Product Data Sheet

Product Name: SR 48692
Cat. No.: GC13242

Chemical Properties

Cas. No.	146362-70-1		
Chemical Name	(1R,2R,3R,5S,7S)-2-(1-(7-chloroquinolin-4-yl)-5-(2,6-dimethoxyphenyl)-1H-pyrazole-3-carboxamido)adamantane-2-carboxylic acid		
SMILES	ClC1=CC=C2C(N3N=C(C=C3C(C(OC)=CC=C4)=C4OC)C(N[C@]5(C(O)=O)[C@H]6C[C@H]7C[C@H]5C[C@H](C7)C6)=O)=CC=NC2=C1		
Formula	$C_{32}H_{31}ClN_4O_5$	M.Wt	587.07
Solubility	DMSO: 20 mM	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Caution: Product has not been fully validated for medical applications. For research use only.
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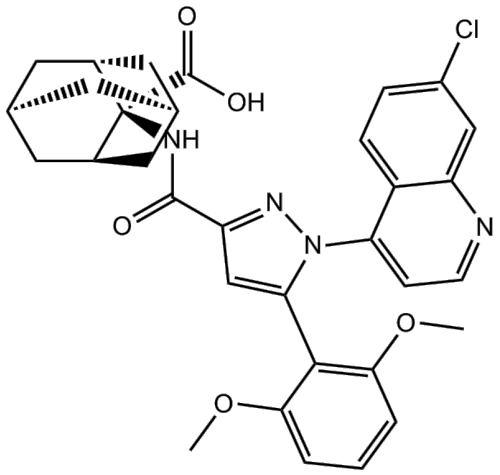
Structure



Protocol

Cell experiment [1]:

Cell lines	A375 melanoma cells
Preparation Method	A375 melanoma cells were treated with 0.01μM neurotensin (NTS) and 0.01μM+5μM SR 48692 seprately, DMSO was used as a control. OD570nm was measured daily from 1 to 4 days.
Reaction Conditions	5μM; 1-4 days

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Applications	SR48692 can inhibit cell proliferation induced by NTS.

Animal experiment [2]:

Animal models	Male athymic nude mice
Preparation Method	Human PC-3M-luc-C6 cells were used in an orthotopic xenograft model in male athymic nude mice. Surgery was conducted to expose the prostate, and 20μL of the tumor cell suspension (5×10^5 cells) was injected into the dorsolateral lobe of the prostate gland. Following closure, mice were treated with SR 48692 (25mg/kg in PEG800) or vehicle control for 5 consecutive days. Drug was administered orally in 0.2mL volumes 4h prior to radiation treatments. Mice were then anesthetized with a ketamine/xylazine mix, and a dose of 2.5 Gy X-ray was given to the prostate area while shielding the body with lead. Animals were imaged on a weekly basis by anesthetizing with isoflurane before and during imaging and injecting intraperitoneally with luciferin. Animals were imaged at a peak time of 10 to 20min post-luciferin injection via a Xenogen IVIS instrument, using exposure times and sensitivity settings to avoid saturation. Image processing was conducted using Living Image software (Xenogen) by region-of-interest analysis of total photons/sec for each tumor, with appropriate background subtraction.
Dosage form	25mg/kg/day; 5 days; p.o.
Applications	Combined treatment of SR 48692 with radiation elicits synergistic antitumor activity against PC-3M tumor xenografts in mice.

References:
[1] Zhang Y, Zhu S, Yi L, et al. Neurotensin receptor1 antagonist SR48692 reduces proliferation by inducing apoptosis and cell cycle arrest in melanoma cells[J]. Molecular and cellular biochemistry, 2014, 389(1): 1-8.
[2]Valerie N C K, Casarez E V, DaSilva J O, et al. Inhibition of neurotensin receptor 1 selectively sensitizes prostate cancer to ionizing radiation[J]. Cancer research, 2011, 71(21): 6817-6826.

Background

SR 48692 (Meclinertant) is an orally bioavailable, allosteric antagonist of the neuropeptide Y receptor NTS1 (K_d=3.4nM)[1, 2]. SR 48692 is the first non-peptide antagonist developed for NTS1, used in scientific research to explore the interactions of neuropeptide Y with other neurotransmitters in the brain[3]. SR 48692 enhances the sensitivity of ovarian cancer cells and experimental tumors to carboplatin[4]. SR 48692, when administered chronically via a central cannula to the paraventricular nucleus (PVN) of the hypothalamus, effectively attenuated the increase in central HPA axis activity caused by circadian rhythm fluctuations and stress responses[5].

In vitro, treatment of A375 melanoma cells with SR 48692 (5μM) for 1-4 days significantly inhibited neuropeptide-induced cell proliferation, inducing cell cycle arrest and apoptosis[6]. SR 48692 (5μM) also antagonized neuropeptide-induced increases in cytosolic Ca^{2+} in NCI-H209 cells[7].

In vivo, oral administration of SR 48692 (25mg/kg/day) for 5 days significantly inhibited tumor growth in mice bearing human prostate cancer cells (PC-3M-Luc cells) xenografts, and showed synergistic anti-tumor activity when combined with radiotherapy[8].

References:
[1] Gully D, Canton M, Boigegrain R, et al. Biochemical and pharmacological profile of a potent and selective nonpeptide antagonist of the neurotensin receptor[J]. Proceedings of the National Academy of Sciences, 1993, 90(1): 65-69.
[2] Labbe-Jullie C, Botto J M, Mas M V, et al. [3H] SR 48692, the first nonpeptide neurotensin antagonist radioligand: characterization of binding properties and evidence for distinct agonist and antagonist binding domains on the rat neurotensin receptor[J]. Molecular pharmacology, 1995, 47(5):

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[3] Iyer M R, Kunos G. Therapeutic approaches targeting the neurotensin receptors[J]. Expert Opinion on Therapeutic Patents, 2021, 31(5): 361-386.
[4] Liu J, Agopiantz M, Poupon J, et al. Neurotensin receptor 1 antagonist SR48692 improves response to carboplatin by enhancing apoptosis and inhibiting drug efflux in ovarian cancer[J]. Clinical Cancer Research, 2017, 23(21): 6516-6528.
[5] Rowe W B, Nicot A, Sharma S, et al. Central administration of the neurotensin receptor antagonist, SR48692, modulates diurnal and stress-related hypothalamic-pituitary-adrenal activity[J]. Neuroendocrinology, 1997, 66(2): 75-85.
[6] Zhang Y, Zhu S, Yi L, et al. Neurotensin receptor1 antagonist SR48692 reduces proliferation by inducing apoptosis and cell cycle arrest in melanoma cells[J]. Molecular and cellular biochemistry, 2014, 389(1): 1-8.
[7] Moody T W, Chiles J, Casibang M, et al. SR48692 is a neurotensin receptor antagonist which inhibits the growth of small cell lung cancer cells[J]. Peptides, 2001, 22(1): 109-115.
[8] Valerie N C K, Casarez E V, DaSilva J O, et al. Inhibition of neurotensin receptor 1 selectively sensitizes prostate cancer to ionizing radiation[J]. Cancer research, 2011, 71(21): 6817-6826.

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