Abstract

Neurosteroids are an important group of substances that affect communication between neurons. They act as allosteric modulators of membrane receptors for neurotransmitters. One of the most important systems influenced by neurosteroids are NMDA receptors; however, a binding site(s) for their inhibition by steroids have not been found yet. This work is focused on the synthesis of fluorescently labeled photoaffinity probe, which may help explain the structure and location of binding site(s) and simplify the development of new neuroprotectives.

A structural analogue of the endogenous neurosteroid, (*20S*)-20-Azido-5β-pregnan-3α-yl N-(7-nitrobenz-2-oxa-1,3-diazole-4-yl)-L-glutamyl 1-ester (**8**), was prepared. The structure of compound **8** includes photolabile azido group, as well as covalently bounded fluorescent NBD group. In addition, a photoaffinity probe with a modified steroid skeleton - pyridinium 17aα-azido-17α-methyl-17a-homo-5β-androstan-3α-yl 3-sulfate (**29**) - was synthesized.

The ability of compound **8** and **29** to inhibit activated NMDA receptor has been verified for recombinant NR1-1a/NR2B receptors expressed in HEK293 cells using a patch-clamp technique. Additionally, the IC_{50} values of compounds **8** and **29** have been calculated. (In Czech)

Key words: neuroactive steroid, NMDA receptor, photoffinity labeling, patch-clamp technique.