# RISK ASSESSMENT OF THE CHIRAL PESTICIDE FIPRONIL IN HUMANS THROUGH *IN VITRO* TOXICITY STUDIES USING HEPG2 CELLS

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Fipronil is a chiral pesticide used worldwide to control insects in crops and urban areas. Although fipronil enantiomers do not present activity differences, they may show enantioselective toxicity differences in non-target species, including humans. Human exposure to fipronil may occur through occupational or environmental contamination. Therefore, its enantioselective risk assessment in humans is important. Previously, *in vitro* metabolism studies have shown that fipronil is mainly metabolized into fipronil sulfone by CYP3A4. Besides that, *in vitro* inhibition studies have demonstrated that *rac*-fipronil (moderate), its enantiomers (moderate), and fipronil sulfone (strong) are inhibitors of CYP2D6 isoform, which could cause pesticide-drug interactions. In this work, *in vitro* cytotoxicity and genotoxicity of these xenobiotics were evaluated in HepG2 cells using the MTT and comet assays, respectively. *Rac*-fipronil significantly decreased cell viability from concentrations of 5.0 µmol $L^{-1}$. *R*-fipronil and fipronil sulfone showed the highest cytotoxic effect, with impairing of cell viability from concentrations of 1.0 µmol $L^{-1}$. *S*-fipronil presented the lowest cytotoxic potential, being significative only at 50.0 µmol $L^{-1}$. The comet assay results indicated potential genotoxic effects of *rac*-fipronil, *R*-fipronil, *S*-fipronil, and fipronil sulfone from concentrations of 1.0, 10.0, 10.0, and 0.5 µmol $L^{-1}$, respectively. Although it was observed cytotoxic differences for *R*-fipronil and *S*-fipronil, both presented similar genotoxic potential. Furthermore, fipronil sulfone presented a higher cytotoxic and genotoxic effect than *rac*-fipronil. Therefore, the metabolism of fipronil into fipronil sulfone may increase the risk of toxic effects. Next, *in vitro* cytotoxicity will be completed using the live/dead assay and *in vitro* mutagenicity will be assessed using the micronucleus assay. The results presented in this work, together with the *in vitro* metabolism and inhibition results (already published), provide important scientific information on the risk assessment of fipronil in humans.