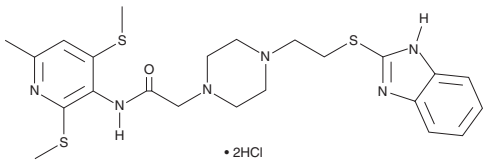
PRODUCT INFORMATION

K-604 (hydrochloride)

Item No. 41119

CAS Registry No.: 217094-32-1
Formal Name: 4-[2-(1H-benzimidazol-2-ylthio) ethyl]-N-[6-methyl-2,4-*bis*(methylthio)-3-pyridinyl]-1-piperazineacetamide, dihydrochloride
MF: $C_{23}H_{30}N_6OS_3 \bullet 2HCl$
FW: 575.6
Purity: ≥98%
Supplied as: A solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

K-604 (hydrochloride) is supplied as a solid. A stock solution may be made by dissolving the K-604 (hydrochloride) in the solvent of choice, which should be purged with an inert gas. K-604 (hydrochloride) is soluble (≥10 mg/ml) in DMSO.

Description

K-604 is an inhibitor of acyl-coenzyme A:cholesterol acyltransferase-1 (ACAT-1; IC_{50} = 0.45 µM).[1] It is selective for ACAT-1 over ACAT-2 (IC_{50} = 102.85 µM). K-604 reduces foaming of J774 macrophages (IC_{50} = 0.026 µM) and reduces cholesterol esterification in monocyte-derived macrophages (IC_{50} = 0.068 µM).[1,2] It decreases lipid-accumulation areas in the aortic arch in atherosclerosis-susceptible Bio F1B hamsters fed a high-fat and high-cholesterol diet when administered at a dose of 10 mg/kg and reduces plasma total cholesterol levels in the same model at 10 and 30 mg/kg.[1] K-604 also increases the LC3-II-to-LC3-I ratio, a marker of autophagosome formation, in Neuro2a (N2a) mouse neuroblastoma cells when used at concentrations of 0.1 and 1 µM.[3] It decreases wild-type and mutant P301L-tau levels in N2a cells overexpressing these proteins but does not affect endogenous tau levels. Intranasal administration of K-604 (105 µg/animal) reduces the level of brain cholesteryl esters in mice.[4]

References

1. Shibuya, K., Kawamine, K., Ozaki, C., *et al*. Discovery of clinical candidate 2-(4-(2-((1 H-benzo[d]imidazol-2-yl)thio)ethyl)piperazin-1-yl)-N-(6-methyl-2,4-bis(methylthio)pyridin-3-yl)acetamide hydrochloride [K-604], an aqueous-soluble acyl-CoA:Cholesterol O-acyltransferase-1 inhibitor. *J. Med. Chem.* **61(23)**, 10635-10650 (2018).
2. Ikenoya, M., Yoshinaka, Y., Kobayashi, H., *et al*. A selective ACAT-1 inhibitor, K-604, suppresses fatty streak lesions in fat-fed hamsters without affecting plasma cholesterol levels. *Atherosclerosis* **191(2)**, 290-297 (2007).
3. Shibuya, Y., Niu, Z., Bryleva, E.Y., *et al*. Acyl-coenzyme A:cholesterol acyltransferase 1 blockage enhances autophagy in the neurons of triple transgenic Alzheimer's disease mouse and reduces human P301L-tau content at the presymptomatic stage. *Neurobiol. Aging* **36(7)**, 2248-2259 (2015).
4. Shibuya, K., Morikawa, S., Miyamoto, M., *et al*. Brain targeting of acyl-CoA:cholesterol *O*-acyltransferase-1 inhibitor K-604 via the intranasal route using a hydroxycarboxylic acid aolution. *ACS Omega* **4(16)**, 16943-16955 (2019).

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