1. Overview

Chlorpromazine was first synthesized in 1950 by the French chemist Paul Charpentier in the laboratories of Rhône-Poulence. Quickly its antipsychotic potential was discovered. In 1952 it was released to the market as „Thorazine“ in the US by Smith Kline and French. In Europe it was marketed as „Largactil“ and in Germany as „Megaphen“.

The structural base of chlorpromazine is phenothiazine. Therefore it is classified as a tricyclic neuroleptic. Indications for the use of chlorpromazine are the following conditions:

- schizophrenia
- psychotic disorders
- bipolar disorders
- amphetamine-induced psychosis
It was also used as a tranquilizer for agitated patients and as a preanesthetic due to its sedative effect. In medication the hydrochloride form is used and its application is either oral as syrup or in pills or intravenous. The pharmacodynamic half-life of chlorpromazine is about 30 hours. Chlorpromazine blocks several neurotransmitter receptors. It acts as an antagonist for the dopamine-receptors D1 and D2, the serotonin-receptors 5-HT1 and 5-HT2, the H1-histamine receptor and adrenergic receptors. The antipsychotic effect is mainly caused by its potential to block the D2-dopamine receptor. Since chlorpromazine does not target a specific receptor and therefore has many side effects it is called a “dirty drug”. By blocking the forementioned receptors especially in the brain it has the following centralnervous effects: sedative, anticholinergic, antihistaminic and antiemetic.

2. Physiological effects

Since the physiological cause for diseases like schizophrenia is not exactly known, so far only theories for the effectiveness of Chlorpromazine exist. One is the hypothesis of dopamine abundance in schizophrenic patients. It is based on the correlation between antipsychotic potency of drugs and their affinity for dopamine-receptors. Similar effects are observed for serotonin. Chlorpromazine has some positive side effects though they are not linked to its psychotic value. Studies showed antiviral and antibacterial effects. In many cases the use of Chlorpromazine caused extrapyramidal symptoms. This has led to the development of newer drugs with a better side effect profile. Other common adverse effects are liver damages, eczemas and anticholinergic effects such as mouth dryness and constipation. Frequently, an increase in prolactin production causes erectile dysfunction, hyperplasia of mammary glands and galactorrhea.
3. Synthesis

The Synthesis is a two-step-reaction from 3-Chlordiphenylamin

1. 3-Chlordiphenylamin is heated up with Sulfur to 2-Chlorphenothiazin
2. 3-dimethylaminopropylchlorid gets alkylated in alkaic medium with Sodium amide as a Catalyst to Chlorpromazine

4. Historical Facts

About 1900 antibiotic potency of dye was discovered by the german company BASF. For example Arsphenamine was used for treatment of syphilis and Methylene blue for Malaria. In World War II drugs for Malaria were rare with the result that the sedative and histaminergic potency of Promethazine were spotted. Promethazine is similar to Chlorpromazine. They both are derivates of Phenothenazine. Soon after antipsychotic potency was discovered. On 11 December 1950 Chlorpromazine was synthesized by Paul Charpentier. He was employed at Rhône-Poulenc. One year later Chlorpromazine was distributed for testing to physicians. It was used as an anaesthetic booster and to reduce shock. In 1953 Chlorpromazine was released onto the market by Rhône-Poulenc. The trade name of Chlorpromazine in europe was Largactil. 2 years later it was released in the USA under the trade name Thorazine. It was used for treatment against mania, schizophrenia and other psychotic affections. After newer psycholocigal drugs were discovered the number of sales of Chlorpromazine decreased. In 1955 about 500.000 patients have taken Thorazine. 35 years later in 1990 about 110.000 - 120.000 people have taken it. There you can see that newer psychological drugs replaced Thorazine. Since 1977 Chlorpromazine is on the World Health Organisation list of essential medicine.
5. Further Information


6. Sources

- www.laborlexikon.de/lexikon/infoframe/p/Prolaktin.htm, 18.01.2015.