POTENT AND SELECTIVE COMPOUNDS AS SEROTONIN 1B RECEPTOR MODULATORS

Field of the invention

This invention relates to new potent and selective compounds as modulators of serotonin receptor 1B (5-HTR_{1B}) also known as 5-hydroxytryptamine receptor 1B (5-HT_{1B}). The compounds are of potential utility in the treatment of diseases and conditions mediated by serotonin receptor type 1B (5-HTR_{1B}), such as cancer, including blood cancer and solid tumors and respiratory diseases and hepatic disorders. The invention also relates to the use of such compounds as medicaments, to pharmaceutical compositions containing them, and to synthetic routes for their production.

Background of the invention

Serotonin (5-hydroxytryptamine, 5-HT) is a biogenic monoamine that acts as a neurotransmitter in the central nervous system (CNS), local mediator in the gut and vasoactive agent in the blood. It is synthesized by a two-step pathway from the essential amino-acid tryptophan. Most of the serotonin of the body is located in the periphery (Sarrouilhe D. et al, *Serotonin and Cancer: What Is the Link?*, Current Molecular Medicine 2015, 15, 62-77).

Serotonin has been linked to a variety of CNS functions such as brain development, circadian rhythm, thermoregulation, cognition, pain, appetite, sexual drive, fear, mood, violent behavior, motor function and neuroendocrine secretion. Moreover, serotonin is implicated in many CNS and psychiatric disorders: Parkinson's disease, depression, hallucination, schizophrenia, bulimia, anxiety, addiction, chronic stress. Consequently, serotoninergic systems are targets for a large array of psychoactive compounds including antidepressants, antipsychotics and hallucinogens (Marin P. et al, *5-HT Receptor-Associated Protein Networks: New Targets for Drug Discovery in Psychiatric Disorders?*, Current Drug Targets, 2012, 13, 28-52).

Mammals employ 5-HT as a neurotransmitter within the central and peripheral nervous systems, and also as a local hormone in numerous other tissues, including the gastrointestinal tract, the cardiovascular system and immune cells. This multiplicity of function implicates 5-HT in a vast array of physiological and pathological processes. This plethora of roles has consequently encouraged the development of many compounds of