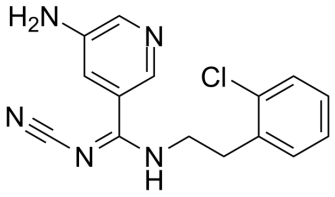
KRN4884

Cat. No.:	HY-U00201
CAS No.:	152802-84-1
Molecular Formula:	$C_{15}H_{14}ClN_5$
Molecular Weight:	299.76
Target:	Potassium Channel
Pathway:	Membrane Transporter/Ion Channel
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	KRN4884 is a K^+ channel opener. In the presence of intracellular ATP (1 mM), KRN4884 (0.1-3 μM) activates K_{ATP} channels in a concentration-dependent manner (EC_{50}=0.55 μM).
IC_{50} & Target	EC50: 0.55 μM (K_{ATP} channel)[1]
In Vitro	KRN4884 (0.3 μM) shifts the concentration-response relationship for ATP-induced K_{ATP} channel inhibition to the right and slightly upward direction without altering the slope. After either the spontaneous or Ca^{2+}-induced channel rundown, KRN4884 (1 and 3 μM) partially restores the K_{ATP} channel activity. Furthermore, the effect of KRN4884 is augmented by the presence of uridine 5′-diphosphate (3 mM). KRN4884 activates cardiac K_{ATP} channels through not only decreasing the sensitivity of the channel to ATP but also directly stimulating the opening of the channel. KRN4884 (0.3 and 3 μM) increases the outward current in a concentration-dependent manner, and the unitary current amplitudes are similar to that of K_{ATP} channels in the ATP-free solution[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The effects of KRN4884, a novel pyridinecarboxamidine type K_{ATP} channel opener, on serum triglyceride levels are investigated in Sprague-Dawley rats. Oral administration of KRN4884 (3 mg/kg) for 10 days causes a significant reduction in serum triglyceride levels, which is comparable to that of Clofibrate (160 mg/kg). Reduction in serum triglyceride levels by KRN4884 and Clofibrate are accompanied by a reduction in triglyceride levels both in chylomicron and in very low density lipoprotein. KRN4884 treatment does not affect serum concentrations of total cholesterol and phospholipid, but increases free fatty acid levels. Rats receiving KRN4884 exhibite an increase in lipoprotein lipase (LPL) activity both in adipose tissue and in skeletal muscle[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	KRN4884 is dissolved in DMSO as a 10 mM stock solution, and diluted in the bath solution. The final concentration of DMSO to which cells are exposed is less than 0.1%[1]. To quantitatively analyze the effect of KRN4884 or other compounds, channel activity is expressed as NP_oi. NP_oi is calculated by integrating a 5- to 15-s continuous current record during the steady effect of each drug. The concentration-response curve for KRN4884 is obtained by normalizing NP_oi to that obtained by superfusing with the ATP-free bath solution, and fit to a Hill equation[1].

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Animal Administration [2]	Rats[2] Five-week old male Sprague-Dawley (Crj; CD) rats are obtained and housed in a temperature-controlled environment with a 12 h daily light cycle with free access to water and chow (CE-2). At 6-weeks old, the animals are assigned to vehicle, Clofibrate (160 mg/kg) or KRN4884 (3 mg/kg) treatment groups. The drug is given daily, by gavage for 10 days at 2 mL/kg as a suspension in 0.5% (w/v) carboxymethyl cellulose. Systolic blood pressure is determined 1 h after administration on day 9 with the tail cu. method by use of a sphygmomanometer. Four hours after the final administration of the drug or vehicle on day 10, non-fasting blood is collected from an abdominal aorta of each rat under ether anaesthesia. Serum is provided for lipid analysis. Epididymal adipose tissue, thigh muscle, and liver are removed and weighed, then immediately immersed in liquid nitrogen and stored at -80°C until use. Epididymal adipose tissue and thigh muscle are used for determining lipoprotein lipase (LPL) activity and the liver is used for de- termining hepatic triglyceride lipase (HTGL) activity. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Shinbo A, et al. Activation of cardiac ATP-sensitive K+ channels by KRN4884, a novel K+ channel opener. J Pharmacol Exp Ther. 1997 Nov;283(2):770-7.

[2]. Yokoyama T, et al. Effects of KRN4884, a novel pyridinecarboxamidine type KATP channel opener, on serum triglyceride levels in rats. Br J Pharmacol. 1997 Apr;120(8):1471-6.

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