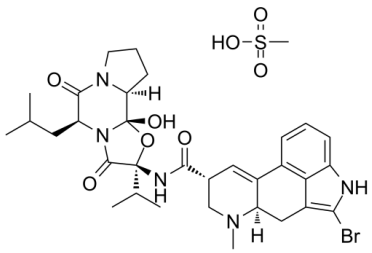
Data Sheet

Product Name:	Bromocriptine (mesylate)
Cat. No.:	CS-6048
CAS No.:	22260-51-1
Molecular Formula:	C33H44BrN5O8S
Molecular Weight:	750.70
Target:	Autophagy; Dopamine Receptor
Pathway:	Autophagy; GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : 75 mg/mL (99.91 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Bromocriptine mesylate is a potent **dopamine D2/D3 receptor** agonist, which binds D2 dopamine receptor with **pK_i** of 8.05±0.2. IC50 & Target: pKi: 8.05±0.2 (dopamine D2 receptor)[1] **In Vitro:** Bromocriptine stimulates [^{35}S]-GTPγS binding at D2 dopamine receptor expressed in CHO cells with pEC_{50} of 8.15±0.05[1]. Bromocriptine also is a strong inhibitor of brain nitric oxide synthase. The ergot alkaloid Bromocriptine (BKT) is found to act as a strong inhibitor of purified neuronal nitric oxide synthase (NOS) (IC_{50}=10±2 μM) whereas it is poorly active towards inducible macrophage NOS (IC_{50}>100 μM) [2]. Bromocriptine is found to inhibit the activity of at least one human cytochrome P450 enzyme. Bromocriptine is a potent inhibitor of CYP3A4 with a calculated IC_{50} value for the interaction of 1.69 μM[3]. **In Vivo:** Bromocriptine mesylate (2 mg/kg, i.p.) is administered for 7 days in groups of mice in forced swimming test (FST) and tail suspension test (TST). Bromocriptine group shows significant anti-immobility action as compared to control. When Bromocriptine administered 30 min after the last dose of 7 days MPE treatment and subjected to FST, this dopaminergic agonist produces significant and dose dependent potentiation of anti-immobility action of MPE (200 mg/kg, p.o.) as compared to MPE treatment alone. Bromocriptine treatment group shows a significant reduction of immobility time as compared to control. Bromocriptine administration after 7 days pretreatment with MPE (100 and 200 mg/kg, p.o.) shows significant and dose dependent potentiation of anti-immobility action of MPE as compared to MPE treatment alone[4]. Intracisternal administration of Bromocriptine decreases significantly the static mechanical allodynia (SMA) score compared to that of sham (saline-injected rats) and its effect lasted for 30 min. Intraperitoneal administration of Bromocriptine induces a significant, dose dependent (0.1 mg and 1 mg/kg) decrease in pain scores in CCI-IoN group when compared to sham and its effect lasted for 6 h. The highest dose induces the highest score decrease (P<0.01). Bromocriptine effect lasts for 20 min. Intraperitoneal administration of Bromocriptine induces a significant dose dependent decrease in SMA score in CCI-IoN+6-OHDA lesioned group compared to that of sham. Its effect lasts for 6 h[5].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]The [^{35}S]-GTPγS binding assay is carried out. Cell membranes (25 ±75 ug) are incubated in Buffer B containing 0.1 mM dithiothreitol (DTT) and 1 uM GDP and drugs in a volume of 0.9 mL for 30 min at 30°C. This preincubation ensures that the agonists tested are at equilibrium when the [^{35}S]-GTPγS (50±150 pM, final concentration) is added (in 100 uL of Buffer B) to initiate the reaction. The assay mixture is incubated for a further 20 min unless otherwise stated. The assays are terminated by rapid filtration and bound radio-activity determined as described for the radio-ligand binding assays above. The total binding of [^{35}S]-GTPγS is less than 20% of that added[1]. **Animal Administration:** Bromocriptine mesylate is dissolved in one drop of glacial acetic acid and made up to volume in distilled water (Mice)[4].

Bromocriptine is prepared in 0.9 % saline (Rat)[5].[4][5]Mice[4]

Swiss mice (20-25 g) of either sex (total 150) are used. Bromocriptine mesylate is used as dopamine receptor (D_2) agonist. Haloperidol is diluted in distilled water which is used for a vehicle of injection. Bromocriptine mesylate is dissolved in one drop of glacial acetic

acid and made up to volume in distilled water. Imipramine is dissolved in 0.9% normal saline. Haloperidol (0.1 mg/kg, i.p.) and Bromocriptine mesylate (2 mg/kg, i.p.) are administered for 7 days in groups of mice in Forced Swimming Test (FST) and Tail Suspension Test (TST). Imipramine (10 mg/kg, p.o.) as a standard is administered in positive control groups for 7 days.

Rat[5]

Adult male Sprague-Dawley rats (N=112, 275-325 g) are used. Two weeks after the 6-OHDA injection, the animals are briefly (<3 min) anesthetized with 2 % halothane using a mask and received for intracisternal administration Bromocriptine (7 µg/kg dissolved in 5 µL vehicle) or the vehicle alone (5 µL of 0.9 % saline). For i.p. injection we used Bromocriptine (1 mg/kg) and SKF81297 (3 mg/kg dissolved in 0.9 % saline) concentrations. Following a recovery period (<2 min), the rats are placed in the observation field for 40 min period-test by a blind-experimenter.

References:

[1]. Gardner B, et al. Agonist action at D2(long) dopamine receptors: ligand binding and functional assays. Br J Pharmacol. 1998 Jul;124(5):978-84.

[2]. Renodon A, et al. Bromocriptine is a strong inhibitor of brain nitric oxide synthase: possible consequences for the origin of its therapeutic effects.FEBS Lett. 1997 Apr 7;406(1-2):33-6.

[3]. Wynalda MA, et al. Assessment of potential interactions between dopamine receptor agonists and various human cytochrome P450 enzymes using a simple in vitro inhibition screen. Drug Metab Dispos. 1997 Oct;25(10):1211-4.

[4]. Rana DG, et al. Dopamine mediated antidepressant effect of Mucuna pruriens seeds in various experimental models of depression. Ayu. 2014 Jan;35(1):90-7.

[5]. Dieb W, et al. Nigrostriatal dopaminergic depletion increases static orofacial allodynia. J Headache Pain. 2016;17:11.

CAIndexNames:

Ergotaman-3',6',18-trione, 2-bromo-12'-hydroxy-2'-(1-methylethyl)-5'-(2-methylpropyl)-, (5α)-, methanesulfonate (1:1)

SMILES:

[H][C@@]12CC3=C(Br)NC4=CC=CC(C1=C[C@@H](C(N[C@@]5(C(C)C)C(N6[C@@H](CC(C)C)C(N7CCC[C@]7([C@]6(O)O5)[H])=O)=O)=O)CN2C)=C43.OS(=O)(C)=O

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