A Cholecystokinin Receptor
Pharmacodynamic Models

Yields refer to raw materials and are not optimized.

Chromatography was performed on silica gel 60 (40-63 pm).

NMR spectra were recorded in deuterated solvents at 200, 300 or 400 MHz (DRX 200, DRX 300, AMX 400, and Bruker.

Synthesis

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New peptide derivatives are clearly available Cholecystokinin Receptor Agonists:

Supporting Information:
The chromatographic data collector was connected to the HPLC-NMR flow-probe via an inert polyethylene capillary (0.25 mm i.D.). The chromatographic data collector (BPSL-12, Bruker, Rheinstetten, Germany) and the chromatography was controlled by Bruker HySS software. The BPSL-12

A Bruker AV 400, equipped with a 4.7 mm NOE probe, was used for the 2D NOE-HETCOR experiments. The NMR system was connected to the HPLC system used for the directly coupled HPLC-NMR experiments.

Chromatography

Under N₂ gas at 40°C, 250 μl of mobile phase was then added to the evaporated sample and analyzed by LC-MS or LC-NMR.

Extract: 1000 μl MeOH, the 3 samples (LC-MS) of 5 samples (LC-NMR) at each time point were pooled and the solvent evaporated.

EtOH: 1000 μl MeOH + 1000 μl NaHPO₄ (pH 7.4), Sample volume: 1000 μl, Washing: 2 X

Spec column. Spec (C₂) SPE cartridges. Activation: 1000 μl MeOH + 1000 μl NaHPO₄ (pH 7.4). Sample volume: 1000 μl, Washing: 2 X

MS method

Microsomal incubations were terminated by applying the samples to solid phase extraction (SPE).

Buffer up to 1000 μl

protein content: 1 mg/ml, NCE concentration: 25 mM, incubation conditions: 37°C, UDP-GA: 1 mM, NADPH: 1 mM, KCl2PO₄ (pH 7.4)

Metabolite profile

Microsomal incubations were terminated by applying 150 μl of MeCN. The metabolitic profiles and metabolite profiles were determined by LC-MS.

Incubations were performed in a 96 well plate format, and a packet of lyophilized material was applied for incubation and lyophilization.

Incubation conditions: 37°C, UDP-GA: 1 mM, NADPH: 1 mM, KCl2PO₄ (pH 7.4). Incubation up to 150 μl. All concentrations were expressed at 90 min, total incubation volume: 150 μl.

Incubation with fat liver microsomes

Incubations were performed in a 96 well plate format, and a packet of lyophilized material was applied for incubation and lyophilization.

Metabolite profile

Microsomal incubations were terminated by applying 150 μl of MeCN.

Incubation profile and metabolite profiles were determined by LC-MS.

Incubation conditions: 37°C, UDP-GA: 1 mM, NADPH: 1 mM, KCl2PO₄ (pH 7.4). Incubation up to 150 μl. All concentrations were expressed at 90 min, total incubation volume: 150 μl.

B. Effect on blood glucose in ob/ob mice

Minimizing the variance of the two basal values.

Responses of &(

The results were expressed as data values calculated as the value obtained 10 min after injection administration of the compound to represent average basal values and again 10 min after administration of & data (mean for peak...