Inhibitors, Agonists, Screening Libraries

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Data Sheet

Product Name: SAR407899 (hydrochloride)
Cat. No.: HY-15687
CAS No.: 923262-96-8
Molecular Formula: C_{14}H_{17}ClN_{2}O_{2}
Molecular Weight: 280.75
Target: ROCK
Pathway: Cell Cycle/DNA Damage; Stem Cell/Wnt; TGF–beta/Smad
Solubility: DMSO: ≥ 2.8 mg/mL; DMSO: < 8.2 mg/mL

BIOLOGICAL ACTIVITY:

SAR407899 HCl is a potent, ATP–competitive ROCK inhibitor with Ki value of 36 nM/41 nM for human ROCK/Rat ROCK respectively. IC50 value: 36 nM/41 nM(Ki, human/Rat ROCK) [1]

Target: ROCK inhibitor

in vitro: SAR407899 is highly selective in panel of 117 receptor and enzyme targets. SAR407899 is ≈8–fold more active than fasudil. In vitro, SAR407899 demonstrated concentration–dependent inhibition of Rho–kinase–mediated phosphorylation of myosin phosphatase, thrombin–induced stress fiber formation, platelet–derived growth factor–induced proliferation, and monocyte chemotactic protein–1–stimulated chemotaxis. SAR407899 potently (mean IC50 values: 122 to 280 nM) and species–independently relaxed precontracted isolated arteries of different species and different vascular beds [1]. SAR407899 dose–dependently relaxed the pre–contracted corpora cavernosa in all species, with similar potency and efficacy in healthy vs diabetic rats, WKY vs SHR rats, healthy vs diabetic rabbits (IC(50) range from 0.05 to 0.29 μM, Emax range 89 to 97%) [3].

in vivo: Over the dose range 3 to 30 mg/kg PO, SAR407899 lowered blood pressure in a variety of rodent models of arterial hypertension [1]. SAR407899 was more effective than Y27632 in reducing ET–1–induced vasoconstriction in ZDF rat renal resistance arteries. Maximum ET–1–induced vasoconstriction in SAR407899–treated and Y27632–treated human renal resistance arteries was 23±5 and 48±6% of control values, respectively [2].

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [3] Rabbits were treated either intravenously (i.v., in an ear vein) with increasing doses of SAR407899 (0.3, 1, 3, 10 mg/kg) or orally with SAR407899 (1, 3, 10, 30 mg/kg) or sildenafil (2 or 6 mg/kg). Each animal was used several times for different doses and different agents, always with a week's washout. The length (mm) of uncovered penile mucosa (penile erection parameter) was measured at different time–points, using a sliding digital caliper. The results were expressed as mean ± SEM penile length of 3–5 rabbits. The area under the curve (AUC) was calculated for each animal in each group, and was expressed as mean ± SEM. For descriptive statistics, one–way ANOVA was done, followed by Newman–Keuls test versus the 6 mg/kg sildenafil group, using SAS v8.2 for Sun Solaris via Everstat v5.0 interface. SAR407899 was prepared in bi–distilled water.

References:
