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Project Aflatox® I – A biotechnological approach for the development of new antifungal compounds to protect the environment and the human health.

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With a steadily increasing world population, a more efficient system of food production is of paramount importance. One of the major causes of food spoilage is the presence of fungal pathogens and the production and accumulation of mycotoxins: due to their implication in crop production, food quality and human and animal health, aflatoxins represent a major concern for both developed and developing Countries. However, despite of countless efforts, to date the problem of food and feed contamination remains unsolved, since the essential factors that affect aflatoxins production are various and hardly to handle together. In this scenario, the exploitation of bioactive natural sources to obtain new agents with novel mechanisms of action may represent a successful strategy to minimize at the same time mycotoxin contamination and the use of harmful pesticides.

In 2015 Aflatox® Project was granted from Cariplo Foundation: purpose of our project was the development of new-generation inhibitors of aflatoxigenic *Aspergillus* spp proliferation and toxin production, through the modification of naturally occurring molecules; a panel of at least 180 compounds, based on a class of molecules named thiosemicarbazones, have been analyzed for their antifungal and antiaflatoxigenic ability. Accordingly with the experimental design, the activities of the different research groups joining the project were organized as follows:

- 1) synthesis and characterization of new bioactives obtained by condensation of thiosemicarbazide with aldehydes or ketones of natural origin;
- 2) evaluation of effect on *A. flavus* growth, development and aflatoxin biosynthesis;
- 3) improvement of compounds performance by modifying the chemical scaffold and/or via complexation with biocompatible metal ions (i.e. copper and zinc);
- 4) evaluation of cytotoxicity, genotoxicity and epi-genotoxicity of new-synthesized compounds through the use of validated assays on human cell lines (colon, epidermis and lung tissues), Salmonella/microsome test and *Allium cepa* micronucleus test;
- 5) *in vitro* evaluation of the best performing compounds effect on maize kernels infection by *A. flavus*;
- 6) creation of a Quantitative Structure-Activity Relationship (QSAR) database correlating chemical structures with biological/toxicological activities.

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