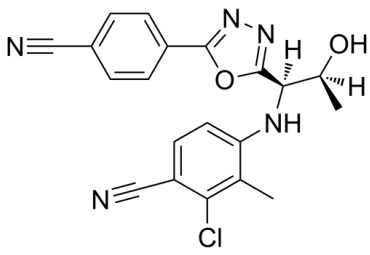
Data Sheet

Product Name:	Vosilasarm
Cat. No.:	CS-4670
CAS No.:	1182367-47-0
Molecular Formula:	$C_{20}H_{16}ClN_5O_2$
Molecular Weight:	393.83
Target:	Androgen Receptor
Pathway:	Vitamin D Related/Nuclear Receptor
Solubility:	DMSO : ≥ 100 mg/mL



BIOLOGICAL ACTIVITY:

Vosilasarm (RAD140) is a potent, orally active, nonsteroidal selective **androgen receptor** modulator (SARM) with a $\mathbf{K_i}$ of 7 nM. Vosilasarm shows good selectivity over other steroid hormone nuclear receptors[1]. IC50 & Target: Ki: 7 nM (Androgen receptor)[1] ***In Vitro:*** Vosilasarm (0-300 nM; pretreated for 1 hour) increases neuron viability against Aβ in a concentration-dependent manner[2]. Vosilasarm (100 nM; 1 hour) protects cultured neurons against apoptotic insults. Vosilasarm shows protective profiles of significantly protecting against neuronal death induced by Aβ and AAII, but not H_2O_2[2].

Vosilasarm (100 nM; 15 minutes) induces a significant increase in levels of phosphorylated but not total ERK in neuronal cultures[2].

In Vivo: The stability of Vosilasarm is high ($t_{1/2}$ > 2 h) in incubations with rat, monkey, and human microsomes, and Vosilasarm also has good bioavailability in rats (F = 27-63%) and monkeys (65-75%)[1].

In castrated immature rats, Vosilasarm (0.03-0.3 mg/kg; for 11 days) stimulates the levator ani bulbocavernosus muscle weight and prostate weight[1].

A high dose of Vosilasarm (10 mg/kg, p.o.) actually antagonizes the effect of testosterone propionate (TP) at 1 mg/kg on the seminal vesicles but adds to the effect of TP on the levator ani muscle. The effective dose for achieving antagonism by Vosilasarm is 0.3-1 mg/kg (p.o.) for 1 mg/kg TP (s.c.). In the young castrate male rat model, Vosilasarm appears to be a potent and complete androgen agonist on the levator ani, but a weaker, partial antagonist on the seminal vesicle and possibly the prostate[1].

Vosilasarm is neuroprotective in vivo using the rat kainate lesion model. In experiments with gonadectomized, adult male rats, Vosilasarm is shown to exhibit peripheral tissue-specific androgen action that largely spared prostate, neural efficacy as demonstrated by activation of androgenic gene regulation effects, and neuroprotection of hippocampal neurons against cell death caused by systemic administration of the excitotoxin kainate[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay (Western blots) [2] Cultures are incubated for 5 minutes with 2 μM calcein acetoxymethyl ester and then examined using an inverted fluorescent IX70 Olympus microscope. The number of healthy, positively stained cells is counted in 4 separate fields (in a predetermined, regular pattern) per well, 3 wells per condition in each experiment (n ≥ 3 independent culture preparations). Counts of viable neurons in vehicle-treated controls ranged from 250-300 per well.Lysates are collected from treated cultures using a reducing sample buffer (62.5 mM Tris-HCl, 1% sodium dodecyl sulfate, 2.5% glycerol, 0.5% 2-β-mercaptoethanol), boiled for 5 minutes, and centrifuged at 13 000 × g for 10 minutes. The supernatants were analyzed by immunoblotting using a standard protocol with 1 μg/mL anti-phosphoERK1/2 primary antibody and corresponding horseradish peroxidase-conjugated secondary antibody (1:5000) and detected using enhanced luminescence. Animal administration [2] GDX rats are administered 1 mg/kg RAD140 suspended in 0.5% methyl cellulose (1 mg/mL) by daily oral gavage for 2 weeks. This dose was chosen based on previous reports for RAD140 efficacy.

Vehicle-treated animals are gavaged with a similar weight/volume of 0.5% methyl cellulose. On day 13 of the 2-week hormone treatment period, kainate (10 mg/kg; Enzo Life Sciences) or sterile water control is injected ip. Kainate is dissolved immediately prior to use in sterile water and lightly heated to fully solubilize. On day 14, SARM-treated rats are administered 1 mg/mL of RAD140 suspended in safflower oil by sc injection because oral gavage is difficult following kainate lesion.

References:

[1]. Miller CP, et al. Design, Synthesis, and Preclinical Characterization of the Selective Androgen Receptor Modulator (SARM) RAD140. ACS Med Chem Lett. 2010 Dec 2;2(2):124-129.

[2]. Jayaraman A, et al. Selective androgen receptor modulator RAD140 is neuroprotective in cultured neurons and kainate-lesioned male rats. Endocrinology. 2014 Apr;155(4):1398-1406.

CAIndexNames:

Benzonitrile, 2-chloro-4-[[(1R,2S)-1-[5-(4-cyanophenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl]amino]-3-methyl-

SMILES:

ClC1=C(C)C(N[C@]([H])([C@@]([H])(O)C)C2=NN=C(O2)C3=CC=C(C#N)C=C3)=CC=C1C#N

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