Design of biocontrolled pesticides based on trehalase inhibition

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Aphids are major pests for forests, cereals, vegetables and fruit crops not only due to their direct action on the plants, but also because they act as vectors of many phytopathogenic viruses. Also, they are difficult to control due to their high reproductive capability, combined with a short development time. Aphid invasions are generally fought against with insecticides such as carbamate compounds or synthetic pyrethrinoids, but more and more cases of resistance have been observed. These compounds, similarly to the very recent neonicotinoids, are neurotoxins and endocrine-disrupting compounds, and they have been found to also be harmful to fish and mammals. Several crops such as sugar beet in Belgium have temporary authorization to continue to be protected with neonicotinoids to control aphids but this will end soon without any actual alternative. Even the very recent sulfoximine-based insecticides were demonstrated to have a serious impact, in particular on insect pollinators, which led many countries to progressively ban their use.

Due to this huge damaging impact on human health and environment, the European Union is now enforcing the reduction of pesticides dissemination. As a result, scientists are urged to find new pathways, alone or in combination with existing strategies that would effectively control aphid populations. Among these, biological control methods have been developed that take advantage of natural predators or parasitoids of aphids. However, in a context of field crops, they do not yet ensure production yields at a competitive price. Among other possibilities currently being considered, is the formulation of new insecticides targeting and disrupting the insect biochemical functions. Thanks to their high specificity, such pest control will pose very little risk to both, environment and human health. As potential safer insecticides, inhibitors reducing the availability of energy for the insect are a good alternative, and since trehalose is a major energetic reserve in insects, the inhibition of its catalysis appears as an effective control strategy. The degradation of trehalose can be achieved by several pathways including hydrolysis, which is performed by the enzyme trehalase (Treh) to produce glucose. In contrast to vertebrates where Treh is only required for the degradation of ingested trehalose, the enzyme is involved in diverse physiological processes in other animal groups.

Consequently, Treh is an ideal pesticide target, leading to a dysfunction in the life-sustaining biological systems of the target insects without inducing any threat to vertebrates. Most of Treh inhibitors reported to date are trehalose mimetics, iminosugars or pseudosaccharides. These investigations were limited either to porcine or insects Trehs, such as *Chironomus riparius* or *Spodoptera littora*lis, while no molecule has yet been considered as aphid Treh inhibitors.