

POSTER PRESENTATIONS

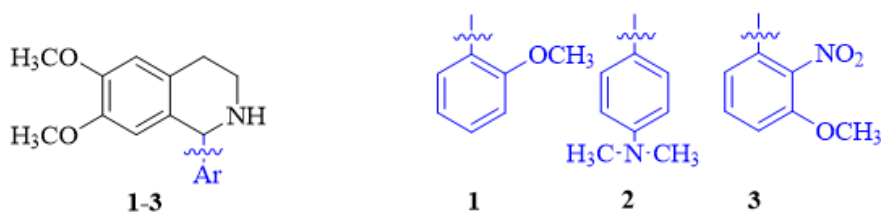
ANTIDOTAL POTENTIAL OF 1,2,3,4-TETRAHYDROISOQUINOLINE DERIVATIVES IN ACUTE ALCOHOL INTOXICATION: ROLE OF GABAERGIC MECHANISMS

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Ethanol enhances GABA-mediated inhibitory neurotransmission by acting as a positive allosteric modulator of GABA_A receptors. Binding of ethanol to specific allosteric sites on the GABA_A receptor increases the probability and duration of chloride channel opening, thereby suppresses synaptic transmission within the central nervous system, contributing to the characteristic depressant effects of ethanol.

The effects of 34 derivatives of 1,2,3,4-tetrahydroisoquinoline and ethalon drugs on the duration of ethanol-induced sleep were investigated in white mice after intraperitoneal administration of ethanol (4.8 g/kg).



It was established, that compounds (1), (2), and (3) showed the strongest effect, significantly exceeding the reference substance cytisine (76.6%, 75.3%, and 73.2% protection, respectively).

The computational analysis revealed strong interactions between the tested ligands and the allosteric pockets of the GABA_A receptor (PDB ID: 6X3W). The binding free energies at these sites ranged from -6.0 to -7.8 kcal/mol, confirming the thermodynamic stability of the resulting ligand–receptor complexes.

Molecular docking results of ligands with GABA_A receptor (6X3W)

Ligands	ΔG (kcal/mol)
Cytisine	-6.6
Ethanol	-2.3
1	-7.2
2	-7.0
3	-6.7

These *in silico* findings provide structural support for the *in vivo* experimentally demonstrated neuroprotective efficacy of the compounds and their ability to counteract central nervous system depression induced by ethanol neurotoxicity.

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