THE PROTECTIVE MECHANISM OF PLANTS IMMUNOMODULATORS IN CADMIUM-INDUCED TOXICITY IN VIVO

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Abstract: Cadmium is an important industrial pollutant, even though its mechanism of toxicity has not been completely clarified. While cadmium is toxic to a wide range of tissues, liver and kidneys are the primary targeted organs of cadmium toxicity. Cadmium induces apoptosis, mitotic activity of cells and also causes necrotic cell death in certain pathophysiological situations. In acute as well in chronic cytotoxicity and cancerogenesis, activation of endonucleases, generation of reactive free radicals such as reactive oxygen species (ROS), and signal transduction pathways involving apoptosis play important roles. Cadmium accelerates peroxidation chain reaction in the targeted organs, resulting in the generation of reactive oxygen species and consequently the induction of cytotoxicity. The introduction and use of herbal immunomodulators, in order to protect cadmium-induced toxic effects, have been increasing in the last few decades. Despite significant advances in studying the protective mechanisms of plants immunomodulators, *Echinacea purpurea (EP)* and *Eleutherococcus senticosus (ES)* were given less attention, in particular in the interaction between these plants extracts and heavy metals. We hypothesized that biologically-active compounds from *EP* and *ES* (polysaccharides, lipopolysaccharides, glycoproteins – lectins, phenolics, flavonoids, carotenoids etc) would have a protective impact during intoxication by heavy metals. To determine whether *EP* and *ES* are able to regulate the process of apoptosis in vivo, we administered these plants extracts intraperitonialy and orally for 6 and 8 weeks respectively to cadmium-treated mice. In addition, mice were treated with the natural substances modulating apoptosis in mice liver cells. We found that administration of *EP* decreased the cadmium-induced mitotic activity of liver cells, and increased the apoptotic activity of these cells. Long-term exposure to cadmium results in the formation of the foci of necrosis in liver, which may be reduced by the application of *EP* extract. We also demonstrated that administration of *ES* normalizes increased mitotic index of liver cells in cadmium-treated mice and protect liver protein synthesis from cadmium toxicity.

Key words: Cadmium, plants immunomodulators, apoptosis, mitosis, necrosis