« PARC « : Towards Next-generation Chemical Risk Assessment

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ABSTRACT:
In May 2022, the European Union launched the „PARC" initiative, a « Partnership for the Assessment of Risks from Chemicals ». The 7-year partnership under Horizon Europe has a total funding volume of €400 million Euro, 50% funded by the European Union and 50% by Member States. PARC involves about 200 institutions working in the areas of the chemical safety from 28 countries and three EU authorities, including the European Chemical Agency (ECHA), the European Food Safety Authority (EFSA) and the European Environment Agency (EEA). The partnership is coordinated by ANSES, the French Agency for Food Safety, Environmental Protection and Occupational Health. PARC aims to develop next-generation chemical risk assessment to protect human health and the environment.

In the field of emerging contaminants, PARC aims to close critical data gaps for comprehensive risk assessment. One line of activity is focused on hazard characterization of the emerging mycotoxins enniatins, beauvericin and *Alternaria* toxins, non regulated contaminants with an increasing data base on occurrence in food and feed. A special challenge is represented by *Alternaria* mycotoxins with more than 70 compounds out of different chemical classes reported so far, which might be formed by these fungi. However, only a limited number of secondary metabolites formed by *Alternaria* fungi are commercially available und thereby accessible as reference material and test compounds for hazard characterization. In the first project period, toxicological characterization of *Alternaria* toxins was focused on alternariol (AOH), alternariol monomethyl ether (AME), tenuazonic acid (TeA), alternuene (ALT), tentoxin (TEN), and altertoxin I (ATX-I), the compounds with most occurrence data available. Within PARC, in close collaboration of 17 Universities, research institutes and regulatory units, genotoxic potential, endocrine disruptive effects and immunotoxic properties were determined. Among the various mycotoxins produced by *Alternaria* spp. some have previously been shown to mediate immunotoxic effects, suppressing lipopolysaccharide (LPS)-induced inflammation as exemplified by downregulation of the NF-κB signaling pathway in THP-1 cells [1,2,3]. In THP-1 monocytes, immunotoxic effects of enniatins (A, A1, B, B1) and beauvericin were observed only in cytotoxic concentrations. In contrast, the selected *Alternaria* toxin showed a differential immunotoxic profile. In THP-1 monocytes as well as THP-1 derived macrophages most of the tested *Alternaria* toxins suppressed the proinflammatory stimulus of LPS. Notably, AME and ATX-I were more active in macrophages, whereas the other *Alternaria* toxins showed higher potency in monocytes. Taken together, these data highlight the ability of selected *Alternaria* mycotoxins to modulate NF-κB signaling in both monocytes and macrophages, with compound- and cell-specific differences in potency and cytotoxicity. Ultimately, these findings contribute to fill data gaps in the hazard characterisation of emerging mycotoxins and provide valuable data for future risk assessment.

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