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Marina Requile, Ovidio Gonzalez Alvarez Duban, Stéphane Delanaud, Larbi Rhazi, Véronique Bach, et al.. STUDY OF THE IMPACT OF A CHRONIC CO-EXPOSURE OF A PESTICIDE AND A PREBIOTIC ON THE INTESTINAL MICROBIOTA USING TWO IN VITRO MODELS. 25th United European Gastroenterology Week, Oct 2017, Barcelone, Spain. hal-04336188

HAL Id: hal-04336188

<https://normandie-univ.hal.science/hal-04336188>

Submitted on 11 Dec 2023

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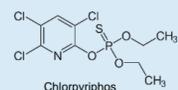
STUDY OF THE IMPACT OF A CHRONIC CO-EXPOSURE OF A PESTICIDE AND A PREBIOTIC ON THE INTESTINAL MICROBIOTA USING TWO *IN VITRO* MODELS

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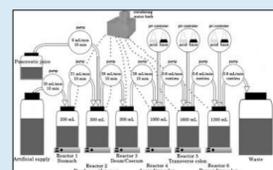
Introduction and goals

The excessive use of pesticides, often found as residues in our diet and as contaminants in drinking water, has become a public health topic. Indeed, preliminary studies have shown that chronic low-dose exposure to **chlorpyrifos** (CPF) (Joly et al. 2013) alone causes an intestinal imbalance (dysbiosis).



Objective: The objective of this study is to evaluate the preventive potential of a prebiotic (inulin) in co-exposition with CPF on intestinal dysbiosis, bacterial translocation and its consequences on the integrity of the intestinal mucosa using two *in vitro* models.

Matérials and Methods

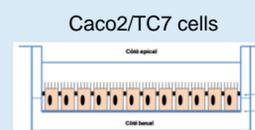


Simulator of the Human Microbial Intestinal Ecosystem: SHIME®



Stabilization of microflora (15 days)

Exposure of SHIME® to CPF (3,5 mg) ± Inulin (10g) per day



Caco2/TC7 cells

Collection of samples at D0, D15 et D30

• Integrity and epithelial function
• Bacterial translocation

• Bacterial profile
• Fermentative activity

Results

Bacterial profile and fermentative activity

• ↓ with CPF 3.5 mg
• ↑ with Inulin

• ↓ with Inulin
• ↑ with CPF 3.5 mg

Beneficial flora

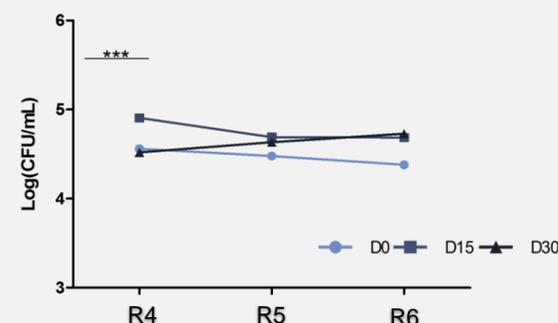


Potentially pathogenic flora

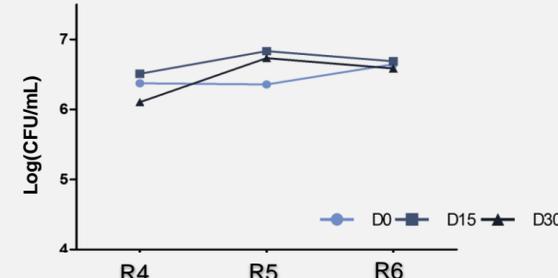


Co-exposition CPF 3,5 mg / Inulin

Potentially pathogenic flora (*Staphylococcus*)



Beneficial flora (*Bifidobacterium*)



→ Prebiotic helps to restore intestinal dysbiosis induced by CPF.

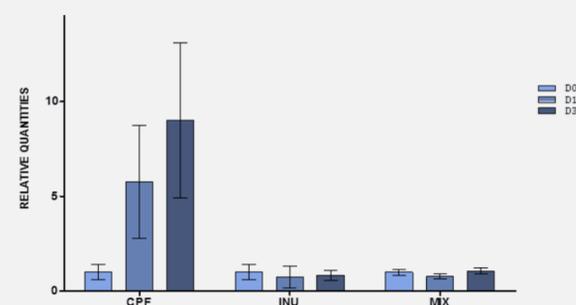
→ Inulin beneficially influenced the fermentative profile, with higher production of VFA (Volatile Fatty Acids), especially propionic acid and butyric acid.

Impact on the functional epithelium

Trans-epithelial resistance (TEER)

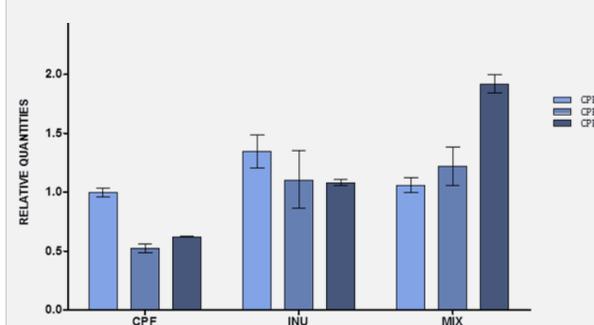
→ Reduced TEER suggest perturbation of the epithelial layer in all conditions.

Inflammation: production of IL8



→ Prebiotic prevents the pro-inflammatory response.

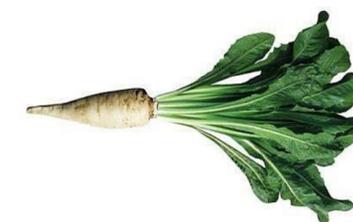
Expression of the Villin gene



→ Increase of the villin gene expression to restore the perturbation caused by the CPF.

Conclusion

CPF / inulin co-exposure has an impact on both the bacterial profile and metabolism, suggesting that prebiotic supplementation could decrease the damages caused by CPF exposure. The combination of two *in vitro* models seems to be an ethical and relevant alternative to animal or human experiments.



Perspective

Preliminary results showed toxicity of SHIME® samples on intestinal epithelial cells. Therefore, an optimization phase is necessary. In order to have a better representation of the complexity of the mucosal tissue, the model could be developed further by the inclusion of mucus-producing cells.