

## Protective effect of 6-Gingerol against oxidative stress induced by zearalenone and its metabolites

Intidhar Ben Salem, Salwa Abid-Essefi, Christophe Lemaire and Hassen Bacha  
Monastir University, Tunisia

**Z**earalenone (ZEN) is a non-steroidal estrogenic mycotoxin produced by several species of *Fusarium* in cereals and agricultural products. ZEN and its metabolites:  $\alpha$ -Zearalenol ( $\alpha$ -Zol) and  $\beta$ -Zearalenol ( $\beta$ -Zol) have been implicated in several mycotoxicosis in farm animals and in humans. Several reports suggest that oxidative damage seems to be a key determinant of ZEN and its metabolites induced toxicity *in vitro* and *in vivo*.

The aim of the current study was to evaluate the protective effects of 6-Gingerol (6-Ging), against ZEN and its metabolites induced cytotoxicity, reactive oxygen species (ROS) and mitochondrial superoxide anion  $O_2^-$  generation, loss of the mitochondrial transmembrane potential ( $\Delta\psi_m$ ), lipid peroxidation (MDA), DNA fragmentation and also against ZEN-induced endoplasmic reticulum (ER) stress in cultured HCT-116 cells. Indeed, cytotoxicity effects were studied using MTT viability assay and flow cytometry analysis, ROS generation and MDA formation measurement. To check whether the oxidative stress induction was associated to DNA lesions, we looked for DNA fragmentation using Comet test. Besides, the implication of ZEN and its metabolites on ER stress and then on the activation of the unfolded protein response (UPR) was demonstrated by Western blot analysis. Our results indicated that ZEN,  $\alpha$ -Zol and  $\beta$ -Zol induced several toxic effects and significant alterations mediated by oxidative stress mechanism. Treatment by ZEN/metabolites combined to the lowest dose of 6-Ging (5  $\mu$ M) showed a significant reduction of ZEN induced damages for all tested markers and a noticeable reduction of DNA fragmentation. It could be concluded that 6-Ging is effective in the protection against ZEN hazards. This could be relevant, particularly with the emergent demand for natural products which may counteract the detrimental toxic effects mediated by oxidative stress process and therefore prevents multiple human diseases.

intidhar.ben.salem@gmail.com