Biological activity and biotransformation of enniatins from Fusarium fungi

October 30 2013

Fusarium Head Blight in wheat. Credit: Courtesy G. Bergstrom

Mould species of the genera Fusarium and Altenaria are considered the most important threats to Norwegian grain cereals because they produce toxins which can be a potential risk to food safety.

F. avenaceum, the fungi most frequently isolated from Norwegian grain, produces enniatins which have been found in large quantities in

Norwegian grain in recent years. A new PhD project concludes that incomplete intestinal absorption and enzymatic metabolic breakdown in the liver may reduce the enniatins' bioavailability so that they are less harmful to humans following oral administration.

To what extent enniatins pose a potential risk to human health due to their stability in the gastrointestinal tract, fat solubility and a number of negative effects found on cells in vitro has been a matter for debate. Lada Ivanova's doctoral thesis has expanded current knowledge about the toxicity of enniatins. She used the human intestinal cell line (Caco-2) to identify the molecular biological mechanisms which lead to the dysfunction of lysosomes, the release of peptides into the cytosol of the cells and a programmed necrosis – morphological changes leading to cell death.

A substance is categorised as toxic if it disturbs biochemical and physiological processes when absorbed into an organism. The substance's absorption and distribution in the organism and its biological transformation and excretion all influence bioavailability. Since a toxic effect in the organism is normally related to bioavailability, knowledge about the absorption from the intestinal tract and the biotransformation (enzymatic degradation) of enniatins is an important factor when it comes to predicting risks to humans.

Ivanova used microsomes from different species to study how important enzymes belonging to the cytochrome P450 group are for the liver's ability to break down enniatin B. She came to the conclusion that enniatin B is primarily transformed by the enzyme CYP3A4 and to some degree by CYP1A2 and CYP2C19. Using different chemical tools, thirteen new metabolites (products of metabolism) of enniatin B were identified and characterised. The model used was confirmed by analysing biological samples from chickens which had been given feed containing specific amounts of enniatins.

The ability of enniatins to pass through the intestinal wall was studied in a model system emulating the function of the intestines. This in vitro model uses Caco-2 cells originating from human colon cancer cells. The general conclusion of this research is that several apical ABC transporters (protein molecules) can prevent the absorption of enniatins from the intestinal lumen. At the same time, there was evidence that enniatins can block important transporters and change the absorption and distribution of other substances from the intestines.

The results of this doctoral project indicate that the bioavailability and toxic effects of enniatins after oral administration may be reduced due to incomplete absorption from the intestines and enzymatic degradation in the liver.

Lada Ivanova, who holds a Master of Food Safety, defended her doctoral research on 25th October 2013 at the Norwegian School of Veterinary Science with a thesis entitled: "Enniatins from Fusarium fungi. Their biological activities and biotransformation in a food and feed safety perspective".

Provided by Norwegian School of Veterinary Science