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(71) Applicant: **MOHAMED ABDULLA ANZAR, Chempattu** [IN/IN]; No.1018/5, In Front Of Hanuman Temple and College of Engineering College and Technology, Ghatikia, Orissa, Bhubaneswar 30 (IN).(72) Inventors: **MISHRA, Dr. Baidyanath**; No.1018/5, In Front Of Hanuman Temple and College of Engineering College and Technology, Ghatikia, Orissa, Bhubaneswar 30 (IN). **GANAPATHY, Sujan**; No. P6 (B), 1 Floor, I Cross, 1 Stage (Opposite To Jalahalli Metro Station and Adjacent to Sai Hero Showroom) Bangalore-Tumkur National Highway, Peenya Industrial Estate, Bangalore 560058 (IN). **SHARIQ AFSAR, T**; No. 165/5 & 5805/05, Near Navayuga Toll Gate Office, Nh-4, Nelamanga, Karnataka, Bangalore 562123 (IN).(74) Agents: **RAKESH PRAHBU** et al.; ALMT Legal Advocates & Solicitors, N°2, Lavelle Road, Bangalore - 560001, Karnatakak (IN).

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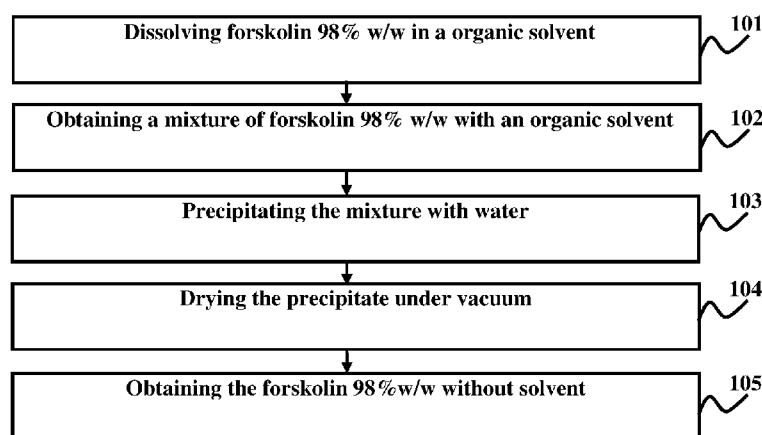


FIG. 1

(57) Abstract: The embodiments herein provides method for synthesizing water soluble forskolin 10% w/w. 250 litres of distilled water, 5 kg of pre-treated forskolin (98% w/w) and 20 kg of synthetic water soluble polymer are added into the reactor to obtain a mixture. 15 kg of modified starch dissolved in 100 litres of water is added to the mixture. The reaction is allowed to take place for 8 hours in the reactor at a temperature of 50-80°C. After 8 hours the reaction is stopped and the reaction mixture comprising water soluble forskolin is cooled to 30-50°C. The mixture is spray dried at 180°C. The mixture after spray drying is milled and sieved. The mixture comprising water soluble forskolin 10% w/w is packaged. The bioavailability of the forskolin 10% w/w is increased and the recommended dosage is 500 mg/day for an individual.



A WATER SOLUBLE 10% W/W FORSKOLIN COMPOSITION AND A METHOD OF SYNTHESIZING THE SAME

CROSS-REFERENCE TO RELATED APPLICATIONS

5 [0001] This application claims the priority of Indian Provisional Patent Application No. 1296/KOL/2015 filed on December 16, 2015, with the tile, “A water soluble 10% w/w forskolin composition and a method of synthesizing the same”, and the content of which is incorporated entirely as reference herein.

BACKGROUND

10 *Technical Field*

[0002] The embodiments herein are generally related to the field of pharmaceutical agents. The embodiments herein are particularly related to the process for solubilizing pharmaceutically active ingredients in water or aqueous solutions. The embodiments herein are more particularly related to a method for synthesizing solution of diterpenes with high concentration.

Description of the Related Art

[0003] It is known that many pharmaceutically active substances are having poor water solubility. The poor water solubility of pharmaceutically active substances results in difficulties such as formulation and administration of homogeneous aqueous solution. The poor solubility of pharmaceutically active substance is observed in topical ophthalmic, rhinologic, otologic, gynecologic, dermatologic drugs or pharmaceutical agents. Further the problem arises when these water insoluble drugs or pharmaceutical agents are used for oral mucous membranes.

[0004] Certain active pharmaceutical ingredients are inherently insoluble or very sparingly soluble in water or aqueous solutions. Achieving therapeutically active concentrations of such water insoluble active pharmaceutical ingredients in stable form has always been actively perused. The methods/techniques of molecular structural manipulation are generally adopted. The molecular structural features that promote aqueous solubility result in an attenuation or modification of the intended desired pharmacological properties.

[0005] The pharmaceutical active ingredients sparingly soluble in water are extremely advantageous and effective, when the pharmaceutical active ingredients are

topically administered in the form of eye-drops or the effectiveness or ease of application is increased when the concentration of the existing preparations are increased. Following are the examples of common drugs having poor solubility in water or very low solubility in water. The drugs are antiglaucoma agents (forskolin, dapiprazol), anti-cataract agents
5 (tolrestat), non-steroidal anti-inflammatory drugs (piroxicam), steroidal anti-inflammatory drugs (formocortal), glucoside vasoprotective agent (rutin), fluoro-quinolone anti-bacterial drugs (rufloxacin), antibiotics (amphotericin B).

[0006] Over the years, various methods have been developed for increasing the solubility, the ease of formulation and bio-availability of water insoluble or sparingly
10 soluble drugs (pharmaceutical agents/drugs). All the said methods are classified into Chemical Modifications and/or Physicochemical Solubilization Techniques.

[0007] The chemical modifications method includes a process of introduction of a ionic or ionizable groups and a process of introduction of a group that lowers the melting point.

15 [0008] The physicochemical solubilization technique includes a method of Micellar solubilization by means of surface-active agents and a method of formation of solid solutions and suspension by means of polymers.

[0009] The transformation of the active ingredients into an ionic or ionizable derivative is a very common solubilization method. The basis of this method lies in the
20 relationship between solubility and pH for weak acids and bases. Said bases are valid only to the point where the total solubility approaches the solubility of the ionic species such as salts.

[0010] The method of lowering the melting point depends on the concept that the molecules have to leave the crystal lattice for solubility. Any modification of the molecule
25 that lowers the melting point and thus reduces the energy of the crystal lattice tends to increase the solubility thereof in any solvent.

[0011] The method of micellar solubilization by means of surface-active agents, has the following limiting factors: (a) the limited solubilizing ability of the micelles, (b) the possible short term and long term toxicity of surfactant and (c) the simultaneous
30 solubilization of other components of the formulation such as preservatives, flavouring agents and dyes with resulting alteration of the stability and activity.

[0012] In order to form solid solutions and suspensions by means of polymers, a composition is to be stored at 4°C for a limited time and the composition must be re-suspended by shaking it every time before use. Such a solution or composition cannot be proposed for development at the industrial and commercial level.

5 [0013] Aqueous solubility of drugs is a desirable feature for several purposes. Aqueous formulations are sterilized by standard techniques such as filtration, to render such preparations suitable for systematic administration. Also aqueous preparations are preferable in dermatological, gynecological, ontological, rhinological and on mucous membrane applications. Aqueous preparations are especially useful in aqueous
10 ophthalmic preparations of drugs.

[0014] Forskolin is a labdanoid diterpene that is produced by the Indian Coleus plant (*Plectranthus barbatus* or *Coleus forskohlii*). Forskolin is commonly used to raise levels of cyclic AMP (cAMP) in the study and research of cell physiology. Forskolin activates the enzyme adenylyl cyclase and increases intracellular levels of cAMP. cAMP
15 is an important secondary messenger necessary for the proper biological response of cells to hormones and other extracellular signals. It is required for cell communication in the hypothalamus/pituitary gland axis and for the feedback control of hormones. cAMP acts by activating cAMP. Sensitive pathways such as protein kinase A and Epac.

[0015] Forskolin directly, rapidly and reversibly activates adenylyl cyclase. The
20 activation of adenylyl cyclase results in increasing the intracellular cAMP level. cAMP increases utilization of body fat, increases basal metabolic rate and regulates the body's thermogenic response to food. Thus forskolin leads to fat loss without muscle mass loss.

[0016] Forskolin has several desirable pharmacological properties. Forskolin displays positive inotropic, anti-hypertensive and broncho-spasmolytic activity. It lowers
25 intraocular pressure.

[0017] Forskolin is poorly soluble in water. Existing technologies provide the forskolin with 6% water solubility. This results in poor absorption of forskolin in gut. After forskolin is soluble in water, it is easily carried from intestine to blood stream.

[0018] Hence, there is a need for a composition with higher percentage of
30 forskolin soluble in water. Also there is a need for a method for synthesizing water soluble forskolin.

OBJECTIVES OF THE EMBODIMENTS

[0019] The primary objective of the embodiments herein is to provide a composition comprising water soluble forskolin 10% w/w.

5 [0020] Another objective of the embodiments herein is to provide a method for the synthesizing water soluble forskolin 10% w/w.

[0021] Yet another objective of the embodiments herein is to provide formulas for producing water soluble forskolin 10 % w/w and compositions for the functional and nutritional support for obese individuals.

10 [0022] Yet another objective of the embodiments herein is to provide a composition comprising water soluble forskolin 10% w/w with higher bioavailability compared to existing products.

[0023] Yet another objective of the embodiments herein is to provide a composition comprising water soluble forskolin 10% w/w with no solvents.

15 [0024] Yet another objective of the embodiments herein is to provide a simple method for the synthesizing water soluble forskolin 10% w/w.

[0025] Yet another objective of the embodiments herein is to provide a composition comprising water soluble forskolin 10% w/w which is used in health drinks, sports drinks, dairy products, capsules and tablets.

20 [0026] These and other objects and advantages of the embodiments herein will become readily apparent from the following detailed description taken in conjunction with the accompanying drawings.

SUMMARY

25 [0027] The various embodiments herein provide a composition comprising water soluble forskolin 10% w/w. The embodiments herein also provide a method for the synthesizing water soluble forskolin.

[0028] According to one embodiment herein, the method of synthesizing a composition comprising water soluble forskolin, comprises the following steps. The forskolin 98% w/w is pretreated for obtaining a solvent free forskolin 98% w/w. A predetermined amount of distilled water is added in a first reactor. The predetermined amount of water added to the first reactor is 250 litres. A predetermined amount of synthetic water soluble polymer is added in the first reactor comprising distilled water. The predetermined amount of synthetic water soluble polymer added to the first reactor is

20 Kg. A predetermined amount of pre-treated forskolin 98% w/w is added to the first reactor comprising distilled water and synthetic water soluble polymer. The predetermined amount of pre-treated forskolin 98% w/w added to the first reactor is 5 Kg.

5 [0029] A predetermined amount of modified starch is dissolved in a second reactor comprising 100 litres of distilled water. The predetermined amount of modified starch added to the second reactor comprising 100 litres of distilled water is 15 Kg. A modified starch solution is obtained.

[0030] The modified starch solution is added to the first reactor comprising
10 distilled water, synthetic water soluble polymer and pre-treated forskolin 98% w/w to obtain a mixture. The mixture is heated in the first reactor for a predetermined amount of time at a predetermined temperature range. The predetermined amount of time is 8 hours. The predetermined temperature is in a range of 50-80°C. The heating reaction is stopped after 8 hours. The reaction mixture is cooled to 30-50°C. A compound comprising a
15 water soluble forskolin is obtained. The compound comprising water soluble forskolin is spray dried at 180°C. The compound comprising water soluble forskolin is collected after the spray drying process. The dried compound comprising water soluble forskolin is milled. The milled compound comprising water soluble forskolin is sieved through 80 mesh. The milled and sieved compound comprising water soluble forskolin is refined.
20 The milled and sieved compound comprising water soluble forskolin is packaged. The water soluble forskolin is administered to the individuals at a predetermined dosage.

[0031] According to one embodiment herein, the method of pre-treating forskolin 98% w/w comprises the following steps. The forskolin 98% w/w is dissolved in an organic solvent. A mixture comprising forskolin 98% w/w and organic solvent is
25 obtained. Water is added to the mixture. A precipitate comprising forskolin 98% w/w is obtained. The precipitate comprising forskolin 98% w/w is dried. The pre-treatment of forskolin 98% w/w makes the forskolin 98% w/w solvent free.

[0032] According to one embodiment herein, the synthetic water soluble polymer is selected from a group consisting of polyvinyl pyrrolidone, poly ethylene glycol,
30 polyvinyl alcohol and polyacrylic acid.

[0033] According to one embodiment herein, the organic solvent is selected from a group consisting of a compound having 2 carbon atoms, a compound having 3 carbon

atoms, a compound having 4 carbon atoms, a compound having 5 carbon atoms, a compound having 6 carbon atoms and a compound having 8 carbon atoms.

[0034] According to one embodiment herein, the modified starch is selected from a group consisting of malto-dextrin, starch sodium octenyl succinate, starch and cyclodextrin.

[0035] According to one embodiment herein, the forskolin is administered in a recommended dosage. The recommended dosage of forskolin 10% w/w is 500 mg/day for an individual.

[0036] According to one embodiment herein, the forskolin is administered for weight management and glaucoma. The water soluble forskolin has a higher bioavailability. The bioavailability of the water soluble forskolin is more than the bioavailability of the existing forskolin compositions.

[0037] According to one embodiment herein, the concentration of water soluble forskolin in the mixture is 10% w/w. The forskolin has a water solubility of 10% w/w.

[0038] According to one embodiment herein, the composition of water soluble forskolin, comprises forskolin with a water solubility of 10% w/w. The water soluble forskolin composition is administered to the individuals at predetermined dosage. The predetermined dosage of forskolin 10% w/w is 500 mg/day for an individual. The concentration of water soluble forskolin in the composition is 10% w/w. The forskolin has a water solubility of 10% w/w.

[0039] According to one embodiment herein, additives are present in the forskolin composition. The additives are selected from a group consisting of polyvinyl pyrrolidone, poly ethylene glycol, polyvinyl alcohol and polyacrylic acid, malto-dextrin, starch sodium octenyl succinate, starch and cyclodextrin.

[0040] According to one embodiment herein, the additives are added to the forskolin composition for promoting physiochemical solubilization. The additives are configured to promote the physiochemical solubilization by presence of surface active agents, formation of solid solutions and formation of suspension by polymers present in additives.

[0041] According to one embodiment herein, the forskolin is administered for weight management and glaucoma. The water soluble forskolin has a higher

bioavailability. The bioavailability of the water soluble forskolin is more than the bioavailability of the existing forskolin compositions.

[0042] According to one embodiment herein, forskolin is a water insoluble pharmaceutical agent which is commonly used in weight management and glaucoma. As
5 forskolin is poorly soluble in water, it is poorly absorbed by the body. The embodiments herein discloses water soluble and solvent free forskolin 10% w/w. The water soluble forskolin is used in synthesis of pharma and dietary supplements. The forskolin is water insoluble and has low or poor absorption in the gut. The water soluble forskolin is easily carried from intestine to blood stream. The water soluble forskolin is administered in
10 form of health drinks, sports drinks, dairy products, capsules and tablets.

[0043] According to one embodiment herein, following are the materials used for the synthesis of the forskolin 10% w/w water soluble. Distilled water (Rankem), polyvinyl pyrrolidone (Thomas baker), polyvinyl alcohol (Thomas baker), poly ethylene glycol (Thomas baker), polyacrylic acid (Thomas baker), malto dextrin (Thomas baker),
15 starch sodium octenyl succinate (Thomas baker), starch (Thomas baker) and Cyclodextrin (Thomas baker).

[0044] According to one embodiment herein, forskolin 98% w/w is used as a precursor for synthesizing water soluble forskolin 10% w/w. The forskolin 98% w/w is pre-treated before synthesis of the water soluble forskolin 10% w/w. The forskolin 98%
20 w/w is dissolved in organic solvent and precipitated with water. The precipitate is dried under vacuum. This pre-treatment of forskolin 98% w/w makes the forskolin 98% w/w solvent free.

[0045] According to one embodiment herein, the synthesis of the water soluble forskolin 10% w/w comprises the following steps. 250 litres of distilled water is added
25 into the reactor. 20 kg of synthetic water soluble polymer is added in the reactor. 5 kg of forskolin is added into the reactor at a concentration of 98% w/w. 15 kg of modified starch is dissolved separately in a reactor comprising 100 litres of water. The modified starch solution is obtained. The modified starch solution is added to the reactor comprising distilled water, water soluble synthetic polymer and forskolin solution. The
30 reaction is allowed to take place for 8 hours in the reactor at a temperature of 50-80°C. After 8 hours the reaction is stopped and the reaction mixture is cooled to 30-50°C. The mixture comprises of water soluble forskolin. The mixture is spray dried at 180°C. The

mixture is collected after spray drying. The dried mixture is milled and sieved through 80 mesh. After sieving and refining the mixture comprising water soluble forskolin 10 % w/w is packaged.

[0046] According to one embodiment herein, the synthetic water soluble
5 polymers are selected from a group comprising of polyvinyl pyrrolidone, poly ethylene glycol, polyvinyl alcohol and polyacrylic acid.

[0047] According to one embodiment herein, the modified starch is selected from a group comprising of malto-dextrin, starch sodium octenyl succinate, starch and cyclodextrin.

10 [0048] According to one embodiment herein, the in-vitro data illustrates that the bioavailability of the forskolin 10% w/w has been increased when compared to the existing forskolin compositions.

[0049] According to one embodiment herein, the recommended dosage of the forskolin 10% w/w is 500 mg/day for an individual.

15 [0050] According to one embodiment herein, the forskolin composition has a solubility of 10%. The bioavailability is a function of absorption of active molecules in the human body. By physiochemical nature forskolin has a very low or very poor solubility in water and hence no bioavailability. The forskolin with 10% water solubility has an increased absorption of forskolin in the gut of an individual. The increased
20 absorption from the gut results in increased concentration of forskolin in the blood. The enhanced availability of forskolin in the blood denotes enhanced bioavailability.

[0051] These and other aspects of the embodiments herein will be better appreciated and understood when considered in conjunction with the following description and the accompanying drawings. It should be understood, however, that the
25 following descriptions, while indicating preferred embodiments and numerous specific details thereof, are given by way of illustration and not of limitation. Many changes and modifications may be made within the scope of the embodiments herein without departing from the spirit thereof, and the embodiments herein include all such modifications.

BRIEF DESCRIPTION OF THE DRAWINGS

[0052] The other objects, features and advantages will occur to those skilled in the art from the following description of the preferred embodiment and the accompanying drawings in which:

5 [0053] **FIG.1** illustrates a flow chart explaining a method for pre-treating forskolin 98% w/w for the synthesis of water soluble forskolin 10 % w/w, according to one embodiment herein.

[0054] **FIG.2A-2B** together illustrates a flow chart explaining a method for synthesizing water soluble 10% w/w forskolin, according to one embodiment herein.

10 [0055] Although the specific features of the embodiments herein are shown in some drawings and not in others. This is done for convenience only as each feature may be combined with any or all of the other features in accordance with the embodiments herein.

DETAILED DESCRIPTION OF THE EMBODIMENTS HEREIN

15 [0056] In the following detailed description, reference is made to the accompanying drawings that form a part hereof, and in which the specific embodiments that may be practiced is shown by way of illustration. These embodiments are described in sufficient detail to enable those skilled in the art to practice the embodiments and it is to be understood that the logical, mechanical and other changes may be made without departing from the scope of the embodiments. The following detailed description is
20 therefore not to be taken in a limiting sense.

[0057] The various embodiments herein provide a composition comprising water soluble forskolin 10% w/w. The embodiments herein also provide a method for the synthesizing water soluble forskolin.

25 [0058] According to one embodiment herein, the method of synthesizing a composition comprising water soluble forskolin, comprises the following steps. The forskolin 98% w/w is pretreated for obtaining a solvent free forskolin 98% w/w. A predetermined amount of distilled water is added in a first reactor. The predetermined amount of water added to the first reactor is 250 litres. A predetermined amount of
30 synthetic water soluble polymer is added in the first reactor comprising distilled water. The predetermined amount of synthetic water soluble polymer added to the first reactor is 20 Kg. A predetermined amount of pre-treated forskolin 98% w/w is added to the first

reactor comprising distilled water and synthetic water soluble polymer. The predetermined amount of pre-treated forskolin 98% w/w added to the first reactor is 5 Kg.

[0059] A predetermined amount of modified starch is dissolved in a second
5 reactor comprising 100 litres of distilled water. The predetermined amount of modified starch added to the second reactor comprising 100 litres of distilled water is 15 Kg. A modified starch solution is obtained.

[0060] The modified starch solution is added to the first reactor comprising
distilled water, synthetic water soluble polymer and pre-treated forskolin 98% w/w to
10 obtain a mixture. The mixture is heated in the first reactor for a predetermined amount of time at a predetermined temperature range. The predetermined amount of time is 8 hours. The predetermined temperature is in a range of 50-80°C. The heating reaction is stopped after 8 hours. The reaction mixture is cooled to 30-50°C. A compound comprising a
water soluble forskolin is obtained. The compound comprising water soluble forskolin is
15 spray dried at 180°C. The compound comprising water soluble forskolin is collected after the spray drying process. The dried compound comprising water soluble forskolin is milled. The milled compound comprising water soluble forskolin is sieved through 80 mesh. The milled and sieved compound comprising water soluble forskolin is refined. The milled and sieved compound comprising water soluble forskolin is packaged. The
20 water soluble forskolin is administered to the individuals at a predetermined dosage.

[0061] According to one embodiment herein, the method of pre-treating forskolin
98% w/w comprises the following steps. The forskolin 98% w/w is dissolved in an
organic solvent. A mixture comprising forskolin 98% w/w and organic solvent is
obtained. Water is added to the mixture. A precipitate comprising forskolin 98% w/w is
25 obtained. The precipitate comprising forskolin 98% w/w is dried. The pre-treatment of forskolin 98% w/w makes the forskolin 98% w/w solvent free.

[0062] According to one embodiment herein, the synthetic water soluble polymer
is selected from a group consisting of polyvinyl pyrrolidone, poly ethylene glycol,
polyvinyl alcohol and polyacrylic acid.

30 [0063] According to one embodiment herein, the organic solvent is selected from a group consisting of a compound having 2 carbon atoms, a compound having 3 carbon

atoms, a compound having 4 carbon atoms, a compound having 5 carbon atoms, a compound having 6 carbon atoms and a compound having 8 carbon atoms.

[0064] According to one embodiment herein, the modified starch is selected from a group consisting of malto-dextrin, starch sodium octenyl succinate, starch and cyclodextrin.

[0065] According to one embodiment herein, the forskolin is administered in a recommended dosage. The recommended dosage of forskolin 10% w/w is 500 mg/day for an individual.

[0066] According to one embodiment herein, the forskolin composition comprises additives. The additives are selected from a group consisting of polyvinyl pyrrolidone, poly ethylene glycol, polyvinyl alcohol, polyacrylic acid, malto-dextrin, starch sodium octenyl succinate, starch and cyclodextrin.

[0067] According to one embodiment herein, the the additives are added to the forskolin composition for promoting physiochemical solubilization. The additives are configured to promote the physiochemical solubilization by presence of surface active agents, formation of solid solutions and formation of suspension by polymers present in additives.

[0068] According to one embodiment herein, the forskolin is administered for weight management and glaucoma. The water soluble forskolin has a higher bioavailability. The bioavailability of the water soluble forskolin is more than the bioavailability of the existing forskolin compositions.

[0069] According to one embodiment herein, the concentration of water soluble forskolin in the mixture is 10% w/w. The forskolin has a water solubility of 10% w/w.

[0070] According to one embodiment herein, the composition of water soluble forskolin, comprises forskolin with a water solubility of 10% w/w. The water soluble forskolin composition is administered to the individuals at predetermined dosage. The predetermined dosage of forskolin 10% w/w is 500 mg/day for an individual. The concentration of water soluble forskolin in the composition is 10% w/w. The forskolin has a water solubility of 10% w/w.

[0071] According to one embodiment herein, the forskolin is administered for weight management and glaucoma. The water soluble forskolin has a higher bioavailability. The bioavailability of the water soluble forskolin is more than the

bioavailability of the existing forskolin compositions. The water soluble forskolin has higher bioavailability when compared to existing forskolin compositions.

[0072] According to one embodiment herein, forskolin activates adenylate cyclase directly, rapidly and reversibly. The activation of adenylate cyclase increases the intracellular cyclic adenosine monophosphate (cAMP) level. The cAMP increases the utilization of the body fat, increases basal metabolic rate and regulates body's thermogenic response to food. The forskolin supplement leads to fat loss without the loss of muscle mass.

[0073] According to one embodiment herein, forskolin is a water insoluble pharmaceutical agent which is commonly used in weight management and glaucoma. As forskolin is poorly soluble in water, it is poorly absorbed by the body. The embodiments herein discloses water soluble and solvent free forskolin 10% w/w. The water soluble forskolin is used in synthesis of pharma and dietary supplements.

[0074] According to one embodiment herein, following are the materials used for the synthesis of the forskolin 10% w/w water soluble. Distilled water (Rankem), polyvinyl pyrrolidone (Thomas baker), polyvinyl alcohol (Thomas baker), poly ethylene glycol (Thomas baker), polyacrylic acid (Thomas baker), malto dextrin (Thomas baker), starch sodium octenyl succinate (Thomas baker), starch (Thomas baker) and Cyclodextrin (Thomas baker).

[0075] According to one embodiment herein, forskolin 98% w/w is used as a precursor for synthesizing water soluble forskolin 10% w/w. The forskolin 98% w/w is pre-treated before synthesis of the water soluble forskolin 10% w/w. The forskolin 98% w/w is dissolved in organic solvent and precipitated with water. The precipitate is dried under vacuum. This pre-treatment of forskolin 98% w/w makes the forskolin 98% w/w solvent free.

[0076] According to one embodiment herein, the synthesis of the water soluble forskolin 10% w/w comprises the following steps. 250 litres of distilled water is added into the reactor. 20 kg of synthetic water soluble polymer is added in the reactor. 5 kg of forskolin is added into the reactor at a concentration of 98% w/w. 15 kg of modified starch is dissolved separately in a reactor comprising 100 litres of water. The modified starch solution is obtained. The modified starch solution is added to the reactor comprising distilled water, water soluble synthetic polymer and forskolin solution. The

reaction is allowed to take place for 8 hours in the reactor at a temperature of 50-80°C. After 8 hours the reaction is stopped and the reaction mixture is cooled to 30-50°C. The mixture comprises of water soluble forskolin. The mixture is spray dried at 180°C. The mixture is collected after spray drying. The dried mixture is milled and sieved through 80 mesh. After sieving and refining the mixture comprising water soluble forskolin 10 % w/w is packaged.

[0077] According to one embodiment herein, the synthetic water soluble polymers are selected from a group comprising of polyvinyl pyrrolidone, poly ethylene glycol, polyvinyl alcohol and polyacrylic acid.

[0078] According to one embodiment herein, the modified starch is selected from a group comprising of malto-dextrin, starch sodium octenyl succinate, starch and cyclodextrin.

[0079] According to one embodiment herein, the in-vitro data illustrates that the bioavailability of the forskolin 10% w/w has been increased when compared to the existing forskolin compositions.

[0080] According to one embodiment herein, the recommended dosage of the forskolin 10% w/w is 500 mg/day for an individual.

[0081] **FIG.1** illustrates a flow chart explaining a method for pre-treating forskolin 98% w/w for the synthesis of water soluble forskolin 10 % w/w, according to one embodiment herein. The forskolin 98% w/w is pre-treated for the removal of solvents. The pre-treatment of the forskolin 98% w/w comprises the following steps. The pre-treatment of the forskolin 98% w/w is dissolved in an organic solvent (101). A mixture of forskolin 98% w/w with an organic solvent is obtained (102). The mixture is precipitated with water (103). The precipitate is dried under vacuum (104). The forskolin 98% w/w is obtained without solvent (105).

[0082] **FIG.2A-2B** together illustrates a flow chart explaining a method for synthesizing water soluble 10% w/w forskolin, according to one embodiment herein. The method for synthesizing water soluble 10% w/w forskolin comprises of the following steps. 250 litres of distilled water is added in a reactor (201). 20 kg of synthetic water soluble polymer is added in the reactor (202). 5 kg of pre-treated forskolin is added into the reactor at a concentration of 98% w/w (203). 15 kg of modified starch is dissolved separately in a reactor comprising 100 litres of water and a modified starch solution is

obtained (204). The modified starch solution is added to the reactor comprising distilled water, water soluble synthetic polymer and forskolin 98% w/w (205). The reaction is allowed to take place in the reactor for 8 hours at a temperature of 50-80°C (206). The reaction is stopped after 8 hours and the reaction mixture is cooled to 30-50°C (207). The
5 reaction mixture is spray dried at a temperature of 180 °C; the reaction mixture comprises water soluble forskolin 10% w/w (208). The mixture comprising water soluble forskolin 10% w/w is collected after spray drying (209). The reaction mixture comprising water soluble forskolin 10% w/w is milled (210). The mixture comprising water soluble forskolin 10% w/w is refined by sieving through 80 mesh (211). The mixture comprising
10 water soluble forskolin 10% w/w is packed (212).

[0083] According to one embodiment herein, the forskolin composition has a solubility of 10%. The bioavailability is a function of absorption of active molecules in the human body. Due to physiochemical nature, forskolin has a very low or very poor solubility in water and hence no bioavailability. The forskolin with 10% water solubility
15 has an increased absorption of forskolin in the gut of an individual. The increased absorption from the gut results in increased concentration of forskolin in the blood. The enhanced availability of forskolin in the blood denotes enhanced bioavailability.

[0084] The foregoing description of the specific embodiments will so fully reveal the general nature of the embodiments herein that others can, by applying current
20 knowledge, readily modify and/or adapt for various applications such specific embodiments without departing from the generic concept, and, therefore, such adaptations and modifications should and are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments.

[0085] It is to be understood that the phraseology or terminology employed
25 herein is for the purpose of description and not of limitation. Therefore, while the embodiments herein have been described in terms of preferred embodiments, those skilled in the art will recognize that the embodiments herein can be practiced with modification within the spirit and scope of the appended claims.

[0086] Although the embodiments herein are described with various specific
30 embodiments, it will be obvious for a person skilled in the art to practice the embodiments herein with modifications.

CLAIMS

1. A method of synthesizing a composition comprising water soluble forskolin, the method comprising the steps of:
 - pretreating forskolin 98% w/w for obtaining a solvent free forskolin 98% w/w;
 - adding a predetermined amount of distilled water in a first reactor, and wherein the predetermined amount water added to the first reactor is 250 litres;
 - adding a predetermined amount of synthetic water soluble polymer in the first reactor comprising distilled water, and wherein the predetermined amount of synthetic water soluble polymer added is 20 Kg;
 - adding a predetermined amount of pre-treated forskolin 98% w/w to the first reactor comprising distilled water and synthetic water soluble polymer, and wherein the predetermined amount of pre-treated forskolin 98% w/w added to the first reactor is 5 Kg;
 - dissolving a predetermined amount of modified starch in a second reactor with 100 litres of distilled water, and wherein the predetermined amount of modified starch added to the second reactor is 5 Kg to obtain a modified starch solution;
 - adding the modified starch solution to the first reactor comprising distilled water, synthetic water soluble polymer and pre-treated forskolin 98% w/w to obtain a mixture;
 - heating the mixture in the first reactor for a predetermined amount of time at a predetermined temperature range, and wherein the predetermined amount of time is 8 hours, and wherein the predetermined temperature is in a range of 50-80°C;
 - cooling the reaction mixture to 30-50°C to obtain a compound comprising a water soluble forskolin;
 - spray drying the compound comprising water soluble forskolin at 180°C;
 - collecting the compound comprising water soluble forskolin after spray drying;
 - milling the dried compound comprising water soluble forskolin;

sieving the milled compound comprising water soluble forskolin through 80 mesh;

refining the milled and sieved compound comprising water soluble forskolin ; and

5 packaging the milled and sieved compound comprising water soluble forskolin, and wherein the water soluble forskolin is administered to individuals at a predetermined dosage.

2. The method according to claim 1, wherein the method of pre-treating forskolin 98% w/w comprises the steps of:

10 dissolving the forskolin 98% w/w in organic solvent;
 obtaining a mixture comprising forskolin 98% w/w and organic solvent;
 adding water to the mixture;
 obtaining a precipitate comprising forskolin 98% w/w; and
 drying the precipitate comprising forskolin 98% w/w, and wherein pre-
15 treatment of forskolin 98% w/w makes the forskolin 98% w/w solvent free.

3. The method according to claim 1, wherein the synthetic water soluble polymer is selected from a group consisting of polyvinyl pyrrolidone, poly ethylene glycol, polyvinyl alcohol and polyacrylic acid.

4. The method according to claim 1, wherein the organic solvent is selected from a
20 group consisting of compounds having 2 carbon atoms, compounds having 3 carbon atoms, compounds having 4 carbon atoms, compounds having 5 carbon atoms, compounds having 6 carbon atoms and compounds having 8 carbon atoms.

5. The method according to claim 1, wherein the modified starch is selected from a
25 group consisting of malto-dextrin, starch sodium octenyl succinate, starch and cyclodextrin.

6. The method according to claim 1, wherein the forskolin is administered in a recommended dosage, and wherein the recommended dosage of forskolin 10% w/w is 500 mg/day for an individual.

7. The method according to claim 1, wherein the forskolin is administered for weight
30 management and glaucoma, and wherein the water soluble forskolin has a bioavailability which is higher than a bioavailability of existing forskolin compositions.

8. The method according to claim 1, wherein a concentration of water soluble forskolin in the mixture is 10% w/w, and wherein the forskolin has a water solubility of 10% w/w.
9. A composition of water soluble forskolin, wherein the composition comprises:
5 forskolin with a water solubility of 10% w/w, and wherein a concentration of water soluble forskolin in the composition is 10% w/w, and wherein the forskolin having a water solubility of 10% w/w, and wherein the water soluble forskolin composition is administered to individuals at a predetermined dosage, and wherein the forskolin is administered to the individuals in a recommended dosage,
10 and wherein the recommended dosage of forskolin 10% w/w is 500 mg/day for an individual, and wherein a concentration of water soluble forskolin in the composition is 10% w/w, and wherein the forskolin has a water solubility of 10% w/w, and wherein the forskolin composition comprises additives, and wherein the additives are selected from a group consisting of a polyvinyl pyrrolidone, an
15 ethylene glycol, an polyvinyl alcohol, an polyacrylic acid, a malto-dextrin, a starch sodium octenyl succinate, a starch and a cyclodextrin.
10. The composition according to claim 9, wherein the forskolin is administered for weight management and glaucoma, and wherein the water soluble forskolin has a bioavailability which is higher than a bioavailability of existing forskolin
20 compositions.

1/3

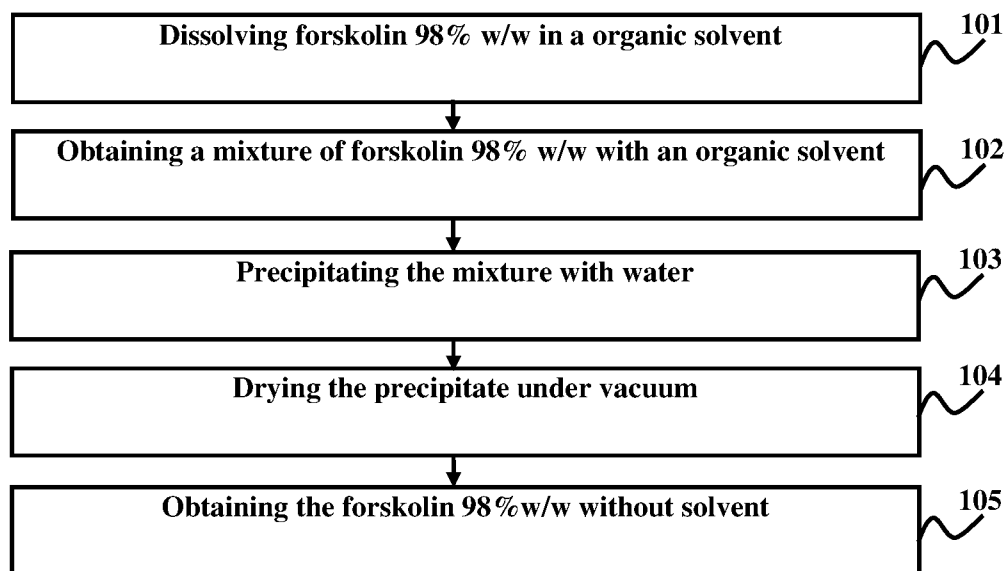


FIG. 1

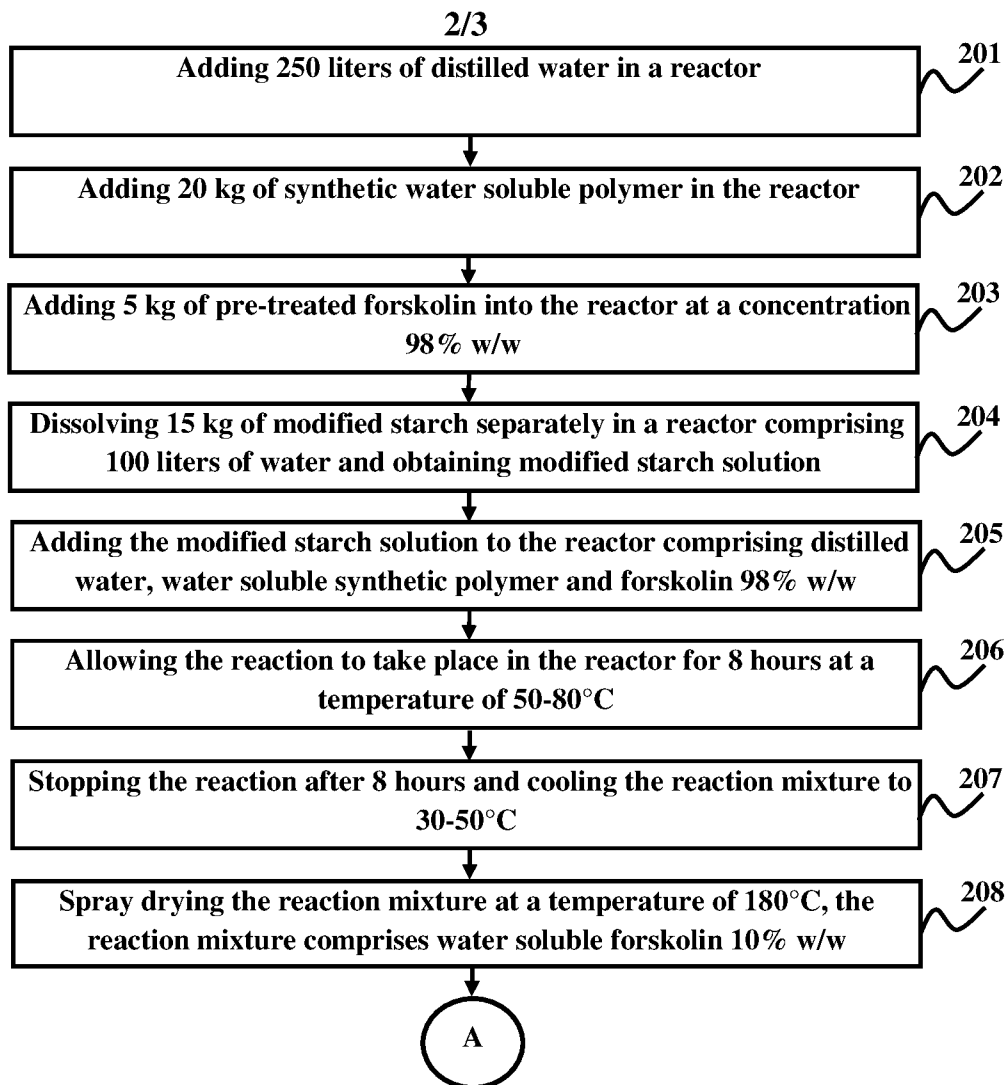


FIG. 2A

3/3

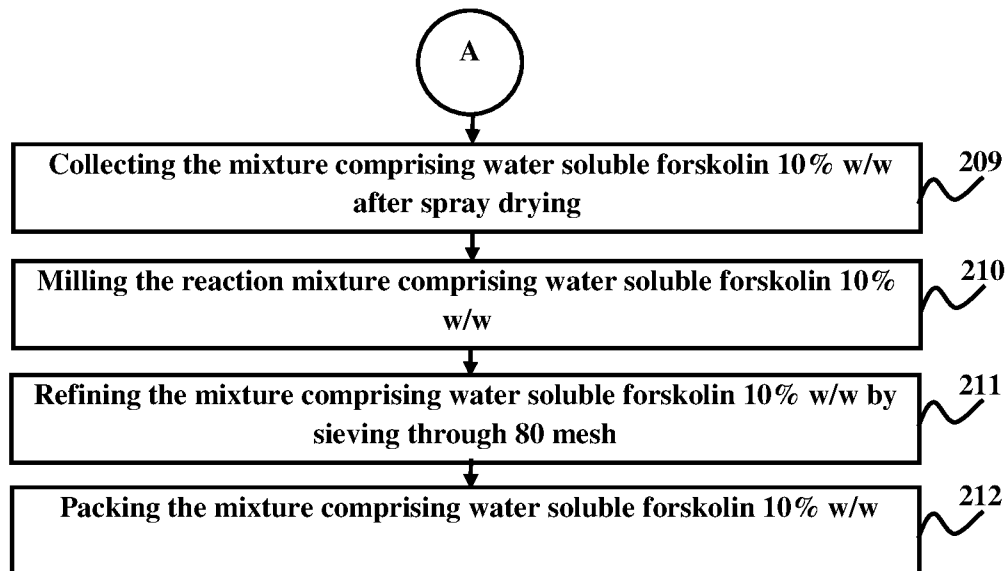


FIG. 2B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2016/057654

A. CLASSIFICATION OF SUBJECT MATTER
C07D311/92 Version=2017.01

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)

C07D

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)

Patseer, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO2005025500A2 (MAJEED, Muhammed et al) 24 March 2005 (24-03-2005). *Claims, paragraph [0026]*	9-10
A	WO2005025500A2 (MAJEED, Muhammed et al) 24 March 2005 (24-03-2005). *Whole document*	1-8
A	US6346273B1 (FARMIGEA S.P.A., SAETTONI Marco Fabrizio, GIANNACCINI Boris) 12 February 2002 (12-02-2002). *Whole document*	1-8
A	S. Sareen et al: "Improvement in solubility of poor water-soluble drugs by solid dispersion" International Journal of Pharmaceutical Investigation; 2012; Volume: 2(1); Pages: 12-17; PMCID: PMC3465159. *Whole document especially abstract*	1-8
A	LA Nikghalb et al: "Solid Dispersion: Methods and Polymers to increase the solubility of poorly soluble drugs" Journal of Applied Pharmaceutical Science; 2012; Volume: 2(10); Pages: 170-175. *Whole document*	1-8

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search

01-03-2017

Date of mailing of the international search report

01-03-2017

Name and mailing address of the ISA/

Indian Patent Office
Plot No.32, Sector 14, Dwarka, New Delhi-110075
Facsimile No.

Authorized officer

Harish Raj

Telephone No. +91-1125300200

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2016/057654

Citation	Pub.Date	Family	Pub.Date
WO 2005025500 A2	24-03-2005	CA 2537820 C	26-03-2013
		CN 1882508 B	14-07-2010
		EP 1718568 B1	26-12-2012
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		EP 0994727 B1	23-10-2002
		WO 1999004823 A1	04-02-1999