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DDA Département Sciences des Denrées alimentaires

Impact of food additives on intestinal microbiota and inflammation

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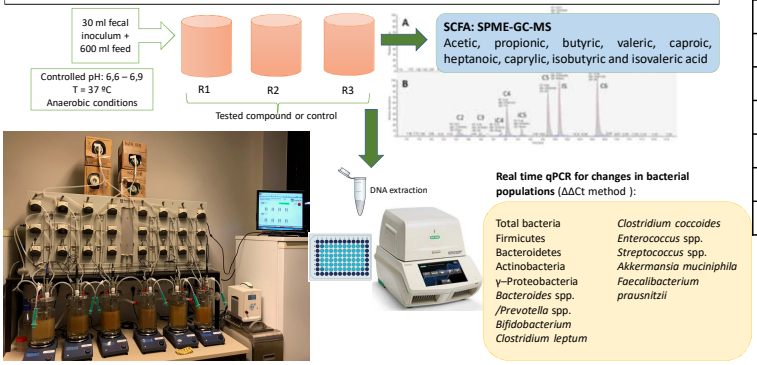
Introduction

Accumulating evidence demonstrates a contribution of dietary emulsifiers in the increase of prevalence of diseases associated with intestinal inflammation, such as inflammatory bowel disease (IBD; Naimi et al., 2021). Two emulsifiers in particular, polysorbate 80 and carboxymethylcellulose, profoundly impact intestinal microbiota leading to gut inflammation (Frolkis et al., 2013; Maaser et al., 2017; Chassaing et al., 2017; Naimi et al., 2021). The impact of other food additives on the intestinal microbiota composition and function is less known. Some mucolytic bacteria, such as *Mucispirillum schaedleri, Ruminococcus* and *Anaeroplasma* have been directly correlated with fibrosis induction while other bacteria such as *Oscillospira* and *Coprococcus* were negatively correlated (Jacob *et al.,* 2018).

The aim of this work is to determine how food additives influence intestinal microbiota towards an inflammation, a dysbiosis and the subsequent formation of fibrosis in the context of IBD.

Materials and Methods

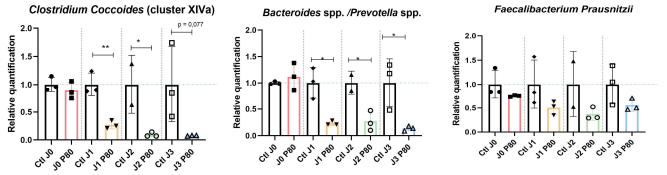
Six food additives (polysorbate 80, maltodextrin, titanium dioxide, sodium nitrite, sucralose and carrageenan) were tested in *in vitro* batch cultures model of intestinal microbiota, using the SHIME ® system, for 72 hours. The tested concentrations were based on the acceptable daily intake (ADI) or on the estimated daily exposure assuming in both cases an average weight of 70 kg. A mix of fecal samples from 5 healthy donors was used in the *in vitro* batch models. Changes in microbiota were assessed every 24h using qPCR targeting bacterial groups involved in short-chain fatty acid (SCFA) production or inflammation. In addition, SCFA production was assessed using GC/MS.



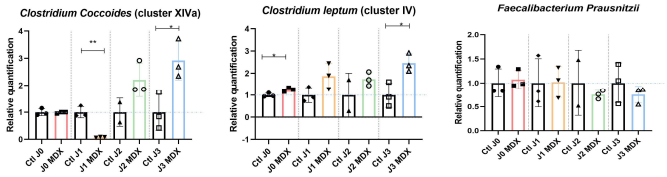
Results – Microbial changes

	Polysorbate 80	Titanium dioxide	Maltodextrin	Carrageenan	Sucralose	Sodium Nitrite
Firmicutes						
Bacteroidetes						
Actinobacteria						
γ-Proteobateria						
***Bacteroides* spp /*Prevotella* spp**						
***Enterococcus* spp**						
***Streptococcus* spp**						
Bifidobacterium						
Clostridium coccoides						
Clostridium leptum						
Faecalibacterium prausnitzii						
Akkermansia Muciniphila						

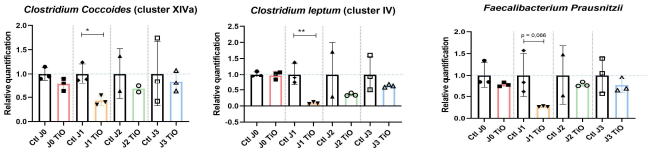
Table 1: Relative increase or decrease of specific groups of bacteria caused by food additives in comparison with control batch culture. refers to a decreasing or increasing trend respectively (0,05 < p < 0,1). means significative decrease or increase (p < 0,05).



Impact of **polysorbate 80** on the relative quantity of *Clostridium coccoides, Bacteroides* spp. / *Prevotella* spp. and *Faecalibacterium prausnitzii* .

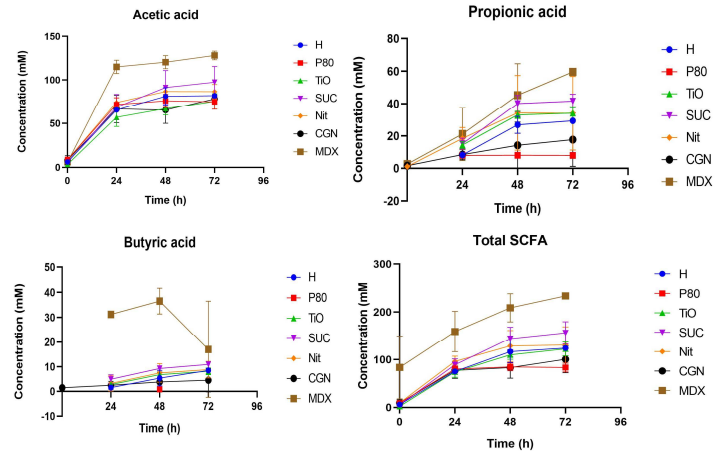


Impact of **maltodextrin** on the relative quantity of *Clostridium coccoides, Clostridium leptum* and *Faecalibacterium prausnitzii* .



Impact of **titanium dioxide** on the relative quantity of *Clostridium coccoides, Clostridium leptum* and *Faecalibacterium prausnitzii.*

Results – SCFA production



H: healthy donors; P80: polysorbate 80; TiO: titanium dioxide; SUC: sucralose; Nit: sodium nitrite; CGN: carrageenan; MDX: maltodextrin
No significant differences were observed regarding the production of branched – chain fatty acids (BCFA)

Discussion and Conclusion

The analysis of SCFA production revealed that polysorbate 80 dramatically decreased the concentration of butyric and propionic acid after 72h of fermentation. After this period, the total production of SCFA was also significantly lower than the control. The qPCR analysis confirmed that this compound inhibited the growth of Bacteroidetes, *Bacteroides/Prevotella* spp. (propionate producing bacteria) and *Clostridium coccoides* group (butyrate producing bacteria). The production of acetic, propionic and butyric acid was significantly higher than the control when maltodextrin was added to the system. Indeed, even after 24h of fermentation, the total quantity of SCFA was significantly higher than the control. The addition of maltodextrin promoted the growth of the phylum actinobacteria in general and the rise of *Bifidobacterium* genus specifically. The growth of *Streptococcus* spp., *Clostridium coccoides* and *Clostridium leptum* group was also promoted with the addition of maltodextrin. On the other side, the relative quantities of Bacteroidetes phylum, *Bacteroides* spp. / *Prevotella* spp., γ – proteobacteria and *Akkermansia muciniphila* were significantly lower than the control after 24h of fermentation. The addition of titanium dioxide negatively impacted the growth of several bacterial groups as *Enterococcus* spp., *Streptococcus* spp., *Bifidobacterium, Clostridium coccoides* group, *Clostridium leptum* group. Sucralose inhibited the growth of bacteria belonging to actinobacteria, γ – proteobacteria, *Enterococcus* spp., *Streptococcus* spp. and *Clostridium leptum* group after 24h of fermentation, while the relative quantity of Bacteroidetes was significatively increased after 48h of fermentation. The effects of sodium nitrite and carrageenan on the intestinal microbiota were limited to the significant diminution of *Clostridium leptum* and *Clostridium coccoides* groups respectively.

It can be concluded that the use of some food additives can lead to a dysbiosis affecting some bacterial groups considered as beneficial for human health such as members of *Clostridium leptum* and *Clostridium coccoides* groups.

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