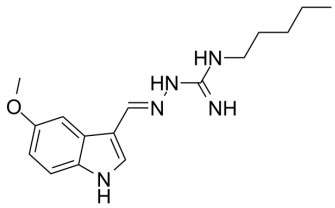
Tegaserod

Cat. No.:	HY-14153
CAS No.:	145158-71-0
Molecular Formula:	$C_{16}H_{23}N_5O$
Molecular Weight:	301.39
Target:	5-HT Receptor; Apoptosis
Pathway:	GPCR/G Protein; Neuronal Signaling; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (165.90 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3180 mL	16.5898 mL	33.1796 mL
	5 mM	0.6636 mL	3.3180 mL	6.6359 mL
	10 mM	0.3318 mL	1.6590 mL	3.3180 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5 mg/mL (16.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (16.59 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (16.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tegaserod is an orally active serotonin receptor 4 (HTR4; 5-HT_4R) agonist and a 5-HT_{2B} receptor antagonist. Tegaserod has pK_is of 7.5, 8.4 and 7.0 for human recombinant 5-HT_{2A}, 5-HT_{2B} and 5-HT_{2C} receptors, respectively. Tegaserod causes tumor cell apoptosis, blunts PI3K/Akt/mTOR signaling and decreases S6 phosphorylation. Tegaserod has anti-tumor activity and has the potential for irritable bowel syndrome (IBS) research[1][2][3].

IC_{50} & Target

5-HT_4 Receptor

In Vitro

Tegaserod (3-5 μM; 24-72 h) causes a significant time and dose-dependent increase in apoptosis[1].
Tegaserod (3-5 μM; 8-18 h) decreases phosphorylation of the kinase directly upstream of S6, p70 S6 at Thr^{421}/Ser^{424}[1].
Tegaserod (0.1-3 μM; 24h) inhibits 5-HT-mediated contraction of the rat isolated stomach fundus potently (pA_2=8.3), consistent with 5-HT_{2B} receptor antagonist activity[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	A375, RPMI-7951 (RPMI), SH4, B16F10, MeWo and MEL-JUSO
Concentration:	3, 5 μM
Incubation Time:	24, 48, 72 h
Result:	There was a significant time and dose-dependent increase in apoptosis in all cell lines.

Western Blot Analysis[1]

Cell Line:	RPMI, SH4 and B16F10 cells
Concentration:	3, 5 μM
Incubation Time:	8 or 18 h
Result:	Decreased phosphorylation of the kinase directly upstream of S6, p70 S6 at Thr^{421}/Ser^{424}.

In Vivo

Tegaserod (5 mg/kg/day; ip; for five consecutive days) delays tumor growth, reduces metastases, increases survival and suppresses p-S6 in vivo[1].
Tegaserod (0.1-2.0 mg/kg; IP 15 min prior to gastric loading) significantly accelerates the gastric emptying rate of glucose in db/db mice, reducing the fraction of the meal remaining in the stomach at 30 min by 80% with 0.1mg/kg[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 J mice were subcutaneously injected with B16F10 cells[1]
Dosage:	5 mg/kg
Administration:	Administered intraperitoneally (i.p.) daily for five consecutive days
Result:	Treatment significantly decreased tumor growth and resulted in only slight decreases in weight following treatment.

Animal Model:	Female C57BLKS/J db/db mice[2]
Dosage:	0.1, 0.5, 1.0, 2.0 mg/kg
Administration:	IP 15 min prior to gastric loading
Result:	Produced a dramatic decrease in the fraction of the meal remaining in the stomach for doses as low as 0.1 mg/kg (0.1 mg/kg). Accelerated gastric emptying, with a reduction of nearly 80% in the fraction remaining at 30 min ($P < 0.0001$) (0.1 mg/kg). Induced a significant decrease in the gastric emptying rate as the amount of the meal remaining at 30 min was significantly greater (2.0 mg/kg). Resulted in inhibition of tegaserod-induced increased gastric emptying (0.1 mg/kg).

REFERENCES

[1]. M D Crowell, et al. The effects of tegaserod, a 5-HT receptor agonist, on gastric emptying in a murine model of diabetes mellitus. Neurogastroenterol Motil. 2005 Oct;17(5):738-43.

[2]. D T Beattie, et al. The 5-HT4 receptor agonist, tegaserod, is a potent 5-HT2B receptor antagonist in vitro and in vivo. Br J Pharmacol. 2004 Nov;143(5):549-60.

[3]. Wei Liu, et al. Repurposing the serotonin agonist Tegaserod as an anticancer agent in melanoma: molecular mechanisms and clinical implications. J Exp Clin Cancer Res. 2020 Feb 21;39(1):38.

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