Product Data Sheet

Product Name: McN5691 (RWJ26240)
Cat. No.: GC32636

Chemical Properties

Cas. No.	99254-95-2		
SMILES	COC1=C(OC)C=CC(CCN(C)C(C)CCC(C=C(OC)C=C2)=C2C#CC3=CC=CC=C3)=C1		
Formula	$C_{30}H_{35}NO_3$	M.Wt	457.6
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	McN5691 (RWJ26240)		

Protocol

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Address: 10292 Central Ave. #205, Montclair, CA, USA

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Animal experiment:

Dogs[2]14C- McN5691 is administered by gavage to male and female beagle dogs (3 of each sex, weight 10.2-12.8 kg) as a single 6 mg/kg (as free base in corn oil) dose. Plasma samples are obtained for 24 hours after dosing. Urine and fecal samples are collected over a 7-day period. Each collected sample is assayed for total radioactivity and analyzed by TLC and HPLC.Rats[3]Studies are conducted in male SHR and control normotensive Wistar-Kyoto (WKY) rats. All animals are housed in constant temperature and environment facilities and given standard lab chow and water ad libitum. Four separate studies are conducted using conscious, age-matched animals:(a) SHR receiving McN5691 as a hydrochloride salt (McN5691) (n=8, body weight=361±7 g); (b) SHR receiving vehicle (VH) (n= 8, bodyweight=381±5g); (C) WKY receiving McN5691(n=9, body weight=355±7 g); and (d) WKY receiving VH (n=6, body weight=342±7g). McN5691 or VH alone is administered i.v. (right jugular vein) as a 15 min continuous infusion for each dose. Each animal receives three doses of McN5691 (0.3, 1.0 and 3.0 mg/kg) in a cumulative fashion or VH infused at an equal rate (0.0408 mL/min).

References:

[1]. Flaim SF, et al. Structurally novel antihypertensive compound, McN-5691, is a calcium channel blocker in vascular smooth muscle. J Pharmacol Exp Ther. 1991 Jan;256(1):279-88.
[2]. Wu WN, et

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al. Excretion and metabolism of the antihypertensive agent, RWJ-26240 (McN-5691) in dogs. Drug Metab Dispos. 1998 Feb;26(2):115-25.
[3]. Flaim SF, et al. Effects of the novel calcium channel blocker, McN-5691, on cardiocirculatory dynamics and cardiac output distribution in conscious spontaneously hypertensive rat. J Cardiovasc Pharmacol. 1988 Apr;11(4):489-500.

Background

McN5691 is a voltage-sensitive calcium channel blocker.

McN5691 (1 and 10 μM) prevents 60 mM KCl-induced contraction and calcium uptake and causes concentration-dependent relaxation (EC50=190 μM) of 30 mM KCl-contracted aortic rings. At or below 10 μM, McN5691 (McN-5691) has no effects on basal tone or calcium uptake (45Ca) in isolated rings of rabbit thoracic aorta. McN5691 causes complete high affinity inhibition (Kd=39.5 nM) of specific diltiazem binding to the benzothiazepine receptor

on the voltage-sensitive calcium channel in skeletal muscle microsomal membranes. In contrast to diltiazem, McN5691 inhibits specific dihydropyridine receptor binding, but the effect is biphasic with high (Kd=4.7 nM) and low (Kd=919.8 nM) affinity components. McN5691 inhibits norepinephrine (NE)-induced contraction (10 μM) and calcium uptake (1 and 10 μM) and causes concentration-dependent relaxation (EC50=159 μM) of 1 μM NE-contracted rings of rabbit thoracic aorta[1].

The excretion and metabolism of a 2-ethynylbenzenealkanamine analog, antihypertensive McN5691 (RWJ-26240), in beagle dogs is investigated. A total of 96.8% and 2.8% of the radioactive dose are excreted in feces and urine, respectively, during the 7 days after oral administration of 14C-McN5691. Of the radioactive dose, 96.8% and 2.8% is recovered in feces and urine, respectively, in the 7 days after oral administration of 14C-McN5691. More than 87% of the dose is excreted in feces during the 48 hours. McN5691 is extensively metabolized in dogs. Unchanged McN5691 is found in less than 0.1% and 19% of the dose in the 0-24 hour urine and 0-48 hour fecal extract, respectively, and 36% of the sample in the 4 hour plasma[2]. In the McN5691 (McN-5691) study, vascular resistances tend to be higher in spontaneously hypertensive rat (SHR) than in Wistar-Kyoto (WKY) but the differences are statistically significant only in the cerebellum and the midbrain[3].

[1]. Flaim SF, et al. Structurally novel antihypertensive compound, McN-5691, is a calcium channel blocker in vascular smooth muscle. J Pharmacol Exp Ther. 1991 Jan;256(1):279-88. [2]. Wu WN, et al. Excretion and metabolism of the antihypertensive agent, RWJ-26240 (McN-5691) in dogs. Drug Metab Dispos. 1998 Feb;26(2):115-25. [3]. Flaim SF, et al. Effects of the novel calcium channel blocker, McN-5691, on cardiocirculatory dynamics and cardiac output distribution in conscious spontaneously hypertensive rat. J Cardiovasc Pharmacol. 1988 Apr;11(4):489-500.

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