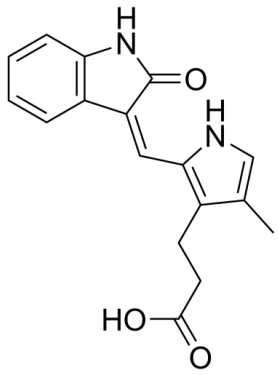
Data Sheet

Product Name:	SU 5402
Cat. No.:	CS-0200
CAS No.:	215543-92-3
Molecular Formula:	$C_{17}H_{16}N_2O_3$
Molecular Weight:	296.32
Target:	FGFR; PDGFR; VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 30 mg/mL (101.24 mM); H2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)



BIOLOGICAL ACTIVITY:

SU 5402 is a potent multi-targeted receptor tyrosine kinase inhibitor with **IC_{50}** of 20 nM, 30 nM, and 510 nM for **VEGFR2**, **FGFR1**, and **PDGFRβ**, respectively. IC50 & Target: IC50: 20 nM (VEGFR2), 30 nM (FGFR1), 510 nM (PDGFRβ)[1] ***In Vitro:*** SU 5402 is cocrystallized with the catalytic domain of FGF-R1 (flg-1) and is found to inhibit tyrosine phosphorylation of VEGF-R2 (Flk-1/KDR) and PDGF-R in NIH 3T3 cells with IC_{50} values of 0.4 and 60.9 μM, respectively[1]. In order to investigate whether phosphorylation of PKM2 and LDHA is mediated in FGFR1-specific manner, FTC-133 are treated with receptor tyrosine kinase inhibitors Dovitinib and SU 5402 (SU-5402). Dovitinib treatment results in significant decrease of phosphorylation status at a concentration of 100 nM after four hours of incubation for both PKM2 and LDHA. No significant changes are seen when administered at concentrations of 1 nM and 10 nM. SU 5402 administration leads to a sigificant decrease of PKM2 and LDHA phosphorylation at a concentration of 20 μM[2]. ***In Vivo:*** Inhibition of FGFR1 with SU 5402 (SU5402) administered to ΔF508-CFTR homozygous mice results in partial ΔF508-CFTR rescue, as shown by an increase in saliva secretion, a surrogate "sweat test" assay in mice. As salivary secretion is often sex dependent, only male mice are chosen for these experiments. Our results indicate that treatment of the ΔF508-CFTR mice with SU 5402 restores the saliva secretion level to ~10% of that observed for the wild-type CFTR mice, which suggests that SU 5402 can have therapeutic benefits to Cystic Fibrosis (CF)[3]. The selective FGFR1 inhibitor SU 5402 (SU5402) prevents and/or reverses PH induced by MCT (monocrotaline) in rats. In rats treated with SU 5402 on days 21 to 42 after the MCT injection, evaluations on day 42 show marked decreases in pulmonary artery pressure (PAP), RV/(LV+S), and distal artery muscularization compare with rats treated with the vehicle (saline)[4].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: SU 5402 (SU-5402) is solubilized in DMSO and stored, and then diluted with appropriate media before use[2].[2]8505C and FTC133 cells are grown in DMEM/F12 suppplemented with 10% FCS and 1% PenStrep and incubated at 37°C, 5% CO_2. For B-CPAP RPMI 1640 medium is used. FGFR1 inhibition experiments are performed on FTC133 cells by employment of Receptor Tyrosine Kinase Inhibitors TKI-258 (Dovitinib) and SU 5402 (20μM). Inhibition is conducted over 4 h with the indicated inhibitor concentrations. Control cells receive corresponding concentrations of DMSO[2]. **Animal Administration:** SU 5402 (SU5402) is dissolved in DMSO and then diluted (Mice)[3].

SU 5402 (SU5402) is prepared in saline (Rats)[4].[3][4]Mice[3]

Male ΔF508 mice ($CFTR^{tm1Eur}$ on a 129/FVB background) and their wild-type littermates of 9-12 weeks are intraperitoneally injected with DMSO or SU 5402 (dissolved in DMSO at the concentration of 6 mg/mL) at 25 mg/kg body weight, every day for 1 week. The mice are weighed daily and the dosages adjusted accordingly. The mice are then anesthetized by inhaling isoflurane until the end of the procedure. Cholinergic antagonist, Atropine (1 mM, 50 μL) is subcutaneously injected into the right cheek to block potential

cholinergic stimulation of the salivary gland. A small strip of filter paper is placed against the injected cheek, for 4 min. Isoprenaline (10 mM, 37.5 μL) is subsequently injected in the same spot to stimulate an adrenergic secretion of saliva (time 0). Filter strips (pre-weighed in an Eppendorf tube) are replaced every 5 min, over a period of 30 min. All six filter strips are weighed at the end of the collection and the results are normalized relative to mg/g body weight.

Rats[4]

To assess the potential effects of the FGFR1 inhibitor SU 5402 on established PH, adult male Wistar rats (200-250 g) are given MCT (60 mg/kg s.c.), left untreated for 21 days, then randomly divided into 2 groups (10 animals in each group), of which one is treated with SU 5402 (25 mg/kg/day) and the other given the vehicle, from day 21 to day 42. All treatments are given once a day by s.c. injection.

References:

[1]. Sun L, et al. Design, synthesis, and evaluations of substituted 3-[(3- or 4-carboxyethylpyrrol-2-yl)methylidenyl]indolin-2-ones as inhibitors of VEGF, FGF, and PDGF receptor tyrosine kinases. J Med Chem. 1999 Dec 16;42(25):5120-30.

[2]. Kachel P, et al. Phosphorylation of pyruvate kinase M2 and lactate dehydrogenase A by fibroblast growth factor receptor 1 in benign and malignant thyroid tissue. BMC Cancer. 2015 Mar 18;15:140.

[3]. Trzcińska-Daneluti AM, et al. RNA Interference Screen to Identify Kinases That Suppress Rescue of ΔF508-CFTR. Mol Cell Proteomics. 2015 Jun;14(6):1569-83.

[4]. Izikki M, et al. Endothelial-derived FGF2 contributes to the progression of pulmonary hypertension in humans and rodents. J Clin Invest. 2009 Mar;119(3):512-23.

CAIndexNames:

1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-

SMILES:

O=C(CCC1=C(NC=C1C)/C=C2C(NC3=C\2C=CC=C3)=O)O

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA