Some of the earliest synthetic organic molecules were dyes. The dyes were of interest not only in industry but also in biology. Dyes were found to be useful in biology for staining certain types of cells. Paul Ehrlich, an immunologist in the late 1800s, realized if dyes can selectively stain certain types of cells, then maybe toxic dyes can selectively *kill* certain types of cells. Ehrlich called this idea of a selective drug a **magic bullet**. After receiving a Nobel Prize in Medicine in 1908 for his work in immunology, Ehrlich developed a new **arsenical** drug with activity against the bacteria that cause syphilis. Arsenicals are a drug class in which each member contains an arsenic atom. The arsenic atom makes the drug toxic, but Ehrlich's drug was much less toxic, and still effective, than other arsenicals.

Gerhard Domagk [incorrectly stated as Georg in the video] of Germany followed in the footsteps of Ehrlich's work and explored the use of dyes as antibiotics. Domagk discovered a particularly effective red dye, which was later called Prontosil Rubrum (1). Prontosil Rubrum was active against multiple different types of bacteria and was an immediate sensation in medicine. Domagk later received the Nobel Prize in Medicine in 1939 for his work on Prontosil Rubrum.

![Prontosil Rubrum](image)

When Prontosil Rubrum reached the market in 1935, a group of French researchers almost immediately discovered that Prontosil Rubrum has little or no antibacterial effect. Instead, Prontosil Rubrum is metabolized in the body to form sulfanilamide (2), which is the active form of the drug. Prontosil Rubrum is therefore classified as a **prodrug**. Prodrugs are inactive compounds that react in the body to form an active drug.

![Sulfanilamide](image)

Sulfanilamide was soon used in place of the more complex and expensive Prontosil Rubrum as an antibacterial. Sulfanilamide itself is the parent structure of an entire class of molecules, the **sulfonamide antibacterials** or just **sulfa drugs**. The entire structure of sulfanilamide is very nearly equivalent to the pharmacophore of the sulfa drugs in general (see a following exercise for more details).

While sulfa drugs were a very successful class of antibacterials, the compounds are not in widespread use today. As with many antibacterials, after prolonged use, sulfa drugs have become less effective against most bacteria. This **mutational resistance** involves genetically mutated bacteria that develop immunity to a drug. One exception is sulfamethoxazole (3). Sulfamethoxazole is occasionally prescribed for inner ear infections.
Although the sulfa drugs are no longer in general use, the drug class is very important as one of the first examples of wholly synthetic medicines.