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Synthesis and biological activity of a new 5-cyanoindole derivatives as a dual D_2/5-HT_{1A} receptor ligands

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The current treatment of central nervous system diseases including depression, schizophrenia or Parkinson's disease is it is not fully effective. Therefore, the need for further research into antidepressants is justified. There are more and more reports in the literature in which the cooperation of two mechanisms of action is described [1,2]. An example for this approach may be Wilazodone well known antidepressant, whose mechanism of action is based on inhibition of serotonin reuptake and it is a 5-HT_{1A} receptor agonist [3]. Another example of a compound used in the treatment of depression is Aripiprazole. Similar to Wilazodone, Aripiprazole also has a dual mechanism of action - it is a partial agonist to D_2 and 5-HT_{1A} receptors [4].

Based on this knowledge, it was decided to synthesize a new group of derivatives of long-chain arylpiperazines (LACPs) with a 5-cyanoindole moiety. These compounds contain a motif from Aripiprazole - chlorophenylpiperazine and from Vilazodone (5-cyanoindolobutyl moiety). Ligands were synthesized in solvent-free reactions supported by microwave irradiation. This method can be regarded as fast, efficient and eco-friendly that fits into the canons of green chemistry. The purified ligands were examined in biological tests to determine the binding to the D_2 and $5HT_{1A}$ receptors. The compounds were also designed for their drug-like properties, calculating for appropriate physicochemical parameters *in-sillico.*

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