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DOXORUBICIN AND TAXOL HEPATOTOXICITY IN RATS

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Doxorubicin (DOX) and paclitaxel (PCL, Taxol) are antitumor drugs widely used in chemotherapy of advanced ovarian and breast cancer. DOX belongs to the group of anthracyclines, while PCL is a novel antineoplastic agent (taxane) extracted from the bark of the Pacific yew *Taxus brevifolia*. Taxol inhibits cell division by the unique mechanism of increasing the rate of microtubule assembly and preventing microtubule depolymerisation. The clinical use of DOX and PCL in long-term treatments is often limited by serious side effects, particularly by the development of a dose-dependent form of cardiomyopathy, which is frequently lethal. Both drugs were reported to exert toxic effects on liver tissue as well. Combined treatment of PCL and DOX has been suggested to account for increased risk of severe side effects in some of the patients. Oxidative stress generated by these drugs is considered as an important mechanism of their side effects.

In this work we evaluated the ability of DOX and Taxol to induce oxidative stress in liver tissue in rats, dependently on the way of their administration – alone or in combination. The drugs were administered i.p. as a single dose of 10 mg/kg each. Our biochemical findings showed that both drugs caused hepatotoxic effects and changed antioxidant defense capacity of liver cells but they differed in their effect on the activity of the particular antioxidant enzymes. SOD level increased significantly in DOX-treated rats, while appreciable increase in CAT activity was observed only in rats injected with PCL. Interestingly, when DOX was administered in combination with PCL substantial changes in SOD level was observed in relation to PCL, but not with regard to DOX. Catalase activity in rats injected with combination of DOX and PCl was higher than that in rats treated with DOX but lower than the activity of CAT in rats that received PCL only.

These results demonstrate that both DOX and PCL increase free radical production in liver tissue and change its ability to detoxify reactive oxygen species (ROS). When used in combination neither addictive nor synergistic effect of both drugs on activity of the SOD and CAT antioxidant enzymes in liver tissue was observed.