Sour grapes: addressing the challenges in utilising vinegar and short-chain fatty acids to treat dysregulated glycaemic responses

Paul A Gill[1,2], Nicole J Kellow[3]

[1]Department of Microbial Diseases, UCL Eastman Dental Institute, Royal Free Campus, University College London, United Kingdom

[2]Department of Gastroenterology, Central Clinical School, Monash University and Alfred Hospital, Melbourne, Victoria, Australia

[3]Be Active Sleep and Eat (BASE) Facility, Department of Nutrition, Dietetics and Food, Monash University, Notting Hill, Australia.

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Corresponding author:

Dr Paul A Gill

Department of Microbial Diseases

Eastman Dental Institute, Royal Free Campus

University College London

London, United Kingdom.

Email: paul-gill@ucl.ac.uk

Dear Editor,

We read with interest the article by Cherta-Murillo et al. (1), in which the authors undertook a systematic literature review and meta-analysis of studies that have investigated the use of short-chain fatty acids (SCFA) and vinegar on glycaemic control. Although pharmacological agents are widely used in the treatment of metabolic conditions such as type 2 diabetes mellitus (T2DM), dietary interventions have been investigated as an alternative strategy to manage disease. Intake of vinegar has been observed to improve post-prandial glucose and insulin responses to a carbohydrate load, with a dose-response effect seen with increasing acetic acid concentrations (2) .

By stratifying the studies obtained to homogenise results from meta-analysis, the authors found that acute consumption of vinegar had a significant effect on blood glucose in healthy volunteers and those with T2DM. However, no effect was seen in studies investigating SCFA or long-term supplementation. Another recently published systematic literature review with meta-analyses found long-term supplementation between 1-12 weeks resulted in statistically and clinically significant reductions in fasting blood glucose and glycated hemoglobin levels in people with T2DM (3). Indeed, the differences in these findings may be due to variation in the meta-analysis approach, as Cherta-Murrilo et al. pooled data from healthy controls and T2DM patients and used standardized mean differences to report meta-analysis outcomes. This may have exacerbated heterogeneity observed in meta-analysis outcomes. Furthermore, chronic interventions were defined as those greater than 24 hours which led to one study investigating vinegar intake that was 2 days in duration being assessed with those of much longer duration (4). We recommend that the authors provide further clarity on the data provided on Figure 9, that appears to be mistakenly labelled as post-prandial blood glucose when elsewhere the outcome data is described as fasting blood glucose. The authors rightly put forward that heterogeneity in study outcomes is also due to the wide variety of vinegar types and doses utilised in the studies examined. Phenolic compounds in various vinegars confound affects,

therefore distilled white vinegar should be utilised in studies going forward to confirm if acetic acid is the main bioactive compound modulating glycaemic control.

The authors found that many studies had a high risk of bias and may not be reliable. We urge the authors to check data for one study (5) that was previously found to contain incorrect standard deviation values for study outcomes. However, we do not expect this to substantially affect the conclusions of the analysis performed. The authors found that many studies examined did not adequately assess confounding variables such as weight or body fat change during study interventions. Given that delivery of SCFA have also been observed to modulate fatty acid metabolism and energy expenditure in humans (6), changes in body weight may be expected if SCFA is provided over a long period of time. However, adequate control over dietary intake and other lifestyle factors is needed to attribute these effects to a SCFA intervention. In addition, lack of reporting of dietary intake in many studies will not recognise additional consumption of SCFA from dietary sources, particularly from fermented foods that can contain 1000 mg of SCFA in a standard serve (7).

Indeed, most studies assessed did not measure changes to circulating SCFA concentrations during the intervention period. These must be included in future randomised control trials to confirm if interventions deliver an adequate amount of SCFA to the colon and peripheral circulation. This is particularly important in those with metabolic disease who may already have existing dysregulated SCFA metabolism (8). The pharmacokinetics of SCFA should be considered when sampling, given that oral intake is likely to produce an acute (1-2 hr) increase to plasma SCFA (7).

There will continue to be great interest in utilising dietary therapies such as vinegar to treat metabolic conditions. Despite some evidence from the authors highlighting that vinegar consumption may regulate acute glycaemic responses, high-quality evidence is required to determine if long-term consumption of vinegar or oral SCFA may result in clinically relevant

changes to glucose regulation. Future studies must be adequately controlled and identify patient cohorts likely to respond to treatment, with follow-up of glycated hemoglobin levels after 4-6 months desirable.

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