SB-258741: A 5-HT₇ Receptor Antagonist of Potential Clinical Interest

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Key Words: SB-258741—Serotonin antagonist—5-HT₇ receptors—Antidepressant—Pharmacology.

ABSTRACT

Recently, series of 5-HT₇ receptor antagonists have been developed (24,29,36,68). Among them SB-258741, R-(+)-1-(toluene-3-sulfonyl)-2-[2-(4-methylpiperidin-1-yl)ethyl]pyrrolidine, (compound “13” in 36,37) was one of the most potent and specific compounds. Due to a lack of specific ligands the pharmacology of 5-HT₇ receptor antagonists is still relatively unexplored. It has been suggested, however, that 5-HT₇ receptor ligands could be useful in the therapy of various disorders such as sleep disorders, schizophrenia, depression, migraine, epilepsy, pain, or memory impairment. Many of these conceivable indications are not supported by pharmacological data. It is, therefore, of particular interest to review the data generated from studies of one of these most potent and specific 5-HT₇ receptor antagonists, SB-258741, with a goal of testing the validity of the proposed clinical indications. In this review, the author describes pharmacology of this compound in order to define its potential clinical use. The available safety pharmacology data are discussed in an attempt to predict potential side effects of specific 5-HT₇ receptor antagonists.