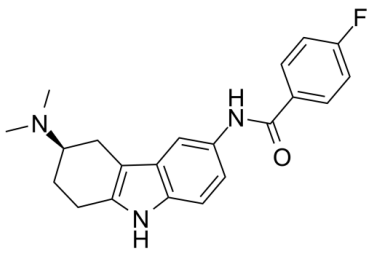
Data Sheet

Product Name:	LY 344864
Cat. No.:	CS-1350
CAS No.:	186544-26-3
Molecular Formula:	C21H22FN3O
Molecular Weight:	351.42
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : ≥ 350 mg/mL (995.96 mM)



BIOLOGICAL ACTIVITY:

LY 344864 is a selective receptor agonist with an affinity of 6 nM (Ki) at the recently cloned 5-HT1F receptor. IC50 Value: 6 nM (Ki) [1] Target: 5-HT1F LY 344864 possesses little affinity for the 56 other serotonergic and non-serotonergic neuronal binding sites examined [1]. in vitro: he 5-HT1A, 5-HT1B and 5-HT1D receptor agonists 8-OH-DPAT (3 microM), CP93129 (3 microM) and L694247 (3 microM), but not the 5-HT1F receptor agonist LY344864 (1 - 3 microM) inhibited evoked IPSCs [2]. in vivo: After an intravenous dose of 1 mg/kg, rat plasma LY 344864 levels declined with time whereas brain cortex levels remained relatively constant for the first 6 hours after injection. Oral and intravenous LY344864 administration potently inhibited dural protein extravasation caused by electrical stimulation of the trigeminal ganglion in rats [1]. Sumatriptan, zolmitriptan, rizatriptan, and naratriptan all contracted the rabbit saphenous vein from baseline tone, whereas LY 344864 in concentrations up to 10(-4) M did not contract the rabbit saphenous vein. Furthermore, vascular contractions to sumatriptan were markedly augmented in the presence of prostaglandin F(2alpha) (PGF(2alpha)). However, even in the presence of PGF(2alpha) (3 x 10(-7) M), LY344864 did not contract the rabbit saphenous vein in concentrations well in excess of its 5-HT(1F) receptor affinity (pK(i) = 8.2) [3].

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [1] LY344864 was dissolved in isotonic saline which had been acidified with HCl to a final pH of between 4-5.5. Male, Wistar rats (275-300 grams) were anesthetized with sodium pentobarbital (65 mg/kg, i.p.) and placed in a stereotaxic frame with the incisor bar set at -3.5 mm. LY344864 was given intravenously 10 minutes before, or orally 75 minutes before trigeminal stimulation. The dose that inhibited plasma protein extravasation by 50% (IDso) was approximated from the dose-response curve. Statistical comparisons were made using a oneway analysis of variance with a post-hoc Tukey-Kramer comparison of confidence limits.

References:

[1]. Phebus LA, Johnson KW, Zgombick JM, Characterization of LY344864 as a pharmacological tool to study 5-HT1F receptors: binding affinities, brainpenetration and activity in the neurogenic dural inflammation model of migraine. Life Sci. 1997;61(21):2117-26.

[2]. Jeong HJ, Chenu D, Johnson EE, Sumatriptan inhibits synaptic transmission in the rat midbrain periaqueductal grey. Mol Pain. 2008 Nov 11;4:54.

[3]. Cohen ML, Schenck K. 5-Hydroxytryptamine(1F) receptors do not participate in vasoconstriction: lack of vasoconstriction to LY344864, a selective serotonin(1F) receptor agonist in rabbit saphenous vein. J Pharmacol Exp Ther. 1999 Sep;290(3):935-9.

CAIndexNames:

Benzamide, N-[(3R)-3-(dimethylamino)-2,3,4,9-tetrahydro-1H-carbazol-6-yl]-4-fluoro-

SMILES:

O=C(NC1=CC2=C(NC3=C2C[C@H](N(C)C)CC3)C=C1)C4=CC=C(F)C=C4

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

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