6.7 Hydroxylmethylfurfural induces reactive oxygen species (ROS)-dependent activation of the Toll pathway in honey bees

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Abstract

Hydroxymethylfurfural (HMF), a common product of hexose degradation occurring during the Maillard reaction and caramelization, has been found toxic for rats and mice. HMF can be consumed by honey bees through bad production batches of sugar syrups that are offered as winter feeding. In Belgium, abnormal losses of honey bee colonies were observed in colonies that were fed with syrup of inverted beet sugar containing high concentrations of HMF (up to 475 mg/kg). These losses suggest that HMF could be implicated in bee mortality, a topic that so far has received only little attention.

We studied the influence of HMF feeding on the gene expression of honey bees. The expression levels of marker genes for different stressors were determined with an in-house developed colorimetric microarray. The targets on the microarray are marker genes for the immune system, *Nosema* infestation, *Varroa* infestation, nutritional stress, pathogens and intoxication. After analysis of the gene expression, profiles were differently expressed in bees exposed to HMF compared to the control group. The data were normalized using the RPL8 reference gene. The most up- and down regulated genes were selected for validation with qPCR.

Statistical analysis of the data revealed that defensin-1 is downregulated after 10 days exposure to 320 ppm but becomes upregulated in the other conditions. Defensin-1 is an end product of the Toll pathway. A recognition protein of the pathway, Bgluc1, is upregulated in all conditions which can explain why the Defensin-1 expression is upregulated. Another end product of the Toll pathway, Abaecin, was upregulated in all conditions except in the 320 ppm after 14 days it was downregulated.

It is clear that HMF is influencing the expression of genes involved in the TOLL pathway. This pathway is normally activated upon microbial infection. In *Saccharomyces cerevisiae*, HMF induce oxidative stress although the exact mechanism has not yet been elucidated. When HMF is inducing oxidative stress in honey bees upon exposure these ROS intermediates may be responsible for the activation of the Toll pathway. This mechanism was recently described in the mosquito *Aedes aegypti.*

We can conclude that HMF induces reactive oxygen species (ROS)-dependent activation of the Toll pathway in honey bees. In addition some detoxification genes were upregulated upon HMF expression.