COLLEGE DOCTORAL BRETAGNE SCIENCES DE LA VIE ET DE LA SANTE

Year 2022-2023

THESIS TOPIC

Subject N° (to be completed by the ED):	**FUNDING:** ☒ **Requested** ☒ **Acquired**	**Funding origin: ILVO (acquired) + ARED (requested)**
Thesis title: Effect of fermentation on mycotoxins: identification and toxicity studies of metabolites formed		3 keywords: Mycotoxins Fermentation Toxicity
Research Unit / team: **ANSES Fougères loboratory (Team Toxicology of Contaminants)**		
Director's name: **FESSARD Valérie**		Phone number: +33 (0)2.99.94.66.85 Email address: valerie.fessard@anses.fr Year of HDR : 2006

Socio-economic and scientific context (approximately 10 lines):

Mycotoxins produced by fungi (Alternaria, Aspergillus, Fusarium and Penicillium) can contaminate a wide range of foodstuffs and generate deleterious effects in exposed humans and animals. Fermented foods have become increasingly popular for several reasons (food preservation, new flavors, possible health benefits). However, they are likely to be contaminated by mycotoxins, especially those made from vegetable raw materials (cereals, rice, soy).The origin of mycotoxins can be diverse (contaminated raw materials or ingredients, fungal contamination during or after processing, use of toxigenic strains with mycotoxin production during fermentation). The inoculated cultures can also affect the mycotoxins during fermentation.

Working hypothesis and aims (approximately 8 lines):

Food safety risks due to mycotoxins or toxic metabolites in fermented products should not be overlooked.
In this project, we will study the impact on mycotoxins of fermentation processes using microorganisms. We will contribute to answer 6 research questions:

1. Does fermentation with these microorganisms induce mycotoxin production?
2. Can fermentation metabolize mycotoxins in contaminated raw starting material?
3. Can we identify the metabolites formed?
4. Can some of them be found in fermented products on the market?
5. Does fermentation lead to a decrease in the toxicity of mycotoxins?
6. What is the toxicity of the metabolites formed after fermentation?.

Main milestones of the thesis (approximately 12 lines):
Our strategy will be split into 4 tasks:
T1 Possible production of mycotoxins and fate of mycotoxins during fermentation (ILVO).
Fermentation will be performed in a controlled system: culture medium with a micro-organism (bacteria, yeast, fungus) supplemented with each selected mycotoxin (2 regulated and one emerging.) Several mycotoxin concentrations and/or fermentation conditions (micro-organism and fermentation time) will be tested. Adequate controls will also be performed to detect, by difference, the molecules of interest produced.
Analyses for the presence of mycotoxins (targeted, quantitative approach) as well as for possible metabolites formed during fermentation (non-targeted, qualitative approach) will be performed by HRMS. To facilitate the identification and purification of the compounds of interest, a directed effect analysis approach with fractionations coupled to cellular tests (even T3) could be considered.
T2 Research of identified compounds in fermented materials on the market (ILVO)
A preliminary market survey will be carried out to investigate the possible presence of both mycotoxins and identified metabolites. Based on the selected microorganisms, a maximum number of 40 relevant samples will be analyzed.
T3 Toxicity study of T1 samples (ANSES)
The toxicity (apoptosis, inflammation, DNA damage, oxidative stress, etc.) of the samples provided in T1 will be evaluated on cell cultures (intestine, liver) according to the mycotoxins tested.
T4 Predictive toxicology (ANSES)
The toxicity of the metabolites characterized from the samples analyzed in T1 will be predicted by in silico approaches. From their chemical formula, the available information will be searched in different databases. Moreover, their toxicity (mutagenicity, carcinogenicity, endocrine disruption, etc.) will be predicted by structure/activity type tools (QSARs).

Scientific and technical skills required by the candidate (2 lines):
Master 2 in analytical chemistry or toxicology
Good level in English

3 publications from the team related to the topic (last 5 years):

- Lemée P, Fessard V, Habauzit D Prioritization of mycotoxins based on mutagenicity and carcinogenicity evaluation using combined in silico QSAR methods. Expo Health (in revision)
- Habauzit, D., Lemée, P., Botana, L.M., Fessard V. Toxicity Predictions for Mycotoxins: A Combined In Silico Approach on Enniatin-Like Cluster. Expo Health (2022).
- Alarcan J, Barbé S, Kopp B, Hessel-Pras S, Braeuning A, Lampen A, Le Hégarat L, Fessard V. Combined effects of okadaic acid and

pectenotoxin-2, 13-desmethylspirolide C or yessotoxin in human intestinal Caco-2 cells. Chemosphere (2019) 228:139-148.;78:105257.

National and international collaborations:

This project will be done in collaboration with the Belgian institute ILVO (Flanders research institute for agriculture, fisheries and food). The thesis will be realized the first 18 months in Belgium (Brussels) on fermentation and chemical analysis by mass spectrometry and the last 18 months in France (Fougères) on the predictive and experimental toxicity of the different samples.