Tegaserod maleate

Cat. No.: HY-14153A

CAS No.: 189188-57-6

Molecular Formula: $C_{20}H_{27}N_5O_5$

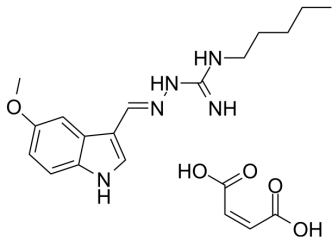
Molecular Weight: 417.46

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)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	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

1. 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
2. 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].

IC_{50} & Target		
	5-HT_4 Receptor (Agonist)	5-HT_{2B} Receptor (Antagonist)

In Vitro

Tegaserod maleate (SDZ-HTF-919; 3-5 μM; 24-72 h) causes a significant time and dose-dependent increase in apoptosis[1].
Tegaserod maleate (3-5 μM; 8-18 h) decreases phosphorylation of the kinase directly upstream of S6, p70 S6 at Thr^{421}/Ser^{424} [1].

Tegaserod maleate (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 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-HT2B receptor antagonist in vitro and in vivo. Br J Pharmacol. 2004 Nov;143(5):549-60.

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