

A cholecystokinin receptor agonist (CCK-8) induces adiponectin production in rat white adipose tissue

Adrián Plaza, Beatriz Merino, Nuria Del Olmo, and Mariano Ruiz-Gayo

Departamento de Ciencias Farmacéuticas y de la Salud. Facultad de Farmacia. Universidad CEU-San Pablo. Madrid, Spain.

Author for correspondence: Mariano Ruiz-Gayo
Departamento de Ciencias Farmacéuticas y de la Salud
Facultad de Farmacia. Universidad CEU-San Pablo
Campus de Montepíncipe. Alcorcón
28925 Madrid, Spain
e-mail: ruigayo@ceu.es
Tel: +34 913 724 700

Short title: Cholecystokinin promotes adiponectin production

Disclosure statement: The authors have nothing to disclose

Funding: Ministerio de Economía y Competitividad (BFU2012-35353, BFU2016-78556-R), European Regional Development Fund, and Fundación Universitaria San Pablo-CEU. A.P. is supported by a grant from Ministerio de Economía y Competitividad, Spain (BES-2013-063773).

Table 1.-Effect of acute and chronic CCK-8 on plasma parameters. Acute treatment with a single dose of CCK-8 (10µg/kg) had no effect on plasma levels of glucose, triglycerides (TG), non-esterified fatty acids (NEFA), insulin, leptin and total cholecystokinin immunoreactivity (CCK). Chronic CCK-8 treatment had no effect on plasma glucose and CCK, but reduced TG, NEFA insulin, and leptin levels.

	Acute treatment		Chronic treatment	
	Saline	CCK-8 (10 µg/kg)	Saline	CCK-8 (10 µg/kg)
Glucose (mg/dl)	110.5±3.4	110.8±2.3	101.9±4.0	90.9±2.6
TG (mg/dl)	159.6±25.7	116.6±20.8	152.6±12.7	114.4±10.3*
NEFA (mg/dl)	43.4±5.1	35.3±3.4	37.8±2.4	31.9±1.2*
Insulin (ng/ml)	0.77±0.13	0.83±0.18	1.85±0.24	0.92±0.14*
Leptin (ng/ml)	2.3±0.5	4.1±1.2	0.87±0.1	0.26±0.1*
CCK (ng/ml)	0.77±0.10	0.74±0.09	0.47±0.01	0.53±0.06

Values are means ± S.E.M. (n=6). *P<0.05 compared to their respective saline control groups (Newman Keuls' test).

This table has been already published in Plaza et al. 2018 (Plaza A, Merino B, Cano V, Domínguez G, Pérez-Castells J, Fernández-Alfonso MS, Sengenès C, Chowen JA & Ruiz-Gayo M 2018 Cholecystokinin is involved in triglyceride fatty acid uptake by rat adipose tissue. *Journal of Endocrinology* 236 137-150.

Figure 1. Effect of CCK-8 on adiponectin production in subcutaneous pre-adipocytes.

Two-way ANOVA revealed an effect of pharmacological treatment ($F_{(1,24)}=4.822$; $P<0.05$) and time ($F_{(2,24)}=13.59$; $P<0.05$), without significant interaction CCK-8 x time. One-way ANOVA indicated only an effect of CCK-8 (ANOVA-1; $F_{(2,12)}=8.739$, $P<0.05$), that was significant 1h after CCK-8 withdrawal ($P<0.05$). In contrast, adiponectin content remained unchanged during the assay in saline-treated cells (ANOVA-1; $F_{(2,12)}=3.059$, $P=0.084$).

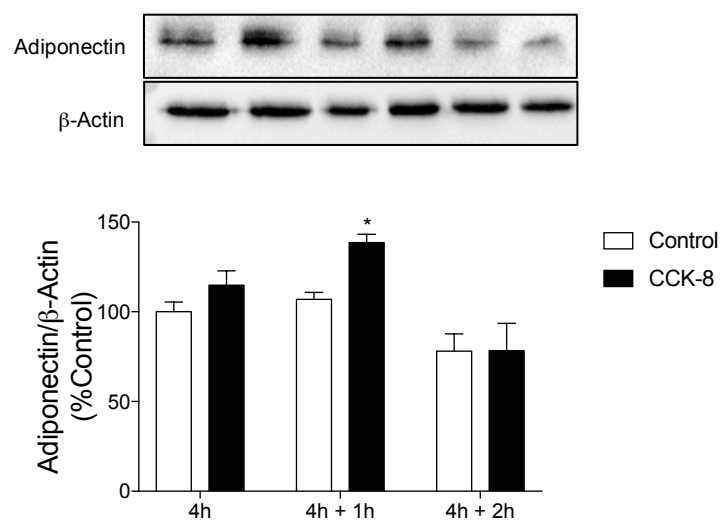


Figure 2: Effect of CCK-8 on the expression of IL1b, IL6, IL10 and TNF α

Acute treatment with CCK-8 suppressed the expression of *Il6* ($t_{(8)}=3.277$; $P<0.05$) and up-regulated *Il10* expression ($t_{(8)}=2.983$; $P<0.05$) in Vis-WAT, whereas chronic CCK-8 repressed the *Il6*, *Il1b* and *Tnfa* expression ($t_{(10)}=2.795$, $P<0.05$; $t_{(10)}=2.957$, $P<0.05$ and $t_{(10)}=2.535$, $P<0.05$, respectively). Regarding Sc-WAT, acute treatment only reduced the expression of *Il1b* ($t_{(8)}=3.039$; $P<0.05$) while chronic treatment reduced the expression of *Il6*, *Il1b* and *Tnfa* ($t_{(10)}=9.312$, $P<0.05$; $t_{(10)}=3.028$, $P<0.05$ and $t_{(10)}=3.705$, $P<0.05$, respectively).

