Impacts of Cadmium on Placental BH4 Cofactors

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Rapid industrial development has led to extensive environmental pollution, particularly from the toxic heavy metal cadmium (Cd). This pollution has negative effects on human health and fetal development through contamination of the atmosphere, water, soil, and food. Cadmium exposure disrupts placental development, gene expression, and nutrient exchange, leading to abnormal fetal development and impaired placental function. It also interferes with the synthesis of the essential cofactor tetrahydrobiopterin (BH4), causing metabolic disorders. Therefore, it is crucial to investigate the impact of cadmium on placental BH4 cofactors and evaluate the potential protective effects of BH4 supplementation. Our hypothesis is that cadmium inhibits the placental BH4 pathway, disrupting essential metabolic processes, and BH4 supplementation can mitigate the detrimental effects of cadmium exposure. Our study confirmed that cadmium was found to inhibit recombinant sepiapterin (SPR) (IC50 = 19.0 µM), it also confirmed direct concentration and time-dependent inhibition of BH4 synthesis and observed its inhibition of BH2 and BH4 production from SPR in human placental cell lines. Furthermore, cadmium specifically inhibited SPR activity (IC50=1.37 µM) and BH2-mediated BH4 formation (IC50=0.85 µM) in cells after a 24-h incubation. These findings support BH4 supplementation as a potential treatment to counteract cadmium-induced inhibition of the BH4 pathway, enhance placental function, and promote normal fetal development. This research project is supported by the NIH R25ES020721 Grant, Society of Toxicology Intern Program, and RISE/SURF program at Rutgers University.