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Toxicological Interactions in Insects Exposed to Binary Mixtures Cointaining a Botanical Monoterpene and a Conventional Insecticide

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Abstract

Due to its low toxicity in mammals and very low environmental impact, some botanical monoterpenes with insecticidal activity are an attractive alternative to conventional insecticides. There is extensive literature on the insecticidal activity of individual monoterpenes, but very few studies about toxicity of simple mixtures containing monoterpenes (2-4 components) or monoterpenes and conventional insecticides (organophosphorus, carbamates, pyrethroids, neonicotinoids). Additive, antagonistic and synergistic interactions have been reported for such a mixtures when applied on several insect pest species. The identification of monoterpenes that increase the toxicity of conventional insecticides has a potential practical application. It could be the first step towards the development of products to control pests by applying lower doses of such insecticides.

Keywords: Botanical monoterpenes; Insecticidal mixtures; Toxicological interactions; Synergism; Conventional insecticides

Introduction

Essential oils are combinations of secondary metabolites synthesized by aromatic plants [1]. Their low toxicity in mammals allows them to be used in aromatherapy, as well as in the production of perfumes and food additives [2]. The main components of essential oils are monoterpenes, molecules with structural skeletons made up by two isoprene units [3]. Monoterpenes have a low molecular weight, are volatile, non-polar and present a characteristic aroma [1]. Some botanical monoterpenes have insecticidal activity [4-8]. In addition to mortality, some of them produce sublethal effects in insects such as repellency, growth inhibition and feeding deterrence [9-13]. Recent findings have shown that, as observed for pyrethroid insecticides, certain botanical monoterpenes produce hyperactivity, an increase in the locomotor activity of the insects [11-13]. The insecticide properties of monoterpenes have received special attention over the last decades. This is because there is a constant search for alternative substances to control insect populations that are resistant to conventional insecticides (organophosphorus, carbamates, pyrethroids, neonicotinoids). In insects, the toxicity of monoterpenes is usually lower than that of conventional insecticides, but their potential insecticidal activity is particularly interesting to investigate due to its aforementioned low toxicity in mammals and its very low environmental impact [14].

Discussion

Essential oils are complex mixtures, in some cases made up by dozens of substances. Hence, their insecticide activity is almost certainly the result of numerous interactions among them (in general terms, the toxicity of a mixture can be higher -synergism- or lower -antagonism- than the sum of the individual toxicities of its components). There is extensive literature on the insecticide activity of essential oils, as well as on their individual components. Studies using simple mixtures of monoterpenes (2-4 components) or monoterpenes and conventional insecticides are much scarcer. In larvae of the tobacco cutworm, *Spodoptera litura*, binary mixtures of *trans*-anethole with citronella, thymol or α-terpineol acted synergistically in terms of both acute toxicity and feeding deterrence [15]. On the other hand, binary combinations of citronella with thymol and α-terpineol showed synergism for feeding deterrence, but additivity (no toxicological interaction) for acute toxicity. Synergism also occurred when some combinations of three or four monoterpenes were applied on *Musca domestica* and the louse *Pediculus humanus capitis* [16,17].

The type of toxicological interaction can vary according to the form of application. Out of fifteen binary mixtures of monoterpenes applied in two different ways to *M. domestica*, twelve interacted synergically and three presented additivity when applied topically [18]. However, when applied in vapor phase, eight were synergistic, six were additive and one antagonistic. Synergism seems to prevail in binary mixtures of monoterpenes. The assessment of 435 mixtures in the cotton leafworm *S. littoralis*, elicited 211 synergistic and 97 antagonistic interactions [19]. Synergic effects were also observed in mixtures of γ-terpinene or terpinen-4-ol with the organophosphorus profenofos and the carbamate methomyl in *S. littoralis* and the bean aphid *Aphis fabae* [20]. In the blood-sucking bug, *Triatoma infestans*, menthol and menthyl acetate synergized the toxicity of the organophosphorus azamethiphos both when applied topically and by exposure to films on filter paper [21]. Eugenol also synergized azamethiphos when the mixture was applied on filter paper; however, no interaction occurred when topical application was performed. Monoterpenes usually increase the toxicity of conventional insecticides in less than one order in magnitude, but a striking exception occurred in *T. infestans.* In first instar nymphs of this species, the toxicity of azamethiphos increased dramatically when applied topically together with menthyl acetate (15 000x) or menthol (49 000x) [21].

Toxicological interactions may occur in any of the toxicokinetic and toxicodynamic processes of the substances involved: absorption, distribution, metabolism and target binding [22,23]. The limited information on the toxicokinetics and toxicodynamics of monoterpenes in insects only allows for very generalized speculations on the possible mechanisms underlying their toxicological interactions. The mechanism of a toxicological interaction between two monoterpenes was carried out in larvae of the cabbage looper, *Trichoplusia ni*, where thymol synergized the toxicity of *p*-cymene by increasing its cuticular penetration [24,25]. There is also a report on a case of behavioral synergism, where a change in the behavior of *T. infestans* produced by a sublethal dose of a monoterpene increased the exposure of the insects to a pyrethroid applied on a filter paper [26]. Toxicological, behavioral, pharmacological and analytical chemistry experiments demonstrated that nymphs of *T. infestans* hyperactivated by eugenol picked up more insecticide, and subsequently become intoxicated faster, than non-hyperactivated nymphs when exposed to a permethrin-treated surface. Some evidence suggest that the octopaminergic system participates in the hyperactivant effect of eugenol in *T. infestans* [27].

Conclusion

The toxicological interactions that involves botanical monoterpenes and conventional insecticides is a field that is only just being explored, but that already sheds promising results for pest control. The examples described in the previous paragraphs suggest that aromatic plants are a rich source of insecticide synergists. The identification of monoterpenes that increase the toxicity of conventional insecticides has a potential practical application. It could be the first step towards the development of products to control pests by applying lower doses of such insecticides. The mixtures that are more efficient synergically, such as menthol and menthyl acetate with azamethiphos in *T. infestans*, should be assessed in different insect pests to confirm whether it is an isolated phenomenon or not. On the other hand, studying the mechanisms underlying these interactions will lead the way towards finding appropriate monoterpenes to be included in new mixtures.

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