ASPET 2026
Advancing Pharmacology. Building Community.
SUN, MAY 17–WED, MAY 20 | MINNEAPOLIS, MN

Topic: Toxicology

Abstract ID: 275480

Board Number: 526

Chronic Exposure to Benzalkonium Chlorides Results in Metagenomic and Metabolic Shifts in Gut-Liver Axis of C57BL/6 Mice (Abstract ID: 275480)

VANESSA A. LOPEZ [1], CORRINA K. COOPER [2], JAKE BARBIERI [2], RYAN P. SEGUIN [1], LIBIN XU [1]

[1] *Univ of Washington*
[2] *University of Washington*

INTRODUCTION: Benzalkonium chlorides (BACs) are disinfectants widely used in consumer, medical, and commercial settings. Persistent exposure to BACs has resulted in detectable levels in human feces and blood samples. Previous work in our lab has shown that a one-week oral exposure of individual chain-length BACs at 120 μg/g/day to C57BL/6 mice produced compositional shifts in the gut microbiome, leading to decreased levels of microbe-dependent secondary bile acids. This finding prompted further investigation into the impact of BACs on the gut-liver axis under chronic low-dose exposure.

METHODS: To mimic BAC exposure in humans, in this study, male and female C57BL/6 mice were orally exposed to a deuterium (d_7)-labeled BAC cocktail consisting of 40% d_7-C12-BAC, 50% d_7-C12-BAC, and 10% d_7-C16-BAC, the composition of common household disinfectant products, at a dosage of 1.2 μg/g/day for 31 days. The animals were then sacrificed, and the cecal contents and livers were harvested. Cecal content underwent metagenomic sequencing, and livers underwent RNA sequencing.

RESULTS: Alpha and Beta diversity metrics revealed distinct shifts in microbial diversity and separation of microbial communities between the control and BAC-exposed groups. Furthermore, in the male cohort, we observed an increase in alpha diversity, whereas in the female cohort, we observed a stark decrease. Metagenomic sequencing enables species-level resolution of taxonomic composition in samples. The male cohort, in particular, showed that several Bacillota species were increased in BAC-exposed mice. For example, *Dysosmobacter welbionis*, *Ruthenibacterium lactatiformans*, *Mediterraneibacter gnavus*, *Anaerobutyricum hallii*, *Roseburia hominis*, and *Lacrimispora saccharolytica* were all increased in male BAC-exposed mice compared to controls. Notably, *D. welbionis*, *R. hominis*, and *A. hallii* play direct roles in butyrate synthesis, an important short-chain fatty acid that supports gut barrier integrity and lipid metabolism. Furthermore, *R. lactatiformans* participates in gut carbohydrate metabolism by producing lactate.

RNA sequencing of the livers revealed that several pathways related to bile acid, sterol, lipid, and xenobiotic metabolism were impacted in BAC-exposed mice. For example, in the male liver, gene expression of xenobiotic-metabolizing enzymes, *cyp4f17*, *cyp4f15*, *cyp21a1*, *cyp3a13*, *cyp7a1*, and *cyp2d26,* all increased. In the female liver, expression of carboxylesterase enzymes *ces1g*, *ces1e*, and *ces1d* was increased, and transcriptional repressor *nr1d1* was decreased. Notably, these enzymes are involved in bile acid, sterol, and fatty acid metabolism and maintenance. Furthermore, expression of aldo-keto reductase and glucuronosyltransferase genes, *akr1c14* and *ugt2b37*, respectively, was increased in female BAC-exposed livers.

CONCLUSION AND SIGNIFICANCE: Together, these data indicate that low-dose, chronic exposure to BACs elicits shifts in gut microbiome composition, congruent with altered expression of genes involved in metabolic processes in the liver, yielding novel insight into BACs' effects on the gut-liver axis.

104885; DOI: https://doi.org/10.1016/j.jpet.2026.104885