

## Effect of Food Additives on the Gut Microbiome in Relation to Human Health

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The interplay between the host and host-associated gut microbiota is an area of increasing interest during the recent decade and the fundamental roles of gut microbiome in human health is incrementally being recognized, though it still needs further in-depth understanding [1]. Accumulating evidence have confirmed the association between the dysbiosis of gut microbial composition and etiology of human metabolic, immunological, neurological diseases [2,3]. Gradually, the causal or consequential relations of gut microbiota with various diseases, including inflammatory bowel disease [4], cancer [5,6], obesity [7,8], diabetes [9], cardiovascular disease [10,11], liver disease, neurodegenerative disorders and autism, are also being revealed [2].

Human gut microbiome composition is largely effected by the genotype and physiology of host [12], as well as many environmental factors associated with lifestyle and diet [13,14]. Particularly, diet could rapidly and reproducibly alter the human gut microbiome in microbial activity and gene expression [15]. Therefore, attempts were carried on targeting the diet-microbiota interaction as moderators of human metabolism [16]. Numbers of studies have also clarified the relationship between gut microbiota and different dietary interventions, such as the plant-based diet, animal-based diet, or western-style diet [15,17]. However, other ingredients in diet, like food additives, did not receive enough attention and are recently being unraveled [18-24], especially when considering their chronic effect on human health in low dosages.

Food additives are synthetic or natural substances that are added to foods to improve food color, aroma and taste, and to meet the needs of preservation and processing technology. The potential effect of food additives on human health has been a long-standing concern, and recently is complicated given the intensive metabolic activities of gut microbes. Non-caloric artificial sweeteners (NAS) were introduced over a century ago as means for providing sweet taste to foods without the associated high energy content of caloric sugars, regularly consumed by lean and obese individuals alike [18]. Studies demonstrate that consumption of commonly used NAS formulations drives the development of glucose intolerance through induction of compositional and functional alterations to the intestinal micro biota [19]. The impact of dietary emulsifiers on the mouse gut micro biota was also conducted by Benoit Chasseing and his colleague [20,21]. Administration of the emulsifier's carboxyl methyl cellulose (CMC) and polysorbate-80 (P80) via drinking water promoted colitis and

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metabolic syndrome in mice, which was associated with micro biota encroachment, altered micro biota composition, and increased pro-inflammatory responses. Furthermore, transplant of low-grade inflammation-associated phenotypes along with the unbalanced suspensions of human intestinal microbial ecosystem indicates that the direct effects of these emulsifiers on the micro biota are sufficient to drive low-grade inflammation and metabolic disease. Titanium dioxide (TiO) nanoparticles, which are also widely used as in food additive industry or in pharmaceutical formulations to provide a whitening effect, were also reported to worsen intestinal inflammation in the dextran sodium sulfate (DSS) mouse model of colitis [22]. Salt, another essential micronutrient with no caloric value, has been associated with the development of obesity, diabetes and other disorders in recent study [23]. Researches show that high intake of salt activates the aldose reductase-fructokinase pathway in the liver and hypothalamus, leading to endogenous fructose production with the development of leptin resistance and hyperplasia that cause obesity, insulin resistance, and fatty liver [23]. Moreover, salt can also lead to hypertension and cardiovascular disease when consumed in excess. Study report that high salt intake affects the gut microbiome in mice, particularly by depleting *Lactobacillus murinus* and drives autoimmunity by inducing T helper 17 (TH17) cells, which can contribute to hypertension [24].

It is becoming increasingly accepted that food additives are safe within specified limits. Some long-term safety assessments have also been carried out according to people's prior understanding on human health. However, as the veil of the new functional organ gut microbiota is being uncovered, health/safety problems related to gut microbiota should be further explored and confirmed. Therefore, improved mechanistic understanding of health/disease implicated with food additives or other risk diet factors and gut microbiome should be paid more effort.

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