Title:
Effects of the artificial sweetener sorbitol on gastrointestinal colonization resistance against Salmonella Typhimurium

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Abstract (300 words maximum): :
The healthy human gastrointestinal tract is colonized by a complex and diverse bacterial consortium known as the microbiota. It provides numerous benefits to the host, including protection against enteropathogenic bacteria, also known as colonization resistance. However, infections caused by diarrhea-inducing bacteria remain common, and the reasons for this are not fully understood. Previous studies on high-fat diets have demonstrated that diet composition can transiently alleviate colonization resistance, thereby increasing the risk for enteropathogenic infections.
We hypothesized that food additives might similarly impair colonization resistance. Here, we investigated the impact of the commonly used artificial sweetener sorbitol on colonization resistance against the foodborne pathogen Salmonella enterica serovar Typhimurium (S. Typhimurium). Our findings revealed that sorbitol substantially enhances S. Typhimurium gut infection in mice harboring a complex gut microbiota. Compared to antibiotic-mediated microbiota disruption or germ-free mouse models, sorbitol application resulted in delayed luminal pathogen growth and slower disease progression. Despite this delay, infection levels eventually reached comparable endpoints after 4 days of infection.
Through a series of experiments, we characterized this treatment and infection regimen, with a focus on its effects on the microbiota, the host inflammatory response, and the challenges S. Typhimurium must overcome to break colonization resistance. The pathogen critically relies on virulence factors necessary for epithelial invasion and replication in the gut tissue. S. Typhimurium mutants lacking these virulence factors failed to proliferate or cause disease in sorbitol-treated mice.
Altogether, we propose that this infection scheme offers a valuable alternative to classical antibiotic pre-treatment models for studying S. Typhimurium infections. It offers insights into the role of the pathogen's virulence factors in vivo while potentially mirroring natural infection dynamics more closely.