



Dear editor,

In a letter in the autumn 2011 edition of World Agriculture, Christopher Jones commented that in my recent article on pesticide toxicity (Pesticide toxicity and public chemophobia: how toxic are modern-day pesticides? World Agriculture 2011, 2 (1), 22-31), I did not discuss the possible adverse effects associated with the simultaneous exposure to the residues of multiple pesticides, so called "cocktail effects". This is quite true and I would like to rectify this situation.

The fear of cocktail effects is predicated on the observation that in certain circumstances mixtures of biologically active chemicals can display synergism. In other words the mixture of chemicals can result in greater biological effects than would be expected from consideration of the biological activity of the individual chemicals alone at the same concentrations.

Since most pesticide toxicity testing is done on individual active ingredients alone, it is therefore proposed that mixtures of pesticide residues in food could possibly be more toxic than testing would predict. I'd like to make a number of points: firstly it will come as no surprise to learn that companies engaged in the invention of new pesticidal active ingredients actively look for combinations of pesticides which have the potential to act synergistically. Such mixtures will be more effective in the field and hence lower spray concentrations will be required.

For instance herbicides which inhibit 4- hydroxyphenylpyruvate dioxygenase (HPPD) are often used in tandem with herbicides which block photosystem-II since these mixtures tend to be especially effective. However it must be emphasised that such genuinely synergistic effects are rare: generally the activity of mixtures of compounds is well predicted by the activity of the

individual components alone. In fact antagonistic effects, where mixtures of compounds are less active than would be predicted, are more common than synergistic effects and this can be a real issue in new product development.

Secondly, where genuine synergy is observed, the magnitude of the effect is invariably small. A factor of three would be considered very significant.

In my paper I show that typical exposure to pesticide residues in food is of the order of a million-fold too low to have any impact on the health of people consuming the food. At such miniscule levels of exposure, even if synergistic effects exist they are of no consequence – the million-fold safety factor is many orders of magnitude greater than any synergistic effect that has ever been established. There are no reports of synergy ever being recorded at doses typical of pesticide exposure in food.

A recently published comprehensive literature review (Boobis *et al.* Critical Reviews in Toxicology, 2011, 41 (5), 369-383) sought to analyse all of the studies that claim synergistic effects of mixtures of compounds in mammalian test systems at "low dose" (i.e. near to the no adverse effect level, still many orders of magnitude higher than actual pesticide exposure in food).

The authors identified 90 studies examining combinations of 204 compounds published in the peer reviewed literature between 1990 and 2008. However convincing, quantitative evidence of synergy was only presented in six of these studies and the magnitude of synergy reported never exceeded a factor of four.

Finally the whole "cocktail effect" concept perpetuates the absurd idea that there is somehow something special about synthetic chemicals and their toxicity relative to natural chemicals. All of the myriad natural

chemical components of our food are capable of being toxic (if the dose is sufficient), and many are present in higher concentrations and are more toxic than pesticide residues. If synergistic toxicity between chemicals present in our food is really considered to be a safety issue, surely we must also consider the possibility of synergism amongst these natural chemicals? It may be argued that these natural chemicals have been in our diets for many years and hence we would have spotted any such toxicological issues by now.

However new types of food are being introduced all the time and chefs delight in combining ingredients in ever more exotic and inventive ways.

It can therefore equally be argued that we are continually being exposed to novel mixtures of potentially toxic natural compounds most of which have never even been isolated and identified, let alone tested for toxicity!

It is perfectly reasonable for the public to demand extremely high standards of safety in the food chain, and that is what is routinely delivered by modern agriculture.

However the issue of "cocktail effects" is often used by those opposed to the use of pesticides in agriculture to imply uncertainty in the safety of this technology. The Precautionary Principle is invoked and ever more testing is demanded, along with guarantees of absolute safety which are of course impossible to provide in any context.

This threat remains entirely hypothetical and these effects have never been measured at realistic concentrations.

The fact remains that pesticide residues in food are irrelevant to our health, and the use of pesticides in agriculture makes our food safer than it has ever been before.

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Comments

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