Ursodeoxycholic acid sensitizes human breast adenocarcinoma cells to doxorubicin-induced apoptosis

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Results and conclusions: Isoflavones as supplements in doses of 40 or 80mg/day taken for several months and even up to several years appear to be without significant negative health effects in peri- and post-menopausal women. These doses taken for one to three months may represent a risk of negative effects on hormone levels and/or menstrual function in adolescent and pre-menopausal women, and on hormone levels in adolescent and adult men, but did not appear to have other significant negative health effects. There was not sufficient data to draw any conclusions on potential negative effects of isoflavones in children.

Implications: This risk assessment will be used to establish a positive list in a national regulation of “other substances”.

P-12-00-34
Assessment of the antioxidant activity of an olive oil total polyphenolic fraction and hydroxytyrosol in endothelial cells and myoblasts

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Olive oil (OO) constitutes the basis of the Mediterranean diet, and it seems that its biophenols, such as hydroxytyrosol (HT) may scavenge free radicals, attracting distinct attention due to their beneficial effects in many pathological conditions, such as cancer. The aim of the present study was to examine the antioxidant properties of an EVOO total polyphenolic fraction (TPF) rich in biophenols, from a Greek endemic variety of Olea europea, grown on Mount Athos, as well as that of pure HT. It is worth noting, that to date, at least to the best of our knowledge, there are no studies available investigating the antioxidant properties of an OO TPF in cell cultures. The antioxidants effects were assessed at a cellular level, particularly in EA.hy926 endothelial cells and C2C12 myoblasts. TPF and HT exhibited potent free radical scavenging activity in vitro. The cells were treated with non-cytotoxic concentrations and their redox status [in terms of glutathione (GSH), reactive oxygen species (ROS), levels] was assessed. TPF extract was less cytotoxic than HT, and the observed differences between the two cell lines used suggest a tissue-specific activity. Finally, flow cytometric analysis revealed that both TPF and HT improved the redox status by increasing the levels of GSH, one of the most important antioxidants molecules, in both endothelial cells and myoblasts, while the ROS levels were not significantly affected. The obtained results will provide important information on the possible use of the TPF as an antioxidant food supplement.

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Ursodeoxycholic acid sensitizes human breast adenocarcinoma cells to doxorubicin-induced apoptosis

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The aim of this study is to evaluate whether ursodeoxycholic acid (UDca) potentiates apoptosis-inducing effects of doxorubicin (DOX) in MCF-7 cell line by measuring expression of apoptosis-regulating genes. MCF-7 cells were treated either with 250 nM of Dox or with combined treatment by adding 0.05 mM UDca. Cell viability was determined by a colorimetric assay using MTT whereas gene expression was analysed using qRT-PCR. The co-incubation of MCF-7 cells with Dox and non-toxic concentration of UDCA...
resulted in significant inhibition of cell growth ($p < 0.05$) compared to Dox alone. Relative expression of gene of Bax was increased in both Dox-treated cells (3.2-fold, $p = 0.001$) and co-treated cells (2.3-fold, $p = 0.007$), compared to control. Relative expression of anti-apoptotic Bcl-2 mRNA was reduced in cells co-treated with Udca (0.8-fold, $p < 0.001$) compared to Dox-treated cells. Bax/Bcl-2 ratio indicated that co-treatment with Udca induced apoptosis in higher level than Dox alone compared to control ($7.9 \pm 1.1$, $p = 0.004$ vs. $6.2 \pm 0.7$, $p = 0.008$). In conclusion, Udca potentiates mitochondrial pathway of Dox-induced apoptosis in MCF-7 cells, suggesting that Udca may be further investigated as novel chemosensitizing agent with aim to improve the therapeutic response to DOX-containing chemotherapy regimens.

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Polyethyleneglycol-serine nanoparticles as novel nanostructure for attenuation of organophosphate poisoning: Synthesise, characterization, in vitro and in vivo studies

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This study attempts to attach the serine amino acid to the polyethyleneglycol (PEG) as a novel nanoparticles (NPs) for treatment of diazinon poisoning. Serine and PEG were conjugated with reductive amination reaction. NPs were purified by ultrafiltration. NP structure was analyzed by $^1$H NMR, $^{13}$C NMR, IR and DSC. Particle size of NPs was determined by dynamic light scattering method. Blood hemolysis and cytotoxicity of synthesised NPs on SKBR3 cell line were assessed. Effectiveness of NPs was evaluated in Albino poisoned mice. NPs at doses of (100, 200, 400 mg/kg) were administered (ip) 20 min after a single dose of diazinon (LD50 = 166 mg/kg). Atropine (20 mg/kg, ip) with pralidoxime (20 mg/kg, ip) or alone as compared to the standard treatment were used. LD50 decreasing, cholinesterase reactivation enzymes in brain, RBC and serum and oxidative damage in brain mitochondria were assessed in mice. According to NMR, IR and DSC data, conjugation of PEG-Serine was achieved successfully. Average particle size of nanomicelle was determined 142.4 nm. Amount of hemolytic activity of this NP was measured 0.867% and IC50 was calculated 36 mg/ml. LD50 significantly decreased (25%) by NPs when compared with only diazinon group. Cholinesterase enzymes activity, lipid peroxidation, protein carbonyl content, and mitochondrial function significantly improved by NPs when compared with diazinon group. In general, it can be concluded that the synthesized NPs are very biocompatible with none toxicity that can successfully decrease the acute toxicity of diazinon as a new combination therapy.

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Severe hyperammonemia without liver failure induced by deferasirox: A biochemical conundrum

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Deferasirox (DFR) is an oral-chelating agent used to treat iron overload in transfusion-dependent hematologic patients. Recently, we and other authors described cases of hyperammonemia (HM) without severe liver injury in few patients treated with DFR. Here we report a new case of DFX-induced HM, looking the pathophysiological mechanisms of this event. We report the case of a 4y girl suffering from thalassemia major, under chronic treatment with DFR. She was hospitalized for fever, vomiting, alteration of consciousness. Lumbar puncture and brain CT scan were negative. Blood tests showed HM (200 mcg/dl), mild metabolic acidosis (ABE-11) and renal tubular acidosis, a biochemical picture similar to reported patients. IV arginine and bicarbonate were given, with normalization of clinical conditions and biochemical parameters. We suggest a multiple interactions of DFR on metabolic pathways involved in ammonia detoxification. The severe depletion of bicarbonates in patients under DFR could have caused a block in the Urea Cycle (UC). UC converts ammonia and Bicarbonate ($\text{HCO}_3^-$) into carbamoylphosphate in the mitochondrial matrix, starting from carbamoylphosphate synthetase (CPS1) activated by mithocondrial N-acetylglutamate (NAG). $\text{HCO}_3^-$ is generated by carboxy anhydrates (CA), and defect of CAs cause secondary HM, due to depletion of crucial intermediates for UC enzymes. We then hypothesize that defective activation of CPS1 due a direct block of mitochondrial pathways (DFR-related depletion of iron from critical mitochondrial iron-containing proteins, disturbed cellular oxidative capacity, and acidosis) is responsible for hepatocyte dysfunction and the HM in DFR-treated patients.

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Optimisation of non-ambulant (clinical) decontamination processes

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Project SULIS was undertaken to establish an effective response for non-ambulant casualties following a CBRN incident. Current practice is based upon a model “rinse-wipe-rinse” process (Home Office, 2004). Guided and unguided NHS decontamination training sessions were observed, through use of video and activity monitors. The observations determined that it can take 12 min to process one non-ambulant casualty by a 4-person decontamination team.