macrocyclic lactone; and sirolimus, another macrocyclic lactone, which is also known as rapamycin. These compounds have molecular weights even exceeding those of many steroids, and are structurally distinctly different from both steroids and common antimalarials. Many solutions of aqueous preparations have been described in the art that closely resemble those mentioned before. However, in all these cases the preparations are either complicated to manufacture, lack proper storage stability, and/or are not at least quasi-homogenous solutions.

It may therefore be inferred from the aforesaid that there still exists a need for augmenting the aqueous solubility of water-insoluble or slightly water-soluble therapeutically or cosmetically useful compounds in order to enable better topical or systemic bioavailability, as well as for improving physical and chemical storage stability.

SUMMARY

In one aspect, the present invention refers to a method of manufacture of a pharmaceutical or cosmetic composition comprising a water-insoluble or slightly water-soluble hydrophobic organic compound dissolved in an aqueous solvent system at an increased concentration, the method comprising: adding a saponin component selected from the group consisting of escin and glycyrrhizin to an aqueous solvent in an amount sufficient to trigger the formation of micelles; wherein the concentration of the saponin component is adjusted to a value of from 0.01 to 0.5% w/v in the case of escin, and to a value of from 0.5 - 5% w/v in the case of glycyrrhizin; adding dex¬panthenol to the aqueous solvent at a concentration of from 0.5% to 5% v/v; and adjusting the pH of the aqueous solvent to a value within a range of from pH 4 to pH 8; wherein the hydrophobic organic compound is already present in the aqueous solvent prior to the addition of the saponin component; or else, wherein in a first step the hydrophobic organic compound is pre-dissolved in a pharmaceutically or cosmetically acceptable organic solvent, whereupon in a second step the organic solvent comprising the pre-dissolved hydrophobic organic compound is admixed to the aqueous solvent; whereupon at least a part of the insoluble or slightly soluble hydrophobic organic compound gets solubilized and dissolved in the aqueous solvent through interaction

with the saponin component to form common micelle structures wherein the said compound gets attached to or entrapped within the micelles formed, yielding an aqueous composition having an increased concentration of said organic compound dissolved therein.

In another aspect, the present invention refers to a pharmaceutical or cosmetic composition comprising a water-insoluble or slightly water-soluble hydrophobic organic compound dissolved in an aqueous solvent system at an increased concentration, characterized in that the aqueous solvent system comprises a buffer adjusted to a pH value in a range of from pH 4 to pH 8 and a saponin component selected from the group consisting of escin and glycyrrhizin at or above a critical micelle concentration, wherein the saponin concentration is in a range of from 0.01 to 0.5% w/v in the case of escin, and in a range of from 0.5 - 5% w/v in the case of glycyrrhizin, wherein the aqueous solvent further comprises dexpanthenol at a concentration of from 0.5% to 5% v/v, and wherein at least a part of the water-insoluble or slightly soluble organic compound is dissolved through solubilization by way of attachment to saponin-micelles present in the solvent. The inventors have surprisingly discovered that the poor solubility of many organic compounds in aqueous media can successfully be overcome and the solubility of such compounds amazingly increased severalfold and in many cases up to several orders of magnitude by the addition of a saponin component at very low concentrations to a said aqueous medium, typically a pharmaceutically or cosmetically acceptable aqueous solvent or solvent system, and admixing to the aqueous solvent or solvent system a portion of a desired water-insoluble or slightly water-soluble hydrophobic organic compound pre-dissolved in a conventional non-aqueous organic solvent.

Experiments conducted by the present inventors have proven that the solubilization effect of the saponins suitable for carrying out embodiments described herein is not limited to the interaction with a particular class of water-insoluble or slightly soluble compounds that share a close chemical, physiological or structural similarity but instead seems to be broadly applicable to a vast variety of

## CLAIMS

What is claimed is:

1. A method of manufacture of a pharmaceutical or cosmetic composition comprising a water-insoluble or slightly water-soluble hydrophobic organic compound dissolved in an aqueous solvent system at an increased concentration, the method comprising:
   - adding a saponin component selected from the group consisting of escin and glycyrrhizin to an aqueous solvent in an amount sufficient to trigger the formation of micelles;
   - wherein the concentration of the saponin component is adjusted to a value of from 0.01 to 0.5% w/v in the case of escin, and to a value of from 0.5 - 5% w/v in the case of glycyrrhizin;
   - adding dexpanthenol to the aqueous solvent at a concentration of from 0.5% to 5% v/v; and
   - adjusting the pH of the aqueous solvent to a value within a range of from pH 4 to pH 8;

   wherein the hydrophobic organic compound is already present in the aqueous solvent prior to the addition of the saponin component;
   or else,
   wherein in a first step the hydrophobic organic compound is pre-dissolved in a pharmaceutically or cosmetically acceptable organic solvent, whereupon in a second step the organic solvent comprising the pre-dissolved hydrophobic organic compound is admixed to the aqueous solvent;

   whereupon at least a part of the insoluble or slightly soluble hydrophobic organic compound gets solubilized and dissolved in the aqueous solvent through interaction with the saponin component to form common micelle structures wherein the said compound gets attached to or entrapped within the micelles formed, yielding an aqueous composition having an increased concentration of said organic compound dissolved therein.

2. The method of claim 1, comprising drying the composition by lyophilisation.

3. The method of claim 1 or 2, wherein the addition of the saponin component is carried out at a temperature of between 20 and 80 degrees C, or between 35 and 50 degC, or within a range of from 30 to 40 degC.

4. The method of any one of claims 1 to 3, wherein escin is added as one or the sole saponin component to the aqueous solvent at a concentration of from 0.02 to 0.5 % w/v.

5. The method of any one of claims 1 to 3, wherein glycyrrhizin is added as one or the sole saponin component to the aqueous solvent at a concentration of from 0.1 to 5 % w/v.

6. The method of any one of claims 1 to 5, wherein the aqueous solvent comprises propylene glycol at a concentration of from 1 to 15% v/v.

7. The method of any one of claims 1 to 6, wherein the organic solvent is selected from the group consisting of DMSO, propylene glycol, polyethylene glycol, propylene carbonate, dimethyl isosorbide, fatty acid alcohols, triacetin monostearate, ethylene glycol distearate, glyceryl monostearate, propylene glycol monostearate, polyvinyl alcohol, carbomers, non-ionic polyethoxylated detergents derived from hydrogenated castor oil, and chemically modified cellulose derivatives.

8. The method of any one of claims 1 to 7, wherein at least one further ingredient selected from the group consisting of propylene glycol, carrageenan, cellulose derivatives, and hyaluronic acid is added to the aqueous solvent.

9. The method of any one of claims 1 to 8, wherein the water-insoluble or slightly soluble hydrophobic organic compound is a pharmaceutically active drug selected from the group consisting of analgesics, antirheumatics, antiallergics, antibiotics, chemotherapeutics, antiepileptics, antimycotics, antimalarials,

corticoids, dermatics, hynotics, sedatives, immunotherapeutics, immuno-suppressants, cytokines, anaesthetics, anti-migraine drugs, parathyroid hormones, calcium metabolism regulators, ophtalmics, psychotropics, sex hormones, inhibitors of sex hormones, cytostatics, and metastasis inhibitors.

10. The method of any one of claims 1 to 9, for the manufacture of a cosmetic preparation or a medicament.

11. A pharmaceutical or cosmetic composition comprising a water-insoluble or slightly water-soluble hydrophobic organic compound dissolved in an aqueous solvent system at an increased concentration, characterized in that the aqueous solvent system comprises a buffer adjusted to a pH value in a range of from pH 4 to pH 8 and a saponin component selected from the group consisting of escin and glycyrrhizin at or above a critical micelle concentration, wherein the saponin concentration is in a range of from 0.01 to 0.5% w/v in the case of escin, and in a range of from 0.5 - 5% w/v in the case of glycyrrhizin, wherein the aqueous solvent further comprises dexpanthenol at a concentration of from 0.5% to 5% v/v, and wherein at least a part of the water-insoluble or slightly soluble organic compound is dissolved through solubilization by way of attachment to saponin-micelles present in the solvent.

12. The pharmaceutical or cosmetic composition of claim 11, characterized in that it further comprises propylene glycol.

13. The pharmaceutical or cosmetic composition of claim 11 or 12, characterized in that it comprises propylene glycol at a concentration of from 1 to 15% v/v.

14. The pharmaceutical or cosmetic composition of any one of claims 11 to 13, characterized in that it the aqueous solvent system comprises a portion of an organic solvent selected from the group consisting of DMSO, propylene glycol, polyethylene glycols, propylene carbonate, dimethyl isosorbide, fatty acid alcohols, triacetin monostearate, ethylene glycol distearate, glyceryl mono-

stearate, propylene glycol monostearate, polyvinyl alcohol, carbomers, non-ionic polyethoxylated detergents derived from hydrogenated castor oil, and chemically modified cellulose derivatives.

15. The pharmaceutical or cosmetic composition of any one of claims 11 to 14, characterized in that it comprises at least one further ingredient selected from the group consisting of iota-carrageenan, kappa-carrageenan, and hyaluronic acid.

16. The pharmaceutical or cosmetic composition of any one of claims 11 to 15, characterized in that the water-insoluble or slightly water-soluble hydrophobic organic compound is a pharmaceutically active drug selected from the group consisting of analgesics, antirheumatics, antiallergics, antibiotics, chemotherapeutics, antiepileptics, antimycotics, antimalarials, corticoids, dermatics, hynotics, sedatives, immunotherapeutics, immunosuppressants, cytokines, anaesthetics, anti-migraine drugs, parathyroid hormones, calcium metabolism regulators, ophtalmics, psychotropics, sex hormones, inhibitors of sex hormones, cytostatics, and metastasis inhibitors.

17. The pharmaceutical or cosmetic composition of any one of claims 11 to 16, characterized in that it is adapted for administration to a mucosal surface, particularly a mucosal surface of the nose, of the mouth, of the eyes, of the respiratory tract, of the lungs, of the genital region, and of the anorectal region.