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Abstract

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Toxicology. 2009 Aug 21;262(3):184-91. doi: 10.1016/j.tox.2009.06.006. Epub 2009 Jun 17.

Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines.

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Abstract

Glyphosate-based herbicides are the most widely used across the world; they are commercialized in different formulations. Their residues are frequent pollutants in the environment. In addition, these herbicides are spread on most eaten transgenic plants, modified to tolerate high levels of these compounds in their cells. Up to 400 ppm of their residues are accepted in some feed. We exposed human liver HepG2 cells, a well-known model to study xenobiotic toxicity, to four different formulations and to glyphosate, which is usually tested alone in chronic in vivo regulatory studies. We measured cytotoxicity with three assays (Alamar Blue, MTT, ToxiLight), plus genotoxicity (comet assay), anti-estrogenic (on ERalpha, ERbeta) and anti-androgenic effects (on AR) using gene reporter tests. We also checked androgen to estrogen conversion by aromatase activity and mRNA. All parameters were disrupted at sub-agricultural doses with all formulations within 24h. These effects were more dependent on the formulation than on the glyphosate concentration. First, we observed a human cell endocrine disruption from 0.5 ppm on the androgen receptor in MDA-MB453-kb2 cells for the most active formulation (R400), then from 2 ppm the transcriptional activities on both estrogen receptors were also inhibited on HepG2. Aromatase transcription and activity were disrupted from 10 ppm. Cytotoxic effects started at 10 ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered, and their classifications as carcinogens/mutagens/reprotoxics is discussed.

PMID:

19539684 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

Publication Types

<u>Research Support, Non-U.S. Gov't</u>

MeSH Terms

- <u>Adolescent</u>
- <u>Aromatase/drug effects</u>
- Aromatase/genetics
- <u>Aromatase/metabolism</u>
- <u>Cell Line, Tumor</u>

Supplemental Content

- DNA Damage/drug effects*
- <u>Dose-Response Relationship</u>, Drug
- Endocrine Disruptors/administration & dosage
- Endocrine Disruptors/toxicity*
- Estrogen Receptor alpha/drug effects
- Estrogen Receptor alpha/metabolism
- Estrogen Receptor beta/drug effects
- Estrogen Receptor beta/metabolism
- Genes, Reporter/drug effects
- <u>Glycine/administration & dosage</u>
- <u>Glycine/analogs & derivatives*</u>
- Glycine/toxicity
- <u>Herbicides/administration & dosage</u>
- <u>Herbicides/toxicity*</u>
- <u>Humans</u>
- <u>Male</u>
- Pesticide Residues/toxicity
- <u>RNA, Messenger/metabolism</u>
- <u>Receptors</u>, <u>Androgen/drug effects</u>
- <u>Receptors</u>, <u>Androgen/metabolism</u>
- <u>Toxicity Tests/methods</u>
- <u>Transcription</u>, Genetic/drug effects

Substances

- Endocrine Disruptors
- Estrogen Receptor alpha
- Estrogen Receptor beta
- Herbicides
- Pesticide Residues
- <u>RNA</u>, <u>Messenger</u>
- <u>Receptors</u>, Androgen
- glyphosate
- <u>Glycine</u>
- <u>Aromatase</u>

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