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Death by Multiple Poisoning, Glyphosate and Roundup

Scientists pinpoint how very low concentrations of the herbicide and other chemicals in Roundup formulations kill human cells, strengthening the case for phasing them out, and banning all further releases of Roundup-tolerant GM crops
[Dr. Mae-Wan Ho](#) and [Brett Cherry](#)

This article was submitted to the USDA on behalf of ISIS

Four different Roundup formulations of the herbicide glyphosate manufactured by Monsanto are highly toxic to human cells, and at concentrations far below the recommended agricultural use levels. Researchers at the Institute of Biology in Caen, France published their latest results in the current issue of *Chemical Research in Toxicology* [1].



Roundup formulations are lethal cocktails

The four Roundup formulations are mixtures of glyphosate with various adjuvants. (An adjuvant is 'helper' substance added to aid the effect of the active ingredient.) The Roundup formulations are currently the top non-selective herbicides worldwide and increasing, as more than 75 percent of genetically modified (GM) crops are Roundup tolerant. Glyphosate and its major metabolite, aminomethylphosphonic acid (AMPA) are main contaminants in rivers. The adjuvants, not often measured in the environment, are usually considered 'inert' and protected as trade secret in manufacturing. Among them, the predominant one is polyethoxylated tallow amine (POEA). POEA is used as a surfactant in Roundup formulations to improve solubility and penetration into plants.

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Three human cell lines were tested; primary cell line HUVEC from umbilical cord vein epithelium, embryonic cell line 293 derived from kidney, and placenta cell line JEG3. All cells died within 24 hours of exposure to the Roundup formulations.

The Roundup formulations (Rs) contain different amounts of the active ingredient glyphosate: Roundup Express, 7.2 g/L (R7.2) ; Roundup Bioforce, 360 g/L (R360) ; Roundup Grand Travaux, 400 g/L (R400); and Roundup Grand Travaux Plus, 450 g/L (R450). They were compared with glyphosate (G), AMPA, and POEA . All Roundup formulations in the study, along with individual chemical ingredients, were tested at concentrations from 10 ppm (parts per million) to 2 percent (the recommended agricultural usage level), which means that the Roundup formulations were diluted up to 100 000 times or more.

The researchers found that the presence of the other chemical ingredients in Roundup formulations, such as POEA, actually amplified glyphosate's toxic effects. The toxicities of the Roundup formulations were not proportional to the amount of glyphosate they contained, and are most likely due to POEA and other as yet undisclosed ingredient(s) present in all the formulations. POEA by itself is much more toxic than the Roundup formulations, while AMPA is more toxic than glyphosate.

Multiple targets in toxicity

The researchers tested Rs, G, AMPA, and POEA for effects on three targets that could kill the cell: damage to the cell membrane, poisoning of the mitochondria (site of energy metabolism), and programmed cell death that results in fragmentation of the DNA in the cell nucleus. They measured specific enzyme markers at different concentrations for each damage at 24 h of exposure, and also obtained images of the cell cultures under the microscope.

All Rs, as well as G, caused cells to die; the results are the same for all human cell types, but at different concentrations. Thus, R400, the most toxic formulation, killed all cells at 20 ppm, which is equivalent to 8ppm in G. However, 4-10 ppm G alone is non-toxic, its toxicity begins around 1 percent (10 000 ppm), and is not connected with the cell membrane. The R formulations damage the cell membrane, and also poison the mitochondria. In contrast, G poisons the mitochondria without damaging the cell membrane

Unexpectedly, R400 is more toxic than R450, the latter in turn more harmful than R360, R7.2 and G. However, the toxicities are not proportional to the concentration of G present. The cell killing power of R7.2 was almost the same as that of R360, and these results are consistent across all cell lines. This suggests other unknown substances are involved in the toxic effects.

Thus AMPA and POEA also kill cells by poisoning the mitochondria and damaging the cell membrane. POEA is so potent that it begins to damage the cell membrane in HUVEC and poison the mitochondria in 2 93 and JEG3 at 1 ppm. Roundup formulations are more toxic than either G or AMPA. AMPA itself destroys the cell membrane, however, which G does not do, though it is 3-8 times more toxic for the mitochondria than AMPA. But as cell membrane damage is more serious for the cell, AMPA is more toxic than G, while POEA is the most toxic of all.

What happens when these ingredients are combined? The researchers found that for HUVEC and 293 cells, combinations of G and POEA, G and AMPA, AMPA and POEA were all more toxic than the same concentration of the single ingredients

For programmed cell death, the action is quicker. The marker enzymes are activated from 6 h of exposure, with a maximum at 12 h in all cases. HUVEC was 60-160 times more sensitive than the other cell lines; G and R360 were effective at exactly the same concentration, from 50 ppm. The adjuvants do not seem necessary. G alone is 30 percent more potent here than Rs; it acted rapidly at concentrations 500 -1 000 times lower than agricultural use

Ban Roundup tolerant GM crops

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These latest studies confirm a wealth of evidence on the toxicities of glyphosate and Roundup formulations [2] ([Glyphosate Toxic & Roundup Worse](#), *SiS* 26), and pinpoint the different sites of action, all of which result in cell death. Epidemiological studies have previously linked glyphosate to spontaneous abortions, non-Hodgkin lymphoma, and multiple myeloma. Laboratory studies showed that glyphosate inhibits transcription in sea urchin eggs and delays development. Brief exposures to glyphosate in rats caused liver damage, and adding the surfactant in Roundup had a synergistic effect, causing greater liver damage. Roundup was also found to be much more lethal to frogs than to weeds, and could have contributed to the global demise of amphibians within the past decades [3] ([Roundup Kills Frogs](#), *SiS* 26).

We have called for a new regulatory review on glyphosate and Roundup in 2005 [2]. There is now a strong case for restricting, if not phasing out glyphosate and Roundup; in the first instance, by banning the release of Roundup tolerant GM crops worldwide. For the same reason, no further Roundup tolerant GM crops should be approved for commercial release.

References

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