

## Effects of artificial sweeteners on glucagon-like peptide 1 secretion in GLUTag cells, an *in vitro* model of enteroendocrine cells

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The effects of artificial sweeteners (AS) on the peptide hormone-producing enteroendocrine cells (EEC) of the gastrointestinal tract are controversial (contradictory studies in humans, animals and cells)<sup>(1)</sup>. Recently, sucralose, a highly potent AS, has been shown to induce secretion of the insulin regulating and blood glucose lowering hormone, glucagon-like peptide 1 (GLP-1), from intestinal *in vitro* models<sup>(2)</sup>. It is suggested that it may be interacting with the sweet taste-receptors found on EECs<sup>(3)</sup>. However the effects of other commonly used AS in the UK, such as aspartame, acesulfame-k and Candere<sup>®</sup> (1.4 % aspartame; 0.95 % acesulfame-k) have not been investigated. The aim of the present study was to assess the effects of these AS on GLP-1 secretion in GLUTag cells (mouse EEC line).

GLUTag cells were incubated with test reagents for 2 hours at 37° C and the supernatant collected. GLP-1 was measured from the supernatant using a GLP-1 (Active) ELISA assay (EMD Millipore<sup>®</sup>, UK). Data is presented as means and standard deviation.

At dietary relevant doses (0.25-5 mM) the individual AS, aspartame and acesulfame-k, and the AS mixture, Candere<sup>®</sup> significantly induced GLP-1 secretion in GLUTag cells when compared to baseline (except for 0.25 mM acesulfame-k) and values were similar to glucose-induced GLP-1 secretion (table 1). Cells incubated in a combination of Candere<sup>®</sup> and glucose (0.4 mM and 5 mM) showed the highest secretion of GLP-1 (table 1); indicating a potential synergistic effect of AS and other nutrients in EEC function. In conclusion, our *in vitro* data suggests certain AS given alone and in combination with glucose may result in a GLP-1 response.

**Table 1.** Values are means (n = 6; different passage numbers). Mean values were significantly different compared to baseline (ANOVA\* or Student's T test□); \*□P < 0.05; a: Candere<sup>®</sup> dose = 0.4 mM aspartame and 0.4 mM acesulfame-k.

Test Reagents mM	Glucose GLP-1(pM)		Aspartame GLP-1(pM)		Acesulfame-K GLP-1(pM)		Candere <sup>®</sup> a GLP-1(pM)		Candere <sup>®</sup> a + 0.4 mM Glucose GLP-1(pM)		Candere <sup>®</sup> a + 5 mM Glucose GLP-1(pM)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0 (baseline)	86	13	86	13	86	13	86	13	86	13	86	13
0.25	123*	16	113*	13	92	15	–	–	–	–	–	–
0.4	134*	17	102*	18	131*	18	122□	8	180□	42	203□	43
2.5	165*	35	142*	15	116*	12	–	–	–	–	–	–
5	145*	20	147*	36	119*	31	–	–	–	–	–	–

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