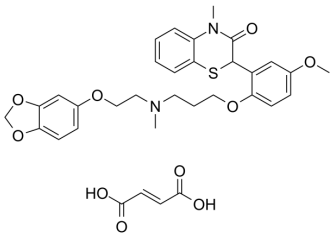
Semotiadil recemate fumarate

Cat. No.:	HY-U00026
CAS No.:	123388-25-0
Molecular Formula:	$C_{33}H_{36}N_2O_{10}S$
Molecular Weight:	652.71
Target:	Calcium Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Semotiadil recemate fumarate is the recemate of Semotiadil fumarate. Semotiadil fumarate is a novel vasoselective Ca^{2+} channel antagonist.
IC_{50} & Target	Ca^{2+} channel[1]
In Vitro	Semotiadil in a concentration of 1 μM produces an inhibition of 12.4±9.7% and in a concentration of 10 μM an inhibition of 25±11.0%[1]. Effects of Semotiadil on the voltage-dependent Ca current (ICa) are investigated in dispersed smooth muscle cells of the rabbit portal vein. At a holding potential of -100 mV, Semotiadil (> or =0.1 μM; dissolved in DMSO) inhibits the ICa in a concentration-dependent manner (IC_{50}=2.0 μM). At a holding potential of -80 mV or -60 mV, the concentration-inhibition curve observed in the presence of Semotiadil is shifted to the left compared with that observed at -100 mV; and Semotiadil shifts the voltage-dependent inactivation curve to the left. The curve for the decay of ICa is fitted with two time constants. Semotiadil (<1 μM) reduces the slow but not the fast time constant. The curve for the recovery from ICa inactivation also consisted of two time constants, and Semotiadil (1 microM) prolongs the slow recovery. Semotiadil dissolved in deionized water more potently inhibits ICa than Semotiadil dissolved in DMSO[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Semotiadil fumarate, a novel benzothiazine calcium antagonist, is given alone or in combination with either Enalapril or trichlormethiazide to conscious, spontaneously hypertensive, rats daily for 2 weeks. When given alone, the antihypertensive effects of Semotiadil (10 mg/kg, p.o.) and Enalapril (5 mg/kg, p.o.) first became apparent after the 3rd dose and thereafter the effects appeared to develop daily although this effect had waned by the time of the next dose. These results indicate that combined daily dosing of Semotiadil, especially with Enalapril, each at relatively low doses may be able to control hypertension in a continuous manner[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Semotiadil is dissolved in DMSO. Appropriate dilutions are made freshly for each experiment[1]. The experiments are performed in an experimental bathing chamber (volume 1 ml) mounted on the stage of an inverted microscope. The cells are superfused with warm (37°C) extracellular solution at the rate of 3 mL/min. The solution could be exchanged for an identical solution containing the substance under study without any significant alteration either in the flow rate or in the temperature of the superfusing fluid. A complete exchange of the bath solution was achieved within 1 min

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Animal Administration [3]	Rats[3] Semotiadil fumarate is given alone or in combination with either Enalapril or trichlormethiazide to conscious, spontaneously hypertensive, rats daily for 2 weeks. Systolic blood pressure and heart rate are recorded 24 h before the start of the regimen and then every 2 and 24 h after the 1st, 3rd, 7th, 10th and 14th doses. When given alone, the antihypertensive effects of Semotiadil (10 mg/kg, p.o.) and Enalapril (5 mg/kg, p.o.) first became apparent after the 3rd dose and thereafter the effects appeared to develop daily although this effect had waned by the time of the next dose. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Koidl B, et al. A novel benzothiazine Ca^{2+} channel antagonist, Semotiadil, inhibits cardiac L-type Ca^{2+} currents. Eur J Pharmacol. 1997 Mar 19;322(2-3):243-7.

[2]. Teramoto N. Mechanisms of the inhibitory action of Semotiadil fumarate, a novel Ca antagonist, on the voltage-dependent Ca current in smooth muscle cells of the rabbit portal vein. Jpn J Pharmacol. 1993 Mar;61(3):183-95.

[3]. Ichikawa M, et al. Antihypertensive effects of a novel calcium antagonist, Semotiadil fumarate (SD-3211), alone and in combination with Enalapril or trichlormethiazide in spontaneously hypertensive rats. Biol Pharm Bull. 1994 Nov;17(11):1513-5.

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