been demonstrated for many pathological conditions including pain (Pasquini, S. J Med Chem 2012, 55(11): 5391), neuropathic pain (Garcia-Gutierrez, M.S. Br J Pharmacol 2012, 165(4): 951), psychiatric disorders (Garcia-Gutierrez, M.S. Br J Pharmacol 2012, 165(4): 951), psychosis (Garcia-Gutierrez, M.S. Br J Pharmacol 2012, 165(4): 951), osteoporosis and inflammation (Sophocleous, A. Calcif Tissue Int 2008, 82(Suppl. 1):Abst OC18), psychiatric diseases and psychosis (Garcia-Gutierrez, M.S. Br J Pharmacol 2012, 165(4): 951), oncology (Preet, A. Cancer Prev Res 2011, 4: 65), encephalitis and malaria (Zimmer, A. WO 2011045068), allergy and inflammation (Ueda, Y. Life Sci 2007, 80(5): 414), encephalitis and malaria (Zimmer, WO 2011045068), asthma (Lunn, C.A. J Pharmacol Exp Ther 2006, 316(2): 780), immunological disorders (Fakhfouri, G. Neuropharmacology 2012, 63(4): 653), rheumatoid arthritis (Chackalamannil, S. US 7776889), arthritis (Lunn, C.A. J Pharmacol Exp Ther 2006, 316(2): 780), and gastrointestinal disorders (Barth, F. FR 2887550).

The compounds of the invention bind to and modulate the CB2 receptor and have lower CB1 receptor activity.

In one aspect, there is provided a compound selected from the group consisting of:

3-Fluoropropyl 2-{[6-(cyclopropylmethoxy)-5-(3-methoxyazetidin-1-yl)pyridine-2-carbonyl]amino}-2-ethylbutanoate;

2-Fluoroethyl N-[6-(cyclopropylmethoxy)-5-(3-methoxyazetidin-1-yl)pyridine-2-carbonyl]-L-leucinate;

2-Fluoroethyl 2-{[6-(cyclopropylmethoxy)-5-(3-methoxyazetidin-1-yl)pyridine-2-carbonyl]amino}-2-ethylbutanoate;

6-(Cyclopropylmethoxy)-N-[(2S)-1-(fluoromethoxy)-4-methylpentan-2-yl]-5-(pyrrolidine-1-yl)pyridine-2-carboxamide;

6-(Cyclopropylmethoxy)-N-[(2S)-1-(2-fluoroethoxy)-4-methylpentan-2-yl]-5-(pyrrolidin-1-yl)pyridine-2-carboxamide; and

6-(Cyclopropylmethoxy)-N-[(2S)-1-(fluoromethoxy)-4-methylpentan-2-yl]-5-(3-methoxyazetidin-1-yl)pyridine-2-carboxamide.

In another aspect, there is provided a compound as defined herein for use as therapeutically active substance.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein and a therapeutically inert carrier.

In another aspect, there is provided use of a compound as defined herein in the preparation of a medicament for the treatment or prophylaxis of pain, atherosclerosis, age-related macular degeneration, diabetic retinopathy, glaucoma, diabetes mellitus, inflammation, inflammatory bowel disease, ischemia-reperfusion injury, acute liver failure, liver fibrosis, lung fibrosis, kidney fibrosis, systemic fibrosis, acute allograft rejection, chronic allograft nephropathy, diabetic nephropathy, glomerulonephropathy,

Claims

1. A compound selected from the group consisting of:

3-Fluoropropyl 2-{[6-(cyclopropylmethoxy)-5-(3-methoxyazetidin-1-yl)pyridine-2-carbonyl]amino}-2-ethylbutanoate;

2-Fluoroethyl N-[6-(cyclopropylmethoxy)-5-(3-methoxyazetidin-1-yl)pyridine-2-carbonyl]-L-leucinate;

2-Fluoroethyl 2-{[6-(cyclopropylmethoxy)-5-(3-methoxyazetidin-1-yl)pyridine-2-carbonyl]amino}-2-ethylbutanoate;

6-(Cyclopropylmethoxy)-N-[(2S)-1-(fluoromethoxy)-4-methylpentan-2-yl]-5-(pyrrolidine-1-yl)pyridine-2-carboxamide;

6-(Cyclopropylmethoxy)-N-[(2S)-1-(2-fluoroethoxy)-4-methylpentan-2-yl]-5-(pyrrolidin-1-yl)pyridine-2-carboxamide; and

6-(Cyclopropylmethoxy)-N-[(2S)-1-(fluoromethoxy)-4-methylpentan-2-yl]-5-(3-methoxyazetidin-1-yl)pyridine-2-carboxamide.

2. The compound of claim 1, wherein the compound is 3-Fluoropropyl 2-{[6-(cyclopropylmethoxy)-5-(3-methoxyazetidin-1-yl)pyridine-2-carbonyl]amino}-2-ethylbutanoate.

3. A compound according to claim 1 or 2 for use as therapeutically active substance.

4. A pharmaceutical composition comprising a compound in accordance with claim 1 or 2 and a therapeutically inert carrier.

5. The use of a compound according to claim 1 or 2 in the preparation of a medicament for the treatment or prophylaxis of pain, atherosclerosis, age-related macular degeneration, diabetic retinopathy, glaucoma, diabetes mellitus, inflammation, inflammatory bowel disease, ischemia-reperfusion injury, acute liver failure, liver fibrosis, lung fibrosis, kidney fibrosis, systemic fibrosis, acute allograft rejection, chronic allograft nephropathy, diabetic nephropathy, glomerulonephropathy, cardiomyopathy, heart failure, myocardial ischemia, myocardial infarction, systemic sclerosis, thermal injury, burning, hypertrophic scars, keloids, gingivitis pyrexia, liver cirrhosis or tumors, regulation of bone mass, neurodegeneration, stroke, transient ischemic attack or uveitis.

6. A compound according to claim 1 or 2 for use in the treatment or prophylaxis of pain, atherosclerosis, age-related macular degeneration, diabetic retinopathy, glaucoma, diabetes mellitus, inflammation, inflammatory bowel disease, ischemia-reperfusion injury, acute liver failure, liver fibrosis, lung fibrosis, kidney fibrosis, systemic fibrosis, acute allograft rejection, chronic allograft nephropathy, diabetic nephropathy, glomerulonephropathy, cardiomyopathy, heart failure, myocardial ischemia, myocardial infarction, systemic sclerosis, thermal injury, burning, hypertrophic scars, keloids, gingivitis pyrexia, liver cirrhosis or tumors, regulation of bone mass, neurodegeneration, stroke, transient ischemic attack or uveitis.

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