

FUNCTIONAL IMPAIRMENT OF PANCREATIC B-CELLS BY GLYPHOSATE AND ITS COMMERCIAL FORMULATION

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INTRODUCTION: Glyphosate (GLY) is the most widely used herbicide globally. Emerging evidence suggests that glyphosate-based herbicides (GBHs), such as RoundUp®, may act as endocrine-disrupting chemicals capable of impairing metabolism homeostasis, however this remains poorly understood. **OBJECTIVES:** Evaluate the direct effects of either GLY or GBHs on pancreatic islets and β -cell function. **MATERIALS AND METHODS:** The MIN6 cell line (mice pancreatic β -cells), was used to assess the cytotoxic effects of GLY and GBHs *in vitro*. Cells were treated with increasing concentrations of pure GLY or GBH (1 nM to 4 mM), and viability was evaluated using the MTT assay. For *ex vivo* analysis, pancreatic islets were isolated from adult mice and divided into control or treatment groups; receiving GLY or GBH at 10 nM, 100 nM and 1 μ M. After 24 hours of exposure, intracellular calcium dynamics were assessed using the calcium-sensitive probe Fura-2 under a perfusion system coupled to an epifluorescence microscope. Islets were stimulated with low (2.8 mM) and high (11.2 mM) glucose, calcium influx was quantified by 340/380 nm fluorescence ratio. Similarly, NADPH levels were measured based on autofluorescence at 360 nm. Glucose-stimulated insulin secretion (GSIS) was also evaluated under the same glucose and compound concentrations. **RESULTS AND CONCLUSION:** Pure GLY did not significantly reduce MIN6 cell viability, even at supraphysiological concentrations (up to 4 mM). In contrast, GBH exposure resulted in a concentration-dependent reduction in viability, beginning at 100 μ M and reaching complete cell death at 400 μ M. Both GLY and GBH reduced intracellular calcium levels at all concentrations tested in the first peak. There was no difference in NADPH autofluorescence in all tested groups. While GLY had no significant effect on GSIS, GBH treatment at 100 nM and 1 μ M significantly attenuated insulin secretion in response to high glucose. These findings suggest that although both compounds disrupt calcium signaling, only GBHs exhibit cytotoxic and functional impairment in β -cells, likely due to formulation-specific additives. Further research is needed to clarify the molecular mechanisms involved on β -cell dysfunction and to determine the long-term metabolic implications of such exposures.

Key words: Pesticides; Pancreatic beta-cells; Metabolism; Insulin; Cytotoxicity;

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