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Combined treatment with escitalopram and cannabidiol in ineffective doses induces antidepressive, but not anxiolytic effect in maternally separated adolescent rats

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**Abstract (approximately 250-300 words limit)**

As drugs currently used in the therapy of depressive disorder in adolescent population present limited efficacy and delayed clinical effect, researchers nowadays pay a great attention into discovering new drugs that stimulate alternative pathways in order to augment treatment with traditional antidepressants. One of such promising substances is cannabidiol, second main cannabinoid derived from *Cannabis sativa,* that seems to be promising in the therapy of affective diseases. The aim of this study was to investigate whether the combined administration of escitalopram with cannabidiol (CB1 and CB2 receptors non-competitive negative allosteric modulator) in ineffective doses, will provide better or similar effects in behavioral tests compared to escitalopram in a dose reversing despair behavior in adolescent rats. For this reason, maternal separation as a form of early life adversity has been used. The pups were separated from their dams for 360 minutes daily from postnatal day (PND) 2 until PND 15. Later, on PND 42 or 44 escitalopram or vehicle were administered in a subacute manner. Before the behavioral assessment was performed, cannabidiol or vehicle were injected in a single dose. Three standard behavioral tests were performed: the elevated plus maze and the open field test on PND 42 and the forced swimming test on PND 43-44 on the subsequent group of rats. Anxiolytic-like effects has not been observed after combined treatment with escitalopram and cannabidiol in ineffective doses but despair behavior in the forced swimming test was successfully relieved showing similar efficacy as treatment with escitalopram in effective dose. This preliminary study might indicate possible positive drug interaction that may be helpful in designing new treatment strategies in the therapy of adolescent depressive disorder.

**Keywords**

*Maternal separation; adolescent rats; cannabidiol; escitalopram; antidepressant and*

*anxiolytic-like effects.*

**Recent Publications:**

Dragon J, Gołyszny M, Zieliński M, Popiołek-Barczyk K, Starowicz K, Obuchowicz E. Escitalopram reverses anxiety-like and despair behavior and affects endocannabinoid-related genes expression in the brain of adolescent male rats subjected to early life stress. Neuroscience. 2025 Feb 16;567:96-108. doi: 10.1016/j.neuroscience.2025.01.001. Epub 2025 Jan 4. PMID: 39761822.

Dragon J, Obuchowicz E. How depression and antidepressant drugs affect endocannabinoid system?-review of clinical and preclinical studies. Naunyn Schmiedebergs Arch Pharmacol. 2024 Jul;397(7):4511-4536. doi: 10.1007/s00210-023-02938-z. Epub 2024 Jan 27. PMID: 38280009.

**Biography** **(150 words limit)**

My name is Jonasz Dragon and since 2019 I am a PhD candidate in the Department of Pharmacology of the Medical University of Silesia in Katowice. Besides my research career, I am a senior resident in the Department of Urology and Urological Oncology of the Provincial Hospital no 2 in Jastrzębie-Zdrój. My scientific interests and also topic of my PhD thesis focus on the endocannabinoid system and its possible impact on the behavior of adolescent rats.

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