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Agonist/antagonist activity of three pesticides on the estrogen receptor alpha in a recombinant yeast assay

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The focus of scientific concern about pesticides is still high due to their continuous use. Pesticides have been found in all compartments from soil to atmosphere, ground and surface waters as well as in human tissues. Despite their environmental low concentrations, they can induce chronic toxic effects on whole aquatic organisms, acting as pseudo-persistent pollutants, given continuous introduction into the environment. Another effect of pesticides might be that, once absorbed, they interfere with the normal functions of the endocrine system by mimicking or antagonizing the action of natural hormone 17 β -estradiol (E2). The aim of the present study was to assess the potential endocrine activity of three pesticides: cyfluthrin, a pyrethroid derivative insecticide, iprodione, an imidazole fungicide and endosulfan, an organochloride insecticide. In addition, the combined effect of the single compounds with E2 and tamoxifen, an anti-estrogen was investigated. The estrogenic activity was investigated *in vitro* by a recombinant yeast system (YES assay) carried out on *Saccharomyces cerevisiae*-RMY326 which expresses the human estrogen receptor α (hER α). It includes expression plasmids carrying the reporter gene lac-Z, encoding the β -galactosidase, used to measure the receptor activity. The β -galactosidase activity was determined by adding the colorimetric substrate, 2-nitrophenyl- β -galactoside; the absorbance of the samples was measured at 420 nm. The results showed that cyfluthrin, iprodione and endosulfan bind to the hER α of yeast cells with a relatively low affinity when compared to estradiol, used as the positive control. Endosulfan was the most potent with EC50 values equal to 1.1 \cdot 10⁻⁸ M (1000 times less than 17 β -estradiol). The results obtained co-incubating different concentrations of single pesticide with increasing concentrations of tamoxifen (1.0 \cdot 10⁻⁷ to 1.0 \cdot 10⁻⁴ M) indicated a non-competitive antagonism of all chemicals while when combined with E2 (1.0 \cdot 10⁻¹¹ to 1.0 \cdot 10⁻⁷ M), cyfluthrin was anti-estrogenic, iprodione and endosulfan anti-estrogenic at lower concentrations and agonist at higher concentrations. No evidence of synergism was observed when the single compounds were tested in combination with tamoxifen or E2. These findings confirm the estrogen mimetic activity of some pesticides and show that *in vitro* estrogenic assays such as YES test could be a useful tool to give an overall knowledge of the estrogenic potency of xenobiotics.

Biography

Margherita Lavorgna has completed her PhD in 2006 from Second University of Naples (Italy). Since 12/2010, she is researcher of General and Applied Hygiene. Her research activity is addressed to toxic, genotoxic and endocrine interference activity of environmental xenobiotics as well as microbiology of waters and food. She has published 26 papers on peer reviewed national and international journals.

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