



TOXICITY OF GLUCOSINOLATE-DERIVED ISOTHIOCYANATES TO GENERALIST-FEEDING CATERPILLARS

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Glucosinolates are major plant defense compounds in the order Brassicales (e.g. cabbage, broccoli, mustard). Upon tissue damage caused e.g. by chewing herbivores, the non-toxic parent glycosides are transformed into toxic isothiocyanates (ITCs) and other metabolites. Still, generalist-feeding insect herbivores sometimes feed successfully on glucosinolate-containing plants. Previous studies in our group revealed that a proportion of ITCs is metabolized to glutathione conjugates; yet, a large amount is excreted in unmodified form [1]. These unmodified ITCs cause decreased rates of growth and delayed development. However, the mode of action of these nucleophilic and lipophilic toxins in caterpillars is poorly understood.

We compared the effects of Met- and Trp-derived glucosinolates, which lead principally to ITC and non-ITC hydrolysis products, respectively, on two generalist-feeding caterpillars in the laboratory. The development of larvae of *Spodoptera littoralis* (African cotton leafworm) and *Mamestra brassicae* (cabbage moth) was investigated from hatching until adult emergence while the larvae were reared on *Arabidopsis thaliana*, accession Col-0, and three different glucosinolate-deficient mutants. We found that both glucosinolate types negatively affected larval development when fed separately, but in combination their effect was significantly stronger. To our surprise, larvae fed on glucosinolates gave rise to heavier pupae and adults. Using artificial diets, we conducted detailed investigations on the effect of the aliphatic 4-methylsulfinylbutyl-ITC (sulforaphane) on the biochemistry and metabolism of *S. littoralis* larvae. The most typical effect was the decrease of glutathione in midgut tissue and hemolymph, likely due to losses by conjugation to ITC during detoxification. As a consequence, the levels of free amino acids were altered, with a sharp decrease in cysteine leading to reductions in protein content, but an increase in lipids. To learn more about the mechanism of glucosinolate toxicity, we are now performing a comprehensive study of the conjugation of ITC to the proteome *in vivo*.

[1] Schramm K, Vassão DG, Reichelt M, Gershenzon J, Wittstock U (2012) Metabolism of glucosinolate-derived isothiocyanates to glutathione conjugates in generalist lepidopteran herbivores. *Insect Biochemistry and Molecular Biology* 42, 174-182.
