The Effects of targeting glucose metabolism in cancer cells usingpyruvate esters and NADH analog

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Introduction: A major hallmark of cancer is defective metabolic pathways. In cancer cells, the Warburg effect ensures that the glycolytic pathway is the main source of energy. Treatment strategies that enable the switch from glycolysis to other metabolic pathways such as OXPHOS could be more effective against cancer cells. Pyruvate esters and NADH analogs may help bypass the glycolytic pathway resulting in anti-cancer properties.

Aim: The study investigated the effect of pyruvate esters and NADH analog drugs on the Warburg effect in cancer.

Methods: Cancer cell line (A549 and MCF 7) and normal cells (HEK 293) were treated with various concentrations of the ethyl pyruvate (a pyruvate ester), NADH analog, and irinotecan as the positive control. Cell viability and cytotoxicity were measured using MTT and LDH assays. Apoptosis and cell cycle analysis were conducted using the MUSE analyser and flow cytometer, respectively. The student T-test was used to determine statistical analysis.

Results: The treatment of A549 and MCF 7 with ethyl pyruvate showed that it reduced the cell viability as the concentration is increased but when compared with HEK 293, there was no notable reduction in cell viability.Treatment with ethyl pyruvate led to an increase in LDH levels after 48hrs, signifying high toxicity in cancer cells. When A549 cells was treated with ethyl pyruvates, death occurs as a result of apoptosis 79.66% and 1.6% for necrotic death wasrecorded, while for MCF 7 was 84.31% for apoptosis and 6.2% necrotic death.

Conclusion: Overall, ethyl pyruvates induced cell death and toxicity in cancer cells while exhibiting reduced cytotoxicity effects in normal cell lines, therefore it may be an effective and potential therapeutic drug for cancer treatment.