

Modified Forms of Alternariol and Alternariol Monomethyl Ether and their Resorption and Metabolism in Human Caco-2-Cells

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Fungi of the genus *Alternaria* are ubiquitous and can contaminate a wide range of food and feed. Some *Alternaria* strains produce toxic secondary metabolites such as Alternariol (AOH) and Alternariol monomethyl ether (AME). Both mycotoxins have already been found in various foods including tomatoes, carrots, and cereals.

Similar to mammalian metabolism, contaminated plants are able to metabolize mycotoxins by altering their chemical structures, e.g. by conjugation with glucose. As a result, compounds are formed that are not detected in routine analysis. Due to the possible release of the parental toxin during digestion, it is important to elucidate the structures of the conjugated mycotoxins and to investigate their bioavailability.

Incubation of tobacco plant cell suspension cultures with AOH and AME resulted in metabolites, which were analyzed with 2D-NMR. For both toxins, AOH and AME, two glucosides and two malonylglucosides as well as one AOH diglucoside were unambiguously identified [1].

In order to assess the relevance of these so-called “modified” mycotoxins in intact plant tissues, tomatoes were infected with spores of *Alternaria alternata*. Besides small amounts of the already mentioned glucosides, sulfate conjugates were detected in large amounts, too. Subsequent studies showed that they were not formed by the tomato but by the mold itself. To study their metabolism in plants, the sulfate conjugates were incubated in tobacco suspension cells, resulting in the formation of three sulfoglucosides of AOH and one sulfoglucoside of AME. Their structures were unambiguously determined by using NMR. These metabolites were also found in *A. alternata* infected tomatoes. Mixed sulfate / glucoside diconjugates may also represent modified forms of other mycotoxins containing two or more hydroxyl groups [2].

Furthermore, first experiments with Caco-2 cells were performed. This system is a common in vitro model to study intestinal absorption as well as the metabolism of xenobiotic substances. Upon incubation of Caco-2 cells with glucosylated AOH and AME conjugates, a partial release of the parental toxins AOH and AME has already been demonstrated leading to an increase in the total exposure to the toxin.

[1] A.A. Hildebrand et al., J. Agric. Food Chem. 2015, 63, 4728-4736

[2] S.T. Soukup et al., J. Agric. Food Chem. 2016, 64, 8892-8901