The disclosure further relates to a pharmaceutical composition comprising an opioid antagonist with κ- opioid receptor activity and vortioxetine or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable excipient, wherein said opioid antagonist with κ- activity is nalmefene or a pharmaceutically acceptable salt thereof .

In one aspect, there is provided the use of an opioid antagonist with κ- activity in the preparation of a medicament for the treatment of depressive disorder with melancholic features, wherein said opioid antagonist with κ- activity is nalmefene or a pharmaceutically acceptable salt thereof, wherein said medicament further comprises vortioxetine or a pharmaceutically acceptable salt thereof.

Also disclosed is the use of an opioid antagonist with κ- activity in the preparation of a medicament for the treatment of depressive disorder with melancholic features, wherein a therapeutically effective amount of said opioid antagonist with κ- activity is to be administered to a patient having depressive disorder with melancholic features.

Brief description of drawings

Figures 1 and 2 illustrate the effect of vehicle and test compounds on chronic mild stress in male Wistar rats (control rats and rats exposed to chronic mild stress).

X-axis: weeks of treatment; Y-axis: sucrose intake (g). Values are means +/- SEM.

Figure 1.

Effects of chronic treatment with vehicle and imipramine (10 mg/kg, IP, once daily).

○= control/vehicle; ◇= control/imipramine; ●= stressed/vehicle; ◆= stressed/imipramine.

* - p<0.05, ** - p<0.01, *** - p<0.001; relative to vehicle- or drug-treated control groups.

- p<0.05, ## - p<0.01, ### - p<0.001; relative to drug-treated stressed animals at Week 0.

Figure 2.

Effects of chronic treatment with vehicle, vortioxetine (10 mg/kg, IP, once daily), nalmefene (1 mg/kg, IP, once daily) and joint administration of both drugs.

○= control/vehicle; △= control/vortioxetine; ◇= control/nalmefene;

▽= control/vortioxetine+nalmefene; ●= stressed/vehicle; ▲= stressed/vortioxetine;

◆= stressed/nalmefene; ▼= stressed/vortioxetine+nalmefene.

** - p<0.01, *** - p<0.001; relative to vehicle- or drug-treated control groups.

- p<0.05, ## - p<0.01, ### - p<0.001; relative to drug-treated stressed animals at Week 0.

Definitions

Throughout the specification “opioid receptor antagonists with κ- opioid receptor activity”, “opioid antagonists with κ- opioid receptor activity”, “opioid receptor antagonists with κ-

activity" and "opioid antagonists with κ- activity" are used interchangeably. All are intended to include opioid antagonists with κ- activity selected from, but not limited to: nalmefene, naltrexone, naloxone, nor-BNI (nor-binaltorphimine), buprenorphine, naltriben, nalorphine, levallorphan, LY2456302 ((S)-3-fluoro4-(4-((2-(3,5-dimethylphenyl)pyrrolidin-1-yl)methyl)phenoxy)benzamide), dynorphin, JDTic ((3R)-7-Hydroxy-N-{(1S)-1-{[(3R,4R)-4-(3-hydroxyphenyl)-3,4-dimethyl-1-piperidinyl]methyl}-2-methylpropyl}-1,2,3,4-tetrahydro-3-isoquinoline-carboxamide), and other opioid antagonists with κ- activity. In one embodiment, opioid antagonists with κ- activity of the present invention are selected from nalmefene, nal

Claims

1. Use of an opioid antagonist with κ- activity in the preparation of a medicament for the treatment of depressive disorder with melancholic features, wherein said opioid antagonist with κ- activity is nalmefene or a pharmaceutically acceptable salt thereof, wherein said medicament further comprises vortioxetine or a pharmaceutically acceptable salt thereof.

2. The use according to claim 1, wherein the dose of nalmefene is between 1 and 30 mg.

3. The use according to any of claims 1-2, wherein the dose of vortioxetine is between 1 and 30 mg.

4. The use according to any of claims 1-3, wherein said opioid antagonist with κ- activity and vortioxetine are contained in separate unit dosage forms.

5. The use according to any of claims 1-3, wherein said opioid antagonist with κ- activity and vortioxetine are contained in the same unit dosage form.

6. A pharmaceutical composition comprising an opioid antagonist with κ- activity and vortioxetine or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable excipient, wherein said opioid antagonist with κ- activity is nalmefene of a pharmaceutically acceptable salt thereof.

7. The pharmaceutical composition according to claim 6, comprising 1-30 mg of nalmefene and 1-30 mg of vortioxetine.

8. The pharmaceutical composition according to claims 6 or 7, comprising 5-20 mg of nalmefene and 5-20 mg of vortioxetine.