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Optimising the carbon 13 sucrose breath test for the assessment of environmental enteric dysfunction

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Environmental enteric dysfunction (EED) is a complex disorder characterised by structural and functional aberrations within the small intestine(1). It is hypothesised that EED is the result of repeated enteric infections combined with under-nutrition and is prevalent throughout low and middle income countries. EED is thought to compromise linear growth potentially leading to stunting in infants(2). Stunting currently affects 144 million children globally under the age of 5(3). ^{13}C-sucrose from naturally enriched maize sources has previously been used in a breath test to assess intestinal sucrase activity as a marker of mucosal integrity and function in enteric enteropathy(4). However, this test requires up to 20 g of naturally ^{13}C enriched sucrose to achieve acceptable signal-to-noise in breath $^{13}CO_2$, making the test unsuitable for routine use in infants. The current study aimed to develop a new ^{13}C sucrose breath test (SBT) protocol using commercially available, highly enriched ^{13}C Sucrose to facilitate a much smaller test dose.

This was a randomised crossover trial of 19 healthy adults recruited in Glasgow, UK. All participants completed a baseline SBT with 20 g naturally enriched sucrose before being randomly assigned to two groups; receiving 20 g unlabelled (beet) sucrose + 50 mg tracer (n = 8) or 50 mg tracer dose alone (n = 11). Participants remained allocated to their group and were given in a random repeated order $^{13}C_{12}$-Sucrose, $^{13}C_6$ Sucrose ($^{13}C_6$-Fructose) and $^{13}C_6$ Sucrose ($^{13}C_6$-Glucose) to assess the effect of labelling position on breath recovery parameters with at least 3 days washout between tests.

Results were expressed as Area Under the Curve (AUC), time of maximum breath $^{13}CO_2$ enrichment (T_{max}, hrs), cumulative percentage dose recovered at 90 mins (cPDR90, %) and time at which 50% AUC had been expired in breath 13CO2 ($T_{1/2}$, hrs).

Highly enriched $^{13}C_{12}$ sucrose yielded significantly improved ^{13}C breath signal to noise compared to the naturally enriched sucrose dose (x20). There were no significant differences in AUC, cPDR90, T_{max} or $T_{1/2}$ between $^{13}C_{12}$ sucrose and naturally enriched sucrose (all $P > 0.05$). Altering the position of the ^{13}C label changed kinetics of breath ^{13}C excretion. $^{13}CO_2$ appeared more rapidly with $^{13}C_6$ sucrose ($^{13}C_6$-fructose) compared with $^{13}C_6$ sucrose ($^{13}C_6$-glucose) (T_{max},(SD) = 1.29 (0.44) vs. 1.87 (0.22), $P < 0.05$ and cPDR90 (SD) = 15.95 (3.88) vs. 12.38 (2.31), $P < 0.05$ respectively). Addition of 20 g unlabelled sucrose appeared to slow down ^{13}C sucrose digestion with significantly lower cPDR90 for all highly enriched variants (all $P < 0.05$).

A dose of 50 mg $^{13}C_{12}$-sucrose gave excellent signal-to-noise in breath $^{13}CO_2$ and there was no statistically significant difference in breath parameters compared with the naturally enriched SBT. The ^{13}C labelling pattern impacted the kinetics of ^{13}C recovery in breath probably reflecting intermediary metabolism. A minimal dose of $^{13}C_{12}$-sucrose is likely to be suitable for studies in infants and children.

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