Abstract

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Title of diploma thesis: The effect of resveratrol and gambogic acid on the DNA damage caused by daunorubicin in neonatal rat cardiomyocytes.

DNA Topoisomerases comprise a family of enzymes that are able to alter DNA topology by transient single- or double-strand breaks (DSB) during fundamental processes such as replication and transcription. Inhibition of topoisomerase II (TOP II) is the main mechanism of action of some antitumour drugs, such as anthracyclines (ANT; e.g., daunorubicin). They stabilize the DNA-TOP II complex, leading to the formation of DSBs and later to apoptosis. Other inhibitors, that interact with the enzyme without the DSB formation, can modulate the effect of ANT.

In this thesis, we studied the DNA damage caused by daunorubicin (DAU) and its main metabolite daunorubicinol (DAUnol) and the effect of two naturally-derived compounds and TOP II catalytic inhibitors resveratrol (RES) and gambogic acid (GA) in neonatal rat cardiomyocytes. The DNA damage was determined as the extent of histone H2AX phosphorylation (γ-H2AX) and by Comet Assay.

It can be concluded that both DAU and DAUnol (1,2 μM) exhibit DNA damage that is dependent on the time of exposure – increases during the 6h period. Nevertheless, this trend was detected only by the γ-H2AX. RES (1, 10, 100 μM) alone did not induced DNA damage and at a concentration of 100 μM it reduced DAU-induced γ-H2AX. GA at higher concentration (1 μM) independently increased both γ-H2AX and Comet Assay signal and also increased DAU-induced DNA damage.