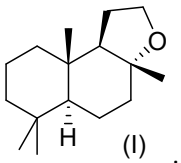
Claims:

1. A method of preparing a solid form of (-)-Ambrox of formula (I)



(I) ,

wherein said solid form is olfactively pure and characterized by the following characteristics:-

- it exhibits an x-ray diffraction pattern having at least one of the following peaks at diffraction angles 2 theta of ~~about~~ 15.6, 16.2, 16.7, 17.0, 17.4, 18.3 +/- 0.2°;
- it comprises elongate crystals having an average diameter of at least ~~about~~ 10 to ~~about~~ 400 microns measured by laser granulometry;
- it comprises elongate crystals having a length along their longest dimension of greater than 100 micron; and
- it has an L* value of 90 or more; an a* value of less than 1 and greater the -1; and a b* value, which is less than 8, wherein L*, a* and b* values represent CIELAB L*a*b* chromaticity coordinates;

wherein the solid form of (-)-Ambrox is formed by a bioconversion process;

said method comprising the steps of:-

I) forming crystalline (-)-Ambrox in a bioconversion medium by means of a biocatalytic process;

II) separating the crystalline (-)-Ambrox from the bioconversion medium~~,~~

iii) wherein the bioconversion medium obtained from the bioconversion process comprises a solid phase containing crude (-)-Ambrox, a liquid phase or phases consisting of water and an oily phase containing residual homofarnesol and other oily or oil-soluble impurities or by-products (II), (III) and (IV) present in the oily phase;

wherein the bioconversion process is an enzyme-catalyzed cyclization of homofarnesol comprising a mixture of 7E,3E and 7E,3Z ~~geometric~~ isomers of homofarnesol ~~,~~ wherein the cyclization reaction is carried out in the presence of an SHC biocatalyst capable of bioconverting a homofarnesol mixture enriched in the 7E,3E isomer to (-)-Ambrox wherein in the presence of

appreciable amounts of homofarnesol, (-)-Ambrox and the by-products remain dissolved together; and wherein a reduction in the level of unreacted homofarnesol in admixture with (-)-Ambrox and the compounds (II), (III) and (IV) results in crystallization of (-)-Ambrox and facilitates downstream processing and isolation/purification of (-)-Ambrox in a solid form from the bioconversion medium.~~.~~

2. The method according to claim 1, wherein the separation step is a filtration step, a decantation step, or a combination of both a filtration step and a decantation step.

3. The method according to claim 1 or claim 2, wherein prior to the separation step, the bioconversion medium is heated to a temperature of at least 55 °C to melt the crystalline (-)-Ambrox; and thereafter slowly cooled in order that the (-)-Ambrox is recrystallized from the bioconversion medium.

4. The method according to any of the claims 1 through 3, wherein the recovered crystals of (-)-Ambrox are solubilized in a solvent, and the solution filtered through a sub-micron filter to remove any residual particulate material that was present in the bioconversion medium, before being rendered in solid form by removing the solvent by evaporation or recrystallization.

5. The method according to any of the claims 1 through 4, wherein the biocatalyst is a recombinant microorganism expressing the gene coding the enzyme, or an isolated enzyme, or an immobilized enzyme.

6. The method according to any of the claims 1 through 5, wherein the enzyme is a wild-type squalene hopene cyclase, or a variant of the wild-type squalene hopene cyclase.

7. The method according to any of the claims 1 through 6, wherein the crystals are washed with water, water-miscible solvents or mixtures thereof, in particular with water.