

# **Setting the Records Straight: The Pioneering Work of Gerhard Domagk**

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## **Abstract**

Heinrich Horlein – who was responsible for the Pharmaceutical Science Laboratories at Bayer, was confident in 1927 that by appointing Gerhard Domagk, he had called upon the right man to the right place and at the right time. He was fascinated by Domagk's thesis which was focused at the annihilation of pathogens from the reticulo-endothelium. Horlein engaged and appointed this young lecturer from Munster University as the head of planned institute for experimental pathology and bacteriology. Domagk built on the studies which had already occupied him as an assistant lecturer for many years. He had already concluded that the infection could either be combatted by increasing the host's immune defenses or by damaging the pathogens, themselves. The studies aimed at the elimination of G+ve cocci started in 1931, and he found some highly effective – a new type of disinfectant, the quaternary ammonium compound or "quits" Zephriol in 1935. This compound was highly effective with good local tolerability to the extent that it could also be used not only as hand disinfectant but also for most medical instruments; it remains the case even today - after more than Fifty years.

**Key words:** Gerhard Domagk; pathology; bacteriology.

## **1. Introduction**

To develop newer compounds and novel test systems, an essential step is to incorporate data from animal experimentations, where countless substances synthesized by the chemist Michts and Klever could be tested by Domagk. The main objective of such experiments was to test their innate propensity as antimicrobial agents by using a mouse model where the animals were infected with staphylococci. Following a flash of inspiration, the animals were subjected to an-azo-dye substituted with one sulphonamide group[1,2], even though it had been completely ineffective in vitro.

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This resulted in a remarkable finding of this compound as a bacteriostatic agent. Simplification of this molecule in 1932 led to the synthesis of prontosil, which was superior to the originally tested compound with unprecedented results. Following confirmation of the test results, careful chemical trials started with surprising success against a wide variety of Coccal infections. In 1935, the substance was introduced in the clinical with an astounding success from the Bayer Laboratories and adopted worldwide soon thereafter. At the Paris world fair in 1937, I.G. Farbenindustric A.G, made up of Bayer plus six other companies [3,4,5] that were operating since 1925, were awarded the “Grand Prix” for the first therapeutically effective sulphonamide. In the subsequent years, over a dozen more sulphonamides, mainly with peak actions against various different organisms made their way from laboratory to the sick-bed and become a major life-saver for humans. This began with Ultron for the oral treatment of Gonorrhea, and ended in 1960 with long acting Durenat with Schering, which is still used today against infection with pathogens that are otherwise insensitive to sulphonamide. During the sulphonamides era mortality from epidemic meningitis fell from 75% to 10% illustrating what a decisive breakthrough Domagk had made in the chemotherapy for bacterial infection in 1939. Shortly after the outbreak of the second world war, Domagk was awarded the Noble prize<sup>2</sup> for medicine in recognition of his revolutionary contribution to novel antibiotics that had revolutionized not only the field of chemistry but also medicine. Unfortunately, the régime’s travel policies prevented him from making a trip to Stockholm so he could not collect the award personally – even after eight years of his breakthrough. His pioneering work archived at the start of a historical epoch for Bayer scientists changed medical aptitude towards the treatment of infection which was otherwise deemed incurable – including tuberculosis, the most famed epidemic of the that time. Domagk [6,7] investigated all the sulphonamides submitted for antimicrobial studies for their antituberculous effects as well. In 1940, he began with specific Hot Inhibitory sulfathiazole. Following on from this discovery came the development of the thiosemicarbazones. Synthesized by Behnisch, of which the substance Known in 1943 [8,9] TBI and later as the active compound in conteban proved the most effective in animal experiments. With this medication it was noted that the tuberculous foci usually appearing after infection were limited or did not develop at all. Domagk spared no efforts in pushing ahead with clinical trials of this first agent against lupus tuberculosis, tuberculosis of the larynx; the kidney, the gut and bladder, and the result were sensational. By its launch in 1949, around 20,000 Pulmonary Patient including Individuals suffering from pulmonary tuberculosis had been treated with the drug. The impressive results achieved with conteban were surpassed in 1951 by isoniazid (INH) which was the Second anti-tuberculosis compound to be synthesized by the Bayer Research Laboratories. It’s powerful, specific effects against tuberculosis strains where were otherwise resistant to thiosemicarbazones, and its good tolerability gave reasons to hope that it could eradicate the source of infection and limit the risk of transmission. With Ncoteban being launched in 1952, and the combination product Nicoteban Compound developed four years later to Combat bacterial resistance with the expectations that the lines of thousands of tuberculosis patients could be saved. INH was discovered separately in three different laboratories, two in the USA (Hattman La Rochie Inc, Squbbe & Sons) [10] illustrating its international significance. Needless to say that for certain, all three routes were based on the Conteban developed by Domagk.

## **2. Conclusion**

Gerhard Domagk was responsible for development of prontosil, the first effective antibacterial agent, although

penicillin was serendipitously discovered by Alexander Fleming before prontosil. The front runner of the Sulfonamides was the first antibiotic produced commercially and patented. Even though his work created the age of antibacterial therapy, in my view, Domagk did not receive the recognition that he so deserved. We can easily examine the circumstances surrounding Domagk's path, and also focus on other individuals who were involved in the project which ultimately contributed to its overall success. This paper also highlighted how biomedical scientists and Chemists integrated their respective expertise to achieve these collective goals. Prior to the work of Domagk, the concept that a bacterial infection could be cured by the systemic administration of chemical substances, was considered unrealistic and foolhardy by most Clinicians. In spite of the fact that Gerhard Domagk was awarded the Nobel Prize in 1939, in my view the Scientific Community tends to view him as a marginal figure as compared to Alexander Fleming and Selman Waksman. This paper is meant to set this record straight. Discoveries of Streptomycin by Domagk not only ushered a new era but also demonstrated to other investigators that the infection could be cured. There has been no greater advancement in clinical medicine then the advent of antibacterial therapy. Domagk's monumental contribution to the welfare of mankind should continue to be revisited and celebrated with the highest accolade.

## References

- [1]. Protocol for sulphanamide studies from Domagk's Laboratory Journal 1934.
- [2]. Certificate confirming the award of the Nobel Prize for Medicine to Gerhard Domagk on 26-10-1939.
- [3]. Bayropharm, a Bayer Subsidiary Germany.
- [4]. Friedr Bayer & co 1988.
- [5]. 100 Years Research and Progress Bayer AG 1988.
- [6]. Domagk 1965 bibliography of Colebrook Royal Society page 44-50.
- [7]. Chemical Heritage Foundation Chemistry Chemical Heritage Press, Philadelphia.
- [8]. Gelmo P (1999) Sulphamides of panico benzene Sulphonic Acid. *Prakt chem* 77369-382.
- [9]. The making of Miracle drug scientific discovery May 31, 2017.
- [10]. Horlein Heinrich (1937) the development of chemotherapy for bacteriological disease 139.635.649.