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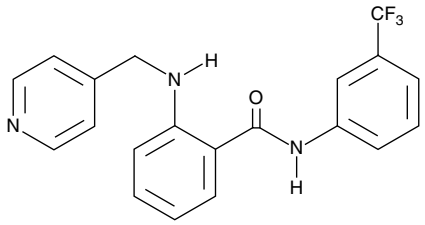
Product Information

AAL-993

Item No. 16351

CAS Registry No.: 269390-77-4
Formal Name: 2-[(4-pyridinylmethyl)amino]-N-[3-(trifluoromethyl)phenyl]-benzamide
Synonyms: VEGFR Tyrosine Kinase Inhibitor VI, ZK 260253
MF: $C_{20}H_{16}F_3N_3O$
FW: 371.4
Purity: ≥95%
Stability: ≥2 years at -20°C
Supplied as: A crystalline solid
UV/Vis.: λ_{max}: 220, 256, 348 nm



Laboratory Procedures

For long term storage, we suggest that AAL-993 be stored as supplied at -20°C. It should be stable for at least two years.

AAL-993 is supplied as a crystalline solid. A stock solution may be made by dissolving the AAL-993 in the solvent of choice. AAL-993 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of AAL-993 in these solvents is approximately 1, 25, and 30 mg/ml.

AAL-993 is sparingly soluble in aqueous solutions. To enhance aqueous solubility, dilute the organic solvent solution into aqueous buffers or isotonic saline. If performing biological experiments, ensure the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. We do not recommend storing the aqueous solution for more than one day.

AAL-993 is a potent inhibitor of VEGF receptors, inhibiting VEGFR1, 2, and 3 with IC_{50} values of 130, 23, and 18 nM, respectively.[1,2] It less potently inhibits c-Kit, colony stimulating factor 1 receptor, PGDF receptor β, and EGF receptor (IC_{50}s = 236, 380, 640, and 1,040 nM, respectively) and is without effect on a number of other tyrosine kinases.[1] AAL-993 is orally bioavailable *in vivo*, blocks VEGF-induced angiogenesis, and prevents the growth of primary tumors and spontaneous peripheral metastases in mice.[1,3] It also inhibits hypoxia-mediated increase in hypoxia-inducible factor-1 transcriptional activity in an ERK-dependent manner (IC_{50} = ~5 µM).[4]

References

1. Manley, P.W., Furet, P., Bold, G., *et al.* Anthranilic acid amides: A novel class of antiangiogenic VEGF receptor kinase inhibitors. *J. Med. Chem.* **45(26)**, 5687-5693 (2002).
2. Honda, T., Tajima, H., Kaneko, Y., *et al.* Conformation-activity relationship on novel 4-pyridylmethylthio derivatives with antiangiogenic activity. *Bioorg. Med. Chem. Lett.* **18(9)**, 2939-2943 (2008).
3. Manley, P.W., Bold, G., Brüggen, J., *et al.* Advances in the structural biology, design and clinical development of VEGF-R kinase inhibitors for the treatment of angiogenesis. *Biochim. Biophys. Acta.* **1697(1-2)**, 17-27 (2004).
4. Ban, H.S., Uno, M., and Nakamura, H. Suppression of hypoxia-induced HIF-1α accumulation by VEGFR inhibitors: Different profiles of AAL993 versus SU5416 and KRN633. *Cancer Lett.* **296(1)**, 17-26 (2010).

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