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THE EFFECT OF TAXOL AND PIROLIN ON RAT HEART MYOCYTES

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Paclitaxel (PCL, Taxol) belongs to taxanes, an important class of anticancer agents increasingly used in the treatment of advanced ovarian or breast cancer. Like other taxanes taxol mainly acts by promotion of polymerization of tubulin. Microtubules formed in the presence of PCL are dysfunctional. They interfere with normal cell division and different interphase processes eventually leading to cell death. Taxol also exhibits numerous undesired actions on normal cells (e.g. cardiotoxicity and hepatotoxicity). Although unequivocal evidence of PCL-induced congestive heart failure is still lacking and little is known about the mechanisms of PCL toxicity towards heart cells, it has been suggested that oxidative stress may play important role. Heart myocytes are provided with poor mechanisms of detoxification of ROS therefore one of the approaches aimed at improving the antioxidant defense of these cells is an employment of antioxidants, which could attenuate oxidative stress generated by anticancer drugs.

In this work we investigated the ability of pirolin (PL), non-immunogenic, low molecular weight nitroxide antioxidant, to reduce the oxidative stress generated by taxol in heart tissue. We have found that PCL had different effect on the activity of the particular antioxidant enzymes. The drug did not change the level of catalase, total superoxide dismutase (SOD) and Cu,ZnSOD in heart tissue, but caused approximately twofold increase in activity of MnSOD. The activities of catalase, SOD and Cu,ZnSOD were not influenced by pirolin either. The nitroxide, similarly to PCL, induced however an increase in MnSOD activity. Both compounds used in combination caused noticeable increase in catalase activity.

Electron microscopic examination of heart tissue from control and treated rats revealed that pirolin did not cause visible changes in ultrastructure of cardiomyocytes. In rats treated with taxol modest changes in ultrastructure of myocardial filaments with concomitant destruction of single myocardial fibers were observed. Another changes involved swelling of some of the mitochondria, vacuolization of cytoplasm, slight lipidization and partial disintegration of mitochondrial cristae. These effects were enhanced in hearts of rats treated with combination of both compounds (PCL and PL).

Our results evidence that taxol generates rather moderate oxidative stress in rat heart and predominantly affects cardiomyocyte mitochondria. Pirolin potentated destructive effect of this anticancer drug on heart muscle.