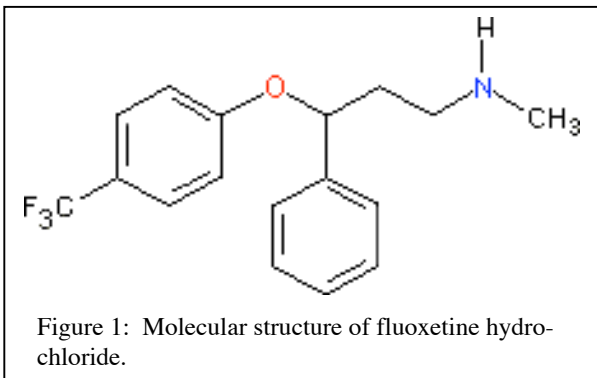
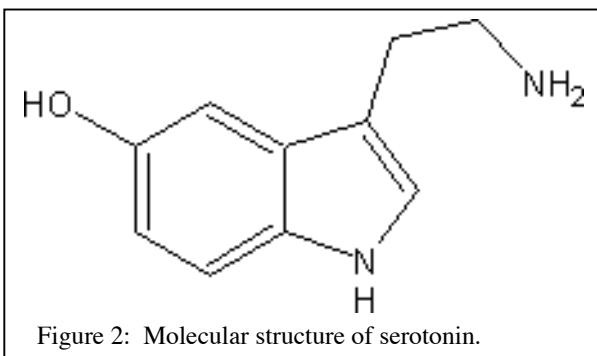


Recitation Handout 13: Maximum Safe Dose of Prozac

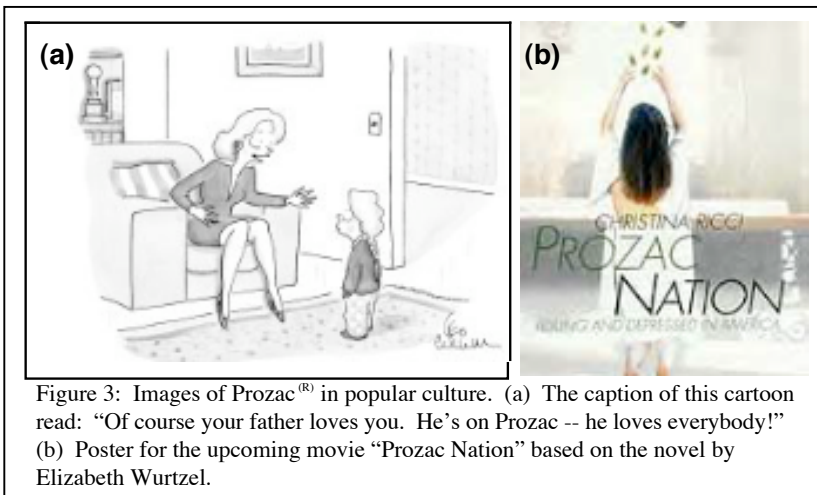


Prozac[®] is the registered trademark for the drug fluoxetine hydrochloride (see Figure 1¹). Fluoxetine hydrochloride may be prescribed for a variety of conditions including mild bulimia and obsessive-compulsive disorder. However, Prozac[®] is best known as an antidepressant, and over the last decade has become the most widely prescribed drug in the history of psychiatry. Prozac[®] is currently prescribed to more

than 38 million people in over 100 countries².



Fluoxetine hydrochloride was the first of a new class of drugs for treating mental illness known as *selective serotonin re-uptake inhibitors*. These drugs help to alleviate depression by increasing the levels of the neurotransmitter *serotonin* (see Figure 2³) in the brain. Serotonin is a chemical that is exchanged by cells in the brain, and is thought to influence sleep, appetite, aggression and mood.



Prozac[®] is also the first prescription medicine to become a cultural phenomenon. During the early and mid-nineteen nineties, Prozac[®] was the subject of intense media scrutiny, being vigorously – if not particularly deeply – discussed on popular television talk shows, magazine articles and

¹ Image source: <http://organic.chem.wisc.edu/>

² Boseley, S. 1999. Revealed: The danger of taking Prozac. *The Guardian*, Saturday September 4.

³ Image source: <http://www.giftplanzen.com/>

best-selling books (see Figures 3 and 4). In March of 2003, the film adaptation of Elizabeth Wurtzel's 1997 novel, *Prozac Nation: Young and Depressed in America*, will be released, starring Christina Ricci and Jason Biggs (the pie guy from *American Pie*). The movie will tell the story of a woman's struggle with depression during her freshman year at a prestigious university, and her interactions with parents, room-mates, psychiatrists and ultimately Prozac®.

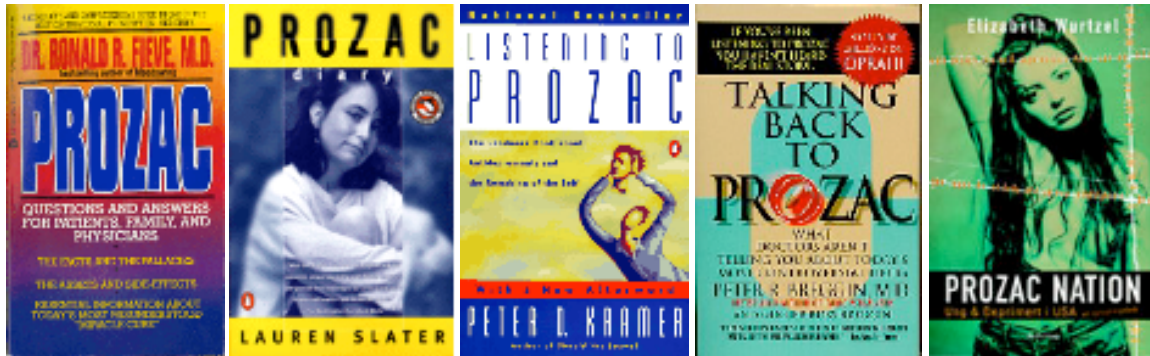


Figure 4: A very small selection of the books that have appeared on the subject of Prozac® over the last ten years.

Prozac® was initially approved for medical use in Belgium in 1986 for the treatment of depression, and was approved by the FDA in 1987. In a very rapid rise to popularity Prozac® achieved its most-widely prescribed psychiatric drug by 1990, a position that it has maintained ever since. According to Eli Lilly and Company⁴ (the manufacturers of Prozac®), the safety and effectiveness of the drug have been "...thoroughly studied in clinical trials with more than 11,000 patients." Eli Lilly and Company further comment, "There have been more than 3,500 publications on Prozac® in medical/scientific journals." This is a surprisingly lukewarm testament to Prozac®'s effectiveness and safety.

The *Physicians' Desk Reference* (PDR) lists critical information on prescription drugs. In the section on "Adverse Reactions," under the entry for Prozac® the PDR devotes approximately one page to simply listing the adverse reactions to the drug that were encountered during the clinical trials alone. Since the conclusion of the clinical trials, tens of thousands of Prozac® users have reported adverse reactions, ranging from occasional diarrhea to attempted murder/suicide. A number of patients who were prescribed Prozac® have sued Eli Lilly and Company. Recently (November 30, 2002) Eli Lilly settled a major case out of court. The plaintiffs, Diane and Melvin Cassidy of Monroeville PA sued Lilly for \$4.84 million in damages, although the actual amount of the settlement has not been made public.

The Cassidy case alleged that Prozac®, prescribed to Diane Cassidy for weight loss, produced suicidal thoughts and eventually led Ms. Cassidy to attempt suicide. The suicide attempt left Ms. Cassidy paralyzed on one side of her body and mentally impaired. The PDR casually mentions "suicide attempt" (in only one place) as an "infrequent whole body" adverse reaction to the drug.

⁴ See: <http://www.prozac.com/>

Although Prozac[®] has been implicated in a number of deaths – some put the number in the thousands, as shown in Figure 5⁵ – that occurred in circumstances like Ms. Cassidy’s there have been very few deaths that can be attributed to overdose of the drug in a purely biochemical sense. That is, deaths that resulted from chemical interference between fluoxetine hydrochloride and the human body’s natural chemical processes.

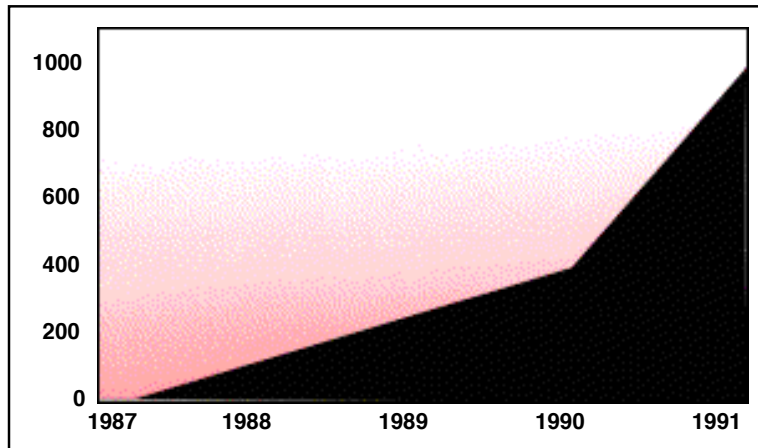


Figure 5: Cumulative total number of deaths among people using Prozac[®] during the five years following the drug’s introduction to the United States.

Prior to the introduction of Prozac[®] into the United States in 1987 there had been only two deaths as a result of acute fluoxetine overdose, and these were both in combination with either alcohol, powerful painkillers or illicit drugs. In the first case, the person was determined to have taken 1800 mg of fluoxetine. Although it was not possible to determine the actual amount of fluoxetine taken by the other person, measurements made during the autopsy were consistent with a dose of 760 mg.



Figure 6: Prozac[®] packaging and 20 mg capsules.

Fluoxetine hydrochloride is a chemical that has an unusually long half-life (5 days) in the human body. (Fluoxetine hydrochloride is broken down by the liver to form a chemical called norfluoxetine, which has an even longer half-life – about 14 days – in the body.)

Until recently, Prozac[®] was only available in capsule form, with each capsule delivering 20 mg of fluoxetine hydrochloride (see Figure 6⁶). The dosage guidelines in the PDR clearly state in several

places that the maximum safe dose of Prozac[®] is 80 mg per day.

How did the scientists at Eli Lilly, Prozac[®]’s manufacturer, arrive at this figure for the maximum daily dose?

⁵ Source: <http://users.actweb.net/>

⁶ Image source: <http://adbusters.cool.ne.jp/prozac.jpg>