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THE EFFECT OF ENTEROLACTONE ON INTRAHEPATOCELLULAR CONCENTRATION AND APOPTOSIS IN HEPG2 CELLS

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Rationale: It is commonly known that sphingolipids are one of the major lipid fractions, which regulate cell functions and play an essential role in cell signalling pathways. Lignans are a group of plant-derived compounds, represented by enterolactone (ENL). Despite the fact that some phytoestrogens were well identified, there are no studies concerning influence of enterolactone on sphingolipid concentration in hepatocytes.

Objective: The main goal of the study was to evaluate if enterolactone, in the presence of elevated bioavailability of palmitic acid (PA), enhances intrahepatic sphingolipid concentration in HepG2 cells and, therefore, leads to apoptosis.

Materials and methods. HepG2 cells were cultured for 5 days in Dulbecco's Modified Eagle Medium (DMEM) with 10% fetal bovine serum and 1% penicillin/streptomycin at 37°C in a humidified atmosphere of 5% CO_2 in air. Subsequently, selected groups were incubated in the presence or absence of palmitic acid (0.5 mM) and/or enterolactone (50 μM). All measurements were performed after 16h incubation period. Sphingolipids contents (ceramide, sphingosine, sphinganine) in HepG2 cells were measured using a HPLC method.

Results and discussion. Although HepG2 cell culture incubation with ENL alone for 16h revealed notable increase of intracellular ceramide, sphingosine and sphinganine content, the highest change was visible in sphinganine concentration compared to control group (CG) of all sphingolipids. Considering the effects in PA+ENL group, there was a marked increase in concentration of all sphingolipids fractions. Exposure to PA+ENL resulted in higher accumulation of ceramide in comparison to sphinganine and sphingosine. Moreover, sphingosine level in PA+ENL group was slightly elevated compared to sphinganine concentration. Caspase-3 expression after exposure to ENL alone and combined with PA was higher in comparison to CG group.

Conclusions. Enterolactone alone and enterolactone combined with palmitic acid increased intrahepatocellular concentration of all three sphingolipids in HepG2 cells. Furthermore, it may be said that higher concentration of sphinganine after exposure to ENL alone and together with PA led to intensified de novo synthesis pathway. An elevated sphingolipid accumulation may enhance apoptosis and a markedly increased caspase-3 expression may confirm that theory.