IN VITRO ASSESSMENT OF ARSENIC BIOACCESSIBILITY AND INTESTINAL TRANSPORT, INCLUDING GUT MICROBIOTA CONTRIBUTION

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Introduction

Contaminated water and food are the main sources of oral exposure to arsenic (As). Assessing the risks from oral As exposure involves an evaluation of its oral bioavailability (fraction of As that reaches the systemic circulation), yet human *in vivo* bioavailability data are scarce. Bioaccessibility (the fraction of As released from its matrix during digestion) and intestinal transport (the fraction of bioaccessible arsenic crossing epithelial membrane) are therefore often used as conservative estimators of oral bioavailability. Several *in vitro* models are available to measure both determinants, yet the contribution of colonic digestion – including microbial metabolism – to either bioaccessibility or intestinal transport has rarely been investigated. Here, we propose a combination of dynamic gut model with models of intestinal epithelial barrier function to predict oral bioavailability and evaluate the gut microbiome's contribution to the different parameters.

Methods

Several food matrices from the Belgian consumer market were subjected to *in vitro* gastrointestinal digestion in the simulator of the human intestinal microbial ecosystem (SHIME) and in the Caco-2/HT29-MTX model of the intestinal epithelium. Total As quantification and As speciation was conducted with ICP-OES and HPLC-ICP-MS, respectively.

Results

Compared to stomach and colon, the small intestine digestion resulted in the highest bioaccessibility percentages for most food matrices (67-113%). Yet, because of microbial fermentation of dietary fiber, As bioaccessibility was the highest upon colonic digestion of brown rice samples and *Hizikia fusiformis* (107-167% of increase compared to small intestine bioaccessibility). Chemical reduction of pentavalent to trivalent As-species occurred upon stomach, small intestine and colon digestion. However, colon digestion also displayed an active metabolism of As by gut microbiota resulting in several speciation changes. Compared to aqueous standards, the modulation of As bioacessibility and As speciation upon digestion was also impacting intestinal transport as measured by Caco-2/HT29-MTX monolayers. Intestinal absorption of As from colonic digests of brown rice was reduced (5-23%) compared to iAs transport. These data demonstrate that As bioaccessibility and intestinal transport are highly influenced by the dietary matrix and further interactions with gastrointestinal secretions or gut microbiota.

Conclusion

The combination of *in vitro* digestion models, including microbial metabolism, with models of the gut epithelium can offer a more accurate prediction of As bioavailability and assessment of risk (figure 1). The health consequences of As interaction with gut microbiota and the possibilities to modulate As bioavailability through gut microbiome shifts or dietary intervention strategies need further research.

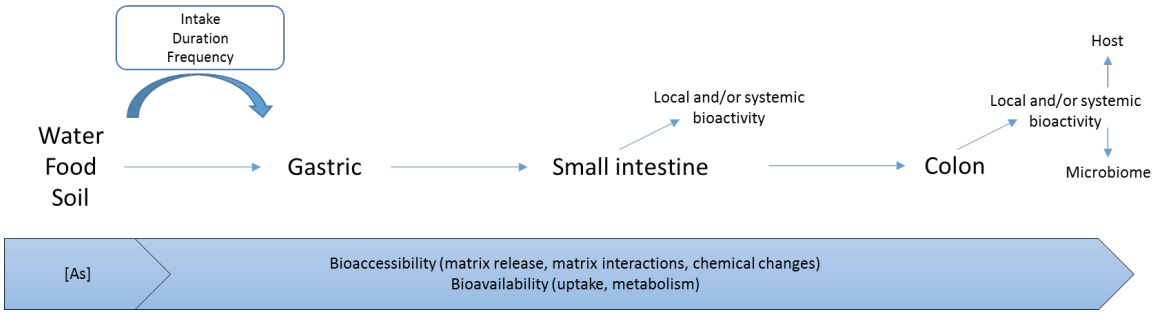

Figure 1. Schematic representation of different stages in exposure and risk assessment to arsenic by oral route.

Synopsis

Oral arsenic (As) exposure is a worldwide health concern. An accurate exposure and risk assessment is needed to achieve a better modelling of internal exposure. Accordingly, the gut is the first line of defense of the human body against the uptake of As and the processess ocurring during the transit of As throught the gastrointestinal tract can affect the exent and As species reaching the target organs. The combination of *in vitro* models including the stomach, small intestine and colonic digestion with models of the gut epithelium could improve our understanding of As toxicokinetics.