HAM-D scale may be used to assess the severity of depression in patients by means of a 24 items questionnaire. According to the outcome of the clinical study compound I is believed to be particularly useful in the treatment of depression avoiding sleep and sexual related adverse events (WO 2008/113359).

For many pharmaceutical compounds, oral administration of a tablet, capsule, pill or similar intended for swallowing is the preferred administration form. However, some patients, e.g. elderly and paediatric patients may have difficulties swallowing, and liquid solutions may be a suitable alternative avoiding the need for swallowing tablets, capsules, pills, etc. A liquid solution further provides a possibility of a flexible dosing regime. In order to limit the volume of a liquid solution it is necessary to have a high concentration of the active ingredient in the solution, which again requires a high solubility of the active ingredient.

The present invention is related to liquid formulations of compound I.

Summary of the invention

The present inventors have surprisingly found that the L-lactic acid addition salt (=L-lactate), the D-lactic acid addition salt (=D-lactate) and the DL-lactic acid addition salt (=DL-lactate) of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine are highly soluble. Accordingly, the present ~~invention~~disclosure relates to a liquid formulation comprising the L-lactic acid addition salt, the D-lactic acid addition salt and/or the DL-lactic acid addition salt of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine.

In one aspect, there is provided a liquid pharmaceutical formulation comprising a salt of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine selected from the DL-lactic acid addition salt, L-lactic acid addition salt and the D-lactic acid addition salt.

In another aspect, there is provided the use of a salt of 1-[2-(2,4-dimethylphenylsulfanyl) phenyl]piperazine selected from the DL-lactic acid addition salt, L-lactic acid addition salt and the D-lactic acid addition salt in the manufacture of a liquid formulation for the treatment of a disease selected from mood disorders; major depressive disorder; general anxiety disorder; panic disorder; post traumatic stress disorder; depression associated with cognitive impairment, Alzheimer's disease or anxiety; depression with residual symptoms; chronic pain; eating disorder or abuse, wherein said salt is in a liquid formulation.

In another aspect, there is provided a salt of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine selected from the DL- lactic acid addition salt, the L-lactic acid addition salt and the D-lactic acid addition salt for use in the treatment of a disease selected from mood disorders; major depressive disorder; general anxiety disorder; panic disorder; post traumatic stress disorder; depression associated with cognitive impairment, Alzheimer's disease or anxiety; depression with residual symptoms; chronic pain; eating disorder or abuse, wherein said salt is in a liquid pharmaceutical formulation.

In one ~~embodiment~~aspect, ~~the invention relates to~~there is provided a compound which is the L-lactic acid addition salt of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine.

In one ~~embodiment~~aspect, ~~the invention relates to~~there is provided a compound which is the D-lactic acid addition salt of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine.

In one aspect, there is provided a compound which is the β form of the DL-lactic acid addition salt characterized by XRDP reflections at 6.01, 10.10, 10.32, 12.06, 12.84, 13.08 and 13.58 (°2θ).

In one embodiment, the ~~invention~~disclosure relates to a method of treatment, said method comprising the administration of a liquid formulation ~~of the present invention~~defined above to a patient in need thereof.

In one embodiment, the ~~invention~~disclosure relates to the use of a salt ~~of the present invention~~disclosed herein in the manufacture of a liquid pharmaceutical composition for the treatment of certain diseases.

In one embodiment, the ~~invention~~disclosure relates to a salt ~~of the present invention~~disclosed herein for use in the treatment of certain diseases, wherein said salts is in a liquid formulation.

In one ~~embodiment~~aspect, ~~the present invention relates to~~there is provided a container comprising a liquid formulation ~~of the present invention~~described above, wherein said container is fitted with a drop aggregate.

Figures

Figure 1: XRPD of L-lactate anhydrate 1 (AH1)

Figure 2: XRPD of L-lactate monohydrate 1 (MH1)

Figure 3: XRPD of L-lactate monohydrate 2 (MH2)

Figure 4: XRPD of DL-lactate alpha form (α)

Figure 5: XRPD of DL-lactate beta form (β)

Figure 6: XRPD of DL-lactate monohydrate (MH), with content of α-form

Figure 7: XRPD of DL-lactate gamma form (γ), with content of α-form

Detailed description of the invention

The formulations to which the present invention relates are all pharmaceutical compositions.

Characterisation of the crystalline base and the previously known salts of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine has been described in WO 2008/113359. The aqueous solubilities of these salts are shown in Table 2. Table 1 shows XRPD reflections, melting points and solubility data of salts of the present invention. As evidenced by the data from Table 1 and 2, the DL-lactic acid addition salt β-form and the L-lactic acid addition salt MH2 have exceptionally high solubilities. Consequently, these salt forms would be suitable for application in liquid formulations comprising 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazin. According to table 2, also the mesylate salt benefits from extremely high solubility. However, use of methane sulfonic acid (mesylate) in combination with alcoholic solvents in the synthesis of pharmaceutical compositions involves a risk of obtaining alkyl mesylate impurities which could be genotoxic (*Mutat. Res.* 581 (2005) 23-34; *Eur. J. Pharm. Sci.* 28 (2006) 1-6). Lactate salts are accordingly superior to mesylate salts for application in pharmaceutical compositions.