

The synergy of xenobiotics in honey bee *Apis mellifera*: mechanisms and effects

Sinergizem ksenobiotikov v medonosni čebeli *Apis mellifera*: mehanizmi in učinki.

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Abstract: During foraging activities honeybees are frequently exposed to different xenobiotics, most of them are agrochemical pesticides and beehive chemicals. Many pesticides are applied together and synergism is likely to occur in different organisms. The risk of synergisms is neglected and relatively few studies were performed concerning the effects and synergy mechanism of different xenobiotic combinations in honeybees. The understanding of synergy mechanisms between xenobiotics is very important for the control of defined mixtures use and also for the prediction of potential toxicity of newly developed substances in agriculture and apiculture. This review is focused on the effects, mechanisms and molecular targets of xenobiotics in honeybees and possible complex mechanisms of their synergisms. The main threat for honeybees are insecticides which primary molecular targets are few neuronal molecules therefore causing the impairment of neuronal system that have a profound effect on honeybee behavior, cognitive functions and physiology. However, the majority of synergistic effects observed in honeybees were ascribed to the inhibition of detoxifying midgut enzymes P450 involved in xenobiotic metabolism since most of studies were done with the mixtures xenobiotic/P450 inhibitor. The main inhibitors of P450 enzymes are specific compounds used to prolong the effects of pesticides as well as some fungicides. Some insecticides can also interact with these enzymes and influence the xenobiotics. Although the primary mechanisms of action of individual xenobiotics especially insecticides are well known and there are possible interactions in honeybees at their primary target sites, this issue is underestimated and it warrants further investigation.

Keywords: synergism, xenobiotic, *Apis mellifera*, mechanism, pesticide, P450

Izvleček: Medonosne čebele so med iskanjem hrane pogosto izpostavljene različnim ksenobiotikom, večinoma so to fitofarmaceutska sredstva in panijske kemikalije. Številna fitofarmaceutska sredstva se uporabljajo skupaj in znano je, da lahko pride do sinergističnih interakcij v organizmih. Tveganje za nastanek sinergizmov je podcenjeno in narejenih je relativno malo študij na čebelah o učinkih in mehanizmih sinergizmov različnih kombinacij ksenobiotikov. Razumevanje mehanizmov sinergizmov ksenobiotikov je zelo pomembno za nadzor nad uporabo definiranih