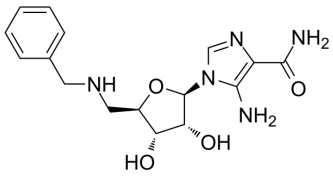
GP531

Cat. No.:	HY-U00116
CAS No.:	142344-87-4
Molecular Formula:	$C_{16}H_{21}N_5O_4$
Molecular Weight:	347.37
Target:	Adenosine Receptor
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (359.85 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8788 mL	14.3939 mL	28.7877 mL
	5 mM	0.5758 mL	2.8788 mL	5.7575 mL
	10 mM	0.2879 mL	1.4394 mL	2.8788 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: ≥ 2.08 mg/mL (5.99 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.99 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GP531 is a potent, second-generation adenosine regulating agent, is pharmacologically silent under basal conditions but increases localized endogenous adenosine during ischemia.

IC_{50} & Target

Adenosine Receptor[1]

In Vivo

Low-dose GP531 reduces infarct size by 34% compared with vehicle and reduces the extent of the anatomic no-reflow zone by 31% compared with vehicle. Infarct size and zone of no-reflow in the high dose are reduced by 22% and 16%,

respectively. GP531 does not affect hemodynamics or blood flow. GP531 is effective at the lower dose in reducing the severity of ischemic/reperfusion injury, without inducing the adverse hemodynamic effects associated with adenosine administration such as bradycardia and hypotension[1]. GP531 infusion has no effect on heart rate or mean aortic pressure but significantly decreases left ventricular end-diastolic pressure, end-diastolic volume, end-systolic volume and end-diastolic wall stress. GP531 significantly increases left ventricular EF, deceleration time of early mitral inflow velocity and the slope of end-systolic PVR without increasing MVO2[2].

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

PROTOCOL

Animal Administration [1]

Rabbits: Baseline hemodynamic parameters and temperature are obtained. The rabbits are randomized to 1 of 3 groups: a low dose of GP531, a high dose of GP 531, or vehicle (10% sodium metabisulfite). The low dose consists of a loading dose of 700 mg/kg given over 10 minutes starting at 12 minutes before coronary artery occlusion, followed by an infusion of 10 mg/kg per minute for the duration of the study. The high dose consists of a loading dose of 2100 mg/kg given over 10 minutes starting at 12 minutes before CAO followed by an infusion of 30 mg/kg per min for the duration of the study. All rabbits receive the same volume (12 mL over the duration of the study), so the concentrations are adjusted for body weight. The rabbits are then subjected to 30 minutes of coronary artery occlusion. The coronary artery is occluded by tightening the snare. Regional myocardial blood flow is measured during the ischemic period at 25 minutes of CAO[1].

Dog: Six dogs with intracoronary microembolizationinduced HF receive a constant intravenous infusion of GP531 (10 μg/kg/min) or vehicle (normal saline) for 6 h in random order 1 week apart. Hemodynamic measurements are made at baseline and at 1, 2, 3, 4, 5 and 6 h after initiating drug infusion. Myocardial oxygen consumption (MVO2) is measured at baseline and 4 and 6 h. LV pressure-volume relationship (PVR) is measured at baseline and 6 h[2].

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

REFERENCES

[1]. Hale SL, et al. Cardioprotection with adenosine-regulating agent, GP531: effects on no-reflow, infarct size, and blood flow following ischemia/ reperfusion in the rabbit. J Cardiovasc Pharmacol Ther. 2010 Mar;15(1):60-7.

[2]. Wang M, et al. Acute intravenous infusion of an adenosine regulating agent improves left ventricular function in dogs with advanced heart failure. Cardiovasc Drugs Ther. 2013 Dec;27(6):489-98.

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