



Reply to the Letter to the Editor by Dan Luo and Xiaobo Xu: Vinegar could act by gut microbiome

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Dear Editor,

We appreciate the comment and interests in our recent report. Citing a reference on renal clearance of radioactively labeled acetate, the authors questioned whether the acetate can be incorporated inside the cells as epigenetic markers due to its rapid metabolism. Aside from the different experimental settings in that reference and in our report, it is reasonable to believe that a continuous intake of acetate will likely increase body's acetate and its biochemical derivatives as absorption of even a minor quantity will shift the equilibrium towards a higher cellular acetate over a long period of time [1,2]. Indeed, our experimental observations provide concrete evidence to support an increase of histone acetylation with consequent transcriptional regulation of miRNAs. Our report does not exclude other mechanistic processes regarding vinegar's anti-nephrolithiasis effect, although we have provided multitude experimental evidence to support epigenetic regulations as an underlying mechanism for vinegar's efficacy. Before we explore a potential role of gut microbiome in mediating vinegar's impact for the kidney, we need to clarify several points raised by the authors. Although mature vinegar is the result of fermentation, there is undetectable living microbiome in the final vinegar due to sterilization at the end of manufacturing process [3]. Therefore, there is no rich microbiome in the vinegar, just the complex mixture of fermentation product, the identity of which is likely varied and undetermined with one component in common, acetic acid. This further suggests that this component is likely the cause of kidney stone reduction associated with vinegar consumption, indeed confirmed by our animal studies using acetic acid. As such, the oxalate degradation effect in semi-finished vinegar can not be transmitted to humans in the form of microbiome by mature

vinegar. One clear example of gut microbiome relating to kidney stone formation is the level of *O. formigenes* which can metabolize oxalate to decrease its homeostatic level to reduce kidney stone formation [4]. However this effect of microbiome on oxalate metabolism is unlikely mediating vinegar's effect on reducing kidney stone formation since we fail to find an association between human vinegar consumption and a decrease in urine oxalate level. Whether and how the observed compositional difference in gut microbiome of Shanxi vinegar consumers is causally connected with a reduction of kidney stone formation remains to be determined. In conclusion, our work is a beginning of rigorous scientific studies of the role of vinegar in preventing kidney stone formation, not the end of it.

Disclosure

Authors do not have any conflicts of interest to declare.

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DOI of original article: <https://doi.org/10.1016/j.ebiom.2019.06.004>.

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<https://doi.org/10.1016/j.ebiom.2019.07.060>

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