Derivatives of N-[2-(dimethylamine)ethyl]-N-(2-phenylethyl)-aniline as potential polypharmacological ligands of SERT/5-HT6/5-HT7

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Depression is a serious mental disorder that cripples the lives of hundreds of millions of people. It is estimated that annual cost associated with depression reaches 800 billion euro (only in Europe).

Most commonly used antidepressant drugs (e.g. Fluoxetine, Sertraline) acts as a selective serotonin reuptake inhibitors (SSRI) by inhibiting the serotonin transporter (SERT). Unfortunately, these substances sometime exhibit low efficacy together with many side effects.

It was revealed, that compounds acting on serotonin receptors (e.g. 5-HT1A, 5-HT6 and 5-HT7) may possess antidepressant properties. This led to the development of an augmentation therapy, where SSRI treatment is supplemented by, for example, buspirone which is a partial agonist of 5-HT1A receptor. Unfortunately, this method brings with it a possibility of dangerous drug interactions and cumulative side effects which can be possibly avoided by a fusion of SERT and agonistic/antagonistic activity in one compound.

Derivatives of N-[2-(dimethylamine)ethyl]-N-(2-phenylethyl)aniline revealed to possess high affinity towards 5-HT6 and 5-HT7 receptors, what more, molecular modeling studies showed their possible high affinity towards SERT. This led to a conclusion that these compounds may act as substances with dual SERT/5-HT6 and/or 5-HT7 activity.


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