

Product Data Sheet

Product Name: BMS-564929

Cat. No.: GC35534

Chemical Properties

Cas. No. 627530-84-1

SMILES N#CC1=CC=C(N(C(N2[C@@]3([H])[C@H](O)CC2)=O)C3=O)C(C)=C1Cl

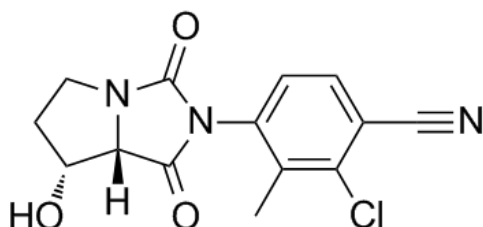
Formula $C_{14}H_{12}ClN_3O_3$ M.Wt 305.72

Solubility DMSO: 50 mg/mL (163.55 mM); Storage Store at -20°C
Water: < 0.1 mg/mL (insoluble)

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.

Structure



Protocol

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

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**Kinase
experiment:**

The human cancer epithelial breast cell lines MDA MB-453 and T47D, which endogenously express AR and progesterone receptor (PR), respectively, are used for radioligand competition binding assays. Binding assays are conducted by incubating BMS-564929 at various concentrations with either [3H]DHT or [3H]progesterone with the cells for 2 h at room temperature. For ER α and ER β , fusion proteins expressed in Escherichia coli, consisting of maltose binding protein, a specific biotinylation sequence, an enterokinase cleavage site, and either the ER α or ER β LBD is used. Binding reactions are conducted by incubating ER α and ER β LBD with BMS-564929 and [3H]E2 for 2 h at room temperature. Specific binding activity to the mineralocorticoid receptor (MR) by BMS-564929 is evaluated by competition binding assay using kidney cytosolic preparations and [3H]aldosterone. The kidneys are obtained from adrenalectomized rats to remove the endogenous source of aldosterone and to increase the MR concentration in the cytosol of kidney cells. Binding reactions are incubated for 2 h on ice in the presence of excess mifepristone (RU486) to block nonspecific glucocorticoid receptor (GR) binding. A fluorescence polarization based assay is used for GR binding, as per manufacturer recommendations. Inhibitory constants (K_i , app) defining apparent binding affinity of test compounds to intracellular receptors are calculated from the observed inhibition of natural ligand binding at multiple concentrations of test compound. SHBG binding is performed using a standard charcoal assay. Reagents: 1 mg lyophilized SHBG powder (Tris), [3H]DHT, 3% charcoal, and 0.4% Dextran in PBS; binding buffer: 50 mM Tris, pH 7.6, 100 mM NaCl, 1 mM EDTA, 1 mM DTT, and mock lysate (3.5 μ g/100 μ L buffer); stock solutions: stock SHBG protein: 1 mg/mL in water=20 μ M; stock [3H]DHT ligand: 9 μ M; DHT: 10 mM in DMSO; BMS 564929: 10 mM in DMSO. Compounds diluted in binding buffer are added to 40 nM [3H]DHT and 20 nM SHBG protein in 200 μ L volume and incubated for 1 h at room temperature. Total binding: 40 nM [3H]DHT and 20 nM SHBG protein in 200 μ L volume; nonspecific binding: 40 nM [3H]DHT and 20 nM SHBG protein and 1 mM cold DHT in 200 μ L volume. At the end of the incubation period, 200 μ L of the charcoal solution (3% containing 0.04% dextran) is added to 200 μ L of the reactions and shaken for 15 min before centrifugation. Supernatant (200 μ L) is then transferred to the wells of a 24-well white Optiplate; 200 μ L of scintillant are added with mixing. Radioactivity counts are read in

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Topcount[1].

Animal experiment:

Rats[1] Matched sets of castrated, sexually mature Harlan Sprague Dawley rats (42-56 d old, 200-250 g) are dosed once daily by oral gavage with BMS-564929 (0.00001-10 mg/kg) in solution/suspension of 80% PEG 400 and 20% Tween 20 for 14 d. Two control groups, one sham operated intact and one castrated, are dosed orally with the PEG/TW vehicle only, beginning on d 15 after surgery. Animals are dosed (vol/wt) at 1 mL/kg body weight. T propionate (TP) is dosed once daily sc in a 10% ethanol/90% peanut oil vehicle as a reference compound (0.03-10 mg/kg). After 14 d of treatment, the animals are killed by carbon dioxide asphyxiation, the levator ani and the ventral prostate are surgically removed and weighed, and serum is collected for LH measurements.

References:

[1]. Ostrowski J, et al. Pharmacological and x-ray structural characterization of a novel selective androgen receptor modulator: potent hyperanabolic stimulation of skeletal muscle with hypostimulation of prostate in rats. *Endocrinology*. 2007 Jan;148(1):4-12.

Background

BMS-564929 is an androgen receptor (AR) agonist, binds to androgen receptor (AR) with a K_i of 2.11 ± 0.16 nM. K_i : 2.11 ± 0.16 nM (Androgen receptor)[1]

BMS-564929 exhibits a potency (EC_{50} , calculated as the concentration at which 50% of the maximum stimulatory effect of DHT is achieved) of 0.44 ± 0.03 nM in the C2C12 myoblast cell line. In the PEC cell line, the EC_{50} for BMS-564929 is 8.66 ± 0.22 nM. BMS-564929 is more than 1000-fold selective for AR vs. estrogen receptors (ER) α and β , glucocorticoid receptor (GR), and mineralocorticoid receptor (MR), and approximately 400-fold selective vs. progesterone receptor (PR). BMS-564929 shows no measurable activity in functional transactivation assays with ER α/β , GR, MR, or PR at concentrations up to 30 μ M[1].

In sexually mature, castrated male rats, a well-characterized animal model, BMS-564929 (p.o.) shows substantially more potent activity in the levator ani, exhibiting an ED_{50} of 0.0009 mg/kg in the

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levator ani and an ED50 of 0.14 mg/kg in the prostate; a net 160-fold selectivity for muscle vs. prostate. Approximately 100% muscle stimulation is achieved at 0.1 mg/kg, reaching greater than 125% stimulation at 0.3 and 1 mg/kg. Compared with T propionate (TP) in the same model, BMS-564929 is more than 200 times more potent in stimulation of muscle and 80 times more selective for muscle vs. prostate[1].

[1]. Ostrowski J, et al. Pharmacological and x-ray structural characterization of a novel selective androgen receptor modulator: potent hyperanabolic stimulation of skeletal muscle with hypostimulation of prostate in rats. *Endocrinology*. 2007 Jan;148(1):4-12.

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