

Product Data Sheet

Product Name: Fluoxetine HCl

Cat. No.: GC11709

Chemical Properties

Cas. No. 56296-78-7

Chemical Name N-methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine;hydrochloride

SMILES CNCCC(C1=CC=CC=C1)OC2=CC=C(C=C2)C(F)(F)F.Cl

Formula $C_{17}H_{18}F_3NO.HCl$ M.Wt 345.79

Solubility $\geq 17.3\text{mg/mL}$ in DMSO Storage Store at 2-8°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.

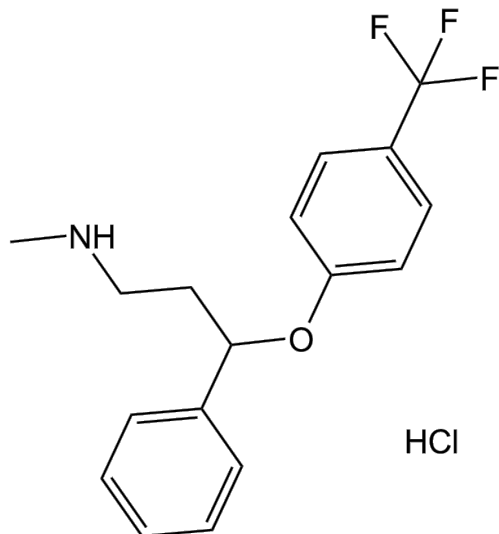
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:

Cell lines Xenopus oocytes expressing 5HT_{2C} receptor or 5HT receptors

Preparation method The solubility of this compound in DMSO is >17.3 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

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Reacting condition 100 μ M

Applications Fluoxetine inhibited the membrane currents elicited by serotonin (5HT) in *Xenopus* oocytes expressing either cloned 5HT_{2c} receptors or 5HT receptors. Responses of 5HT_{2c} receptors, elicited by nM concentrations of 5HT, were rapidly and reversibly blocked by micromolar concentrations of fluoxetine. In accord with the electrophysiological results, fluoxetine inhibited the binding of [³H]5HT to 5HT_{2c} receptors, and the binding to 5HT receptors in rat cortex membranes was also inhibited but less efficiently.

Animal experiment [2]:

Animal models Male Sprague-Dawley rats

Dosage form 5 mg/kg/day, i.p.

Application Olanzapine or fluoxetine treatment also increased the number of proliferating cells in the prelimbic cortex. In contrast, there was no effect of either drug in the subventricular zone or primary motor cortex. Subchronic (7 days) administration of olanzapine had no effect on cell proliferation in hippocampus or prelimbic cortex, consistent with the time course for the effect of fluoxetine and the therapeutic actions of antidepressant treatment. The combination of olanzapine plus fluoxetine did not result in a greater induction of cell proliferation in either brain region.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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- [1] Ni Y G, Miledi R. Blockage of 5HT_{2C} serotonin receptors by fluoxetine (Prozac)[J]. Proceedings of the National Academy of Sciences, 1997, 94(5): 2036-2040.
- [2] Kodama M, Fujioka T, Duman R S. Chronic olanzapine or fluoxetine administration increases cell proliferation in hippocampus and prefrontal cortex of adult rat[J]. Biological psychiatry, 2004, 56(8): 570-580.

Background

Fluoxetine is a specific presynaptic serotonin-reuptake inhibitor (SSRI) at the neuronal membrane, used in the treatment of depression.

The serotonin receptor, also known as 5-HT receptor, is a member of G protein-coupled receptor found in the central and peripheral nervous systems. The serotonin receptors, activated by the natural ligand serotonin, have been involved in a variety of biological and neurological processes such as aggression, anxiety, cognition, learning, memory, mood[1].

In vitro: In *Xenopus* oocytes expressing either cloned 5HT_{2C} receptors or 5HT receptors, micromolar concentrations of fluoxetine (Prozac) inhibited the membrane currents elicited by serotonin (5-hydroxytryptamine; 5HT). For responses elicited by 1 μ M 5-HT, the IC₅₀ of fluoxetine was about 20 μ M. Fluoxetine also inhibited the binding of [3H]5HT to 5HT_{2C} receptors expressed in HeLa cells and the binding of [3H]5HT to 5HT receptors in rat cortex membranes, with K_i of $\approx$ 65–97 nM and $\approx$ 56 μ M, respectively[2]. Administration of fluoxetine blocked the downregulation of cell proliferation of hippocampal cells resulting from inescapable shock (IS), which resulted in a state of behavioral despair[3]. Fluoxetine increased the number of newborn cells in the dentate gyrus of the hippocampus of adult rat. Fluoxetine also increased the number of proliferating cells in the prelimbic cortex[4]. Fluoxetine accelerated the maturation of immature neurons. Fluoxetine enhanced neurogenesis-dependent long-term potentiation (LTP) in the dentate gyrus [5]. Fluoxetine, but not other selective serotonin uptake inhibitors such as citalopram, fluvoxamine, paroxetine and sertraline, increased norepinephrine and dopamine extracellular levels in prefrontal cortex. Fluoxetine produced robust and sustained increases in extracellular concentrations of norepinephrine and dopamine after acute systemic administration [6].

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In vivo: Fluoxetine reversed the deficit in escape latency observed in animals exposed to inescapable shock in adult male Sprague–Dawley rats [3]. The combination of olanzapine and fluoxetine produced robust, sustained increases of extracellular levels of dopamine ([DA](ex)) and norepinephrine ([NE](ex)) up to $361 \pm 28\%$ and $272 \pm 16\%$ of the baseline, respectively[7]. Fluoxetine (5 and 10 mg/kg) reduced cocaine infusions (0.2 mg/kg), and cocaine infusions returned to baseline levels within 48 hr after fluoxetine treatments were terminated [8]. In sham-operated or adrenalectomized/castrated (ADX/CX) male rats, administration of fluoxetine dose-dependently (2.9-58 $\mu\text{mol/kg}$ i.p.) increased the brain content of the neurosteroid 3 α -hydroxy-5 α -pregnan-20-one (allopregnanolone, 3 α , 5 α -TH PROG)[9].

Clinical trials: In a 5-wk double-blind, parallel study with 40 depressed 23–69 yr olds, fluoxetine(20–80 mg/day) provided effective antidepressant activity, with fewer and less side effects[10].

References:

- [1]. Hoyer D, Clarke DE, Fozard JR, Hartig PR, Martin GR, Mylecharane EJ, Saxena PR, Humphrey PP (1994). "International Union of Pharmacology classification of receptors for 5-hydroxytryptamine (Serotonin)". Pharmacol. Rev. 46(2): 157–203.
- [2]. Ni Y G, Miledi R. Blockage of 5HT_{2C} serotonin receptors by fluoxetine (Prozac)[J]. Proceedings of the National Academy of Sciences, 1997, 94(5): 2036-2040.
- [3]. Malberg J E, Duman R S. Cell proliferation in adult hippocampus is decreased by inescapable stress: reversal by fluoxetine treatment[J]. Neuropsychopharmacology, 2003, 28(9): 1562-1571.
- [4]. Kodama M, Fujioka T, Duman R S. Chronic olanzapine or fluoxetine administration increases cell proliferation in hippocampus and prefrontal cortex of adult rat[J]. Biological psychiatry, 2004, 56(8): 570-580.
- [5]. Wang J W, David D J, Monckton J E, et al. Chronic fluoxetine stimulates maturation and synaptic plasticity of adult-born hippocampal granule cells[J]. The Journal of neuroscience, 2008, 28(6): 1374-1384.
- [6]. Bymaster F P, Zhang W, Carter P A, et al. Fluoxetine, but not other selective serotonin uptake inhibitors, increases norepinephrine and dopamine extracellular levels in prefrontal cortex[J]. Psychopharmacology, 2002, 160(4): 353-361.
- [7]. Zhang W, Perry K W, Wong D T, et al. Synergistic effects of olanzapine and other antipsychotic agents in combination with fluoxetine on norepinephrine and dopamine release in rat prefrontal cortex[J]. Neuropsychopharmacology, 2000, 23(3): 250-262.
- [8]. Carroll M E, Lac S T, Asencio M, et al. Fluoxetine reduces intravenous cocaine self-administration in rats[J]. Pharmacology Biochemistry and Behavior, 1990, 35(1): 237-244.

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- [9]. (Uzunov D P, Cooper T B, Costa E, et al. Fluoxetine-elicited changes in brain neurosteroid content measured by negative ion mass fragmentography[J]. Proceedings of the National Academy of Sciences, 1996, 93(22): 12599-12604.
- [10]. Bremner J D. Fluoxetine in depressed patients: a comparison with imipramine[J]. Journal of Clinical Psychiatry, 1984.

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