



Effects of two isomers of DDT and their metabolite DDE on CYP1A1 and AhR function in human placental cells

Anna K. Wójtowicz¹, Ewelina Honkisz¹, Dorota Zięba-Przybylska¹,
Tomasz Milewicz², Małgorzata Kajta³

¹Laboratory of Genomics and Biotechnology, University of Agriculture, Rzędzina 1B, PL 30-274 Kraków, Poland

²Department of Gynecological Endocrinology, Jagiellonian University, Kopernika 23, PL 31-501 Kraków, Poland

³Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Smętna 12, PL 31-343 Kraków, Poland

Correspondence: Anna Wójtowicz, e-mail: anna.wojtowicz@ur.krakow.pl

Abstract:

The aim of this study was to investigate the actions of two isomers of DDT (*p,p'*-DDT, *o,p'*-DDT) and DDE (*p,p'*-DDE, *o,p'*-DDE) on the human placenta. We studied the effects of DDT and its metabolite DDE on CYP1A1 activity and on CYP1A1 and aryl hydrocarbon receptor (AhR) protein expression in placental cells. We used explants from third-trimester human placental tissue and JEG-3 cells, which are first-trimester human placenta cells. The main finding of this study was that the activity of CYP1A1 in the human placenta, measured in terms of ethoxyresorufin-O-deethylase (EROD) activity, was suppressed by treatment of 1, 10, and 100 ng/ml *p,p'*-DDT, *o,p'*-DDT, *p,p'*-DDE and *o,p'*-DDE. Immunoblot analyses indicated that both isomers of DDT and DDE inhibited the expression of CYP1A1 most effectively at 48 h and/or 72 h after the treatment. Because CYP1A1 activity is mediated by AhR, we evaluated the expression of AhR in placental tissue exposed to DDT and DDE for 1 h to 72 h. Our data showed that DDT and DDE gradually decreased the level of AhR protein, starting at 3 h or 24 h after the start of the experiment. Our results strongly support the involvement of the AhR/CYP1A1 signaling pathway in the mechanism of action of DDT and DDE in the human placenta.

Key words:

human placental explant, JEG-3 cells, pesticide, EROD, AhR protein expression, CYP1A1 protein expression
