Punicalagin Attenuates Chemotherapy-Induced Hepatotoxicity in Normal Cells

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Current research is focused on identifying drugs that can mitigate chemotherapy-induced injury to normal tissues, while being cytotoxic to cancer cells. This study was designed to evaluate the potential protective effects of punicalagin against doxorubicin and cyclophosphamide induced injury in normal liver cells and its parallel cytotoxic effects in cancer cells. Clone 9 cells were pretreated with punicalagin (50 µM, 24 h) followed by doxorubicin (1 µM, 24 h) and cyclophosphamide (25 µM, 24 h). Cell morphology, intracellular reactive oxygen species (DCDFA Assay), protein levels of SOD2, catalase and GPx (western blotting) and intra cellular glutathione content were studied. Mitochondrial functions were measured with intracellular ATP assay, MTT assay, TMRM uptake, JC-1 assay, Swelling Assay and protein levels of SDH, VDAC, DRP1, and PGC-1α (Western Blotting) were analyzed. Effects of punicalagin with and without doxorubicin and cyclophosphamide in MCF7 cells was investigated by measuring cell viability, ROS and morphology. Punicalagin exhibited robust protection against chemotherapy-induced ROS generation and cell morphology. Punicalagin pretreatment also protected mitochondrial functions by significantly preserving ATP content, maintaining mitochondrial membrane potential with reduced swelling and preserving levels of critical proteins. Punicalagin in combination with doxorubicin and cyclophosphamide killed 90% of the breast cancer cells than alone. In conclusion, punicalagin mitigated chemotherapy-induced damage to normal liver cells, while augmenting the cytotoxic effects in cancer cells when combined with chemotherapeutic drugs. Hence, punicalagin may be considered as a potential adjuvant drug during and after chemotherapy to benefit cancer patients.

Awards Won:

Third Award of $1,000