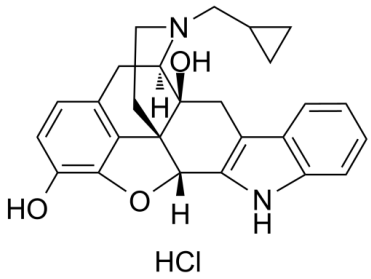
Data Sheet

Product Name:	Naltrindole (hydrochloride)
Cat. No.:	CS-6914
CAS No.:	111469-81-9
Molecular Formula:	C26H27ClN2O3
Molecular Weight:	450.96
Target:	Opioid Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : ≥ 188 mg/mL (416.89 mM)



BIOLOGICAL ACTIVITY:

Naltrindole hydrochloride is a highly potent and selective non-peptide **δ opioid** receptor antagonist with a **K_i** of 0.02 nM. IC50 & Target: Ki: 0.02 nM (δ opioid), 64 nM (μ opioid), 66 nM (κ opioid)[1] **In Vitro:** Opioid drugs exert a wide spectrum of physiological and behavioral effects. These effects are mediated via membrane-bound receptors, of which the best characterized are the kappa, delta, and mu receptors[1]. Naltrindole inhibits the proliferation of cultured human U266 MM cells in a time- and dose-dependent manner with an EC_{50} of 16 μM. Treatment of U266 cells with naltrindole significantly decreases the level of the active, phosphorylated form of the kinases, extracellular signal-regulated kinase and Akt, which may be related to its antiproliferative activity[2]. Naltrindole inhibits growth and induces apoptosis in the three characteristic SCLC cell lines, NCI-H69, NCI-H345, and NCI-H510. Naltrindole treatment reduces constitutive phosphorylation of Akt/PKB on serine 473 and threonine 308 in cells and also its downstream effectors glycogen synthase kinase-3β and the Forkhead transcription factors AFX and FKHR[3]. **In Vivo:** Naltrindole significantly decreases tumor cell volumes in human MM cell xenografts in severe combined immunodeficient mice[2]. In mice, naltrindole at 20 mg/kg s.c. antagonizes the δ-selective agonist effect of [D- Ser, Leu, Thr]enkephalin (DSLET) without blocking the antinociceptive effect of morphine or U50488H. Naltrindole is the only highly selective δ antagonist that is active upon peripheral administration[4]. Acute naltrindole induces significant decreases in external and total ambulation (horizontal activity) and rearing behaviour (vertical activity), as well as a significant increase in grooming frequency. In animals chronically treated with naltrindole there is an increase in total ambulation one day after the discontinuation of the treatment[5].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]U266 cells are plated in 96-well plates at 2000 cells per well in 100 μL of RPMI 1640 medium, supplemented with 10% fetal bovine serum, 100 U/mL penicillin, and 100 μg/mL streptomycin sulfate. Cells are incubated in quadruplicate in the presence of the various antineoplastic agents to construct dose-response curves, alone or in combination with various doses of naltrindole. At the end of the incubation 10 μL of WST-1 cell proliferation reagent is added to each well, and the plates are returned to the incubator for 1 h. Absorbance is then measured[2].

Animal Administration: Naltrindole is dissolved in distilled water or saline.[2][5]Rat:

Effects of neonatal naltrindole treatments on open field activity is tested in 20-day old rats. The animals are injected chronically with saline or naltrindole (1 mg/kg, s.c.) (from birth to day 19), and 1 day after the discontinuation of this treatment are studied for the acute effects of naltrindole (1 mg/kg, i.p.)[5].

Mouse:

Naltrindole is dissolved in distilled water to make a 3 mg/mL solution, and mice are injected with 10 mL/kg daily. Human RPMI 8226 multiple myeloma cells are inoculated subcutaneously into both flanks of SCID mice (10 million cells per flank). After 8 days, 12 mice are divided into two groups of six mice each: vehicle-injected and naltrindole-injected (30 mg/kg). Animals are dosed daily for 36

days, and body weights and xenograft tumors are measured twice a week with a digital caliper[2].

References:

[1]. Raynor K, et al. Pharmacological characterization of the cloned kappa-, delta-, and mu-opioid receptors. Mol Pharmacol. 1994 Feb;45(2):330-4.

[2]. Mundra JJ, et al. Naltrindole inhibits human multiple myeloma cell proliferation in vitro and in a murine xenograft model in vivo. J Pharmacol Exp Ther. 2012 Aug;342(2):273-87.

[3]. Chen YL, et al. Inhibition of akt/protein kinase B signaling by naltrindole in small cell lung cancer cells.

[4]. Portoghese PS, et al. Naltrindole, a highly selective and potent non-peptide delta opioid receptor antagonist. Eur J Pharmacol. 1988 Jan 27;146(1):185-6.

[5]. Fernández B, et al. Postnatal naltrindole treatments induce behavioural modifications in preweanling rats. Neurosci Lett. 2000 Mar 31;283(1):73-6.

CAIndexNames:

4,8-Methanobenzofuro[2,3-a]pyrido[4,3-b]carbazole-1,8a(9H)-diol, 7-(cyclopropylmethyl)-5,6,7,8,14,14b-hexahydro-, hydrochloride (1:1), (4bS,8R,8aS,14bR)-

SMILES:

O[C@@]1(CC(C(C=CC=C2)=C2N3)=C3[C@]4([H])OC5=C6O)[C@]74C5=C(C=C6)C[C@@]1([H])N(CC8CC8)CC7.Cl

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