In this regard, alternative forms of the compound may have widely different properties such as, for example, enhanced thermodynamic stability, higher purity or improved bioavailability (e.g. better absorption, dissolution patterns). Specific compound forms could also facilitate the manufacturing (e.g. enhanced flowability), handling and storage (e.g. non-hygroscopic, long shelf life) of the compound formulations or allow the use of a lower dose of the therapeutic agent, thus decreasing its potential side effects. Thus it is important to provide such forms, having desirable properties for pharmaceutical use.

SUMMARY~~BRIEF DESCRIPTION OF THE INVENTION~~

The inventors of the present ~~invention~~disclosure, after an extensive research on different forms of 4-[2-[[5-methyl-1-(2-naphthalenyl)-1H-pyrazol-3-yl]oxy]ethyl]morpholine (herein referred as "compound 63"), have surprisingly found and demonstrated that some of its salts and specifically its hydrochloride salt provides advantageous production, handling, storage and/or therapeutic properties.

Thus, ~~in a first aspect~~ the present ~~invention~~disclosure relates to a 4-[2-[[5-methyl-1-(2-naphthalenyl)-1H-pyrazol-3-yl]oxy]ethyl]morpholine salt selected from the group consisting of ethanesulfonate, fumarate, hydrochloride, malate, maleate, malonate and methanesulfonate.

In an aspect, there is provided a ~~preferred embodiment, the present invention is directed to the~~ hydrochloride salt of 4-[2-[[5-methyl-1-(2-naphthalenyl)-1H-pyrazol-3-yl]oxy]ethyl]morpholine (herein referred as "P027" or "example 1").

The P027 compound has a molecular weight 373.88 uma, a pKa of 6.73 and a melting point of 194.2 °C. The compound is very soluble in water and freely soluble in methanol, 1N hydrochloric acid and dimethyl sulphoxide. It is sparingly soluble in ethanol, slightly soluble in acetone and practically insoluble in ethyl acetate and in 1N sodium hydroxide. The product exhibits a better dissolution and absorption profile in vivo than its related base.

In another aspect, there is provided~~the present invention is directed to~~ a process for the preparation of the hydrochloride salt of 4-[2-[[5-methyl-1-(2-naphthalenyl)-1H-pyrazol-3-yl]oxy]ethyl]morpholine which comprises:

a) mixing 4-[2-[[5-methyl-1-(2-naphthalenyl)-1H-pyrazol-3-yl]oxy]ethyl]morpholine and a solution containing hydrochloric acid, and
b) isolating the resulting hydrochloride salt.

TA further aspect of the present inventiondisclosure includes pharmaceutical compositions comprising 4-[2-[[5-methyl-1-(2-naphthalenyl)-1H-pyrazol-3-yl]oxy]ethyl]morpholine hydrochloride and a pharmaceutically acceptable carrier, adjuvant or vehicle.

In a further aspect, there is provided a pharmaceutical composition comprising the hydrochloride salt as defined above.

TIn a further aspect the inventiondisclosure is also directed to 4-[2-[[5-methyl-1-(2-naphthalenyl)-1H-pyrazol-3-yl]oxy]ethyl]morpholine hydrochloride for use as medicament, preferably as sigma ligand, i.e., for use the treatment and/or prophylaxis of a sigma receptor mediated disease or condition.

In another aspect, there is provided the hydrochloride salt as defined above for use as medicament.

The disclosure alsoAnother aspect of this invention relates to a method of treating and/or preventing a sigma receptor mediated disease which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a compound as above defined or a pharmaceutical composition thereof.

In another aspect, there is provided the hydrochloride salt as defined above for use in the treatment and/or prophylaxis of a sigma receptor mediated disease or condition.

In another aspect, there is provided the hydrochloride salt as defined above for use in the treatment and/or prophylaxis of a disease selected from the group consisting of diarrhoea; lipoprotein disorders; migraine; obesity; arthritis; hypertension; arrhythmia; ulcer; learning, memory and attention deficits; cognition disorders; neurodegenerative diseases; demyelinating diseases; addiction to drugs and chemical substances including cocaine, amphetamine, ethanol and nicotine; tardive diskinesia; ischemic stroke; epilepsy; stroke; stress; cancer; psychotic conditions, in particular depression, anxiety or schizophrenia; inflammation; or autoimmune diseases.

These aspects and preferred embodiments thereof are additionally also defined in the claims.

BRIEF DESCRIPTION OF THE FIGURES

Figure nº 1: differential scanning calorimetry (DSC) of example 1

Figure nº 2: thermogravimetry (TGA) of example 1

Figure n° 3: proton nuclear magnetic resonance (^{1}HNMR) of example 1

Figure n° 4: proton nuclear magnetic resonance (^{1}HNMR) of compound 63

Figure n° 5: proton nuclear magnetic resonance (^{1}HNMR) of example 2

Figure n° 6: differential scanning calorimetry (DSC) of example 2

Figure n° 7: thermogravimetry (TGA) of example 2

Figure n° 8: FTIR analysis of example 2

Figure n° 9 proton nuclear magnetic resonance (^{1}HNMR) of example 3

Figure n° 10: differential scanning calorimetry (DSC) of example 3

Figure n° 11: thermogravimetry (TGA) of example 3

Figure n° 12: FTIR analysis of example 3

Figure n° 13 proton nuclear magnetic resonance (^{1}HNMR) of example 4

Figure n° 14: differential scanning calorimetry (DSC) of example 4