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- Trockeneiszuschlag
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SZABO-SCANDIC Handels GmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

mail@szabo-scandic.com

www.szabo-scandic.com

[linkedin.com/company/szaboscandic](https://www.linkedin.com/company/szaboscandic) 

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: $C_{23}H_{30}N_6OS_3 \cdot 2HCl$

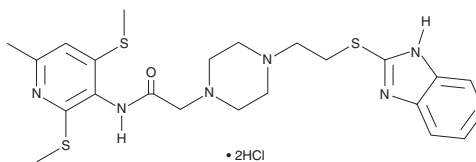
FW: 575.6

Purity: $\geq 98\%$

Supplied as: A solid

Storage: $-20^{\circ}C$

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; $IC_{50} = 0.45 \mu M$).¹ It is selective for ACAT-1 over ACAT-2 ($IC_{50} = 102.85 \mu M$). K-604 reduces foaming of J774 macrophages ($IC_{50} = 0.026 \mu M$) and reduces cholesterol esterification in monocyte-derived macrophages ($IC_{50} = 0.068 \mu M$).^{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 solution. *ACS Omega* **4**(16), 16943-16955 (2019).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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CAYMAN CHEMICAL

1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA

PHONE: [800] 364-9897

[734] 971-3335

FAX: [734] 971-3640

CUSTSERV@CAYMANCHEM.COM

WWW.CAYMANCHEM.COM