

New research finds common herbicides cause antibiotic resistance

- the full paper is available at: <http://mic.microbiologyresearch.org/content/journal/micro> -

New University of Canterbury research confirms that the active ingredients of the commonly used herbicides, RoundUp, Kamba and 2,4-D (glyphosate, dicamba and 2,4-D, respectively), each alone cause antibiotic resistance at concentrations well below label application rates.

UC Molecular Biology and Genetics academic, Professor [Jack Heinemann](#), of the School of Biological Sciences, in UC's College of Science, says the key finding of the research was that "bacteria respond to exposure to the herbicides by changing how susceptible they are to antibiotics used in human and animal medicine."

The herbicides studied are three of the most widely used in the world, including New Zealand, Professor Heinemann says.

"They are among the most common manufactured chemical products to which people, pets and livestock in both rural and urban environments are exposed. These products are sold in the local hardware store and may be used without training, and there are no controls that prevent children and pets from being exposed in home gardens or parks. Despite their ubiquitous use, this University of Canterbury research is the first in the world to demonstrate that herbicides may be undermining the use of a fundamental medicine-antibiotics."

The new paper led by University of Canterbury (UC) researchers also finds that inert ingredients (surfactants) that are commonly used in some herbicide formulations and processed foods also cause antibiotic resistance. The new study found an antibiotic resistance response was caused by both the tested surfactants, Tween80 and CMC. Both are also used as emulsifiers in foods like ice cream and in medicines, and both cause antibiotic resistance at concentrations allowed in food and food-grade products.

With expertise in genetic engineering, bacterial genetics and biosafety, Professor Heinemann has some recommendations: "The sub-lethal effects of industrially manufactured chemical products should be considered by regulators when deciding whether the products are safe for their intended use," he says.

"More emphasis needs to be placed on antibiotic stewardship compared to new antibiotic discovery. Otherwise, new drugs will fail rapidly and be lost to humanity."

The researchers first observed this antibiotic resistance in their [paper published in the American Society of Microbiology's journal mBio in 2015](#). This follow-up study was conducted in order to identify which ingredients in herbicides were responsible.

Antibiotic resistance is the cause of nearly a million additional deaths worldwide from infectious diseases, Professor Heinemann says.

"The United States, for example, estimates that more than two million people are sickened every year with antibiotic-resistant infections, with at least 23,000 dying as a result. By 2050, resistance is estimated to add 10 million annual deaths globally with a cumulative cost to the world economy of US\$100 trillion. In other words, roughly twice the population of New Zealand will be lost annually to antibiotic resistance."

The paper, "Herbicide ingredients change *Salmonella enterica* sv. Typhimurium and *Escherichia coli* antibiotic responses", is published online in the peer-reviewed journal *Microbiology* (see abstract below).

Background

Herbicides are chemicals used to control weeds. Because they kill organisms, they are biocides. As their primary purpose is to kill plants, their effects on some non-target organisms are not as well

studied.

Antibiotics are also biocides. Antibiotic resistance allows bacteria that previously could be controlled by antibiotics to continue to cause disease and remain infectious for longer, even in the presence of antibiotics. Resistance to at least one major clinical antibiotic is now found in all human pathogens, and some important pathogens can be resistant to all but one antibiotic, or even all antibiotics. Even in wealthy countries, antibiotic resistance is responsible for billions of dollars of increased health care costs, additional suffering and tens of thousands of deaths each year.

Many biocides have effects on either target or non-target organisms at concentrations that do not kill. These are called sub-lethal effects. When pesticides, including herbicides, are reviewed for their safety by regulators, the focus is on acute and sometimes chronic toxicity using mortality as an endpoint. Much less information is sought on potential sub-lethal effects, particularly for microbes.

“Where this information is sought, it is usually only for people or animals. We are unaware of any regulator ever considering the risk of sub-lethal effects on bacteria. That is what makes this new research so important.”

Herbicide ingredients change *Salmonella enterica* sv. Typhimurium and *Escherichia coli* antibiotic responses

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Brigitta Kurenbach, Paddy S. Gibson, Amy M. Hill, Adam S. Bitzer, Mark W. Silby, William Godsoe and Jack A. Heinemann

Abstract

Herbicides are frequently released into both rural and urban environments. Commercial herbicide formulations induce adaptive changes in the way bacteria respond to antibiotics. *Salmonella enterica* sv. Typhimurium and *Escherichia coli* were exposed to common co-formulants of formulations, and *S. enterica* sv. Typhimurium was exposed to active ingredients dicamba, 2,4-D and glyphosate to determine what ingredients of the commercial formulations caused this effect. Co-formulants Tween80 and carboxymethyl cellulose induced changes in response, but the pattern of the responses differed from the active ingredients, and effect sizes were smaller. A commercial wetting agent did not affect antibiotic responses. Active ingredients induced changes in antibiotic responses similar to those caused by complete formulations. This occurred at or below recommended application concentrations. Targeted deletion of efflux pump genes largely neutralized the adaptive response in the cases of increased survival in antibiotics, indicating that the biochemistry of induced resistance was the same for formulations and specific ingredients. We found that glyphosate, dicamba, and 2,4-D, as well as co-formulants in commercial herbicides, induced a change in susceptibility of the potentially pathogenic bacteria *E. coli* and *S. enterica* to multiple antibiotics. This was measured using the efficiency of plating (EOP), the relative survival of the bacteria when exposed to herbicide and antibiotic, or just antibiotic, compared to survival on permissive media. This work will help to inform the use of non-medicinal chemical agents that induce changes in antibiotic responses.