Synthesis, docking and pharmacological evaluation of novel homo- and hetero-bis 3-piperazinylpropylindole derivatives at SERT and 5-HT1A receptor

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A series of 3-(3-(4-(3-(1H-indol-3-yl)propyl)piperazin-1-yl)propyl)-1H- indole derivatives (3a-d and 5a-f) as homo- and hetero-bis-ligands, were synthesized and evaluated for in vitro affinity at the serotonin transporter (SERT) and the 5-HT1A receptor. Compounds 5b and 5f showed nanomolar affinities for both targets. The experimental data were rationalized according to results obtained from docking experiments. These findings are in agreement with our proposal that bis-indole derivatives can bind both targets, and might serve as leads in the quest of ligands endowed with a dual mechanism of action.

5-Hydroxytryptamine 1A receptor

Bivalent ligands

Docking

Piperazinylpropylindole derivatives

Serotonin transporter

1,4 bis[3 (1h 3 indolyl)propyl]piperazine

1,4 bis[3 (5 bromo 1h 3 indolyl)propyl]piperazine

1,4 bis[3 (5 fluoro 1h 3 indolyl]propyl)piperazine

1,4 bis[3 (5 methoxy 1h 3 indolyl]propyl)piperazine

3 [3 [4 [3 (1h 3 indolyl)propyl] 1 piperazinyl]propyl] 5 bromo 1h indol

3 [3 [4 [3 (1h 3 indolyl)propyl] 1 piperazinyl]propyl] 5 fluoro 1h indol

3 [3 [4 [3 (1h 3 indolyl)propyl] 1 piperazinyl]propyl] 5 methoxy 1h indol

3 [3 [4 [3 (1h indol 3 yl)propyl]piperazin 1 yl]propyl] 1h indole derivative

5 bromo 3 [3 [4 [3 (5 fluoro 1h 3 indolyl)propyl]piperazinyl]propyl] 1h indol

5 bromo 3 [3 [4 [3 (5 methoxy 1h 3 indolyl)propyl]piperazinyl]propyl] 1h indol

5 fluoro 3 [3 [4 [3 (5 methoxy 1h 3 indolyl)propyl]piperazinyl]propyl] 1h indol

citalopram

indole derivative

serotonin 1A receptor

serotonin transporter

unclassified drug

animal tissue

article

binding affinity

controlled study

drug structure

drug synthesis

human

human cell

in vitro study

molecular docking

nonhuman

rat

5-Hydroxytryptamine 1A receptor

Bivalent ligands

Docking

Piperazinylpropylindole derivatives

Serotonin transporter

Dose-Response Relationship, Drug

Humans

Indoles

Models, Molecular

Molecular Docking Simulation

Molecular Structure

Piperazines

Receptor, Serotonin, 5-HT1A

Serotonin Plasma Membrane Transport Proteins

Structure-Activity Relationship