

Product Data Sheet

Product Name: SSR128129E

Cat. No.: GC10491

Chemical Properties

Cas. No. 848318-25-2

Chemical Name sodium;2-amino-5-(1-methoxy-2-methylindolizine-3-carbonyl)benzoate

SMILES CC1=C(N2C=CC=CC2=C1OC)C(=O)C3=CC(=C(C=C3)N)C(=O)[O-].[Na+]

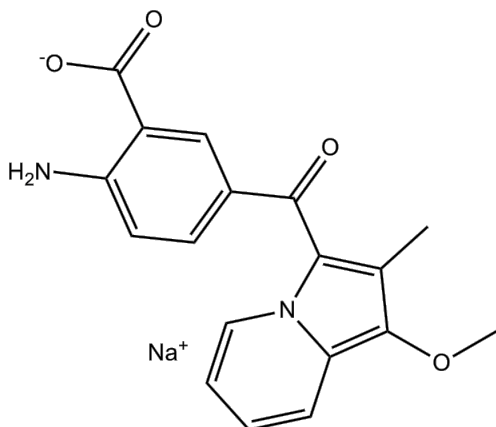
Formula $C_{18}H_{15}N_2O_4 \cdot Na$ M.Wt 346.31

Solubility $\geq 17.3\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment: HUVECs, freshly isolated from different donors and used between passage two and five, are cultured in M199 medium supplemented with 20% fetal bovine serum (FBS), 2 mM L-glutamine, 30 mg/L endothelial cell growth factor supplements (EGCS), 10 units/mL heparin, and penicillin/streptomycin. For proliferation, ECs are starved overnight in growth factor-depleted M199 medium containing 2% FBS and stimulated for 24 hr with 10 ng/mL bFGF with SSR128129E or DMSO. Proliferation is assessed the last 2 hr by incubation with 1 μ Ci/mL [3H]thymidine[1].

Animal experiment: Mice: Anesthetized BALB/c mice are inoculated with murine 4T1 mammary carcinoma cells. After randomization of tumor bearing mice for tumor size on day 5 after tumor cell inoculation, SSR128129E or vehicle (0.6 % methylcellulose) is administered daily via oral gavage at a dose of 30 mg/kg until the end of the experiment at day 21. Tumor volume is measured. At the end of the experiment, mice are sacrificed by pentobarbital injection, and lungs and tumors are dissected. Visible metastatic nodules on the lungs are counted by using a dissecting microscope[1].

References:

[1]. Bono F, et al. Inhibition of tumor angiogenesis and growth by a small-molecule multi-FGF receptor blocker with allosteric properties. Cancer Cell. 2013 Apr 15;23(4):477-88.

Background

SSR128129E is an allosteric inhibitor of FGFR1 with IC50 value of 1.9 μ M [1].

The fibroblast growth factor receptors (FGFRs) are receptor tyrosine kinases for fibroblast growth factors (FGFs) and play an important role in cancer and inflammation. FGF2 plays an important role in angiogenesis [1] [2].

SSR128129E is an orally-active and allosteric FGFR1 inhibitor. In human umbilical venous endothelial cells (HUVECs), SSR128129E inhibited FGF2-induced endothelial cells (ECs)

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proliferation and migration with IC50 values of 31 and 15.2 nM respectively and also inhibited lamellipodia formation. SSR128129E inhibited responses mediated by FGFR1-4. In FGFR2-expressing HEK293 cells, SSR128129E inhibited phosphorylation of FRS2 and ERK1/2 induced by FGF2 [1].

In arthritis mice, SSR128129E inhibited bone and joint damage and reduced angiogenesis in the inflamed joints. In orthotopic Panc02 tumor model, SSR128129E (30 mg/kg) inhibited tumor growth by 44%. In murine 4T1 breast tumors, SSR128129E (30 mg/kg) reduced tumor weight and size by 40% and 53%, respectively [1]. In atherosclerosis-prone apolipoprotein E (apoE)-deficient mice, SSR128129E (50 mg/kg) reduced neointimal proliferation and reduced FGFR2 mRNA levels and lesion size in the aortic sinus [2].

References:

- [1]. Bono F, De Smet F, Herbert C, et al. Inhibition of tumor angiogenesis and growth by a small-molecule multi-FGF receptor blocker with allosteric properties. *Cancer Cell*, 2013, 23(4): 477-488.
- [2]. Dol-Gleizes F, Delesque-Touchard N, Marès AM, et al. A new synthetic FGF receptor antagonist inhibits arteriosclerosis in a mouse vein graft model and atherosclerosis in apolipoprotein E-deficient mice. *PLoS One*, 2013, 8(11): e80027.

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