# Data Sheet

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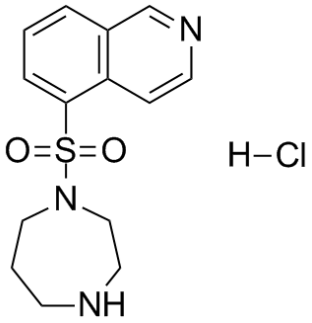
| **Product Name:** | Fasudil (Hydrochloride) |
| **Cat. No.:** | HY-10341 |
| **CAS No.:** | 105628-07-7 |
| **Molecular Formula:** | C14H18ClN3O2S |
| **Molecular Weight:** | 327.83 |
| **Target:** | Autophagy; PKC; ROCK |
| **Pathway:** | Autophagy; Cell Cycle/DNA Damage; Epigenetics; Stem Cell/Wnt; TGF–beta/Smad |
| **Solubility:** | DMSO: ≥ 31 mg/mL |




## BIOLOGICAL ACTIVITY:

Fasudil (Hydrochloride) is a potent inhibitor of **ROCK–II**, **PKA**, **PKG**, **PKC**, and **MLCK** with **Ki** of 0.33 μM, 1.6 μM, 1.6 μM, 3.3 μM and 36 μM, respectively.

IC50 & Target: Ki: 0.33 μM (ROCK–II), 1.6 μM (PKA), 1.6 μM (PKG), 3.3 μM (PKC), 36 μM (MLCK)

***In Vitro:*** Fasudil (Hydrochloride) has vasodilatory action and occupies the adenine pocket of the ATP–binding site of the enzyme[1]. Fasudil is a class of calcium antagonists. Fasudil produces a competitive inhibition of the $Ca^{2+}$–induced contraction of the depolarized rabbit aorta. Fasudil is able to inhibit contractile responses to KCl, phenylephnne (PHE) and prostaglandin (PG) F2a[2]. Fasudil also exhibits vasodilator actions by inhibition of 5–hydroxytryptamine, noradrenaline, histamine, angiotensin, and dopamine induced spiral strips contraction[3]. Fasudil induces disorganization of actin stress fiber and cell migration inhibition[4]. Fasudil inhibits hepatic stellate cells spreading, the formation of stress fibers, and expression of α–SMA with concomitant suppression of cell growth, but does not induce apoptosis. Fasudil suppresses the LPA–induced phosphorylation of ERK1/2, JNK and p38 MAPK[5].

***In Vivo:*** Fasudil (30 μg) produces an approximate 50% increase in CBF via intra–coronary injection to dogs. Fasudil (0.01, 0.03, 0.1 and 0.3 mg/kg, bolus, i.v.) dose–dependently decreases MBP and increases HR, VBF, CBF, RBF, and FBF. A total dose of 1.0 ng/mL Fasudil increases cardiac output. The infusion of Fasudil i.v. produces a significant fall in MBP, left ventricular systolic pressure and total peripheral resistance with an increase in HR and cardiac output, but without significant changes in right atrial pressure, dP/dt or left ventricular minute work in dogs[3]. Fasudil administration displays protectable effects on cardiovascular disease and reduces the activation of JNK and attenuates mitochondrial–nuclear translocation of AIF under ischemic injury[6]. The oral administration of Fasudil (a dosage of 100 mg/kg/day) significantly reduces incidence and mean maximum clinical score of EAE in SJL/J mice immunized with PLP p139–151. Treatment of mice with Fasudil suppresses the proliferative response of splenocytes to the antigen. Oral administration of Fasudil decreases inflammation, demyelination, axonal loss and APP positivein spinal cord of Fasudil–treated mice[7].

## PROTOCOL (Extracted from published papers and Only for reference)

**Kinase Assay:** [1]Cyclic AMP–dependent protein kinase activity is assayed in a reaction mixture containing, in a final volume of 0.2 mL, 50 mM Tris–HCl (pH 7.0), 10 mM magnesium acetate, 2 mM EGTA, 1 μM cyclic AMP or absence of cyclic AMP, 3.3 to 20 μM [r–$^{32}$P] ATP ($4\times10^5$ c.p.m.), 0.5 μg of the enzyme, 100 μg of histone H2B and compound. The mixture is incubated at 30°C for 5 min. The reaction is terminated by adding 1mL of ice–cold 20% trichloroacetic acid after adding 500 μg of bovine serum albumin as a carrier protein. The sample is centrifuged at 3000 r.p.m. for 15min, the pellet is resuspended in ice–cold 10% trichloro–acetic acid solution and the centrifugation–resuspension cycle is repeated three times. The final pellet is dissolved in 1 mL of 1 N NaOH and radioactivity is measured with a liquid scintillation counter.

## References:

[1]. Ono–Saito N, et al. H–series protein kinase inhibitors and potential clinical applications. Pharmacol Ther. 1999 May–Jun;82(2–3):123–31.

[2]. Asano T, et al. Mechanism of action of a novel antivasospasm drug, HA1077. J Pharmacol Exp Ther. 1987 Jun;241(3):1033–40.

[3]. Asano T, et al. Vasodilator actions of HA1077 in vitro and in vivo putatively mediated by the inhibition of protein kinase. Br J Pharmacol. 1989 Dec; 98(4):1091–100.

[4]. Negoro N, et al. The kinase inhibitor fasudil (HA–1077) reduces intimal hyperplasia through inhibiting migration and enhancing cell loss of vascular smooth muscle cells. Biochem Biophys Res Commun. 1999 Aug 19;262(1):211–5.

[5]. Fukushima M, et al. Fasudil hydrochloride hydrate, a Rho–kinase (ROCK) inhibitor, suppresses collagen production and enhances collagenase activity in hepatic stellate cells. Liver Int. 2005 Aug;25(4):829–38.

[6]. Zhang J, et al. Inhibition of the activity of Rho–kinase reduces cardiomyocyte apoptosis in heart ischemia/reperfusion via suppressing JNK–mediated AIF translocation. Clin Chim Acta. 2009 Mar;401(1–2):76–80.

[7]. Sun X, et al. The selective Rho–kinase inhibitor Fasudil is protective and therapeutic in experimental autoimmune encephalomyelitis. J Neuroimmunol. 2006 Nov;180(1–2):126–34.



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