Screening of selected pesticides for oestrogen receptor activation in vitro - DTU Orbit (02/11/2019)

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Twenty pesticides were tested for their ability to activate the oestrogen receptor in vitro using an MCF7 cell proliferation assay and a Yeast Oestrogen Screen. The fungicides fenarimol, triadimefon, and triadimenol were identified as weak oestrogen receptor agonists, which at 10 μM induces a 2.0, 2.4, and 1.9-fold increase in proliferation of human MCF7 breast cancer cells (E3 clone). The relative proliferation efficiency (RPE) was 43-69%, indicating partial agonism at the oestrogen receptor. Several pesticides did not have any effect on the proliferation response after 6 days of exposure, including, chlorpyrifos, diuron, iprodion, linuron, pentachlorphenol, prochloraz, propiconazol, propyzamine, quintozen, tetrachlorvinphos and tetradifon. Some pesticides resulted in a negligible proliferation response, which was not statistically significant under the present experimental conditions. These were, bromopropylate, chlorfenvinphos, chlorobenzilate, dicofol, heptachlor, and imazalil. Fenarimol and dicofol also gave rise to a positive oestrogenic response in yeast cells transfected with rite oestrogen receptor alpha, whereas the remaining compounds resulted in a negative response due either to biological inactivity or cytotoxicity to the yeast cells. The EC50 for fenarimol has estimated to be 13 μM in the yeast cells, compared with an EC50 of 3 μM in the MCF7 cells, indicating higher sensitivity of the latter assay. No in vivo data for fenarimol, triadimefon or triadimenol have previously been published that support oestrogenic activity in the intact animal, Thus, from the present results Mie suggest that oestrogen receptor activation may not be an important mode of action for these compounds. The need to include at least two bioassays in a screening procedure and for combining in vitro and in vivo data is emphasized.

General information
Publication status: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Technical University of Denmark
Contributors: Vinggaard, A., Breinholt, V., Larsen, J. C.
Pages: 533-542
Publication date: 1999
Peer-reviewed: Yes

Publication information
Journal: Food Additives and Contaminants
Volume: 16
Issue number: 12
ISSN (Print): 0265-203X
Ratings:
Scopus rating (1999): SJR 0.802 SNIP 1.017
Original language: English
Keywords: oestrogen receptor, endocrine disruption, pesticides, fenarimol
DOIs:
10.1080/026520399283678
Source: orbit
Source ID: 230902
Research output: Contribution to journal › Journal article – Annual report year: 1999 › Research › peer-review