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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).[1]

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.[2]

It was revealed, that compounds acting on serotonin receptors (e.g. 5-HT1A, 5-HT6 and 5-HT7) may possess antidepressant properties.[3] 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.[4]. 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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