NIVALENOL AND DEOXYNIVALENOL INDUCE INFLAMMATION AND INCREASE LIPOPOLYSACCHARIDE AND INTERFERON-GAMMA EFFECTS ON INTESTINAL EPITHELIAL CELLS

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Mycotoxins are toxic secondary metabolites produced by various molds. These toxins are found all around the world as natural contaminants in numerous commodities of plant origin, especially in cereals grains (Bennett and Klich 2003). Worldwide surveys indicate that 72% of all agricultural commodities are contaminated with different mycotoxins (Streit et al. 2013) and they can also be found in animal-derived food if animals eat contaminated feed (Bryden 2012; Marin, et al. 2013). Mycotoxins ingestion may induce various chronic and acute effects on humans and animals; moreover they are not are not completely eliminated during food processing operations and can contaminate finished processed food products (Da Rocha et al. 2014; Bullerman and Bianchini 2007). Trichothecenes mycotoxins are chemically related compounds produced by different fungal genera. After the ingestion, the intestinal epithelium is the first host defence barrier and it can be exposed to high concentrations of toxins (Maresca et al. 2008). Oral exposure to trichothecenes causes gastrointestinal effects as well as severe damage to the lymphoid and epithelial cells of the gastrointestinal mucosa (Pestka and Smolinski 2005). Thus the intestinal epithelial cells (IECs) are especially sensitive to trichothecenes and their exposure to these toxins may induce toxicity (Pinton et al. 2010).

The aim of this study was to evaluate the effect of two trichothecenes, Nivalenol (NIV) and Deoxynivalenol (DON), alone and in combination, on the inflammatory response in the non-tumorigenic intestinal epithelial cell line IEC-6, at concentrations consistent with the levels plausibly encountered in the gastrointestinal tract after consumption of contaminated food (0.5-5 μM). Our results indicate a consistent NIV and DON pro-inflammatory effect on IEC-6. We observed a significant increase of tumor necrosis factor-α production, inducible nitric oxide synthase and cyclooxygenase-2 expression, nitrotyrosine formation, reactive oxygen species release, Nuclear Factor-kB, Nuclear factor (erythroid-derived 2)-like 2 and inflammasome activation. The pro-inflammatory effect resulted increased strongly by NIV and by the mycotoxins mixture compared to DON alone. Moreover our results also indicate that NIV and DON, alone and even more in combination, are able to exacerbate an existing inflammation state in IEC-6 cells induced by Lipopolysaccharide plus Interferon-γ. Considering that range concentration used in this study for NIV and DON are consistent with the levels plausibly encountered in the gastrointestinal tract after consumption of heavily contaminated food (Leblanc et al. 2005) these evidences are very important for NIV and DON risk assessment. These results highlight the importance of the toxic effect of these mycotoxins, mostly in combination, also during conditions of intestinal inflammation.

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