

Fluvoxamine

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Fluvoxamine (**Luvox**) is an antidepressant which functions as a selective serotonin reuptake inhibitor (SSRI). Fluvoxamine is used for the treatment of major depressive disorder (MDD), obsessive compulsive disorder (OCD),^[1] and anxiety disorders such as panic disorder and post-traumatic stress disorder (PTSD).^[2] Fluvoxamine CR (controlled release) is approved to treat social anxiety disorder.^[3]

The FDA has added a Black box warning for this drug in reference to increased risks of suicidal thinking and behavior in young adults and children. A study from the Institute for Safe Medication Practices identified Luvox as being 8.4 times more likely than other medications to be associated with violence.^[4]

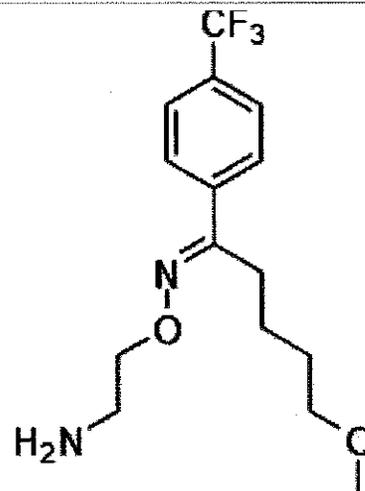
Contents

- 1 History
- 2 Medical uses
- 3 Adverse effects
- 4 Pharmacology
- 5 Pharmacokinetics
 - 5.1 Metabolism
 - 5.2 Elimination
- 6 Drug interactions
- 7 Synthesis
- 8 References
- 9 External links

History

Fluvoxamine was developed by Solvay Pharmaceuticals, Belgium now Abbott Laboratories and introduced as *Floxyfral* in Switzerland in 1983.^[5] It was approved by FDA on 5 Dec, 1994 and introduced as *Luvox* in US.^[6] In India it is available as *Uvox* by Abbott. It was one of the first SSRI antidepressants to be launched. It was the first SSRI, a non-TCA drug approved by the U.S. Food and Drug Administration (FDA) specifically for the treatment of OCD.^[7] At the end of 1995, more than 10 million patients worldwide had been treated with fluvoxamine.^[8] Fluvoxamine was the first SSRI to be registered for the treatment of obsessive compulsive disorder in children by the FDA in 1997.^[9] Fluvoxamine was the first drug approved for the treatment of social anxiety disorder in Japan in 2005.^[10]

Fluvoxamine



Systematic (IUPAC) name

(*E*)-5-methoxy-1-[4-(trifluoromethyl)phenyl]pentan-1-one *O*-2-aminoethyl oxime

Clinical data

Trade names	Luvox, Floxyfral
AHFS/Drugs.com	monograph
MedlinePlus	a682275
Pregnancy cat.	C
Legal status	Prescription Only (S4) (AU) R-only (US)
Routes	Oral

Pharmacokinetic data

Bioavailability	77%
Metabolism	Hepatic
Half-life	15.6 hours
Excretion	Renal

Identifiers

CAS number	54739-18-3 [↗]
ATC code	N06AB08
PubChem	CID 5324346
DrugBank	DB00176
ChemSpider	4481878 [↗]
UNII	O4L1XPO44W [↗]

In 1999, fluvoxamine came under great public scrutiny after it was discovered that Eric Harris, one of the two teenage shooters involved in the Columbine High School massacre, had been taking the drug after switching from Zoloft. Many immediately pointed fingers at fluvoxamine and its manufacturer Solvay Pharmaceuticals.^[11] Sales fell, and Solvay withdrew the medication from the U.S. market in 2002.^[12] In 2007, Solvay re-introduced Luvox to the U.S. market, which is now manufactured by Palo Alto, California-based Jazz Pharmaceuticals, Inc. On February 28, 2008, the FDA approved a controlled-release formulation of fluvoxamine for Solvay Pharmaceuticals, to be marketed as *Luvox CR*.^{[13][14]}

Chemical data	
Formula	C₁₅H₂₁F₃N₂O₂
Mol. mass	318.335
SMILES	
InChI	
	X (what is this?) (verify)

Medical uses

Fluvoxamine's primary use is the treatment of obsessive compulsive disorder (OCD). Fluvoxamine has been found to be useful in the treatment of major depressive disorder (MDD), and anxiety disorders such as panic disorder, social anxiety disorder, post-traumatic stress disorder (PTSD), and obsessive-compulsive spectrum disorders. Fluvoxamine is indicated for children and adolescents with OCD.^[15] The drug works long-term, with research showing that fluvoxamine retains its therapeutic efficacy for at least a year.^[16]

Adverse effects

Side effects most commonly observed with fluvoxamine include nausea, vomiting, drowsiness, insomnia, dizziness, nervousness, anxiety, dry mouth, abdominal pain, constipation, diarrhea, heart burn, appetite suppression, muscle weakness, "pins and needles" sensation, abnormal taste, headache, faster heart beat, sweating, weight gain, weight loss or unusual bruising. Other side effects which are observed more frequently in children include abnormal thoughts or behaviour, cough, increased menstrual pain, nose bleeds, increased restlessness, infection and sinusitis.^[17]

Pharmacology

Fluvoxamine is a potent and selective serotonin reuptake inhibitor with approximately 100-fold affinity for the serotonin transporter over the norepinephrine transporter. It has negligible affinity for the dopamine transporter or any other receptor, with the sole exception of the σ_1 receptor. It behaves as a potent agonist at this receptor and has the highest affinity of any SSRI for doing so. This may contribute to its antidepressant and anxiolytic effects. Reports indicate confusion, decreased anxiety to the point of negative affect, and aggressiveness.

Pharmacokinetics

The oral bioavailability of fluvoxamine is 53%. The plasma protein binding is about 80%.^[18]

Metabolism

Fluvoxamine is strongly metabolized in the liver, mostly by the processes of oxidative demethylation (producing fluvoxamine acid and its N-acetyl analog) and deamination (producing fluvoxethanol). Only fluvoxamine acid has been shown to have SERT inhibitor activity, roughly 1-2 orders of magnitude less potent than the parent compound.^[19]

Radio-labeled administration of a dose of fluvoxamine produced nine identifiable metabolites, constituting 85% of the absorbed dosage (thus 15% of the fluvoxamine remained unchanged). This isolate of metabolites was empirically proven to contain 60% fluvoxamine acid and its N-acetyl analog, and 10% fluvoxethanol, with the other six metabolites making up 30%.^[19]

Elimination

Fluvoxamine has the shortest serum half-life of all SSRIs, with a mean of 15.6 hours.^[20]

Drug interactions

Fluvoxamine inhibits cytochrome P450 enzyme CYP1A2, which metabolises agomelatine, caffeine, clozapine, duloxetine, haloperidol, phenacetin, tacrine, theophylline, and olanzapine. These substances can cause increased serum levels when administered together with fluvoxamine. Of major concern is the fact that the polycyclic aromatic hydrocarbons found in tobacco smoke are potent inducers of CYP1A2 so that smokers may require significant modification of medication dosage.^[21] A recent warning has been published regarding potentially serious interaction with tizanidine, based on CYP1A2 metabolism.^[22] The half-life of caffeine is significantly extended by the use of fluvoxamine, which can cause insomnia and irritability in coffee drinkers.

Fluvoxamine inhibits metabolism of diazepam and phenytoin via CYP2C19 and metabolism of aripiprazole, chlorpromazine, clozapine, haloperidol, olanzapine, perphenazine, risperidone, thioridazine and zuclopenthixol via CYP2D6 as well as of aripiprazole, clozapine, haloperidol, quetiapine and ziprasidone via CYP3A4.^[23]

Fluvoxamine has low potential for the drug interactions which are based on inhibition of enzyme Cytochrome P450 CYP2D6, less than most other SSRIs.^{[24][25][26]} Naturally the other SSRIs which are metabolized by CYP2D6 will have more CYP2D6-based interactions with TCAs, antiarrhythmics, B-blockers, phenytoin, opioids and neuroleptics.

The plasma protein binding of fluvoxamine is about 77%. Drugs with low protein binding are less likely to displace other protein bound drugs, and therefore have a lower potential to cause protein binding-related drug interactions.

Fluvoxamine also inhibits CYP2C9.^{[19][27]}

Synthesis

Fluvoxamine is one of only two SSRIs (along with alaproclate) to have a monocyclic structure.^{[28][29]}

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External links

- Fluvoxamine consumer information from Drugs.com (<http://www.drugs.com/cons/Fluvoxamine.html>)

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Categories: Selective serotonin reuptake inhibitors | Sigma agonists | Oximes | Ethers | Organofluorides

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