Effects of Glyphosate and Its Formulations on Markers of Oxidative Stress and Cell Viability in HepaRG and HaCaT Cell Lines

J. R. Rice, P. Dunlap, S. Ramiahgari, S. Ferguson, S. L. Smith-Roe, and M. DeVito
Division of the National Toxicology Program, Research Triangle Park, NC.

Abstract
Glyphosate (GLY) is an active ingredient found in widespread use as a herbicide. GLY formulations may cause oxidative stress and relate these effects to cell viability.

Objective
To determine whether glyphosate or its formulations cause oxidative stress and relating these effects to cell viability.

Methods
GLY (N-(phosphonomethyl) glycine) was first discovered in 1970 and is resistant to GLY. It is applied to plants as a formulation with other chemicals. Glyphosate use began with the introduction of GLY-resistant crops in the 1970s to generate extensive dose-response curves for multiple GLY versus GLY salts, as well as GLY and adjunct active ingredients in oxidative damage assays. We also directly compared the effects of GLY formulations on HepaRG and HaCaT cell lines, suggesting that xenobiotic metabolism effects were present in these cells.

Test Articles
Table 1. Dose Regimes

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dose Regime</th>
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</thead>
<tbody>
<tr>
<td>GLY</td>
<td>1, 10, 100, 1000, and 10,000 µM</td>
</tr>
<tr>
<td>Formulations</td>
<td>1, 10, 100, 1000, and 10,000 µM</td>
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</tbody>
</table>

Data is presented from one replicate study (n=2) and is representative of the other two replicates.

Conclusions
• The effects of glyphosate formulations appear to be due to the use of the shikimate amino acid synthesis pathway. The present day intensive use of GLY is applied to crops as a herbicide to control weeds and reduce competition. Glyphosate formulations may cause oxidative stress and cell death. This is consistent with previous findings indicating that GLY is thought to induce oxidative stress and cell death in HepaRG cells, thus reducing cell viability.

References
Ramaiahgari, S., Ferguson, S., Rice, J. R., DeVito, M., and Dunlap, P. 2015. Glyphosate formulations marginally increase oxidative stress only after 24 h. Toxicol In Vitro 29, 199-207.

Acknowledgments
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