GS967

Cat. No.: HY-12593
CAS No.: 1262618-39-2
Molecular Formula: C₁₄H₇F₆N₃O
Molecular Weight: 347.22
Target: Sodium Channel
Pathway: Membrane Transporter/Ion Channel
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: 50 mg/mL (144.00 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg</td>
<td>2.880 mL</td>
</tr>
<tr>
<td>5 mg</td>
<td>0.576 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.288 mL</td>
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</tbody>
</table>

Preparing Stock Solutions

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: 2.5 mg/mL (7.20 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.20 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
GS967 (GS-458967) is a potent, and selective inhibitor of cardiac late sodium current (late $I_{Na}$) with $IC_{50}$ values of 0.13 and 0.21 μM for ventricular myocytes and isolated hearts, respectively.

$IC_{50}$ & Target
$IC_{50}$: 0.13 μM (late $I_{Na}$, ventricular myocytes) and 0.21 μM (late $I_{Na}$, isolated hearts)[1]

In Vitro
GS967 (10, 100, 300 nM) completely attenuates the effect of ATX-II (10 nM) to increase action potential duration (APD) and APD variability in ventricular myocytes, with an apparent $IC_{50}$ value of -10 nM and decreased the beat-to-beat variability of APD[2].
**In Vivo**

GS967 prevents and reverses proarrhythmic effects of the late $I_{Na}$ enhancer ATX-II and the $I_{Kr}$ inhibitor E-4031. GS967 significantly attenuates the proarrhythmic effects of methoxamine 1 clofilium and suppressed ischemia-induced arrhythmias.[1]. GS967 causes a reduction of $I_{NaP}$ in a frequency-dependent manner, consistent with use-dependent block (UBD). GS967 evokes more potent UDB of $I_{NaP}$ ($IC_{50}=0.07 \mu M$) than ranolazine (16 $\mu M$) and lidocaine (17 $\mu M$). GS967 is found to exert these same effects on a prototypical long QT syndrome mutation (delKPO)[2]. GS967 prevents ischemia-induced increases in alternans in the left atrium and left ventricle. GS967 reduces ischemia-induced increases in depolarization heterogeneity and repolarization heterogeneity. GS967 does not alter heart rate, arterial blood pressure, PR and QT intervals, or QRS duration, but it mildly decreased contractility during ischemia, which was consistent with late INa inhibition.[3].

**PROTOCOL**

**Animal Administration[1][2]**

Rats: Ventricular tachycardia or fibrillation are induced either by local aconitine injection (50 $\mu g$) in the left ventricular muscle of adult male rats or by arterial perfusion of 0.1 mM hydrogen peroxide in aged male rats. The left ventricular epicardial surface of the isolated-perfused hearts is optically mapped using fluorescent voltage-sensitive dye, and microelectrode recordings of action potentials are made adjacent to the aconitine injection site. The suppressive and preventive effects of GS967 (1 $\mu M$) against EAD/DAD-mediated ventricular tachycardia or fibrillation are then determined[2].

Rabbits: To determine the effect of GS967 on the inducibility of TdP by clofilium in the presence of methoxamine, rabbits are first treated with either vehicle or GS967 (in randomized manner) given as a 60 $\mu g$/kg bolus, followed by a 16 $\mu g$/kg/min infusion that is maintained for the duration of an experiment. After 10 minutes, methoxamine is infused intravenously at 15 $\mu g$/kg/min, followed 10 minutes later by clofilium at 100 nmol/kg/min. The incidences of premature ventricular contractions (PVCs), ventricular tachycardia (VT; defined as three or more consecutive abnormal beats), and TdP are determined from the ECG recordings[1].

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

**CUSTOMER VALIDATION**

- Br J Pharmacol. 2018 Dec;175(23):4325-4337.

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**REFERENCES**

