Haazekamp A and Verpoorte R. describe solubility testing of classical naturally occurring cannabinoid Tetrahydrocannabinoid in the presence of various cyclodextrins (European J. of Pharm Sciences 29 (2006), 340-347).

Souter R., "Nabilone", Analytical Profiles of Drug Substances, vol. 10, 1981, 499-512 describes the physical-chemical characteristics of Nabilone.

Szejtli J., "Cyclodextrins in Pharmaceuticals", 1988, Cyclodextrin Technology, 186-307 describes the use of cyclodextrin as auxiliary substance.

Mannila J. et al.,Europ.J.Pharm.Sciences, 26 (2005), 71-77 disclose sublingual formulations of cannabinoids.

Any increase of solubility of synthetic cannabinoids was not disclosed.

The object of the present invention is to provide Nabilone in a formulation which can overcome the disadvantages as listed above.

The object is solved by the embodiments of the present invention.

Summary

In one aspect, there is provided a composition comprising Nabilone and randomly methylated ß cyclodextrin (RAMEB) in the weight ratio (dry weight to dry weight) of 1:60 - 1:140, preferably in the weight ratio of 1:90 – 1:110 and wherein Nabilone and RAMEB are comprised as an aqueous soluble complex.

In another aspect, there is provided a composition comprising a complex of Nabilone and RAMEB, sodium-hydrogen carbonate, citric acid anhydride and crospovidone.

In another aspect, there is provided a composition as defined above for use as a medicament.

In another aspect, there is provided a composition as defined above for use in the treatment of nausea, muscular spasm, multiple sclerosis, uterine and bowel cramps, movement disorders, pain, including migraine headache, glaucoma, asthma, inflammation, insomnia, high blood pressure and/or a condition responsive to an appetite stimulating, amyotrophic lateral sclerosis, anti-cancer, oxytoxic, anxiolytic, anti-convulsive, anti-depressant and anti-psychotic agent.

In another aspect, there is provided a method for producing a complex of RAMEB and Nabilone as defined above, wherein said RAMEB is combined with Nabilone in a heterogeneous state or in the solid state, including using methods

selected from freeze drying, spray-drying, kneading, grinding, slurry-method, co-precipitation, and neutralization, and optionally separating the obtained complex.

In another aspect, there is provided a method for increasing the bioavailability of Nabilone in a sublingually or buccally administered preparation comprising the step of complexing Nabilone with RAMEB as defined above, and formulating the complex obtained as a sublingually or buccally administerable dosage form.

In another aspect, there is provided a method for increasing the solubility of the Nabilone in aqueous solution by complexing Nabilone and RAMEB wherein Nabilone is stirred for about 96 h in the presence of 25% or 30 weight % RAMEB and maintaining a constant reaction temperature of about 25°C.

Brief description of the invention:

The present invention provides a formulation preferably for a fast disintegrating administration form like, for example, a tablet, containing Nabilone wherein Nabilone has increased solubility in aqueous solutions and increased stability. The better solubility can thus overcome the high first-pass metabolism and low dissolution properties.

The inventive composition specifically comprises Nabilone and randomly methylated ß-cyclodextrin (RAMEB), wherein the weight ratio (dry weight to dry weight) between Nabilone and RAMEB is about 1:60 - 1:140, preferably the weight ratio is about 1:90 – 1:110. Specifically, the inventive composition comprises Nabilone and randomly methylated ß-cyclodextrin (RAMEB) in the weight ratio (dry weight to dry weight) of 1:60 - 1:140, preferably in the weight ratio of 1:90 – 1:110, wherein Nabilone and RAMEB are comprised as an aqueous soluble complex. It has been surprisingly shown that the solubility of Nabilone was highly increased when RAMEB was used as complex-forming agent, being present in the composition in the above mentioned range.

According to an embodiment of the invention, Nabilone is present in the composition in an amount of 0.01 to 100mg, preferably of 0.1 to 50mg, more preferred of 0.25 to 40mg, more preferred in an amount of approx. 30mg with regard to the medication form.