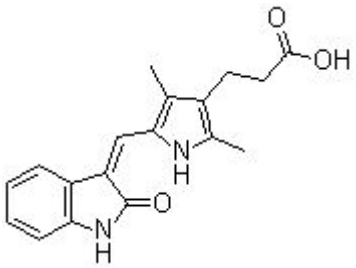
Product Introduction

TSU-68 (SU6668, Orantinib)

SU6668 has greatest potency against **PDGFR** autophosphorylation with K_I of 8 nM, but also strongly inhibits Flk-1 and FGFR1 trans-phosphorylation, little activity against IGF-1R, Met, Src, Lck, Zap70, Abl and CDK2; does not inhibit EGFR. Phase 3.

Technical Data:

Molecular Weight (MW):	310.35	
Formula:	$C_{18}H_{18}N_2O_3$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 62 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	252916-29-3	

Biological Activity

TSU-68 is a competitive inhibitor, with regard to ATP, to Flk-1/KDR trans-phosphorylation, FGFR1 trans-phosphorylation, and PDGFRβ kinases autophosphorylation. TSU-68 (0.03-10 μM) inhibits tyrosine phosphorylation of KDR in VEGF stimulated HUVECs. TSU-68 also inhibits PDGF-stimulated PDGFRβ tyrosine phosphorylation in NIH-3T3 cells overexpressing PDGFRβ at a minimum concentration of 0.03-0.1

μM. TSU-68 inhibits acidic FGF-induced phosphorylation of the FGFR1 substrate 2 at 10 μM and higher. However, TSU-68 (up to 100 μM) has no effect on EGF-stimulated EGFR tyrosine phosphorylation in NIH-3T3 cells overexpressing EGFR. TSU-68 inhibits VEGF-driven and FGF-driven mitogenesis of HUVECs with mean IC50 of 0.34 μM and 9.6 μM, respectively. [1] In human myeloid leukemia MO7E cells, TSU-68 inhibits the tyrosine autophosphorylation of stem cell factor (SCF) receptor, c-kit, with IC50 of 0.1-1 μM, as well as ERK1/2 phosphorylation, a signaling event downstream of c-kit activation. TSU-68 also inhibits SCF-induced proliferation of MO7E cells with IC50 of 0.29 μM, and induces apoptosis. [2]

TSU-68 (75-200 mg/kg) induces tumor growth inhibition against a broad range of tumor types in xenograft models in athymic mice, including A375, Colo205, H460, Calu-6, C6, SF763T, and SKOV3TP5 cells. TSU-68 (75 mg/kg) also suppresses tumor angiogenesis of C6 glioma xenografts. [1] In a tumor model of HT29 human colon carcinoma, TSU-68 (200 mg/kg) decreases the average vessel permeability and average fractional plasma volume in the tumor rim and core. TSU-68 promotes abnormal stromal development at the periphery of carcinomas. [3] In a rabbit VX2 liver tumor model, TSU-68 (200 mg/kg) augments the effect of chemotherapeutic infusion. [4]

References

[1] Laird AD, et al. Cancer Res, 2000, 60(15), 4152-4160.

[2] Smolich BD, et al. Blood, 2001, 97(5), 1413-1421.

[3] Marzola P, et al. Clin Cancer Res, 2004, 10(2), 739-750.

[4] Kim HC, et al. Cardiovasc Intervent Radiol, 2012, 35(1), 168-175.

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