Abstract:
We have evaluated the effect of diabetes-mimicking conditions on the inhibition of kynurenic acid (KYNA) production exerted by mitochondrial toxins: 3-nitropropionic acid (3-NPA) and aminooxyacetic acid (AOAA), by endogenous agonists of glutamate receptors: L-glutamate and L-cysteine sulfinate, and by a risk factor of atherosclerosis, D,L-homocysteine. Hyperglycemia (30 mM; 2 h) itself did not influence KYNA synthesis in brain cortical slices. However, it significantly enhanced the inhibitory effects of 3-NPA, AOAA and D,L-homocysteine, but not of L-glutamate and L-cysteine sulfinate, on KYNA production. Their IC values were lowered from 5.8 (4.5–7.4) to 3.7 (3.1–4.5) mM (p < 0.01), from 11.6 (8.6–15.5) to 7.1 (4.9–10.3) μM (p < 0.05), and from 4.5 (3.5–5.8) to 2.4 (1.8–3.2) mM (p < 0.01), respectively. The obtained data suggest that during hyperglycemia, the mitochondrial impairment and high levels of D,L-homocysteine evoke stronger inhibition of KYNA synthesis what may further exacerbate brain dysfunction and play a role in central complications of diabetes.

Key words:
rat brain, kynurenic acid, hyperglycemia, mitochondrial toxins, in vitro