

Original article

Protective Effects of Agmatine against Chlorpromazine-Induced Toxicity in the Liver of Wistar Rats

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SUMMARY

The metabolic pathways of chlorpromazine (CPZ) toxicity were tracked by assessing oxidative/nitrosative stress markers. The main objective of the study was to test the hypothesis that agmatine (AGM) prevents oxidative/nitrosative stress in the liver of Wistar rats 15 days after administration of CPZ. All tested substances were administered intraperitoneally (i.p.) for 15 consecutive days. The rats were divided into four groups: the control group (C, 0.9 % saline solution), the CPZ group (CPZ, 38.7 mg/kg b.w.), the CPZ+AGM group (AGM, 75 mg/kg b.w. immediately after CPZ, 38.7 mg/kg b.w. i.p.) and the AGM group (AGM, 75 mg/kg b.w.).

Rats were decapitated 15 days after the appropriate treatment. In the CPZ group, CPZ concentration was significantly increased compared to C values ($p < 0.01$), while AGM treatment induced the significant decrease in CPZ concentration in the CPZ+AGM group ($p < 0.05$) and the AGM group ($p < 0.01$). CPZ application to healthy rats did not lead to any changes of lipid peroxidation in the liver compared to the C group, but AGM treatment decreased that parameter compared to the CPZ group ($p < 0.05$). In CPZ liver homogenates, nitrite and nitrate concentrations were increased compared to controls ($p < 0.001$), and AGM treatment diminished that parameter in the CPZ group ($p < 0.05$), as well as in the AGM group ($p < 0.001$). In CPZ animals, glutathione level and catalase activity were decreased in comparison with C values ($p < 0.01$ respectively), but AGM treatment increased the activity of catalase in comparison with CPZ animals ($p < 0.05$ respectively). Western blot analysis supported biochemical findings in all groups. Our results showed that treatment with AGM significantly suppressed the oxidative/nitrosative stress parameters and restored antioxidant defense in rat liver.

Key words: agmatine, antioxidant defense, chlorpromazine, liver, oxidative stress

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