Hepatoprotective and antioxidant potential of apigenin in paracetamol-induced hepatotoxicity in rats

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**Background:** Apigenin is known to have various pharmacological properties without causing significant toxicity. However, hepatoprotective effects of apigenin are not often reported. The aim of our study was to investigate whether the alterations in lipid peroxidation and antioxidant status are in favor to prove the efficacy of apigenin against paracetamol-induced hepatotoxicity.

**Methods:** The effect of apigenin on paracetamol-induced hepatotoxicity was examined in rats by determining biochemical parameters, histological assessment and oxidative status in liver homogenates.

**Results:** Treatment of animals with apigenin attenuated the parameters of paracetamol-induced hepatotoxicity, especially for ALT and ALP activity, which was significantly lower compared to animals treated with saline and instead of paracetamol. Hepatotoxicity induced by a toxic dose of paracetamol was revealed also by notable histopathological alterations, which were not observed in the group treated with paracetamol together with apigenin. Apigenin also prevented paracetamol-induced increases in malondialdehyde (MDA) levels. The activities of both catalase (CAT) and glutathione reductase (GR) in liver homogenates were significantly increased after a toxic dose of paracetamol compared to the control group. Apigenin reversed these parameters to values near to those of the control group.

**Discussion:** According to the results of our study, hepatotoxicity induced by a toxic dose of paracetamol was revealed not only by a noticeable elevation of AST and ALT activities, but also by notable histopathological alterations. As expected, these alterations were not detected in the group treated with paracetamol together with apigenin. Our study is comparable with the results of an earlier study using a model of N-nitrosodiethylamine (NDEA)-induced liver damage, where necrosis of hepatocytes was confirmed histologically. Apigenin showed an ability to prevent paracetamol-induced increases in MDA levels, which suggests that apigenin can preserve cellular integrity. Previous findings also showed that the administration of apigenin in NDEA-induced and phenobarbital-promoted hepatocarcinogenesis in rats could decrease lipid peroxidation. In our study, the activities of antioxidant enzymes were significantly changed after the administration of paracetamol. The antioxidant enzymes GPx and CAT catalyze the reduction of peroxides to alcohols or water, whilst GR reduces glutathione disulfide (GSSG), generated during the reduction of peroxides, to the sulfhydryl form of glutathione (GSH). A toxic dose of paracetamol induced a significant reduction of GR activity, which might be explained by inactivation induced by extreme creation of free radicals. Apigenin exhibited an ability to reverse GR activity to values near those of the control group. CAT activity was increased significantly after paracetamol, while apigenin restored the changes near to values of the control group. On the contrary, in the early study enzymatic antioxidant CAT was decreased significantly in carcinogen-administered animals; however, apigenin restored the changes to near normal by its antioxidant activity.

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