Central effects of nafadotride, a dopamine D$_3$ receptor antagonist, in rats. Comparison with haloperidol and clozapine*  

Grzegorz Kuballa$^1$, Przemysław Nowak$^1$, Łukasz Labus$^1$, Aleksandra Bortel$^1$, Joanna Dąbrowska$^1$, Marek Swoboda$^1$, Adam Kwieciński$^1$, Richard M. Kostrzewa$^2$, Ryszard Brus$^1$

$^1$Department of Pharmacology, Medical University of Silesia, Jordana 36, PL 41-806 Zabrze, Poland  
$^2$Department of Pharmacology, Quillen College of Medicine, East Tennessee State University, Johnson City, TN 37614, USA

**Correspondence:** Ryszard Brus, e-mail: phbrus@am.ka.edu

---

**Abstract:**  
The aim of this study was to examine behavioral and biochemical effects of nafadotride, the new dopamine D$_3$ receptor antagonist, and to compare it with haloperidol (dopamine D$_2$ receptor antagonist) and clozapine (predominate dopamine D$_4$ receptor antagonist). Each drug was injected to adult male Wistar rats intraperitoneally, each at a single dose and for 14 consecutive days. Thirty minutes after single or last injection of the examined drugs, the following behavioral parameters were recorded: yawning, oral activity, locomotion, exploratory activity, catalepsy and coordination ability. By HPLC/ED methods, we determined the effects of the examined antagonists on the levels of biogenic amines in striatum and hippocampus: dopamine (DA), 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), 3-methoxytyramine (3-MT), 5-hydroxtryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA) and noradrenaline (NA). Additionally, DA and 5-HT synthesis rate was determined in striatum and 5-HT in hippocampus. The results of the study indicate that nafadotride, the dopamine D$_3$ receptor antagonist, has a behavioral and biochemical profile of action different from that of haloperidol but partially similar to that of clozapine.

**Key words:**  
nafadotride, haloperidol, clozapine, behavior, brain biogenic amines, rats