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Polyphenols potentialize the cytotoxic activity of gemcitabine on pancreatic cancer cell line AsPC-1

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Pancreatic cancer is one of the most aggressive cancers, with only about 5% of patients surviving 5 years past the initial diagnosis. Gemcitabine monotherapy is the standard of treatment for patients with metastatic pancreatic cancer since several decades. Despite advances with current chemotherapy combinations, overall survival outcomes are still require novel therapeutic approaches. Here, we examined the efficacy of combined treatments of polyphenols and gemcitabine in human pancreatic cancer cells. For that purpose, the proapoptotic effects of gemcitabine were studied on the human pancreatic cell line AsPC-1 in presence or absence of several polyphenols, in order to evaluate if they latter are able to potentialize gemcitabine cytotoxicity. Our study aims to investigate the implication of MDR1 (multidrug transporter) in resistance to gemcitabine and if the studied polyphenol could target this drug efflux pump in AsPC-1 cells by flow cytometric analysis. We observed that 5 µM/ml gemcitabine in combination with 50 µM of selected polyphenol (catechin, quercetin, bergamottin, rhamnetin) was more effective than gemcitabine alone, as shown by increased in the percentage of dead cells up to 60%. In addition, our results indicate that the combination of gemcitabine and each polyphenol increased the expression levels of cleaved caspase-3 and the regulator of apoptosis p53. Moreover our results demonstrated that some polyphenols inhibit the efflux activity of MDR1. Our study *in vitro* suggests therefore that chemotherapy with gemcitabine might be significantly increased upon combination with specific polyphenol. In conclusion, polyphenols may be promising agents for novel combination therapy since they potentialize the cytotoxic activity of gemcitabine to eradicate pancreatic cancer and therefore the cellular resistance.

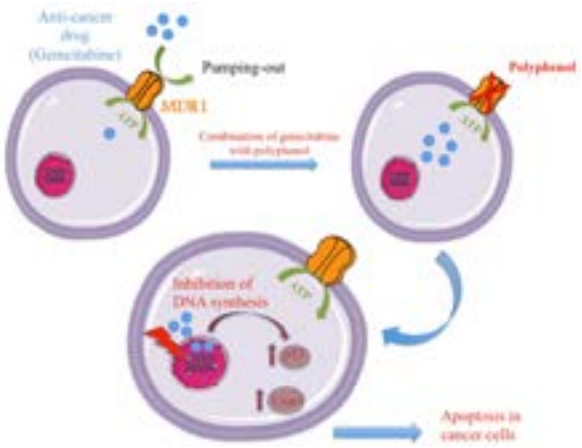

Figure1: Intracellular accumulation of anti-cancer drug by inhibition of MDR1 with polyphenols

Biography

Sarah Hassan is a PhD student at University of Strasbourg. She holds Master's degree in Pharmacology from Holy Spirit University of Kaslik and BS in Biochemistry from Lebanese University. Her research and thesis focused in anticancer drugs, enhancing their efficacy and reducing their toxicity potential by their combination with natural substances..

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