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Human estrogen receptor agonistic effects on organophosphorus pesticides in human breast cancer cell line by modulating p38 MAP kinase activity

HeeSeok Lee
Ministry of Food and Drug Safety, Republic of Korea

More than 260,000 chemicals have been distributed to meet the needs of industrial growth, and over 40,000 chemicals are used in Korea. Despite the benefits, these products afford, humans and wildlife are continuously exposed to the potentially hazardous chemicals present in them. Over the last two decades, there has been international attention on environmental exposure and the effects of endocrine disrupting chemicals (EDCs) in humans and wildlife. EDCs interfere with function of endocrine system by agonistic and antagonistic effects against endocrine-related receptor such as estrogen receptor (ER), androgen receptor (AR) and thyroid receptor (TR), directly. Especially, endocrine disrupting pesticides have been frequently exposure from foodstuff, cosmetics and personal care products as well as environment. However, In this study, we confirmed ER agonistic effects on three organophosphorus pesticides (phoxim, terbufos and tolclofos-methyl) at range of non-intrinsic toxic concentrations by the Organization for Economic Cooperation and Development (OECD) test guideline no. 455, VM7Luc ER transcriptional activation assay. The phoxim, terbufos and tolclofos-methyl exhibited ER agonistic effects with PC20 values of 3.59×10-6, 3.99×10-5 and 3.57×10-6 M, respectively. These pesticides also found to observe the binding affinities to human ER. To investigate the ER agonistic pathway of three organophosphorus pesticides, their transcriptional activities were confirmed with co-treatment of p38, JNK and ERK inhibitors. Among the inhibitors of MAP kinase families, the ER agonistic effects on three organophosphorus pesticides were blocked by p38 inhibitor as well as ER antagonist, ICI182780. Our findings indicated that organophosphorus pesticides can mimics ER-dependent estrogenic activity by targeting proteins that regulate the p38 MAP kinase.

Biography

HeeSeok Lee has completed his PhD from Chung-Ang University in Republic of Korea and Postdoctoral studies from Department of Food Science of University of Massachusetts Amherst. He is working for risk assessment of hazardous chemicals in Korea Ministry of Food and Drug Safety from 2012. His major research field is development of endocrine disrupting chemicals screening methods using cell culture system. He is OECD Expert Member of Validation Management Group of non-animal testing for endocrine disrupting chemicals testing and assessment. He has published more than 30 academic papers to his credit.

hslee0515@gmail.com

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