Aurothiomalate sodium

Cat. No.: HY-106381

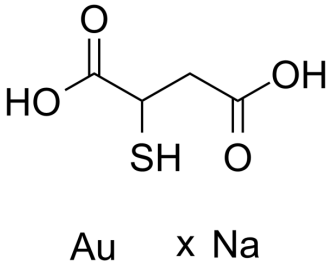
CAS No.: 12244-57-4

Molecular Formula: $C_4H_6O_4S.Au.xNa$

Target: PKC

Pathway: Epigenetics; TGF-beta/Smad

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro	H_2O : 250 mg/mL (Need ultrasonic)
In Vivo	1. Add each solvent one by one: PBS Solubility: 50 mg/mL (Infinity mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description	Aurothiomalate sodium is a potent and selective oncogenic PKC_ι signaling inhibitor. Aurothiomalate sodium inhibits tumor cell proliferation and not cell apoptosis. Aurothiomalate sodium is a potent thioredoxin reductase (TrxR) inhibitor. Aurothiomalate sodium, an anti-rheumatoid agent, exhibits potent anti-tumor activity[1][2][3].
IC_{50} & Target	PKCι
In Vitro	Aurothiomalate sodium (0.001, 0.01, 0.1, 1, 10, 100, 1000 uM) induces dose-dependent inhibition of anchorage-independent growth in all cell lines tested (A549, H1437, H2170, H460, H510, H187, H1703 and A427 lung cancer cell lines) with IC_{50}s ranging from 300 nM-107 μM. The lung adenocarcinoma (LAC) and small cell lung carcinoma (SCLC) cells tends to be more sensitive and lung adenocarcinomas (LACs) less sensitive to Aurothiomalate sodium[1]. Aurothiomalate sodium (25 uM; 6 hours) suppresses TNFa-induced activation of NF-kB and the expression of NF-kB-targeted proinflammatory genes such as E-selectin and cyclooxygenase-2[3]. Aurothiomalate sodium inhibits non-small lung cancer (NSCLC) growth by binding PKC_ι and blocking activation of a PKC_ι-Par6-Rac1-Pak-Mek 1,2-Erk 1,2 signaling pathway[1]. Aurothiomalate sodium inhibits Mek/Erk signaling and decreases proliferative index without effecting tumor apoptosis or vascularization in vivo[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	Bovine arterial endothelial cells (BAEC)
Concentration:	25 uM
Incubation Time:	6 hours

Result:	Suppressed TNFa-induced NF-kB-dependent gene expression in a dose-dependent manner. Did not affect TrxR1 mRNA level in COS7 cells.

In Vivo

Aurothiomalate sodium (2, 6, 20 or 60 mg/kg/day; intramuscular injections; 40 days) exhibits statistically significant inhibition of tumor growth at all concentrations tested in A427 cell tumors because A427 cells are highly responsive[1]. Aurothiomalate sodium (20, 60 mg/kg/day; intramuscular injections; 15 days) shows a statistically significant response (~50% reduction in tumor size) only at the 60 mg/kg dose in H460 tumors because H460 cells are less responsive[1]. Aurothiomalate sodium (60 mg/kg/day; IP; for six weeks) exhibites a decrease in tumor growth in Three-week-old KrasLA2 mice. Aurothiomalate sodium inhibits Kras-mediated bronchioalveolar stem cells (BASCs) expansion and lung tumorigenesis in vivo[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	4-6-week-old female nude mice with A427 or H460 cells[1]
Dosage:	2, 6, 20 or 60 mg/kg
Administration:	Intramuscular injections; daily; 40 days
Result:	Exhibited statistically significant inhibition of tumor growth at all concentrations tested in A427 cell tumors because A427 cells are highly responsive.

REFERENCES

[1]. Roderick P Regala, et al. Atypical protein kinase C iota expression and aurothiomalate sensitivity in human lung cancer cells. Cancer Res. 2008 Jul 15;68(14):5888-95.

[2]. Roderick P Regala, et al. Atypical protein kinase C{iota} is required for bronchioalveolar stem cell expansion and lung tumorigenesis. Cancer Res. 2009 Oct 1;69(19):7603-11.

[3]. Atsuko Sakurai, et al. Overexpression of thioredoxin reductase 1 regulates NF-kappa B activation. J Cell Physiol. 2004 Jan;198(1):22-30.

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