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Undergraduate

HOW MAUVE CURED SYPHILIS

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Accidents are by no means unusual. In a world run by the forces of nature, the unexpected is always expected. Occasionally, however, these so-called accidents advance our individual lives, society, and the future. One particular accident occurred in the realm of chemical science where a young chemist in search of a cure for malaria stumbled upon the first-ever synthetic dye that subsequently pioneered contemporary immunology and chemotherapy, even playing a role in the treatment of syphilis.

In 1856, an eighteen-year-old chemist at the Royal College of Chemistry in London was trying to develop an artificial quinine – a crystalline alkaloid with antipyretic (fever-reducing), anti-malarial, analgesic (pain killing), and anti-inflammatory properties – particularly for the treatment of malaria post-infection. This student, William Henry Perkin, was challenged by his professor, German chemist August Wilhelm von Hofmann, to produce the drug since the only known natural source for quinine was the bark of the cinchona tree from South America; thus, the synthesis of this product would have had obvious economical and medical benefits for the Old World (Butler et al. 2010). Perkin's experiments failed to produce quinine; rather, the two organic compounds he used (oxidized aniline and toluidine) reacted together to produce a black solid. He then began to clean his experimental setup since black solids are common results in "failed" organic synthesis experiments. While cleaning out his flask, Perkin noticed that some components of the black solid dissolved in alcohol, releasing a beautiful, lavender-lilac color like pale purple, which – unbeknownst to Perkin – was the first ever synthetic dye.

Although a handful of chemists first began to prepare aniline dyes (synthetic dyes) decades before Perkin's discovery, they produced identical substances that had no commercial use. Perkin's, however, developed a dye capable of being manufactured commercially, thus, Perkin developed the first truly useful synthetic dye (Johnston, 2007). Perkin saw in his discovery a lucrative enterprise. He patented the dye the following year, and opened a dyeworks in Greenford on the banks of the Grand Union Canal in London. His aniline dye was brighter, more vibrant, and more resistant than any of the natural dyes that came from animals, minerals, or plants.

These natural dyes were characteristic of aristocracy since the natural substances from which they came were expensive and labor-intensive to extract (Tyle, 2002). A brilliant entrepreneur, Perkin manufactured the dye as Tyrian purple to exploit the name's synonym with the rare and affluent dye derived from glandular mucus of snails (Matthew and Harrison, 2004). Tyrian purple was renamed to mauve from the French name for the mallow flower which is violet in color. Chemists later changed the name to mauveine .

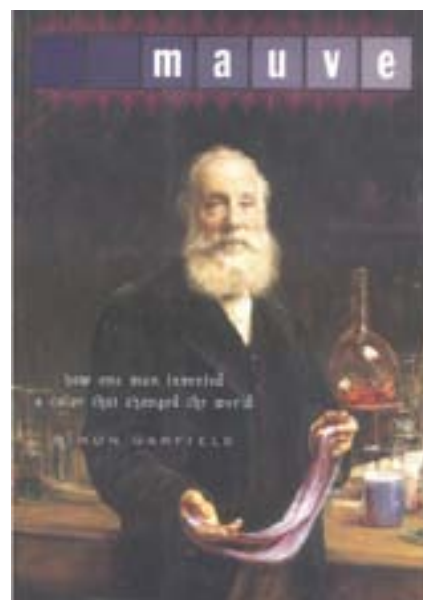


Figure 1. Cover of Simon Garfield's biography titled Mauve: How One Man Invented a Color that Changed the World depicts chemist Sir William Perkin holding a cloth with his emblematic color.

The consequences of this accidental discovery were immediate and widespread. For one, Perkin's discovery motivated German chemists to capitalize on a newfound industry such that by 1912 German dye manufacturers dominated the European market. So much so, in fact, that London, where the first dye was originally made, soon imported 95% of their dyes from Germany (Johnston 2007). What followed is history. Author J.G. Crowther claims in *British Scientists of the Nineteenth*



Figure 2. Greenford Green Works, 1858, was built in 1857 by Perkin, his father, and his brother to mass-produce Perkin's aniline purple.

highlighting the revolutionary effect a simple dye had on commoners and royalties alike. Since Perkin's invention established a cheap and easy method for dye production, nearly two thousand artificial colors were developed within fifty years of Perkin's initial discovery in 1856. Besides applications in the textile industry, these dyes have also been used to color food, hair, and furniture. Essentially, mauve and every subsequent dye attributable to Perkin's accidental breakthrough were deemed immensely valuable in varying industries. The methodology itself also became revolutionary when many industries began looking into other possible applications of coal tar from which the aniline dye was originally synthesized. Coal tar



Figure 4. Dr. Paul Ehrlich.

Century that "Perkin was the creator of modern chemical industry, [which] was imitated [and superbly utilized] in Germany, [and] had a profound influence on the destiny of nations;" thus, the dye has had grand implications outside of chemistry, even rooting itself in the realm of political science. Moreover, Perkin's original dye had influences on popular culture partially due to Perkin's commercial savvy. Perkin, for instance, changed the name of his dye from Tyrian purple to mauve in order to attract the French people since French designers were admired for their fashion sense and were trend setters (Garfield, 2001). Mauve became particularly fashionable when Queen Victoria wore it to one of her daughter's weddings,



Figure 3. The Perkin Medal, awarded annually to a scientist for his or her innovation in applied chemistry resulting in outstanding commercial development. The first Medal was awarded to none other than Sir William Perkin in 1956 commemorating the 50th anniversary of the discovery of mauveine.

was used to develop films and plates, and it improved the sensitivity of photographic emulsions (Fifer, 2002). In addition to improving the art of photography, coal tar has been used as a vital component of sealed, or tarmac, roads; to treat dandruff and psoriasis when in the form liquor carbonis detergens (Paghdal & Schwartz, 2009); and to heat boilers.

Sir Perkin's legacy is indisputable. Some alternatives to dye production have been in effect, but the relative simplicity of Perkin's methods explains its persistence and pertinence. The American section of the Society of Chemical Industry established the Perkin Medal in 1906 in his honor, which is still widely viewed as the highest honor in American industrial chemistry. This honor was first bestowed upon none other than Perkin who is regarded as the father of industrial chemistry for transitioning chemistry from a theoretical to an applicable science (Garfield, 2002; Johnston, 2008; Fifer, 2002).

This remarkable story of how a dye – simply, a coloring substance – changed the world does not end with

recognition for Perkin's achievements, fortuitousness, or contributions to chemistry and industry. Mauve's journey into our modern-day civilization travels through the revolutionary works of microbiologists, particularly Nobel laureate Dr. Paul Ehrlich. With a traceable material at their disposal, microbiologists were able to selectively target bacterium without affecting other organisms, a concept known as the "magic bullet" that was first derived by Dr. Paul Ehrlich (Tan & Grimes). Evidence of Ehrlich's interest in Perkin's anilines dyes began with his dissertation on the theory and practice of staining animal tissue, which earned him his doctorate in medicine in 1878. He subsequently had the unrestricted use of every facility at the Berlin Medical Clinic to further his study of these dyes. In 1882, Ehrlich published his method of staining Tubercle bacillus, which, after few modifications, is still in use today. This method is also the basis of the Gram method of staining bacteria widely used by modern bacteriologists, supporting mauve's enduring legacy.

Ehrlich began his immunological and chemotherapeutical studies in 1890, basing his works on the idea that the chemical constitution of drugs used must be studied in relation to their mode of action and their affinity for the cells of the organisms against which they were directed (Nobel Fnd.), a notion developed via his study of aniline dyes. Ehrlich theorized that living cells have "side-chains" – now known as antibodies – that link with particular toxins to elicit a biological response much like dyes have side-chains related to their specific coloring properties in fabric. Ehrlich's Side-Chain Theory explained the immune response in living cells at a time when very little was known about the nature of toxins and pathogens. His aim then was to expand his theory into practical applications.

He and his assistants developed hundreds of drugs to act like "magic bullets" that directly target particular pathogens and alter their biological make-up so that they are rendered harmless. The first of many modified dyes they produced was Trypan Red in 1904, a red dye with modified sulfo-groups to cure sleeping sickness.

In 1909, Ehrlich set his sights on the newly isolated spirochetal bacteria *Treponema pallidum* that caused syphilis. Ehrlich had developed so many "magic bullets" prior to this finding and not all had specific, designated uses. He tried Compound 606, the 606th arsenical drug that originally tested ineffective for other purposes, on a syphilis-infected rabbit and found it to be very effective (Nobel Fnd.). Compound 606, marketed as Salvarsan, and the later variant Compound 914, called Neosalvarsan, would remain the treatment of choice until penicillin became widely available (Heynick, 2009). Thus, Ehrlich's practical experimentation prevailed, and he became famous as one of the main founders of chemotherapy. In

recognition of his work on immunity, Ehrlich was awarded the Nobel Prize in Physiology or Medicine in 1908 (shared with Ilya Ilyich Mechnikov) one year before he conquered *Treponema pallidum*.

In conclusion, Perkin's dye and method of production was utilized by Ehrlich to develop "magic bullets" that targeted specific pathogens, effectively treating fatal diseases like syphilis.

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