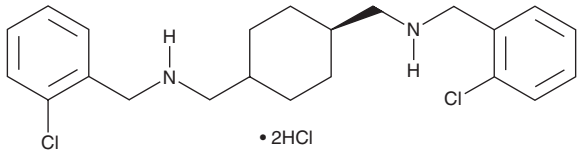
PRODUCT INFORMATION

AY 9944

Item No. 14611

CAS Registry No.: 366-93-8
Formal Name: *trans*-N^1,N^4-bis[(2-chlorophenyl) methyl]-1,4-cyclohexanedimethanamine, dihydrochloride
MF: $C_{22}H_{28}Cl_2N_2 \bullet 2HCl$
FW: 464.3
Purity: ≥98%
UV/Vis.: λ_{max}: 212 nm
Supplied as: A crystalline 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

AY 9944 is supplied as a crystalline solid. AY 9944 is soluble in organic solvents such as ethanol and DMSO, which should be purged with an inert gas. The solubility of AY 9944 in these solvents is approximately 10 mg/ml when briefly exposed to high temperature.

Organic solvent-free aqueous solutions of AY 9944 can be prepared by directly dissolving the crystalline solid in aqueous buffers. AY 9944 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.

Description

AY 9944 prevents cholesterol biosynthesis by inhibiting the 7-dehydro cholesterol Δ^7-reductase (DHCR7) enzyme (IC_{50} = 13 nM), which interferes with the conversion of 7-dehydro cholesterol (Item No. 14612) to cholesterol.[1,2] Furthermore, by upregulating the expression of DHCR7, AY 9944 can block Hedgehog signaling at the level of Smoothened or by loss of Suppressor of Fused.[3] AY 9944 inhibition of DHCR7 has been used to recapitulate phenotypes of Smith-Lemli-Opitz syndrome, a disorder brought about by mutations in the *DHCR7* gene, in animal models.[2,4] However, AY 9944 is highly teratogenic, producing congenital defects in offspring when fed to pregnant animals.[5]

References

1. Horlick, L. Effect of a new inhibitor of cholesterol biosynthesis (AY 9944) on serum and tissue sterols in the rat. *J. Lipid Res.* **7(1)**, 116-121 (1966).
2. Moebius, F.F., Fitzky, B.U., Lee, J.N., *et al*. Molecular cloning and expression of the human Δ7-sterol reductase. *Proc. Natl. Acad. Sci. USA* **95(4)**, 1899-1902 (1998).
3. Lauth, M., Rohnalter, V., Bergström, A., *et al*. Antipsychotic drugs regulate hedgehog signaling by modulation of 7-dehydrocholesterol reductase levels. *Mol. Pharmacol.* **78(3)**, 486-496 (2010).
4. Keller, R.K., Mitchell, D.A., Goulah, C.C., *et al*. Hepatic isoprenoid metabolism in a rat model of Smith-Lemli-Opitz Syndrome. *Lipids* **48(3)**, 219-229 (2013).
5. Xu, G., Salen, G., Shefer, S., *et al*. Reproducing abnormal cholesterol biosynthesis as seen in the Smith-Lemli-Opitz syndrome by inhibiting the conversion of 7-dehydrocholesterol to cholesterol in rats. *J. Clin. Invest.* **95(1)**, 76-81 (1995).

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