. The use of caralluma in the abovementioned three conditions and the method of treatment thereof using caralluma was first studied/investigated by these inventors. These inventors are also the first to study the related subject of increase of muscle mass in subjects by use of caralluma and the method of treatment for the same using caralluma. Said and other uses of caralluma and method of treatment investigations involving caralluma are the subjects of other applications for patents by these inventors.

An interesting fact first observed by these inventors is that said caratuberside-bouceroside synergy is found to be substantially at the maximum thereof at the caratuberside-bouceroside ratio found in c. indica. Three other species, namely, fimbriata, attenuata and tuberculata have substantially the same said ratio value and substantially the same glycoside content as c. indica. These four species are referred to hereinafter as Group I caralluma species. A further four more species, namely, stalagmifera, umbellata, lasiantha and edulis also have substantially the same said ratio but somewhat lesser content of glycosides than said Group I species. Said further four species are referred to hereinafter as Group II species and said ratio is referred to as the CB ratio, or the CBR for short.

Prior art provides a process for extraction of caralluma wherein the aerial parts of caralluma plants are extracted by means of 10% aq. ethanol. Said prior art process has a number of drawbacks and furthermore results in only a crude extract product that is not standardised, that is non-reproducible and that is not representative of the original plant material from which it is extracted. These drawbacks of the prior art product and process are elaborated further hereinbelow.

In this specification, depending on the context the term 'extraction' refers either to the process of extraction as a whole or to the individual step of extraction (leaching) that forms a part of said process. In said individual step of extraction, Caralluma plants, or parts thereof, are contacted with a suitable solvent that extracts out(leaches out) one or more constituents/components thereof. Similarly, the term 'extract' refers, depending on the context, either to the solution that is obtained during, and/or at the end of said extraction step, or to the solid mass that would be obtained upon removal by evaporation or otherwise, of the solvent contained in said solution. Said solid mass is also sometimes referred to herein as the 'solute', which term has also been used herein to refer also to the one or more components of Caralluma that are soluble in said solvent. Said soluble components may be desired ones from the point of view of extraction or otherwise.

In the first prior art reference(M.N.M. Zakaria, M.W.Islam, R. Radhakrishnan, H.B.Chan, M. Kamil, A.N. Gifri, K. Chan, A. Al-Attas, J. of Ethnopharmacology, 76(2001), 155-158) c. arabica, a caralluma species found in West Asia, was extracted using 10% aq. ethanol. The aerial parts of the plant were dried in the shade, powdered and then extracted with 10% aq. ethanol. Solvent was removed from the extract by evaporation under vacuum at 40 degrees C using a

rotary evaporator. The dried extract was re-suspended in distilled water and the slurry used for a pharmacological investigation to establish the anti-nociceptive and anti-inflammatory properties of c. arabica with respect to mice and rats.

In the second prior art reference(M. Kamil, A.F. Jayaraj, F. Ahmed, C. Gunasekhar, S. Samuel, K. Chan, M. Habibullah, J. Pharm. Pharmacology, 1999,5 (Supplement), 225) powdered c. arabica plant material was extracted using 10% aq. ethanol in a soxhlet extractor for eight hours. The flavone glycosides, luteolin-4'-O-nehesperidoside and kaempferol-7-O-nehesperidoside were isolated from the extract and the concentrations thereof in c. arabica established.

In the third (R. Radhakrishnan, M.N.M. Zakaria, M.W. Islam, X.M. Liu, K. Chan, M. Habibullah, J. Pharm. Pharmacology, 1999,5(Supplement) 116) and fourth references(M.N.M. Zakaria, M.W. Islam, R. Radhakrishnan, H.B. Chan, A. Ismail, K. Chan, M. Habibullah, J. Pharm. Pharmacology, 1999, 5(Supplement), 117) aerial parts of c. arabica are stated to have been extracted by means of 10% ethanol. No further details of the adopted process are disclosed.

The first and chief drawback of the prior art process is that decomposition of the caralluma glycosides occurs during processing. This fact has not been recognised in the prior art and was first observed by these inventors. These inventors have observed that when a caralluma extract(solution) is concentrated by evaporation of solvent therein, charring and overheating of material occurs at higher concentrations. Said overheating/charring causes said decomposition which was found to occur despite the provision of considerable agitation.

Said charring/overheating is primarily caused by the high viscosities of the caralluma extracts of high concentrations. The high viscosities are caused by the presence of the resinous matter of caralluma plants that gets extracted out in the extract along with said glycosides and the decomposition products arising out of said decomposition occurring during the extraction step. These inventors observe that under certain conditions of extraction considerable quantities of said resins are extracted out along with the glycosides.

Said decomposition was first observed by these inventors both in the concentration step and the extraction step. Where the extraction temperature is held at levels higher than 75 degrees C, thermal decomposition of the glycosides was found to occur giving high temperature products

that further enhance the viscosity of the extract and increase the risk of said decomposition in the concentration step.

In a soxhlet type apparatus, because of the column effect the caralluma plant matter would come into contact with solvent vapours that have a much greater ethanol content than the 10% that is used to charge the apparatus. The extraction temperature would also remain generally above 75 degrees C. Under these conditions, these inventors have observed that considerable decomposition occurs during extraction and furthermore large quantities of the resinous matter in caralluma plant matter gets extracted out into the extract leading to further decomposition in the concentration step.

The process conditions are not fully disclosed in said third and fourth references but it is fair to assume that the extracts are evaporated to dryness to obtain the product in a solid form suitable for pharmacological studies. Thus, in the view of these inventors said decomposition must certainly occur in the method adopted by said third and fourth references.

The second drawback of the prior art process is the simultaneous extracting out of the non-glycoside components in caralluma along with the glycosides thereof. Said non-glycoside components are tannins, pectins, said resinous matter and others. The present inventors have found that at low ethanol concentrations, for example at 10%, considerable quantities of tannins and pectins are extracted out with the glycosides while at high aq. Ethanol concentrations the resins go preferentially into solution. These inventors observe that when 10% aq. ethanol is used one gets a glycoside extract that contains considerable percentage of said tannins and pectins. So, in the process conditions adopted in said first, third and fourth references the caralluma extract obtained would have considerable impurities in the form of tannins and pectins that have a deleterious effect on the shelf life of the glycoside product. In said second reference, ethanol concentrations of over 80% are likely to be encountered by the caralluma plant matter in the soxhlet apparatus. These inventors have found that the extract under these conditions would contain high amounts of the caralluma resins.

The third drawback of prior art is that the caralluma extract product obtained by the prior art process is non-standard in so far as the composition thereof would vary from one extraction to another. It is unrepresentative in so far as it would not reflect fully either the various constituents of caralluma glycosides or their relative proportions that are found in the original plant matter.

Further, as the composition would vary from extract to extract the caralluma extract product of the prior art process cannot be considered to be reproducible.

Apart from said pharmacological studies of a few of the medicinal aspects of caralluma, prior art does not provide for any concrete medical applications of caralluma. These inventors have pioneered such applications. Said applications would require caralluma constituents in various forms such as tablets, injectables and others which would have to be made starting from a suitable intermediate that contains the principles of caralluma. Such an intermediate that contains the principles of caralluma and that could be said starting point is neither known or defined in the prior art.

In summary, the drawbacks of said prior art process are:

i. non-standardised , non-representative and non-reproducible product;
ii. process conditions conducive to said decomposition of the glycosides of caralluma;
iii. extracting out of undesirable non-glycoside components of caralluma in the extracts, such as said tannins, pectins and resins that would affect the purity and storage properties of the product and/or that have side effects on the subjects treated with caralluma glycoside products;
iv. no provision for removal of said undesirable non-glycoside components from the extracts in the process of prior art; and
v. process parameters not optimised from the point of view of process economics or from the point of view of obtaining said desirable caralluma intermediate product(s).

SUMMARY OF THE INVENTION

It is the object of this invention to eliminate the abovementioned drawbacks and to define one or more suitable Caralluma Extract products(pharmaceutical compositions) that are standardised, representative of the caralluma plant material from which they are derived, are reproducible and which form suitable starting materials(intermediates) for the medicinal, nutraceutical and food products of caralluma and which are, furthermore, suitable for direct administration to subjects.

It is another object of this invention, to devise processes for making said Caralluma Extract products wherein said decomposition is minimised or prevented; wherein the extraction of said undesirable non-glycoside components along with the glycosides is minimised or prevented and

wherein purification means are provided for removal of said undesirable components from said extracts substantially totally or down to low unobjectionable levels.

A still further object of the invention is to define said caralluma extract products at least one of which is a solid and another a liquid and to optimise the specifications thereof considering the process economics, the requirements of said applications of caralluma and the downstream processes for the same.

It is a still further object of this invention to maintain substantially the same CBR in the caralluma extract products as found in said Group I and II caralluma species in view of the presence of said synergy maximum.

According to the invention, therefore, there is provided a First Caralluma Extract, also referred to as Caralluma Extract Technical.

Further according to the invention, there is provided a Second Caralluma Extract, also referred to as the Standardised Caralluma Extract.

Still further this invention provides for a process for making a composition for medicinal, nutraceutical and food applications, that chiefly comprises one or more pregnane glycosides, from plant matter wherein the nature of the solvent/solvent mixture for extraction and the conditions of extraction and of concentration of the extract are selected such as to prevent/minimise the decomposition of said glycosides and the simultaneous extraction of non-glycoside matter such as the pectins, tannins and the resinous matter contained in said plant matter.

Still further according to the invention there is provided a process for making one embodiment of said First Extract(Caralluma Extract Technical) from caralluma plants, one embodiment of said process comprising the steps of:

i. pre-treatment of the caralluma plant material by one or more optional operations such as washing, cleaning, soaking, drying, cutting, chopping, blanching, and others, if and as necessary;

ii. crushing and/or grinding of the plant material obtained from step (i), if, and to the extent, desired;

iii. extracting the material obtained from step (ii) in one or more stages by means of a suitable solvent/solvent mixture and/or with a solution obtained from another extraction, the nature of said solvent/solvent mixture and the concentration thereof and the temperature of extraction being selected such as to minimise or substantially prevent the extraction of the tannins, pectins and resinous mater therein;

iv. concentrating the extract batch(es)(solutions) obtained from step (iii) either singly or as mixtures of one or more thereof in a first concentration stage and further optionally in a second concentration stage by removal of said solvent/solvent mixture by any of known means such as the evaporation of said solvent/solvent mixture to yield the First Caralluma Extract(Caralluma Extract Technical), said solvent/solvent mixture being recovered, if desired;

v. optionally returning one or more said extract batch(es) or parts thereof before said first concentration stage to step(iii) for contacting with the said plant material to be extracted, said batch(es) being subjected optionally to filtration so as to remove particulate solid matter, if any;

vi. optionally subjecting the material-in-process to a resin extracting operation by means of a resin dissolving solvent as part of said step (i), or immediately following said steps (i) or (ii) or (iii) or immediately after said first concentration stage.

Still further, according to the invention, there is provided a process for making an embodiment of said Second Extract(Standardised Caralluma Extract) from said First Extract(Caralluma Extract Technical) one embodiment of said process comprising the steps of:

i. contacting said First Caralluma Extract(Caralluma Extract Technical) with a suitable excipient and further with a suitable binder as necessary, and subjecting the materials to a mixing/blending operation;

ii. drying the material obtained from step (i) by any of the known methods;

iii. powdering the material obtained from step (ii) if required and to the size required by any one of the known methods of grinding/milling; and

iv. sifting the ground/milled material of step (iii) and subsequently blending the sifted material to yield said Second Caralluma Extract(Standardised Caralluma Extract).

Still further, according to the invention, there is provided a process for making an embodiment of said Second Caralluma Extract(Standardised Caralluma Extract) from caralluma plant material, one embodiment of said process comprising the steps of:

i. pre-treatment of the caralluma plant material by one or more optional operations such as washing, cleaning, soaking, drying, cutting, chopping, blanching, and others, if and as necessary;

ii. crushing and/or grinding of the plant material obtained from step (i), if, and to the extent, desired;

iii. extracting the material obtained from step (ii) in one or more stages by means of a suitable solvent/solvent mixture and/or with a solution obtained from another extraction, the nature of said solvent/solvent mixture and the concentration thereof and the temperature of extraction being selected such as to minimise or substantially prevent the extraction of the tannins, pectins and resinous mater therein;

iv. concentrating the extract batch(es)(solutions) obtained from step (iii) either singly or as mixtures of one or more thereof in a first concentration stage and further optionally in a second concentration stage by removal of said solvent/solvent mixture by any of known means such as the evaporation of said solvent/solvent mixture to yield said First Caralluma Extract(Caralluma Extract Technical), said solvent/solvent mixture being recovered, if desired;

v. optionally returning one or more said extract batch(es) or parts thereof before said first concentration stage to step(iii) for contacting with the said plant material to be extracted, said batch(es) being subjected optionally to filtration so as to remove particulate solid matter, if any;

vi. optionally subjecting the material-in-process to a resin extracting operation by means of a resin dissolving solvent as part of said step (i), or immediately following said steps (i) or (ii) or (iii) or immediately after said first concentration stage;

vii. contacting said First Caralluma Extract(Caralluma Extract Technical) with a suitable excipient and further with a suitable binder as necessary, and subjecting the materials to a mixing/blending operation;

viii. drying the material obtained from step (vii) by any of the known methods;

ix. powdering the material obtained from step (viii) if required and to the size required by any one of the known methods of grinding/milling; and

x. sifting the ground/milled material of step (ix) and subsequently blending the sifted material to yield said Second Caralluma Extract(Standardised Caralluma Extract).

The First Caralluma Extract product of this invention is preferably a liquid product containing the caralluma glycosides and other caralluma components in solution and that is designed to be a suitable starting material, intermediate, for a number of pharmaceutical, nutraceutical and food products containing the principles of caralluma. Said product contains the pregnane glycosides and may contain one or more or all said glycosides within the scope of the invention. Similarly, the proportions of said glycosides therein can have any set of values within the scope of the invention. Preferably, said product contains at least, both said major pregnane glycosides(including the isomers), namely, the caratubersides and boucerosides. Further, preferably said two major glycosides are substantially in the proportions corresponding to the proportions found in the caralluma species of said Groups I and II. That is, the CBR, the ratio of caratubersides and boucerosides therein is preferably 9:1 to 11:1. Further, preferably the resin content in said product does not exceed 0.5% by wt. Preferably, the pregnane glycoside content in said First extract is either 5% to 15% w/w or is above 15% w/w. Preferably, said product is suitable for direct administration to subjects without any conversion or treatment.

The glycoside content of said Technical Extract of the invention may have any value within the scope of the invention, that is, said Caralluma Extract Technical may be of any desired concentration. This invention has considered the economics of the process, including extraction and concentration costs and the requirements of the downstream processes and further the different glycoside contents of said Groups I and II and has arrived at two preferred concentrations of said glycosides in said product, namely, above 15% by wt. of glycosides and from 5-15% by wt. glycosides. The first extract may also contain some or all of the saponin glycosides of caralluma and the bitters of caralluma.

The Standardised Caralluma Extract of the invention is preferably a solid form product that is designed to be a suitable starting material(intermediate) for several pharmaceutical, nutraceutical and food products containing the principles of caralluma. Preferably said second extract comprises the said pregnane glycosides adsorbed on a suitable excipient. Said Extract contains the said pregnane glycosides and may contain one, more or all of said glycosides within the scope of the invention. Similarly, said glycosides may be in any relative proportions within the scope of the invention. Preferably, said Extract contains both said pregnane glycosides, namely, the caratubersides and the boucerosides and preferably they are substantially in the proportions as found in caralluma species of said Group I and II, that is, having a CBR of 9:1 to 11:1. Preferably the resin content in said extract does not exceed 1.0% by wt. Preferably, said product is suitable for direct administration to subjects, if desired without the necessity of any conversion or treatment.

The glycoside content of said Standardised Extract can have any value within the scope of the invention.

After considering the process economics including the costs of extraction and concentration and the desirable specification of said Extract for downstream processes for the pharmaceutical, nutraceutical and food products of caralluma and also the glycoside contents of said Group I and II species this invention has arrived at two preferred concentrations of said Standardised Caralluma Extract, namely, a pregnane glycoside content of over 30% and from 25% to 30% w/w. Said two glycoside contents are the specifications obtained by extracting said Group I and II species respectively using the processes of the inventions in a generally optimised manner. Said second extract may also contain one or more of the saponin glycosides of caralluma and/or the bitters thereof.

Said first and second extracts defined by this invention are pharmaceutical compositions in so far as they may be directly administered to subjects. Similarly, they are directly usable as nutraceutical products and food products. Thus, said pharmaceutical composition may comprise said first or second extracts or others in their unconverted form or in the form of any of the pharmaceutically acccepted salts thereof. Said composition may be in the form of a tablet, or injectable or suspension or other pharmaceutical forms. Said compositions may comprise one or

more further therapeutical components and may include any of the known pharmaceutically acceptable additives such as for taste, colour, flavour and others.

BRIEF DESCRIPTION OF THE DRAWINGS

A more complete appreciation of the invention, and many of the attendant advantages, thereof, will be readily apparent as the same becomes better understood by reference to the following detailed description when considered in conjunction with the accompanying drawings in which like reference symbols indicate the same or similar components, and wherein:

Fig. 1 shows an example of the process of the invention for making the first Caralluma extract from Caralluma plant matter;

Fig. 2 shows an example of the process of the invention for making the second Caralluma extract from the first Caralluma extract;

Fig. 3 shows one of the preferred processes of the invention for making the first Caralluma extract from Caralluma plant matter; and

Fig. 4 shows one of the preferred processes of the invention for making the second Caralluma extract from the first Caralluma extract.

DETAILED DESCRIPTION OF THE INVENTION

The First Caralluma Extract product of this invention is preferably a liquid product containing the caralluma glycosides and other caralluma components in solution. It is designed to be a suitable starting material, intermediate, for a number of pharmaceutical, nutraceutical and food products containing the principles of caralluma. Said product may contain any of the pregnane glycosides or mixtures thereof. Similarly, the proportions of said glycosides therein can have any set of values within the scope of the invention. Preferably, said product contains at least, both said major pregnane glycosides of caralluma, namely, the caratubersides and boucerosides. Further, preferably said two major glycosides are substantially in the proportions corresponding to the proportions found in the caralluma species of said Groups I and II. That is, the CBR, the ratio of caratubersides and boucerosides therein is preferably 9:1 to 11:1. Further, preferably the resin content in said product does not exceed 0.5% by wt. Preferably, the pregnane glycoside content in said First extract is either 5% to 15% w/w or is above 15% w/w.

The glycoside content of said Technical Extract of the invention may have any value within the scope of the invention, that is, said Caralluma Extract Technical may be of any desired concentration. This invention has considered the economics of the process, including extraction and concentration costs and the requirements of the downstream processes and further the different glycoside contents of said Groups I and II and has arrived at two preferred concentrations of said glycosides in said product, namely, above 15% by wt. of glycosides and from 5-15% by wt. glycosides. The first extract may also contain some or all of the saponin glycosides of caralluma and the bitters of caralluma.

Typical composition of the Caralluma Extract Technical product of the invention of said two preferred concentrations are given below.

TABLE I

First Caralluma Extract(Caralluma Extract Technical)
(from Group I Species)

Test parameter	Specification
Appearance	brown to dark brown liquid
Solubility in water	soluble
Total dissolved solids	65% minimum w/w
Total Bitters	1.5% minimum w/w
Total Saponin Glycosides	5% minimum w/w
Total pregnane glycosides	Above 15% w/w
Resinous matter	not more than 0.5% w/w
Total microbial count	5000 cfu/gm. maximum
E. coli and salmonella	absent
Coliforms	absent
P. aeruginosa	absent
S. aureus	absent
Heavy metals	10 ppm maximum

TABLE II

First Caralluma Extract(Caralluma Extract Technical)
(from Group II Species)

Test parameter	Specification
Appearance	brown to dark brown liquid
Solubility in water	soluble
Total dissolved solids	65% minimum w/w
Total Bitters	0.5% minimum w/w
Total Saponin glycosides	2% minimum w/w
Total pregnane glycosides	5%-15% w/w
Resinous matter	not more than 0.5% w/w
Total microbial count	5000 cfu/gm. maximum
E. coli and salmonella	absent
Coliforms	absent
P. aeruginosa	absent
S. aureus	absent
Heavy metals	10 ppm maximum

The Standardised Caralluma Extract of the invention is preferably a solid form product that is designed to be a suitable starting material(intermediate) for several pharmaceutical, nutraceutical and food products containing the principles of caralluma. Said Extract may contain any of the said pregnane glycosides or mixtures thereof within the socpe of the invention. Preferably said glycosides and other components are adsorbed on a suitable excipient. Similarly, said glycosides may be in any relative proportions within the scope of the invention. Preferably, said Extract contains both said major pregnane glycosides, namely, caratubersides and boucerosides and preferably they are substantially in the proportions as found in caralluma species of said Group I and II, that is, a CBR of 9:1 to 11:1. Preferably the resin content in said extract does not exceed 1.0% by wt.

The glycoside content of said Standardised Extract can have any value within the scope of the invention. After considering the process economics including the costs of extraction and concentration and the desirable specification of said Extract for downstream processes and also the glycoside contents of said Group I and II species this invention has arrived at two preferred

concentrations of said Standardised Caralluma Extract, namely, a pregnane glycoside content of over 30% w/w and from 25% to 30% w/w. Said two glycoside concentrations are the specifications obtained by extracting said Group I and II species respectively using the processes of the inventions in a generally optimised manner.

Said Standardised Caralluma Extract of the invention comprises the said caralluma glycosides adsorbed on an excipient and is in the powder form. Typical analysis of said Standardised Caralluma Extract of said preferred concentrations(compositions) are given hereinbelow.

TABLE III

Standardised Caralluma Extract
(from Group I caralluma species)

Test parameter	Specification
Appearance	brown to dark brown powder
Solubility in water	75% minimum w/w
Loss on drying	10% maximum w/w
Total Bitters	3% minimum w/w
Total saponin glycosides	10% minimum w/w
Total pregnane glycosides	above 30% w/w
Resinous matters	Not more than 1% w/w
Total microbial count	5000 cfu/gram maximum
E. coli and salmonella	absent
Coliforms	absent
P. aeruginosa	absent
S. aureus	absent
Heavy metals	10 ppm maximum

TABLE IV

Standardised Caralluma Extract
(from Group II caralluma species)

Test parameter	Specification
Appearance	brown to dark brown powder
Solubility in water	75% maximum w/w
Loss on drying	10% maximum w/w
Total bitters	1% minimum w/w
Total saponin glycosides	3% to 5% w/w
Total pregnane glycosides	25%-30% w/w
Resinous matters	not more than 1% w/w
Total microbial count	5000 cfu/gm. maximum
E. coli and salmonella	absent
Coliforms	absent
P. aeruginosa	absent
S. aureus	absent
Heavy metals	10 ppm. Maximum

Within the scope of the invention, said Caralluma Extract Technical and the Standardised Caralluma Extract of the invention may be made by a process of admixture of the constituents thereof or by the employing the extraction processes of the invention or by others.

However, by adoption of the process of the invention, Caralluma Extract Technical and the Standardised Caralluma Extract are obtained containing substantially all the glycosides of caralluma, the desired said CBR, a low resin content , that is, not exceeding the specified limits and low contents of said pectins and tannins.

The processes of the invention for Caralluma Extract Technical and Standardised Caralluma Extract can provide any desired concentration of said glycosides in the products by suitable operation of said extraction and concentration steps and of the other steps.

Said two preferred concentration ranges of the Caralluma Extract Technical and the Standardised Caralluma Extract of the invention are by way of example, that is, by way of preferred embodiments and are without limitation to the scope of the invention. The process of the invention can be operated to give said products of invention having any

concentration(composition) of glycosides therein whether the starting material is said Group I or II species. Said two composition ranges have a certain amount of practical and commercial significance in that they are obtained by processing said Group I and II caralluma species by operating the processes of the invention in a generally optimum manner. The association of said two preferred concentration ranges with said Group I and II species is entirely from the point of view of process economics and downstream processing requirements and is without limitation to the scope of the invention.

Within the scope of the invention, said first and second extracts may additionally contain other components of caralluma such as the saponin glycosides and bitters of caralluma.

The purpose of said excipient in the Standardised Caralluma Extract product of the invention is to adsorb the caralluma glucosides thereon and further to provide an extended surface area for rapid and substantially complete removal of the traces of water, the extraction solvent and the resin dissolving solvent if used. The use of any of the known excipients is within the scope of the invention, the preferred excipients being Malto Dextrin and Magnesium Carbonate.

Within the scope of the invention, the Caralluma Extract Technical and the Standardised Caralluma Extract of the invention, may be made by any of the processes of the invention outlined hereinabove or by a process of admixture of the constituents thereof or by other processes. Said first and second extracts of the invention may be used in medicines having at least one of, but not limited to, the following pharmacological effects: carminative, febrifugal, anti-rheumatic, anti-diabetic and anti-hyperglycaemic, anti-pyretic, anti-inflammatory, anti-hypertensive, anti-nociceptive, anti-oxidant, anti-arthritic, anti-obesity, reduction of BMI(body mass index) and increase of BMR(Basal Metabolic rate) and others.

The present invention and, particularly, the terms 'caralluma extract', 'caralluma plant matter' and 'caralluma plant material' refer to any of the caralluma group species and are not limited to the caralluma species listed herein.

The first step in the process of the invention for making Caralluma Extract Technical from caralluma plant matter, an example of which is shown in Fig. 1 comprises one or more optional operations that may be required considering the condition of the caralluma plant material. The factors to be considered are the size of the plant material and the moisture content thereof, the

amount of foreign matter therein and others. In tropical regions solar drying of the plant material is adequate.

Said first step 110 comprises one or more optional pre-treatment operations such as washing, cleaning, soaking, drying, cutting, chopping, blanching, and others, if and as necessary.

The plant material is preferably extracted as a powder. Thus, if the plant material is in large pieces, a cutting/chopping operation would be desirable to reduce it to a smaller size so that it can be ground to the desired mesh size for the extraction operation. Reducing the plant material size provides better contact during extraction and consequently faster extraction and also better heat transfer and uniformity of bed temperature in the extractor. Very fine plant material may tend to form lumps during extraction reducing the solid-liquid contact.

The crushing and/or grinding 120 of the raw plant material or the plant material obtained from the pretreatment is also optional. In this application, the term "crushing" includes crushing or grinding, or both. A number of grinding apparatus/equipments are available and are within the scope of the invention. A swing hammer mill is preferably used. If the plant material is in pieces rather than a powder, larger equipment is required for the same batch size, and a larger amount of solvent (or mixture) would also be necessary per batch. The batch times would also be correspondingly higher. The preferred size of the material-in-process after grinding is -10 BSS to +80 BSS. The extraction step 130 may be carried out by any of the several known methods such as batch, continuous, counter-current, series arrangement, parallel arrangement and others, by combinations of one or more of these, by hybrid schemes formed by fusing one or more of the methods.

One preferred example of the extraction method is of semi-parallel batch extraction with semi-countercurrent solvent feed. For instance, where a batch of plant material undergoes three separate extraction operations, a plurality of extractors are used. The three operations are referred to herein as "E1", "E2" and "E3". The solvent feed in the operation "E1" is not pure solvent but the somewhat weak extract obtained from the operation E3 of extraction. The solvent feed charged in the operations "E2" and "E3" is substantially pure solvent, which may be either fresh solvent or recovered solvent. The "A", "B" and "C" refer to the extracts(solutions) obtained in the operations, E1, E2 and E3, respectively. In the extraction step 130, undesirable non-glycoside components of Caralluma are also extracted, such as the tannins, pectins and resins that would

affect the purity and storage properties of the product and that have side effects on the subjects treated with Caralluma glycoside products or Caralluma extracts.

Numerous combinations of the extraction methods, extraction schemes and solvent feed systems are possible. The choice of the extraction method is governed by process economics factors such as solvent costs and availability, solvent recovery costs, batch times, energy costs for the heating of extractor contents, capital costs of various types of extraction equipment and others. Such factors vary from region to region and location to location. A wide range of extraction equipment is available. The choice is usually made on cost considerations and with the idea of keeping the batch times to the minimum. One preferred example of the extractor equipment is a jacketed stainless steel extractor.

The selection of the solvent is important. In view of the problems recognized by the inventors, a solvent should offer a good rate of extraction at low temperature and possess low solubility for the resins and also for the tannins and pectins. The rate of solubility of resins, tannins and pectins should also be as low as possible at the conditions adopted for extraction. That is, it is important to optimize the selection of the solvent and conditions of extraction (e.g., temperature and duration of extraction) so that the dissolution of the resinous matter is so reduced as to eliminate the necessity of the optional resin removal step and so that the entire concentration can be carried out in the first stage of concentration.

The present inventors have investigated a number of solvents for the extraction such as for example, acetone, iso-propyl alcohol, ethylene dichloride, n-hexane, n-butanol, water, methanol, ethanol, aq. methanol and aq. ethanol in view of the above factors.

100% methanol gives a poor yield of glycosides and extracts a large amount of resinous matter. This pushes up the solvent costs and solvent recovery costs of resin extraction. Similar results are obtained with methanol of 40% to 100% strength. The best yield of glycosides with a particular batch time is found to be with 20%-40% methanol. But the resin extraction is still high. Because of the resin extraction, the product turns out to be sticky and hygroscopic. Accordingly, a resin removal operation is preferably performed. For example, when methanol is used as a solvent for extraction, n-hexane can be used for resin removal.

Use of ethylene dichloride as solvent without resin removal gives a sticky and hygroscopic Caralluma extract product. If resin removing solvent such as high strength aq. ethanol is used, the product is better but the yield of glycosides with ethylene dichloride is low compared to the use of 30% aq. ethanol where other parameters are substantially the same. The solvent costs and solvent recovery costs are high for both the extracting solvent and for the resin dissolving solvent.

Use of iso-propyl alcohol as solvent gave a good yield of glycosides. n-Hexane was used as the resin removing solvent. When iso-propyl alcohol was used, the Caralluma extract product was found to be of acceptable quality. However, iso-propyl alcohol is a costly solvent.

If water is used as a solvent with the resin dissolving solvent being n-butanol, the yield as well as the product quality are poor. In addition, n-butanol is an expensive solvent.

Costwise, ethanol is preferable to other solvents. Aqueous ethanol gives a good yield of glycosides. It is observed that, at higher strengths, the aqueous ethanol tends to extract more resin than at lower strengths, and that, at lower strengths, it tends to pick up more of the tannins and pectins than at higher strengths. Accordingly, the optimization of the concentration is important. It is preferred that the aq. ethanol is of 10%-85% strength. It is also preferred that the ethanol concentration is 20%-40% by volume to get a good yield of glycosides and simultaneously minimise the extraction of the tannins, pectins and resins.

Various solvent mixtures were investigated by these inventors such as mixtures of n-butanol, ethyl acetate and ethylene dichloride with ethanol, methanol, aq. ethanol, aq. methanol and others. The yields and the product quality were good. The cost is the constraint in their adoption as n-butanol, ethylene dichloride and ethyl acetate are expensive solvents.

While the extraction at the higher temperature tends to keep the batch times shorter, the decomposition of glycosides increases with temperature. Therefore, the optimization of the temperature should be considered. Preferably, the extraction should be done in the temperature range of 70-80 degrees C when using aq. ethanol as solvent. More preferably, the extraction should be done in the temperature range of 70-75 degrees C because, where the extraction temperature is held at levels higher than 75 degrees C, thermal decomposition of the glycosides occurs. Such high temperatures enhance the viscosity of the extract and increase the risk of decomposition in the concentration step.

Batch times can be controlled by controlling the temperature of extraction and the scheme of extraction adopted, solvent used, degree of agitation and others. With 20-40% aq. ethanol as solvent and extraction at 70-80 degrees C preferably the extraction is carried out in 3-4 stages, of which each batch time is about 5-8 hours. In these stages, either fresh solvent or weak solution(s) from other extractions are used.

Step 140 is a concentration step. Numerous methods of desolventification (solvent removal) including evaporation are available. It will be apparent to those skilled in the art that any of the numerous methods available for the concentration step 140 will serve effectively.

The evaporated solvent may be recovered if desired.

The temperature of the evaporation is important. Where aq. ethanol is used, the evaporation is more preferably carried out at temperatures from 40 to 50 degrees C under vacuum.

A plurality of extract batches may come out from the extraction step 130. In the first stage of the concentration step 141, the concentration of the extract batch(es) may be carried out in a single operation or in a plurality of operations. Still further, where the plurality of batch(es) are present, the concentration operation may be carried out singly on each batch or on mixtures of one or more of the batches. Such combinations offer plant operational flexibility and scope for optimizing usage of plant.

For example, with regard to the extract batches "A" and "B" coming out from the extraction step 130, the batches "A" and "B" may undergo a first concentration operation singly to about one-tenth of the original volumes thereof. Subsequently, the batches "A" and "B" may be mixed and then concentrated further to about one fifth of the starting volume thereof. The concentration of the pregnane glycosides at the end of concentration of the mixed batch is preferably about 3-8% by wt. This preferred concentration is below the range at which any significant decomposition of the glycosides occurs.

The viscosity of an extract being concentrated goes up with increasing glycoside concentration. This problem is further compounded by the presence of the resinous matter in the extract. In fact, where glycoside concentration is above 3-8% by wt., overheating and/or charring may occur due

to the high viscosity. Therefore, if the extract contains a large amount of resinous matter, it is advisable to terminate the first stage of concentration at this concentration and undertake the resin removal step 160 as it is the resin that is responsible for the high viscosities. After the resin removal, further concentration (i.e., the second stage of concentration 142) may be taken up. The first and second concentration stages 141, 142 may comprise a plurality of individual concentration operations. Accordingly, it is preferred that the resin removal step 160, if required, be carried out after the first stage of concentration 141 and before the second stage of concentration 142. The reduced volume of the partially concentrated solution(s) can reduce the requirement of the resin dissolving solvent.

The partially concentrated solution(s) at the end of the first concentration step 141 may include particulate impurities. An optional filtration operation 150 may be taken up at this stage to remove the particle impurities before sending the solution(s) to the second stage of concentration 142, or to the optional resin removal step 160 or before returning one or more solution(s) to the extractor(s) to form the solvent feed for one of the stages of the extraction step 130.

Whether or not the resin extraction option is exercised depends on the resin content of the original plant material and how much of the resin is extracted into the extract (i.e., solution). The latter depends on the nature of solvent and its concentration, and the conditions of extraction such as temperature and duration, agitation and others.

The resin removal 160 may be done as part of the pretreatment step 110. n-Hexane can be used as the resin dissolving solvent. Where substantially complete resin removal is achieved, the concentration step 140 can be done in one stage because the entire concentration even up to substantial total dryness could then be done in the first stage 141 without any noticeable decomposition. The resin removal 160 with n-hexane may be done with or without refluxing of the solvent. The drawback in this embodiment is that the consumption of n-hexane, which is expensive, is high.

The resin removal step 160 can also be done between the pretreatment step 110 and the crushing/grinding step 120. After the pretreatment step 110, the plant material is generally of a reduced size so that the requirement of the resin dissolving solvent is reduced.

The resin removal step 160 can be carried out after the crushing/grinding step 120. In this arrangement, there would be further reduction in the amount of solvent required because the crushing/grinding step 120 makes the material to be contacted with the solvent still finer. This has the effect of reducing the batch times for resin extraction.

The resin removal step 160 may be carried out also after the extraction step 130. If done at this stage, it would be a liquid-liquid extraction operation. Contacting of two liquids is a far more efficient operation and consequently the required amount of the solvent would be still less at this stage, all other conditions being equal. Batch times are also reduced.

While it is preferred that the resin removal step be carried out after the first stage of concentration 141 and before the second stage of concentration 142, the determining factors are the cost and availability of the resin extracting solvent. The decision as to where to locate said resin removal step may be made on the basis of the cost and the availability of the resin solvent.

A number of resin dissolving solvents were tried in this invention, such as n-hexane, petroleum ether, benzene, toluene, diethyl ether, methylene dichloride and ethylene dichloride. The resin dissolving solvent can be selected on the basis of the cost of the process and on the cost and availability of the solvent and on considerations such as toxicity, ease of trace removal and others. In the present invention, n-hexane is preferred.

Generally speaking, if the resin content is desired to be reduced to the preferred values of not more than 0.5% w/w for the first Caralluma extract product and not more than 1.0% by wt for the second Caralluma extract product, it would be necessary to carry out the resin removal step 160. However, as mentioned hereinabove, this depends on the original resin content in the plant material and how much of it comes out in the extracts (solutions) during the extraction step.

The resin removal step 160 may include the step of washing the optionally filtered first concentrate, (the solution(s) obtained after the first concentration stage 141) with a suitable solvent that can dissolve the resinous matter contained in the filtrate. The washing (leaching) may be carried out one or more times. The washing step is preferably a liquid-liquid extraction process and any of the various equipment known in the art for the purpose may be used.

The washed filtrate is subjected to a separation operation that results in two layers, the heavy layer being the glycosides in solution and the light layer being the resin dissolving solvent with the resin matter in solution. The separation can be carried out in any of the known equipment/apparatus available in the art for the purpose and adoption of any of them is within the scope of the invention.

The light layer having the resinous matter in solution is either discarded or subjected to a solvent recovery operation by any of the known means of solvent removal provided in the art. Preferably the solvent recovery is done by evaporation and condensation of the solvent.

The heavy layer contains the Caralluma glycosides and is subjected to the second concentration stage 142. Like the first concentration stage 141, the conventional concentration steps and their variations will be apparent to those skilled in the art. Preferably, the concentration 140 is done by evaporation of the solvent under vacuum using thin film evaporators.

The preferred temperature range for the evaporation is 40 to 50 degrees C when aq. ethanol is used as the extracting solvent. The evaporation is done under vacuum. The evaporated solvent can be recovered by condensation. The selection of the method of solvent removal and of the equipment therefor is to a large extent based on cost factors.

The concentration is continued until the desired concentration of glycosides is reached. The heavy layer, that is, the concentrated solution at this stage constitutes the first Caralluma extract product of the invention.

As shown in FIG. 2, the second Caralluma extract product can be made from the first Caralluma extract.

The first Caralluma extract is first contacted with a suitable excipient 210. The contact may be carried out in any of the mixing apparatus/equipment such as, for example, planetary mixers, rapid mixers, granulators, slurry tanks and others that are found in the art. A number of suitable excipients are available in the art and may be used in the process of the invention. The preferred excipients are maltodextrin and magnesium carbonate.

Along with the excipient, the binders (binding agents) may be added if required or desired. Any of the known binding agents may be used in the process of the invention. Preferably, the binder

is selected from the following, starch, gum Acacia, guar gum and polyvinyl pyrolidone. The mixing is continued till the adsorption of the first Caralluma extract on the excipient particles is completed, and the particles have a homogeneous coating of the glycosides and the binder, if used.

At this stage the material-in-process is removed and subjected to the drying step 220. The drying 220 is carried out by any of several methods of drying and by any of the many drying apparatus/equipment that are available in the art. Tray driers, fluid bed dryers, spray driers and vacuum driers are some of the drying apparatus/equipment available in the art. A tray drier and a spay dryer are preferred. The spray drying makes the product sticky and hygroscopic. For example, the blended material from the excipient step 210 may be thinly spread on the trays of the tray drier. This assists and accelerates the evaporation of the final traces of moisture, extraction solvent and the resin dissolving solvent. Accordingly, the excipient may be used for performing both an adsorption function and the function of facilitating drying.

The dried material is basically the second Caralluma extract of the invention. Preferably, it is subjected to a grinding/milling (powdering) operation 230 to obtain a fine powder. The conventional equipment/apparatus such as multi-millers, hammer mills and pulverizers can be used for the grinding/milling step 230.

The product from the grinding/milling step 230 is then sifted in any of the known sifting, equipment/apparatus such as, but not limited to, a sieve shaker or sifter 240.

The sifted material is then blended in a blending machine such as, but not limited to, double cone blender, a ribbon blender, or an octagonal blender 250.

The output from the blending step 250 is the second Caralluma extract of the invention in a powder form.

The process of the invention for making said Standardised Caralluma Extract starting with caralluma plant matter comprises a total of ten steps including optional ones out of which the first six steps are in fact, identical with the steps in the process of the invention for making said Caralluma Extract Technical. It will be seen therefore, that Caralluma Extract Technical is an intermediate product in the process of the invention for making said Standardised Caralluma

Extract starting with caralluma plant material. The remaining four steps are identical with and are taken from the process of the invention for converting Caralluma Extract Technical to the Standardised Caralluma Extract. It will be seen that each of said six steps and four steps have been covered in detail in the foregoing description and that said description and the comments therein are applicable to the corresponding steps in this process of the invention, namely, making said Standardised Extract, starting with caralluma plants. Said description and comments are therefore referred to here at this point for elaborating this process of the invention and are not repeated at this point in the interests of conciseness.

References to solvent hereinabove and in other parts of this specification also include solvent mixtures unless the context requires otherwise, that is, the expression 'solvent/solvent mixture' has been shortened to 'solvent' in the interests of clarity and conciseness.

The terms 'caralluma plant material' or 'plant material' or 'plant matter' refer to the raw material at the commencement of the process, said 'plant material' at various stages of processing in the processes of the invention being referred to as 'material-in-process'. However, for the sake of clarity, conciseness and convenience the terms, 'plant material', 'plant matter' and 'material-in-process' are used somewhat interchangeably. Their meaning would, however, will be found to be quite clear from the context.

In order to provide a clearer understanding of the invention and without limitation to the scope thereof, some examples will now be described and are illustrated in Figs. 3 and 4.

Example-1

The aerial parts of Caralluma fimbriata plant were collected and dried in open-air under a shade 310. The dried material was ground in a swing hammer mill 320. For the extraction step 330, about 500 kgs. of this dry powder material was charged to an extractor. The extractor includes a stainless steel vessel of about 5,000 liters capacity provided with an agitator system and a surrounding jacket for steam heating. About 2,000 liters of about 30% aq. ethanol solvent was charged into the extractor. The solvent charged was formed by mixing about 600 liters of rectified spirit with about 1400 liters of water. The extractor contents were maintained at about 70-75 degrees C by heating with steam and the extraction was carried out for about six hours. This extract is referred to as "A". The volume of extract "A" was about 1,500 L.

The residue in the extractor comprising the partly-extracted Caralluma plant material was subjected to a second extraction (leaching) operation. About 2,000 liters of about 30% aq. ethanol was charged into the extractor and the extraction carried out at about 70-75 degrees C. The extract was taken out of the extractor. The quantity of extract obtained was about 1,500 L. This extract is referred to as "B".

The plant residue in the extractor, comprising the twice-extracted Caralluma matter was subjected to the third extraction. About 1,500 L of about 30% aq. ethanol solvent was charged into the reactor(extractor) to yield about 1,500 L of extract at the end of the extraction operation which was carried out at about 70-75 degrees C. This extract is referred to as "C".

For the first concentration step 341, the extracts "A" and "B" were both separately concentrated in concentrators down to a volume of about 150 L each. The extract "C" was used as solvent charge (solvent feed) for the first stage extraction of the next batch of Caralluma plant material. In this example, the solvent charge in the first extraction is solute-free aq. ethanol of about 30% strength. In the normal course, the solvent charge to the first extraction would be the "C" extract obtained from another batch. But being a freshly commenced extraction operation, the "C" extract was yet to become available and hence solute-free solvent was used.

At this stage, the concentrated extracts "A" and "B" are combined giving about 300 L of material (step 344). This was filtered in a stainless steel Nutsche type Filter using a filter aid (step 350). The filter bed was washed with about 50 L of about 30% aq. ethanol.

The filtrate contains the glycosides. About 300 L of n-hexane is added to the glycosides solution to dissolve out and remove the resinous matter therein (step 360). After allowing a period of time for the hexane to dissolve the resinous matter the material-in-process was subjected to a separation operation 370 resulting in separation into a light hexane-rich layer and the heavier glycoside solution. The hexane-rich layer was sent for hexane recovery while the glycoside solution layer was subjected to another treatment with n-hexane. Again about 300 L of hexane was used. The separation procedure was repeated giving the said two layers out of which the lighter hexane layer was sent for hexane recovery and the heavier glycoside layer was sent for the second concentration step 342 where concentration was carried out in a thin film evaporator at about 45 degrees C and under a vacuum of less than 20 mm. of Hg. The concentrated material

constituted the first Caralluma extract product. The above procedure was carried out five times to check whether the yields are reproducible. The amount of product obtained ranged between 55-65 kgs. The composition/analysis of the product obtained is given hereinbelow.

TABLE 5

Product: First Caralluma Extract (From Caralluma fimbriata)		
Test Parameters	Specification	Actual Values
Appearance	Brown to dark brown liquid	Complies
Solubility in water	Soluble	Soluble
Total dissolved Solids	65% minimum w/w	71% w/w
Total Bitters	1.5% minimum w/w	2% w/w
Total Saponin Glycosides	5% minimum w/w	7% w/w
Total Pregnane Glycosides	Above 15% w/w	19.6% w/w
Resinous matters	Not more than 0.5% w/w	0.05% w/w
Total microbial count	5,000 cfu/gram max	25 cfu/g
E.coli & Salmonella	Absent	Absent
Coliforms	Absent	Absent
P. Aeruginosa	Absent	Absent
S.Aureus	Absent	Absent
Heavy metals	10 PPM maximum	Complies

Example 2:

The solid type Caralluma extract product of the invention was prepared starting with the product of Example 1.

About 60 kgs. of the product obtained in Example 1 was mixed with the required quantity of maltodextrin, starch and gum acacia in a mixer and blended for about 30 minutes to get a homogeneous mass (the step 410).

The homogeneous mass was dried in a tray drier. The material was spread in a thin layer over the stainless steel trays of the drier and dried at a temperature of about 60 degrees C (step 420).

The dried product from the foregoing step was powdered by, for example, a micropulverizer (step 430) and then sifted in an S.S. Sifter to a particle size of about 40-80 mesh (step 440). The sifted material was blended in a double cone blender for about one hour to get a homogeneous powder (step 450).

The homogeneous powder was the second Caralluma extract product of the invention. The abovementioned procedure was repeated five times. The analysis range of the product obtained is given hereinbelow.

TABLE 6

Product: Second Caralluma Extract (Standardized)(from Caralluma fimbriata)		
Test Parameters	Specification	Actual Values
Appearance	Brown to dark brown powder	Complies
Solubility in water	75% minimum w/w	97.0% w/w
Loss on Drying	10% maximum w/w	2.8% w/w
Total Bitters	3% minimum w/w	6.3% w/w
Total Saponin Glycosides	10% minimum w/w	17.8% w/w
Total Pregnane Glycosides	Above 30% w/w	55.2% w/w
Resinous matters	Not more than 1% w/w	0.15% w/w
Total microbial count	5,000 cfu/gram max	25 cfu/g
E.coli & Salmonella	Absent	Absent
Coliforms	Absent	Absent
P. Aeruginosa	Absent	Absent
S.Aureus	Absent	Absent
Heavy metals	10 PPM maximum	Complies

Example 3

The same steps as outlined in the embodiment 2 were followed with the following differences. In Example 3, drying was conducted in a spray drier instead of a tray drier, and the homogeneous

mass was dissolved in water as is required for feeding to a spray drier. Minimum quantity of water was used.

The spray dried Caralluma extract was found to be finer and more uniform in size and consequently it was not necessary to carry out the optional steps of powdering and sifting.

Example 4

100% methanol was used as solvent for extraction while the resin dissolving solvent was n-hexane, to make the Caralluma extract technical starting with Caralluma plant material. The yield of glycosides was relatively low in comparison to the use of 30% aq. ethanol as in example 1. n-Hexane consumption was high because of the higher amount of the resins extracted out by 100% methanol.

Methanol solvents of strengths 60%, 70%, 80% and 90% were also used. The observations of the inventors for these methanol concentrations are generally as for 100% methanol.

Example 5

Aqueous methanol of 30% strength was used. The yield of glycosides was better than for the higher strengths. The yield is optimum at around 30% strength of methanol and is comparable to that for 30% aq. ethanol under comparable conditions. The product was the first Caralluma extract and the resin dissolving solvent used was n-hexane. A tray drier was used for drying.

Example 6

Extraction was done with ethylene dichloride as solvent to produce the second Caralluma extract. The optional resin removal step was carried out for which n-hexane was used. Adsorption was done on maltodextrin. The product was found to be hygroscopic. The glycoside yield was lower than with 30% aq. ethanol solvent under similar conditions.

Example 7

Aqueous methanol of 30% strength was used as the extraction solvent and n-hexane was used for resin removal. The product was the second Caralluma extract. Spray drying was adopted. The yield was equivalent to that of 30% aq. ethanol under comparable conditions. The product was hygroscopic.

Although the present invention has been described in considerable detail with reference to certain preferred versions thereof, other versions are possible. Therefore, the spirit and scope of the appended claims should not be limited to the description of the preferred versions contained herein.

While the invention has been described in connection with specific and preferred embodiments thereof, it is capable of further modifications without departing from the spirit and scope of the invention. This application is intended to cover all variations, uses, or adaptations of the invention, following, in general, the principles of the invention and including such departures from the present disclosure as come within known or customary practice within the art to which the invention pertains, or as are obvious to persons skilled in the art, at the time the departure is made. It should be appreciated that the scope of this invention is not limited to the detailed description of the invention hereinabove, which is intended merely to be illustrative, but rather comprehends the subject matter defined by the following claims.

We claim :

1. A composition for medicinal, nutraceutical and food applications comprising one or more pregnane glycosides as the major and chief constituent(s) thereof.

2. A composition as claimed in the preceding claim 1 and which is obtained by a process of extraction of plant matter.

3. A composition as claimed in the preceding claim 2 wherein said plant matter comprises one or more of the caralluma group of plants belonging to the Asclepiadaceae family.

4. A composition as claimed in the preceding claim 3 wherein said plant matter comprises one or more of the caralluma species of plants of said Group I.

5. A composition as claimed in the preceding claim 4 wherein said plant matter comprises one or more of the caralluma species: fimbriata, indica, attenuata, tuberculata and the like.

6. A composition as claimed in the preceding claim 5 wherein said plant matter comprises c. fimbriata.

7. A composition as claimed in the preceding claim 3 wherein said plant matter comprises one or more of the caralluma species of plants of said Group II.

8. A composition as claimed in the preceding claim 7 wherein said plant matter comprises one or more of the caralluma species of plants, stalagmifera, umbellate, lasiantha, edulis and the like.

9. A composition as claimed in any of the preceding claims 1 to 8 wherein said pregnane glycosides contained therein mainly comprise one or more of the caratubersides (isomers of caratuberside) and boucerosides (isomers of bouceroside).

10. A composition as claimed in any of the preceding claims 1 to 9 wherein the ratio of the caratubersides to boucerosides, referred to as the CB ratio, is preferably substantially equal to that found in any of the caralluma species of said Groups I and II.

11. A composition as claimed in any of the preceding claims 1 to 10 wherein said CB ratio is substantially equal to that found in the caralluma species, fimbriata.

12. A composition as claimed in any of the preceding claims 1 to 11 wherein said CB ratio preferably ranges from 9: 1 to 11: 1.

13. A composition as claimed in any of the preceding claims 1 to 12 and which is in liquid form and is referred to herein as the first caralluma extract.

14. A composition as claimed in any of the preceding claims 1 to 12 and which is in the solid form and is referred to herein as the-second caralluma extract.

15. A composition as claimed in the preceding claim 13 and comprising said glycosides and other matter, if any, in solution.

16. A composition as claimed in the preceding claim 14 wherein said glycosides and other matter, if any, is adsorbed on a suitable excipient.

17. A composition as claimed in the preceding claim 16 wherein said excipient is selected from maltodextrin and magnesium carbonate.

18. A composition as claimed in any of the preceding claims 16 and 17 and comprising a suitable binder.

19. A composition as claimed in the preceding claim 18 wherein said binder is selected from starch, guar gum, gum acacia and polyvinyl pyrolidone.

20. A composition as claimed in the preceding claim 19 wherein said binder is polyvinyl pyrolidone.

21. A composition as claimed in any of the preceding claims 1 to 20 wherein the content of said pregnane glycosides is from 5% to 15% w/w.

22. A composition as claimed in any of the preceding claims 1 to 20 wherein the content of said pregnane glycosides is over 15% w/w.

23. A composition as claimed in any of the preceding claims 1 to 20 wherein the content of said pregnane glycosides is from 25% to 30% w/w.

24. A composition as claimed in any of the preceding claims 1 to 20 wherein the content of said pregnane glycosides is over 30% w/w.

25. A composition as claimed in any of the preceding claims 21 and 22 and which is in the liquid form.

26. A composition as claimed in any of the preceding claims 23 and 24 and which is in the solid form.

27. A composition as claimed in the preceding claim 26 wherein said glycosides and other matter, if any is adsorbed on an excipient selected from maltodextrin and magnesium carbonate.

28. A composition as claimed in any of the preceding claims 1 to 27 wherein the resin content is not more than about 0.5% w/w and which is preferably in liquid form.

29. A composition as claimed in any of the preceding claims 1 to 27 wherein the resin content is not more than about 1.0% w/w and which is preferably in solid form.

30. A composition as claimed in any of the preceding claims 1 to 29 wherein the glycosides therein are in the form of any of the pharmaceutically accepted salts.

31. A composition as claimed in any of the preceding claims 1 to 30 and which further comprises one or more therapeutic agents for treatment and/or management of/for obesity, arthritis, rheumatism, diabetes and reduction of blood sugar, hypertension and reduction of blood pressure, weight reduction, reduction of waist, arm and hip circumference, reduction of BMI (body mass index), increase of BMR (Basal Metabolic Rate), increasing lean mass, reduction of appetite, fat loss or, is carminative, febrifugal, anthelmintic, anti-pyretic, anti-inflammatory, anti-oxidant and/or anti-nociceptive.

32. A composition as claimed in any of the preceding claims 1 to 31 and which further comprises one more nutraceutical agents and/or food additives.

33. A composition as claimed in any of the preceding claims 1 to 32 and which further comprises one or more of the saponin glycosides of caralluma and/or the bitters of caralluma.

34. A composition as claimed in any of the preceding claims 1 to 33 and which is in admixture with one or more of the pharmaceutically accepted agents for taste, colour and flavour and the like.

35. A process for making a composition for medicinal, nutraceutical and food applications chiefly comprising one or more of the pregnane glycosides, said process comprising the extraction of plant matter by means of a solvent/solvent mixture, the parameters of said extraction and of said solvent/solvent mixture being such as to minimise/prevent the decomposition of said glycosides so as to yield a standardised and reproducible extract.

36. The process as claimed in the preceding claim 35 wherein said parameters are such as to yield said extract that is representative of said plant matter particularly with regard to the major pregnane glycosides present, and the proportions thereof, therein.

37. The process as claimed in any of the preceding claims 35 and 36 wherein the major glycosides present in said plant matter are the caratubersides (the various isomers of caratuberside) and the boucerosides (the various isomers of bouceroside).

38. The process as claimed in any of the preceding claims 35 to 37 wherein the CB ratio (the caratubersides to the boucerosides ratio) present in said plant matter is from 9: 1 to 11: 1.

39. The process as claimed in any of the preceding claims 35 to 38 wherein said CB ratio in said extract is from 9: 1 to 11 : 1 obtained where required by admixture of the said extract with the deficient component.

40. The process as claimed in any of the preceding claims 35 to 39 wherein said parameters are such as to minimise/prevent the extraction of the non-pregnane glycoside matter during said extraction.

41. The process as claimed in any of the preceding claims 35 to 40 wherein said parameters are such as to minimise/prevent the extraction of the resinous matter during said extraction.

42. The process as claimed in any of the preceding claims 35 to 41 wherein said parameters are such as to minimise/prevent the extraction of the tannins and pectins during said extraction.

43. The process as claimed in any of the preceding claims 35 to 42 wherein said extract is concentrated to the desired concentration of said glycosides in one or more stages of concentration.

44. The process as claimed in the preceding claim 43 and comprising a first and second said concentration stages.

45. The process as claimed in any of the preceding claims 43 and 44 wherein said concentration is by the evaporation of said solvent/solvent mixture in said extract by heating and optionally under vacuum, said evaporation being carried out in any known evaporator equipment but preferably in a thin film evaporator.

46. The process as claimed in any of the preceding claims 43 to 45 wherein said evaporated solvent/solvent mixture is recovered.

47. The process as claimed in any of the preceding claims 35 to 46 wherein said plant matter is additionally subjected to one or more of pre-treatment operations such as washing,

cleaning, soaking, drying, cutting, chopping, blanching, crushing, grinding and the like, before undergoing extraction.

48. The process as claimed in any of the preceding claims 35 to 47 and comprising an additional operation of resin removal wherein the resinous matter contained in said plant matter is extracted out by treating the said plant matter or material-in-process with a resin dissolving solvent.

49. The process as claimed in the preceding claim 48 wherein said resin removal is carried out either at the commencement of, or during said pre-treatment but preferably after size reduction of said plant matter has been carried out.

50. The process as claimed in the preceding claim 48 wherein said resin removal is carried out after said pre- treatment, if any and before said extraction.

51. The process as claimed in the preceding claim 48 wherein said resin removal is carried out after said extraction but before said concentration step.

52. The process as claimed in the preceding claim 48 wherein said resin removal is carried out between any two said concentration stages but preferably between said first and second concentration stages.

53. The process as claimed in any of the preceding claims 48 to 52 wherein said resin dissolving solvent is recovered after the resin removal step by evaporation and condensation, or other method.

54. The process as claimed in any of the preceding claims 35 to 53 wherein said extraction is carried out in a plurality of stages resulting a plurality of extracts (solutions).

55. The process as claimed in any of the preceding claims 35 to 54 wherein said extract (s) are optionally subjected to filtration to remove solid matter, if any.

56. The process as claimed in any of the preceding claims 54 and 55 wherein one or more said solutions are returned to said extraction step to constitute said solvent/solvent mixtures for one or more of said extraction stages the remaining said solution (s) being subjected to said concentration in either one batch or a plurality of batches.

57. The process as claimed in any of the preceding claims 54 to 56 wherein the combination of said concentration batches and extraction stages is selected such as to maximise production and plant utilisation and minimise costs.

58. The process as claimed in any of the preceding claims 35 to 57 wherein said composition is in the liquid form.

59. The process as claimed in the preceding claim 58 wherein the resin content in said liquid form composition does not exceed 0.5%.

60. The process as claimed in any of the preceding claims 58 and 59 wherein said composition comprises 5% to 15% w/w of pregnane glycosides.

61. The process as claimed in any of the preceding claims 58 and 59 wherein said composition comprises over 15% w/w of pregnane glycosides.

62. The process as claimed in any of the preceding claims 35 to 57 wherein said composition is in the solid form.

63. The process as claimed in the preceding claim 62 wherein the resin content in said solid form composition does not exceed 1.0%.

64. The process as claimed in any of the preceding claims 62 and 63 wherein said composition comprises 25% to 30% w/w of pregnane glycosides.

65. The process as claimed in any of the preceding claims 62 and 63 wherein said composition comprises over 30% w/w of pregnane glycosides.

66. The process as claimed in any of the preceding claims 62 to 65 wherein said composition further comprises a suitable excipient such as malto dextrin or magnesium carbonate or the like.

67. The process as claimed in any of the preceding claims 35 to 66 wherein said plant matter comprises one or more of the caralluma group of plants belonging to the Asclepiadaceae family.

68. The process as claimed in any of the preceding claims 35 to 67 and comprising the steps of :

i. pre-treatment of the caralluma plant material by one or more optional operations such as washing, cleaning, soaking, drying, cutting, chopping, blanching, and others, if and as necessary;
ii. crushing and/or grinding of the plant material obtained from step (i), if, and to the extent, desired;
iii. extracting the material obtained from step (ii) in one or more stages by means of a suitable solvent/solvent mixture and/or with a solution obtained from another extraction, the nature of said solvent/solvent mixture and the concentration thereof and the temperature of extraction being selected such as to minimise or substantially prevent the extraction of the resinous matter and the tannins and pectins in therein;
iv. concentrating the extract batch(es)(solutions) obtained from step (iii) either singly or as mixtures of one or more thereof in a first concentration stage and further optionally in a second concentration stage by removal of said solvent/solvent mixture by any of known means such as the evaporation of said solvent/solvent mixture to yield said composition referred to as the Caralluma Extract Technical (or the First Caralluma Extract) said solvent/solvent mixture being recovered if desired;
v. v. optionally returning one or more said extract batch(es) or parts thereof before said first concentration stage to step (iii) for contacting with the said plant material to be extracted, said batch(es) being subjected optionally to filtration so as to remove particulate solid matter, if any;
vi. optionally subjecting the material-in-process to a resin extracting operation by means of a resin dissolving solvent as part of said step (i), or immediately following said steps (i) or (ii) or (iii) or immediately after said first concentration stage.

69. The process as claimed in any of the preceding claims 35 to 68 wherein said plant material comprises one or more of the caralluma species of Group I such as fimbriata, indica, tuberculata, adscendens and others.

70. The process as claimed in any of the preceding claims 35 to 68 wherein said plant material comprises one or more of the caralluma species of Group II such as stalagmifera, umbellate, lasiantha, edulis and others.

71. The process as claimed in any of the preceding claims 35 to 70 wherein said CB ratio in the said composition product is substantially equal to that in the caralluma species from which is extracted.

72. The process as claimed in any of the preceding claims 35 to 70 wherein the said CB ratio of the said composition product is from 9: 1 to 11 : 1.

73. The process as claimed in any of the preceding claims 35 to 72 wherein said solvent/solvent mixture is selected from the group of solvents, methanol, ethanol, aqueous methanol, aqueous ethanol, i-propyl alcohol, n-butanol, water and ethylene dichloride and others and from the group of solvent mixtures comprising mixtures of n-butanol, ethyl acetate and ethylene dichloride with ethanol, methanol, aqueous ethanol, aqueous methanol and others.

74. The process as claimed in any of the preceding claims 35 to 73 wherein said solvent for extraction is aqueous ethanol.

75. The process as claimed in the preceding claims 74 wherein said aqueous ethanol is preferably of strength 10-80% v/v and more preferably of 20-40% v/v.

76. The process as claimed in any of the preceding claims 35 to 75 wherein said extraction step is carried out at temperatures ranging from 70 to 80 degrees C but more preferably from 70 to 75 degrees C.

77. The process as claimed in any of the preceding claims 74 to 76 wherein said concentration is carried out by evaporation of said solvent at from 40 to 50 degrees C under vacuum in any of the known evaporator equipment but preferably in a thin film evaporator.

78. The process as claimed in any of the preceding claims 35 to 77 wherein said resin dissolving solvent is selected from n-hexane, diethyl ether, ethylene dichloride, petroleum ether, benzene, toluene and methylene dichloride.

79. The process as claimed in the preceding claim 78 wherein said resin dissolving solvent comprises n-hexane.

80. The process as claimed in any of the preceding claims 35 to 79 wherein the said concentration of pregnane glycosides in said solution obtained from said first concentration step and going to undergo said resin extraction is from 3 to 8% w/w.

81. The process as claimed in any of the preceding claims 35 to 80 wherein the step of resin removal from said extract or said first concentrate comprises contacting (washing) said extract or first concentrate with the resin dissolving solvent one or more times, separating the contacted liquid after each said washing /contacting into a heavy layer comprising the solution of said glycosides and a light layer comprising said resin dissolving solvent with the extracted out resin in solution, said light layer being discarded or sent for recovery of the said resin dissolving solvent.

82. The process as claimed in any of the preceding claims 68 to 81 wherein said first caralluma extract comprises from 5% to 15% w/w pregnane glycosides.

83. The process as claimed in any of the preceding claims 68 to 81 wherein said first caralluma extract comprises more than 15% w/w pregnane glycosides.

84. The process as claimed in any of the preceding claims 68 to 83 wherein the resin content of said composition does not exceed 0.5%.

85. The process as claimed in any of the preceding claims 35 to 84 wherein said plant matter comprises the plants, or parts thereof, of the species caralluma fimbriata.

86. The process as claimed in any of the preceding claims 35 to 85 wherein said composition further comprises either the caralluma saponin glycoside (s) or the caralluma bitters or both obtained by extraction of the same from the caralluma plant matter or incorporated in said composition by admixture thereof with the same.

87. A process for making a solid form composition (Standardised Caralluma Extract or Second Caralluma Extract), for medicinal, nutraceutical and food applications, chiefly comprising one or more of the pregnane glycosides, from said first caralluma extract comprising contacting said first extract with a suitable excipient and subjecting the material to a mixing/blending operation followed by the drying of the material by any of the known methods to give the product.

88. The process as claimed in the preceding claim 87 wherein said excipient is either maltodextrin or magnesium carbonate.

89. The process as claimed in any of the preceding claims 87 and 88 wherein in addition to said excipient, said first caralluma extract is also contacted with a suitable binding agent (binder).

90. The process as claimed in the preceding claim 89 wherein said binder is selected from starch, guar gum, gum acacia and polyvinyl pyrolidone.

91. The process as claimed in the any of the preceding claims 87 to 90 wherein said mixing/blending is carried out in an apparatus/equipment selected from a planetary mixer, rapid mixer, granulator, slurry tank or other.

92. The process as claimed in any of the preceding claims 87 to 91 wherein said drying is carried out in one selected from a tray drier, a spray drier, a vacuum drier, fluid bed drier or other.

93. The process as claimed in the preceding claim 92 wherein said drying is carried out in a tray drier.

94. The process as claimed in the preceding claim 92 wherein said drying is carried out in a spray drier.

95. The process as claimed in any of the preceding claims 87 to 84 wherein said solid form composition product is preferably additionally subjected to a grinding/milling operation to obtain a fine product.

96. The process as claimed in the preceding claim 95 wherein said grinding/milling operation is carried out in one selected from a multi-miller, a hammer rnill or other.

97. The process as claimed in any of the preceding claims 87 to 96 wherein said solid form composition product is preferably additionally subjected to a sifting operation in a sifter, or a sieve shaker or other to obtain a uniform sized product.

98. The process as claimed in the preceding claim 97 wherein said sifted product is preferably additionally subjected to a blending operation in blending equipment such as a Double Cone Blender, Ribbon Blender, Octagonal Blender or other known blending equipment.

99. The process as claimed in any of the preceding claims 87 to 98 wherein said solid form composition comprises from 25% to 30% w/w of pregnane glycosides.

100. The process as claimed in any of the preceding claims 87 to 98 wherein said solid form composition comprises over 30% w/w of pregnane glycosides.

101. A process for making a solid form composition (Standardised Caralluma Extract or Second Carallum Extract), for medicinal, nutraceutical and food applications, chiefly comprising one or more of the pregnane glycosides, from said caralluma plant matter comprising the steps of the process for making said first caralluma extract as disclosed in the preceding claims 70 to 89 followed by the steps of the process for making said second caralluma extract from said first caralluma extract as disclosed in the preceding claims 87 to 100.

102. A use of a composition as claimed in any of the claims 1 to 34 in the manufacture of a medicament for the treatment of obesity.

103. A use of a composition as claimed in any of the claims 1 to 34 in the manufacture of a medicament for the treatment of obesity-related disorders.

104. A use as claimed in claim 103, wherein said obesity-related disorders include

i. Overweight and obesity;
ii. Hypertensive;
iii. Type 2 diabetes;
iv. Hyperglycaemia;
v. Hypercholesterolemia;
vi. Osteo-arthritis;
vii. Erectile dysfunction;
viii. Joint inflammation/degradation;
ix. Alteration, or improvement, or regulation of the following functions, conditions or parameters:

    a. Body Mass Index;
    b. Basal Metabolic Rate;
    c. Blood pressure;
    d. Blood sugar;
    e. Waist, Hip and arm circumferences;
    f. Total cholesterol;
    g. HDL/LDL ratio and other cholesterol ratios;
    h. Appetite reduction;
    i. Weight reduction;
    j. Fat levels;
    k. Lean body mass; and
    l. Joint mobility.

105. A use of a composition as claimed in any of the claims 1 to 34 in the manufacture of a medicament for the treatment of non-obesity related disorders.

106. A use as claimed in claim 105, wherein said non-obesity related disorders include

i . Hypertensive;
ii. Type 2 diabetes;
iii. Hyperglycaemia;
iv. Hypercholesterolemia;
v. Migrane;
vi. Osteo-arthritis;
vii. Erectile dysfunction;
viii. Low stamina, endurance and energy levels;
ix. Reduced cognitive and memory function;
x. Capillary degeneration;
xi. Joint inflammation/degradation;
xii. Menopausal syndrome;
xiii. Ageing syndrome;
xiv. Circulation disorder;
xv. Hearing loss;
xvi. Clinical depression;
xvii. Alteration, or improvement, or regulation of the following functions, conditions or parameters:

a. Body Mass Index;
b. Basal Metabolic Rate;
c. Blood pressure;
d. Blood sugar;
e. Waist, Hip and arm circumferences;
f. Total cholesterol;
g. HDL/LDL ratio and other cholesterol ratios;
h. Appetite reduction;
i. Weight reduction;
j. Fat levels;
k. Lean body mass;
l. Mood elevation;
m. Circulation and capillary health;
n. Joint mobility;
o. Sexual power, drive, stamina and libido;and
p. Skin nourishment.

107. A use of a composition as claimed in any of the claims 1 to 34 as an anti-oxidant.

108. A use of a composition as claimed in any of the claims 1 to 34 as an anti-inflammation agent.