Fluoxetine (Prozac)

General aspects
Fluoxetine is a drug which is used against physical disorder. The antidepressant is a selective serotonin reuptake inhibitor (SSRI). 1975 received the American pharmaceutical company Eli Lilly a patent for this active ingredient and began to market in 1985. It was celebrated at this time as an auspicious miracle drug, not least because it was considered stimulus enhancing. Meanwhile, however, serious doubts about the drug have arisen. Therefore, the manufacturer warns in the package insert of suicidal thoughts and behavior. Fluoxetine is commercially known inter alia under the name Prozac.

View of the molecule:
Fluoxetine may occur as R- and S- enantiomer (see Figure 2). In the marketed drug both enantiomers are included. Although only the R- enantiomer is considered to be effective, though no hazards of the S- enantiomer are known, therefore separation of the in the synthesis resulting of racemic is not required.

Fig.1 Fluoxetine.

Fig.2 Structures of the two enantiomers of fluoxetine
Synthesis:

Fluoxetine can be synthesized in various ways. In the following, a retrosynthetic view is performed referring to the synthesis by Eli Lilly.

From the schematic representation it appears that starting from methylamine (F), formaldehyde (G) and acetophenone (H) a Mannich reaction is carried out, which leads to E. By reducing the carbonyl function the alcohol (D) is formed. For the following ether synthesis, it is to be considered that the alcohol group on D must be converted into a better leaving group, so we get C. C is to be reacted with 4- trifluor – methylphenol (B) to fluoxetine (A).
Mechanism of Action:

Fluoxetine belongs to the selective serotonin reuptake inhibitors (SSRI). The mode of action is consistent with the monoamine – deficiency hypothesis that depressions are traced back to a lack of monoamine, such as serotonin or norepinephrine in the synaptic cleft. The mode of action of fluoxetine is based on the inhibition of protein for reuptake of serotonin (serotonin transporter). This has the consequence that the nerve cell, which secretes serotonin on nerve conduction, does not reuptake. Thus, serotonin lingers much longer in the synaptic cleft and thus aroused a lot longer to do the following nerve cell. However, there are reasons to doubt the monoamine - deficiency hypothesis, as for example, other antidepressants do not increase the concentration of monoamine in the synaptic cleft.

Side Effects:

As with many other medicines against depression, side effects may also occur with fluoxetine. The most common side effects: insomnia, headache, diarrhea, nausea, fatigue.

Sources:

- http://de.wikipedia.org/wiki/Fluoxetin
- https://www.youtube.com/watch?v=s48PbbE7E5Q
- http://www.taz.de/1/archiv/?dig=2007/01/12/a0259