OBSERVATIONS

Artificial Sweeteners Have No Effect on Gastric Emptying, Glucagon-Like Peptide-1, or Glycemia After Oral Glucose in Healthy Humans

Intestinal exposure to glucose stimulates the release of glucagon-like peptide-1 (GLP-1), slows subsequent gastric emptying, and reduces appetite. These responses are signaled, at least in part, by intestinal "sweet taste receptors" (STRs), including taste receptor type 1 members 2 and 3 (T1R2, T1R3), and their cellular signaling partners α-gustducin and transient receptor potential cation channel subfamily M member 5 (TRPM5) (1). A recent study by Brown et al. (2) in healthy humans reported that oral ingestion of "diet soda," containing both sucralose (46 mg) and acesulfame potassium (AceK) (26 mg), augmented GLP-1 release by more than one-third after an oral glucose load given 10 min later compared with carbonated water, suggesting a potential synergy between artificial sweeteners and glucose in stimulating GLP-1 secretion. The design of that study was, however, suboptimal, as the diet soda contained a number of substances (including caramel color, gum acacia, natural flavors, citric acid, potassium benzoate, phosphoric acid, and potassium citrate) that were not controlled for. Therefore, we evaluated whether oral administration of sucralose and AceK in doses comparable with those used by Brown et al. (2) would augment the GLP-1 response to oral glucose and modulate gastric emptying or glycemia in healthy humans.

Ten healthy males (mean age 33.6 ± 5.9 years; BMI: 25.5 ± 1.0 kg/m^2) were studied on four occasions each, separated by ≥3 days, in single-blinded randomized fashion. Informed consent and ethics approval were obtained. After an overnight fast, each subject consumed either 240 mL water alone or equivalently sweetened with *1*) 52 mg sucralose, *2*) 200 mg AceK, or *3*) 46 mg sucralose plus 26 mg AceK (3). Ten minutes later, each drank 75 g of glucose, made up to 300 mL with water, and containing 150 mg ^{13}C-acetate. Blood glucose (glucometer), plasma insulin (ELISA), total GLP-1 (radioimmunoassay), and gastric emptying (breath test) were evaluated over 240 min.

Blood glucose, plasma insulin, and total GLP-1 concentrations did not change after either water or sweetened drinks, prior to glucose ingestion, but all increased after oral glucose ($P < 0.001$ for each), without any difference between the 4 days (Fig. 1*A*–*C*). Neither the $^{13}CO_2$:$^{12}CO_2$ ratio nor the half-emptying time (T_{50}) differed between the 4 days (Fig. 1*D* and *E*).

These observations differ from those of Brown et al. (2), although the doses of sucralose and AceK and the load and timing of the subsequent glucose drink were identical in our study. It is unclear whether other components of diet soda that were not controlled for by Brown et al. may have had the capacity to stimulate GLP-1 secretion. Our findings are, however, consistent with previous reports that sucralose or AceK alone has no effect on GLP-1 secretion, insulin, or blood glucose concentrations (3,4) and our observations that sucralose had no effect on GLP-1 secretion or the glycemic response to intraduodenal glucose in healthy humans (5). That the STR antagonist, lactisole, attenuates glucose-stimulated GLP-1 secretion suggests that activation of STRs is necessary, but not sufficient, to stimulate L-cell secretion (1). In conclusion, sucralose and AceK, either alone or in combination, have no acute effect on gastric emptying, GLP-1, or glycemic responses after oral glucose in healthy humans.

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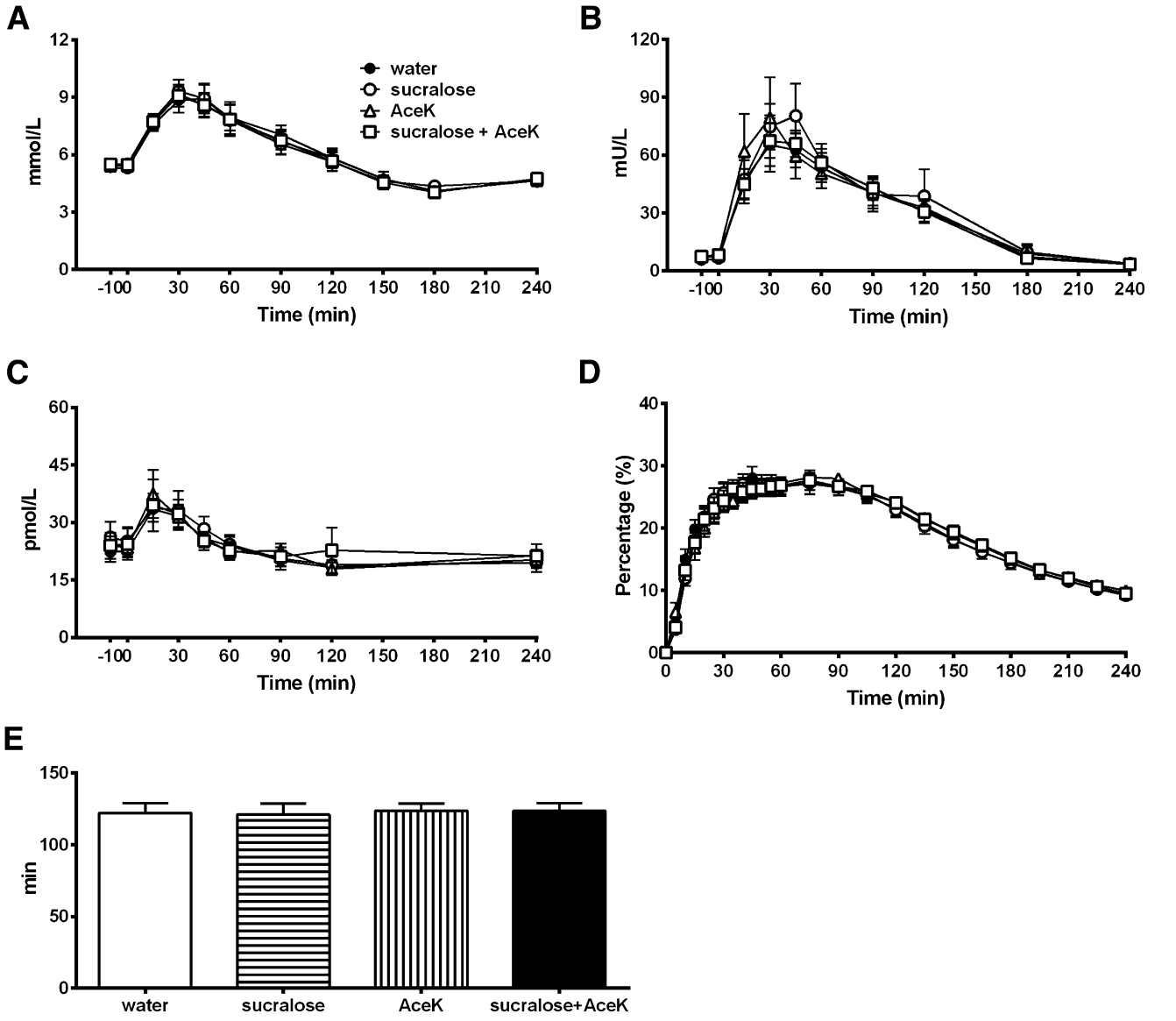

Figure 1—*Effects of ingestion of either water or artificial sweeteners (sucralose, AceK, or sucralose plus AceK) (at* t *= −10 min) on* (A) *blood glucose,* (B) *plasma insulin,* (C) *GLP-1,* (D) $^{13}CO_2$*-to-*$^{12}CO_2$ *ratio, and* (E) T_{50} *in response to 75-g oral glucose (at* t *= 0 min) in healthy humans* (n *= 10). Data are means ± SEM. The area under the curves for blood glucose, plasma insulin,* $^{13}CO_2$*-to-*$^{12}CO_2$ *ratio, and* T_{50} *did not differ between the 4 study days before and after 75-g oral glucose (one-factor repeated-measures ANOVA). There was a time effect* ($P < 0.001$) *but not a treatment effect or treatment × time interaction for blood glucose, plasma insulin, and* $^{13}CO_2$*-to-*$^{12}CO_2$ *ratio (two-factor repeated-measures ANOVA with treatment and time as factors).*

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