The neuroactive steroid pregnanolone glutamate (Pg glu), a synthetic analogue of the naturally occurring pregnanolone sulfate (3alpha5betaS), has neuroprotective properties and a minimum of adverse effects. The subject of my thesis is the influence of selected structural modifications of the molecule Pg glu on biological effects. The first modification involves an increase of lipophilicity, the second involves the attachment of a positively charged group to C3. All these neuroactive steroids are use-dependent inhibitors of NMDA receptors.

The first aim of this thesis was to determine the neuroprotective effectiveness of the neuroactive steroids chosen. The second aim was to explore the influence of selected neuroactive steroids on motor coordination, reflexes, anxiety and locomotor activity, as well as the effect of their high doses. The third aim was to create a battery of behavioural tests for screening the biological effects of analogues of Pg glu in laboratory rodents.

The neuroprotective effects were evaluated in a model of excitotoxic damage of hippocampus in the rat on the basis of its behavioural consequences. The neuroprotective efficacy of androstane glutamate (And glu) and Pg glu was demonstrated. In the case of positively charged molecules, neuroprotective efficacy was not demonstrated.

Neuroprotective doses (1 mg/kg) of And glu and Pg glu did not unfavourably influence motor skills, reflexes and locomotor activity. These findings lend support to the importance of research and development of steroidal inhibitors of NMDA receptors as potential neuroprotectants.

In addition, anxiolytic effects of And glu and Pg glu were ascertained.