Camicinal (GSK962040) is a small molecule, selective motilin receptor agonist with pEC50 of 7.9.

IC₅₀ & Target

pEC5₀: 7.9 (Motilin Receptor)[1].

In Vitro

Camicinal (GSK962040) had no significant activity at a range of other receptors (including ghrelin), ion channels and enzymes. In rabbit gastric antrum, Camicinal (GSK962040) 300 nmol L⁻¹ 10 μmol L⁻¹ caused a prolonged facilitation of the amplitude of cholinergically mediated contractions, to a maximum of 248 ± 47% at 3 μmol L⁻¹. The pEC5₀ values for motilin, erythromycin and Camicinal (GSK962040) were, respectively, 10.4 ± 0.01 (n = 770), 7.3 ± 0.29 (n = 4) and 7.9 ± 0.09 (n = 17) [1]. Camicinal (GSK962040) activated the dog motilin receptor (pEC5₀ 5.79; intrinsic activity 0.72, compared with [Nle13]-motilin) [2]. Camicinal (GSK962040) was preferred because its initial IC₅₀ values at CYP3A4 were significantly higher than our preferred threshold of 10 μM [3].

In Vivo

Camicinal (GSK962040) (5 mg free base kg⁻¹) also produced an increase in total faecal weight over the 2-h postdose period (21.2 ± 4.5 g; P < 0.05) [1]. Camicinal (GSK962040) induced phasic contractions, the duration of which was
dose-related (48 and 173 min for 3 and 6 mg kg⁻¹), driven by mean plasma concentrations >1.14 μmol L⁻¹. After the effects of GSK962040 faded, migrating motor complex (MMC) activity returned. Migrating motor complex restoration was unaffected by 3 mg kg⁻¹ GSK962040 but at 6 mg kg⁻¹, MMCs returned 253 min after dosing, compared with 101 min after saline (n = 5 each) [2]. The oral bioavailability (Fpo) of Camicinal (GSK962040) was found to be 48% [13]. Camicinal (GSK962040) shows a long lasting effect (T1/2) 46.9 (5.0 min at 3 μM) when compared with the short-lived effect of [Nle13]motilin (T1/2) 11.4 (1.5 min at 0.3 μM) [3]. Camicinal (GSK962040) strongly facilitated cholinergic activity in the antrum, with lower activity in fundus and small intestine only [4].

REFERENCES