



COMMENTARY

Putting concerns for caution into perspective: microbial plant protection products are safe to use in agriculture

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Abstract

In a recent publication in this journal, Deising et al. (J Plant Dis Prot 124:413–419, 2017. <https://doi.org/10.1007/s41348-017-0109-5>) stated that the application of microbial plant protection products poses a serious unpredictable health risk. Here I discuss why I disagree with their assessment and argue instead that microbial plant protection products are not posing serious health risks and therefore are safe to use in agriculture.

Keywords Beneficial microbes · Biocontrol · Carcinogens · Plant protection products · Secondary metabolites · Toxins

Many plant diseases can be controlled by chemical pesticides. Because of problems with their toxicity and/or the development of pathogen resistance, there is an increasing trend to replace chemicals by beneficial microbes which directly or indirectly inhibit the pathogen (Lorito et al. 2010; Haas and Defago 2005; Lugtenberg and Kamilova 2009). Examples of such beneficial microbes, which are used as active ingredients of PPPs (plant protection products), are species from the fungal genus *Trichoderma* (Lorito and Woo 2015) and from several species of the bacteria *Bacillus* (Borriss 2015) and *Pseudomonas* (Haas and Defago 2005; Lugtenberg and Kamilova 2009; Lugtenberg et al. 2013).

The reason for writing this communication is to question the caution raised in a recent publication in this journal in which Deising et al. (2017) argue that microbial agents used for biological control of plant diseases pose a serious and unpredictable health risk. The central issue they discuss is the possibility that toxic secondary metabolites can be produced by the newly formed microbial communities. The basis of this assumption is the fact that gene clusters encoding secondary metabolites may be expressed in co-culture with other microorganisms (Abrudan et al. 2015; Brakhage 2013; Wu et al. 2015), while they are not

expressed when microbes are cultured alone. Deising et al. argue that because applied biocontrol microbes will become part of the plant's microbiome, interaction with the resident microbiome may lead to the production of novel perhaps toxic and even carcinogenic metabolites.

I have the following disagreements with several of their assumptions.

1. Let us start with putting the risk of applying biological PPPs into perspective.
 - (a) The examples of toxic secondary metabolites produced by microbes which are given by Deising et al. are mycotoxins produced by plant pathogenic fungi and a neurotoxin produced by a human and animal bacterial pathogen, and thus not by biocontrol microbes.
 - (b) It was estimated that fungi can produce more than 200,000 secondary metabolites, only 300 of which may be regarded as mycotoxins (Cole and Cox 1981). This is far less than one percent. It is unlikely that the percentage of mycotoxins has increased significantly in the past decades since highly toxic metabolites would be the first to be discovered because of their serious health effects.
 - (c) Almost all mycotoxins are produced by fungi belonging to the phylum Ascomycota. The majority of toxigenic species can be found in the genera *Aspergillus*, *Fusarium* and

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Penicillium (Waalwijk and de Nijs, 2013). None of these are used as PPP.

- (d) A very rigid registration procedure (Regulation (EC) No 1107/2009; Commission Regulation (EU) No 283/2013; Commission Regulation (EU) No 284/2013) is required before a PPP can be brought to the market. A registration dossier must contain all requested information of the active microorganism, including its identification at the strain level, its biological properties, its safety for humans and the environment, and its efficacy (Pliego et al. 2011).
 - (e) In the past decades the European Commission has spent tens of millions of Euro's on risk assessment studies on the application of beneficial microbes and these studies did not show any serious risk (Ehlers 2011). Furthermore, in numerous studies, it was shown that the effect of the application is transient: the concentration of the microbe returns to the natural level within months or even faster (van Veen et al. 1997; Grosch et al. 2006; Scherwinski et al. 2008; Schreiter et al. 2014).
 - (f) The highest number of bacteria or fungal propagules of a PPP applied per hectare is 10^{13} .¹ Comparison with the number of microbes applied per hectare, when fertilizing a field with cow manure, learns that in the latter case the number of applied microbes is at least three orders of magnitude higher (see footnote for estimation).
 - (g) The facts mentioned under (a)–(f) indicate that the chance, that the application of microbial PPPs results in the production of novel perhaps toxic and even carcinogenic metabolites due to co-culture of microbes, is negligible.
2. Deising et al. suggest that introduction of a biocontrol microbe in an agricultural ecosystem creates a novel

¹ To compare the numbers of microbes used when applying PPPs versus manure, the following data were used. (a) The highest number of bacteria or fungal propagules of a PPP applied per hectare is 10^{13} (F. Kamilova, *personal communication*). (b) A cow produces per day 20 kg of feces and 60 kg of urine. This, together with 8 kg of rinsing water constitutes 88 kg of manure (Tom Lugtenberg and Ellis Oosterhuis, *personal communication*). So, feces in manure is 4.4 (88:20) times diluted. (c) The amount of manure applied is 60–70 tons per hectare (Tom Lugtenberg and Ellis Oosterhuis, *personal communication*). So, 65,000 kg of manure corresponds with 65,000: 4.4 = 14,773 kg feces per hectare. (d) Human feces contains 2.7×10^{13} bacteria per kg. We assume that this number is similar in feces of cows. (e) Then, 14,773 kg of cow feces corresponds with $14,773 \times 2.7 \times 10^{13} = 39,886 \times 10^{13}$ or approximately 4×10^{17} bacteria per ha. This is approximately 4000 times more than the maximal number of PPPs applied.

and therefore unpredictable situation. However, here they neglect the fact that microbes used as the active ingredients of microbial PPPs were all isolated from nature, often from the habitat in which the product is meant to be active. So, if interactions of this microbe with resident microbes lead to the production of toxic or carcinogenic products, this is already happening in nature. Therefore, the suggestion of a novel situation is not warranted. Moreover, not a single report on detrimental effects due to the application of microbiological PPPs on human or animal health has been published. This also indicates that the risk is negligible.

3. The result of practically all interventions in agriculture has some sort of unpredictability for the simple reason that one cannot predict the future in such a dynamic environment as soil. The truly discriminating aspect of applying microbial PPPs is that it will temporarily result in a much higher local concentration of the beneficial microbe. However, sufficient regulatory measures are in place before such a product is allowed for application in agriculture. Therefore, using the word unpredictable in relation to biological PPPs has an undeserved negative connotation to both the scientific reader and the general public.
4. Whereas Deising et al. claim that the toxicity of microbial secondary metabolites produced by using PPP's is strongly underestimated, they also state that the risk imposed by synthetic (i.e., chemical) pesticides is strongly overestimated. Here they should have used the same scrutiny for synthetic (chemical) pesticides as for microbial secondary metabolites. Using their lines of reasoning, also synthetic chemical pesticides, by definition being biologically active compounds, could interact with the existing microbiome and pose the same proposed unpredictable risk.
5. Conclusions (a) Based on the facts presented in this paper, the application of microbial PPPs is not posing any serious health risks for humans and for the environment. (b) The reasons for questioning the safety of microbial control of plant diseases by Deising et al. are unwarranted and biased. (c) Following the line of reasoning of Deising et al. with respect to unpredictability, there is more reason to worry about chemicals than about microbials used in the control of plant diseases. (d) The use of both biologicals and chemicals should be regulated thoroughly, reasonably, and with equal scrutiny.

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Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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