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# Pharmacology

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## Environmental factors and apoptotic indices in patients with intrauterine growth retardation: A nested case-control study

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Egypt has one of the highest incidences of IUGR. The current study investigates the effect of heavy metals toxicity as risk factors of IUGR and determines the possible role of increased apoptosis in their pathogenesis. This study was conducted in Assiut, Egypt which included 60 women diagnosed to have IUGR. We measured lead and cadmium levels in blood besides arsenic and cadmium levels in urine. Neonatal scalp hair sample were analyzed for arsenic content. Quantitative determination of human placental Bcl-2 and caspase-3 were performed. There were significantly higher levels of heavy metals and caspase-3 and lower levels of placental Bcl-2 in the IUGR group. The levels of heavy metals were positively correlated with caspase-3 while negatively correlated (except cadmium) with Bcl-2 levels. There is an alarming high level of heavy metals toxicity in Egypt that was positively correlated to IUGR. Increased placental apoptosis may be one of the possible mechanisms behind the effect.

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## Phenolics-enriched extracts from Brazilian native fruits: *In vitro* and *in vivo* evaluation of the metabolism and health effects

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**P** roanthocyanidins, flavonoids and ellagic acid derivatives are polyphenols found in high concentrations in Brazilian native fruits such as Jaboticaba (*Myrciaria jaboticaba* Vell. Berg), Camu-camu (*Myrciaria dubia* (Kunth) McVaugh) and Cupuassu (*Theobroma grandiflorum* (Willd. ex Spreng.) K. Schum). Those compounds are known due to their cancer chemopreventive, cardioprotective and antioxidant potential. However, little is known about their bioavailability and metabolites, which are the biologically active compounds indeed. Here, the aim is to investigate the metabolism of different classes of polyphenols present in the native fruits, and the potentially health-beneficial biological activity, in both *in vitro* and *in vivo* assays. The metabolites formed from the Jaboticaba polyphenols were identified in an *in vitro* fermentation model using human feces. In addition, the fate of a wide variety of metabolites was monitored after intragastric administration of Jaboticaba extract (15 min – 8 h) in Wistar rats, using an UPLC-MS. The *in vitro* experiment showed that the ellagic acid derivatives were metabolized by the intestinal microbiota and degraded under testing conditions. Two compounds were identified after fermentation with fecal inoculum, *p*-hydroxybenzoic and *p*-hydroxyphenylacetic acids. *In vivo*, thirty eight metabolites were identified in plasma, stomach, liver, kidneys, brain, muscle and colon, and most of them were formed from ellagic acid derivatives. Further investigations were also made on the role of phenolic-rich extracts from those fruits upon oxidative stress and metabolic changes associated with a high fat (HFD) or a high-fat, high-sucrose (HFHS) diet in Wistar rats and C57BL/6J mice.

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