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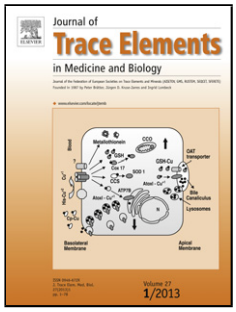

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Authors: Thalita Alves Zanetti, Bruna Isabela Biazi, Adrivanio Baranoski, Gláucia Fernanda Rocha D'Epiro, Amanda Cristina Corveloni, Simone Cristine Semprebon, Giuliana Castello Coatti, Mário Sérgio Mantovani

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Response of HepG2/C3A cells supplemented with sodium selenite to hydrogen peroxide-induced oxidative stress

Thalita Alves Zanetti[1*]; Bruna Isabela Biazi[1]; Adrivanio Baranoski[1]; Gláucia Fernanda Rocha D'Epiro[1]; Amanda Cristina Corveloni[1], Simone Cristine Semprebon[1], Giuliana Castello Coatti[2]; Mário Sérgio Mantovani[1]

[1]Department of General Biology, Center of Biological Sciences, Londrina State University – UEL, Rodovia Celso Garcia Cid, Pr 445 Km 380, Londrina, Paraná – Brazil.

[2]Human Genome and Stem-Cell Research Center. Institute of Biosciences, University of São Paulo – USP, Rua do Matão – Travessa 13, n. 106, São Paulo, São Paulo – Brazil.

* Corresponding Author – tah_zanetti91@hotmail.com, Phone: 55 (43) 3371 4977

HepG2/C3A cells supplemented with sodium selenite and hydrogen peroxide

Abstract

Oxidative stress (OS) is involved in the onset of various pathological processes, and sodium selenite (Na_2SeO_3) is known to have antioxidant activity. This study evaluated the cellular response of human HepG2/C3A cells supplemented with Na_2SeO_3 when exposed to hydrogen peroxide (H_2O_2)-induced OS. We analyzed cytotoxicity, cell proliferation, and genotoxicity in comparison with molecular data of mRNA and protein expression. The MTT and comet assays revealed that Na_2SeO_3 conferred cytoprotective and anti-genotoxic effects. In contrast, RTCA (Real-Time Cell Analysis) and flow cytometry analysis revealed that Na_2SeO_3 did not inhibit H_2O_2-induced anti-proliferative effects or cell cycle arrest (G2/M). Cells exposed simultaneously to Na_2SeO_3 and H_2O_2 showed overexpression of *GPX1* mRNA, indicating that Na_2SeO_3 influenced the cellular antioxidant system. Furthermore, downregulation of *CAT* mRNA and SOD1 and PRX2 proteins induced by H_2O_2, was minimal after the Na_2SeO_3+H_2O_2 treatment. Although normalization of *CCN2B* mRNA expression by Na_2SeO_3 was observed after the Na_2SeO_3+H_2O_2 treatment, this was not observed for other genes such as *CDKN1A*, *CDKN1C*, and *CDKN2B*, which are related to cell cycle control, nor for *GADD45A*, which is involved in the cellular response to DNA damage. Furthermore, both *CDKN1B* and *CDKN1C* expression were downregulated in HepG2/C3A cells treated with Na_2SeO_3 only. Our results indicate that cellular response to Na_2SeO_3 involved the modulation of the antioxidant system. Na_2SeO_3 was unable completely recover HepG2/C3A cells from H_2O_2-induced oxidative damage, as evidenced by analysis of cell proliferation kinetics, cell cycle assay, and expression of key genes involved in cell cycle progression and response to DNA damage.

Key words: anti-genotoxic, cytoprotective, cell cycle, DNA damage, protective.