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Isoniazid modulates Nrf2 through ERK1 phosphorylation and induces apoptosis in Hep3B cells

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Isoniazid is used either alone or in combination with other drugs for the treatment of tuberculosis. It is also used for the prevention of tuberculosis. Chronic treatment of Isoniazid may cause severe liver damage leading to acute liver failure. The mechanism through which Isoniazid causes liver damage is investigated. Isoniazid treatment generates reactive oxygen species and induces apoptosis in Hep3B cells. It induces anti-oxidative and apoptotic genes leading to increase in mRNA expression and protein levels in Hep3B cells. Whole genome expression analysis of Hep3B cells treated with Isoniazid has resulted in differential expression of various genes playing prime role in regulation of apoptotic, anti-oxidative, DNA damage, cell signaling, cell proliferation and differentiation pathways. Isoniazid increased cytosolic Nrf2 protein level while decreased nuclear Nrf2 protein level. It also decreased ERK1 phosphorylation and treatment of Hep3B cells with ERK inhibitor followed by Isoniazid resulting in increased apoptosis in these cells. Two dimensional gel electrophoresis results have also shown differential expression of various protein species including heat shock proteins, proteins playing important role in oxidative stress, DNA damage, apoptosis, cell proliferation and differentiation. Results suggest that Isoniazid induces apoptosis through oxidative stress and also prevents Nrf2 translocation into the nucleus by reducing ERK1 phosphorylation thus preventing cytoprotective effect.

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Effluent toxicity assay of wastewater treatment plant using *Daphnia magna* and its relation to physicochemical parameters

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Evaluation of wastewater treatment plants efficiency to toxicity reduction by application of D. Magna as test organism is very important to study the likely adverse effects of the treated wastewater on the aquatic ecosystem of receiving waters. Toxicity of Urmia municipal wastewater treatment plant effluent was evaluated using bio-assay with Daphnia magna. Acute toxicity tests were performed on effluent samples of Urmia wastewater treatment plant (Biolack system) according to the USEPA methods and 24, 48, 72, and 96 h lethal concentration 50 (LC_{50}) were calculated by application of Probit analysis. Besides, interrelationship between main effluent physicochemical parameters of wastewater (BOD5, COD, and TSS) and 24h-LC_{50} were studied. Results show that effluent of Urmia wastewater treatment plant, according to the standards recommended by Iran Department of Environment (DOE), based on physicochemical parameters and acute toxicity unit (TUa) was safe to be discharged to the surface waters. Relationship between effluent COD and 24h-LC_{50} show that as increase in effluent COD, wastewater toxicity was increased and there was no relationship between BOD_5, TSS and toxicity of effluent wastewater. D. magna can serve as valuable tools for bio-monitoring of wastewater treatment plant effluent, as it is highly sensitive to pollutants.

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