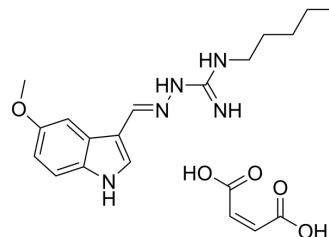


Tegaserod maleate

Cat. No.:	HY-14153A
CAS No.:	189188-57-6
Molecular Formula:	C ₂₀ H ₂₇ N ₅ O ₅
Molecular Weight:	417.46
Target:	5-HT Receptor; Apoptosis
Pathway:	GPCR/G Protein; Neuronal Signaling; Apoptosis
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 35 mg/mL (83.84 mM)
 H₂O : < 0.1 mg/mL (insoluble)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.3954 mL	11.9772 mL	23.9544 mL
	5 mM	0.4791 mL	2.3954 mL	4.7909 mL
	10 mM	0.2395 mL	1.1977 mL	2.3954 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.99 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tegaserod maleate (SDZ-HTF-919) is an orally active serotonin receptor 4 (HTR₄; 5-HT_{4R}) agonist and a 5-HT_{2B} receptor antagonist. Tegaserod maleate 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 maleate causes tumor cell apoptosis, blunts PI3K/Akt/mTOR signaling and decreases S6 phosphorylation. Tegaserod maleate has anti-tumor activity and has the potential for irritable bowel syndrome (IBS) research^{[1][2][3]}.

IC₅₀ & Target

5-HT ₄ Receptor (Agonist)	5-HT _{2B} Receptor (Antagonist)
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In Vitro

Tegaserod maleate (SDZ-HTF-919; 3-5 μ M; 24-72 h) causes a significant time and dose-dependent increase in apoptosis^[1]. Tegaserod maleate (3-5 μ M; 8-18 h) decreases phosphorylation of the kinase directly upstream of S6, p70 S6 at Thr⁴²¹/Ser⁴²⁴ [1].

Tegaserod maleate (0.1-3 μ M; 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 μ M
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 μ M
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 maleate (SDZ-HTF-919; 5 mg/kg/day; ip; for five consecutive days) delays tumor growth, reduces metastases, increases survival and suppresses p-S6 in vivo^[1].

Tegaserod maleate (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]. 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.
- [2]. 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.
- [3]. D T Beattie, et al. The 5-HT₄ receptor agonist, tegaserod, is a potent 5-HT_{2B} receptor antagonist in vitro and in vivo. *Br J Pharmacol.* 2004 Nov;143(5):549-60.
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Caution: Product has not been fully validated for medical applications. For research use only.

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