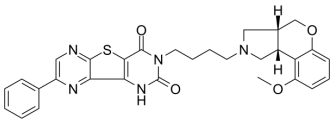
Fiduxosin

Cat. No.:	HY-U00399
CAS No.:	208993-54-8
Molecular Formula:	$C_{30}H_{29}N_5O_4S$
Molecular Weight:	555.65
Target:	Adrenergic Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Fiduxosin is a potent α1-adrenoceptor antagonist, with K_i of 0.160 nM, 24.9 nM, and 0.920 nM for α1a-, α1b-, and α1d-adrenoceptors, respectively.
IC_{50} & Target	Ki: 0.16 nM (α1a-adrenoceptor), 24.9 nM (α1b- adrenoceptor), 0.92 nM (α1d-adrenoceptor), 92 nM (Human α2a-adrenoceptor), 22 nM (Human α2c-adrenoceptor), 21 nM (Rat α2b-adrenoceptor), 29 nM (Rat 5HT1A receptor)[1]
In Vitro	Fiduxosin displays low affinity for other adrenoceptors, including cloned human α2a- (92 nM) and α2c-adrenoceptors (22 nM) and rat neonatal lung α2b-adrenoceptors (21 nM), in addition to β-adrenoceptors (2-5 μM). Fiduxosin also has low affinity for 5HT1A receptors in rat cortex (29 nM) compared with its affinity at α1a-adrenoceptors (0.16 nM). Fiduxosin antagonizes competitively PE-induced responses with a pA2 value of 7.58, in the rabbit urethra[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Fiduxosin (30, 100, and 300 μg/kg, i.v.) antagonizes IUP responses to i.v. EPI in anesthetized dogs. Fiduxosin (178, 592, and 1780 μg/kg, i.v.) elicits transient effects on blood pressure, with no effect of the lowest dose on MAP in spontaneously hypertensive rats (SHR). Fiduxosin (3 μmol/kg or 1780 μg/kg i.v.) slightly reduces MAP, but head-up tilt causes further diminution of MAP at only the 15-min observation with minimal additional changes in MAP at times ≥30 min postdosing in SHR[1]. Fiduxosin (0.1, 0.3, 1.0, and 3.0 mg/kg p.o.) blocks prostatic intraurethral pressure (IUP) responses to a greater extent than MAP responses. The IUP ED_{50} values of fiduxosin is 0.24 mg/kg[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Male beagle dogs (>2 years old, 12-15 kg) are chronically instrumented for the continuous measurement of arterial blood pressure by implanting a telemetry transducer/transmitter (TA11PA-C40) into a carotid artery. On test day, dogs are placed in sling restraints and an Abbocath-T i.v. catheter (18-G) is inserted into a cephalic vein for blood sampling and for the administration of agonist. Prostatic intraurethral pressure (IUP) is measured using a transurethral 7F Swan-Ganz balloon catheter (41224-01). Dose responses of the intraurethral and arterial pressor effects of 8, 16, and 32 μg/kg i.v. phenylephrine (PE) are obtained before and at various time points after a single p.o. dose of an antagonist. Fiduxosin is dissolved in a vehicle of 20% ethanol, 30% propylene glycol, and 50% water. Terazosin and tamsulosin are dissolved in water. All antagonists are given by gavage in a volume of 1 mL/kg. PE is dissolved in saline and administered in a volume of 0.1 mL/kg. The increase in IUP or mean arterial pressure (MAP) caused by PE is allowed to return to baseline before the next dose is

administered.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Hancock AA, et al. Preclinical pharmacology of fiduxosin, a novel alpha(1)-adrenoceptor antagonist with uroselective properties. J Pharmacol Exp Ther. 2002 Feb;300(2):478-86.

[2]. Brune ME, et al. Effect of fiduxosin, an antagonist selective for alpha(1A)- and alpha(1D)-adrenoceptors, on intraurethral and arterial pressure responses in conscious dogs. J Pharmacol Exp Ther. 2002 Feb;300(2):487-94.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA