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Hermann Emil Fischer – The most outstanding chemist in history

Hermann Emil Fischer was an eminent German organic chemist who made brilliant contributions to the chemistry of natural products. He was an exemplary chemist and an excellent model for all future generations of chemists. He is considered one of the great "discoverers" of biochemistry. His main studies addressed the molecular structures of various biochemical molecules, especially sugars. He was the first to clarify the structures of various sugars and enzymes as well as of several other natural products, including glucose, caffeine, and uric acid, and to demonstrate the mechanisms of their formation. He synthesized several amino acids and created small chains thereof as precursors to protein formation. He defined the "lock-and-key" mechanism to explain how enzymes can catalyze certain reactions, but not others. He discovered the chemical compound phenylhydrazine, which later proved to be very useful for a variety of purposes and has been found to induce eczema. His work included methods of managing the chemistry of carbohydrates, thanks in part to the use of phenylhydrazine. This research resulted in the synthesis of a series of sugars; his greatest success was the synthesis of glucose, fructose, and mannose. He was awarded the 1902 Nobel Prize in chemistry in recognition of his achievements in sugar and purine synthesis. He was the first organic chemist to receive this honor. He laid the chemical foundations for biochemistry through his study of sugars, enzymes, purines, and proteins, thereby establishing a close relationship between chemistry and biology.

This year, the French Academy of Science is celebrating its 350th anniversary, which is the perfect occasion to remember Fischer, as he was also a member of the French Academy of Sciences.

1. The life of Fischer

Gaudeamus! Hermann Emil Fischer was born to Julie Poensen Fischer and Laurenz Fischer on 9 October 1852, in Euskirchen, a beautiful town near Bonn, Germany. He was the only male child, the youngest of five children. This was the year, 1852, in which Beer's law was proposed by August Beer. Also born in the same year as Fisher were the German bacteriologists Friedrich August Johannes Loeffler and Julius Richard Petri, the winner of the Nobel Prize in Physics in 1907, Albert Abraham Michelson, the winner of the Nobel Prize in Physics in 1903, Antoine Henri Becquerel, the winner of the first Nobel Prize in Chemistry in 1901, Jacobus Henricus van't Hoff, Jr., the winner of the Nobel Prize in Chemistry in 1906, Ferdinand Frédéric Henri Moissan, the winner of the Nobel Prize in Chemistry in 1904, William Ramsay, the winner of the Nobel Prize in Physiology or Medicine in 1906, Santiago Ramón y Cajal, the Dutch physician and feminist Catharine van Tussenbroek, the Nobel Peace Prize winner Paul-Henri-Benjamin Balluet d'Estournelles, and the famous German musicians Robert Hausmann and Otto Neitzel.

Fischer attended the Gymnasium in Bonn. He was an eminent pupil, and he graduated at the top of his class. Although his father wished that Emil would follow him into the business world, Emil showed interest in scientific subjects. Through his obstinacy, Emil convinced his father of his aptitude for science, and finally, his father agreed to his pursuit of a university education. This was the turning point in Emil's life and laid the foundation for his later scientific achievements. Emil wished to become a mathematician or a physicist, but his father considered these professions to be without economic potential and instead persuaded his son to study chemistry. In 1871, Fischer began his studies in chemistry at the University of Bonn and became a pupil of August Kekulé and Rudolf Clausius. In 1872, he transferred to Strasbourg (along with his cousin Otto Fischer), where he studied chemistry with Adolf von Baeyer, who had recently been appointed the director of the chemical institute. In 1874, he received his doctorate from the Strasbourg University for his research on coal tar dyes that he had performed while working with Adolf von Baeyer. Von Baeyer chose Fischer to be a private assistant in his research laboratory. In 1875, he followed von Baeyer to Munich, where he qualified as Privatdozent in 1878, and joined the University as an

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Assistant Professor in 1879. In 1882, he was promoted to Professor of Chemistry at Erlangen, and in 1885, he became Professor of Chemistry at Wurzburg. In 1892, he succeeded A.W.V. Hofmann as the Director of the Chemistry Institute of Berlin, where he remained until the end of his career.

2. Research activities or a love of science is only the way to achieve conquest

The beginning of Fischer's most important work was his accidental discovery, in 1875, of phenylhydrazine and this random event ultimately proved to drive his destiny.

Under von Baeyer, Fischer performed research on phthalein dyes and wrote his Ph.D. thesis on fluorescein and orcin-phthalein. He was appointed assistant instructor at the Strasbourg University, and there he discovered the first hydrazine derivative, phenylhydrazine, and demonstrated its relationship to hydrazobenzene. Fischer's doctoral thesis had concerned the chemistry of colors and dyes. He extended this interest to new synthetic dyestuffs. Together with his cousin, Otto Fischer, he examined the composition of rosaniline. At that time, there were several conjectures regarding the composition of this substance, but no satisfactory solution was reached until the Fischers succeeded in showing that it was a triphenylmethane derivative. They reduced rosaniline to a colorless derivative, which they called leucaniline, and by removing its nitrogen atoms, they converted it into a hydrocarbon with the composition $C_{20}H_{18}$. They performed similar reactions with pararosaniline, obtaining a hydrocarbon with the formula $C_{19}H_{16}$, which proved to be identical to triphenylmethane. In 1878, they proved that these rosaniline dyes were homologs and were triamine derivatives of triphenylmethane and its homologs, rosaniline being a derivative of metatolyldiphenylmethane and *p*-rosaniline a derivative of triphenylmethane. Fischer's first publications (1875) were concerned with the organic derivatives of hydrazine. He discovered this new group of compounds, considering them to be derivatives of the as-yet-unknown compound N_2H_4, which he named hydrazine to reflect its relation to nitrogen. Fischer prepared phenylhydrazine itself and established its formula by 1878. The reaction of hydrazines with carbon disulfide was found to yield various dyestuffs. Oxidation produced tetrazenes, compounds with chains containing four nitrogen atoms. He found that aryl hydrazines reacted with ketones and keto acids to form derivatives of indole (Fischer indole synthesis, 1886). In 1884, Fischer discovered that phenylhydrazine was a valuable reagent for aldehydes and ketones. By 1888, he had established the structures of hydrazones and osazones. He would later utilize these reactions of phenylhydrazine to elucidate the chemistry and structures of carbohydrates. Fischer studied uric acid and related substances between 1881 and 1914, when he achieved the first synthesis of a nucleotide. In 1882, he published structural formulas for uric acid, caffeine, theobromine, xanthine, and guanine. He synthesized theophylline and caffeine (1895) as well as uric acid (1897), but further research convinced him that his structures were incorrect, since his reaction products were not reconcilable with his formulas. In 1897, he published a new set of formulas. In 1914, he prepared glucosides of theophylline, theobromine, adenine, hypoxanthine, and guanine. Xanthine, hypoxanthine, adenine, and guanine are all present in the nuclei of animal cells. Theobromine, caffeine, and theophylline are stimulants found in plants.

From theophylline-D-glucoside, he prepared the first synthetic nucleotide, theophylline-D-glucoside phosphoric acid. Fischer's purine research was of considerable interest to the German drug industry. His laboratory methods became the basis for the industrial production of caffeine, theophylline, and theobromine. In 1903, he synthesized 5,5-diethyl-barbituric acid. Under various trade names—Barbital, Veronal, and Dorminal—this compound proved to be a valuable hypnotic. Another commercially valuable purine prepared by Fischer, in 1912, was phenylethylbarbituric acid, also known as Luminal or phenobarbital. Fischer became the prime investigator in the field, and it is to him that almost all knowledge of the purines can be attributed. He explored the entire series, established their structures, and synthesized approximately 130 derivatives by 1900.

2.1. Success is not luck but rather ideal means and hard work

Fischer conducted his purine research simultaneously with his carbohydrate studies and became the prime investigator in both fields. When he began his carbohydrate studies in 1884, there were four known monosaccharides, namely, two aldohexoses (glucose and galactose) and two ketohexoses (fructose and sorbose), and three known disaccharides (sucrose, maltose, and lactose). Glucose and galactose are straight-chain pentahydroxy aldehydes, and ketohexoses are straight-chain pentahydroxy ketones. Through an enormous effort, Fischer elaborated the complex structures and chemistry of carbohydrates, synthesized many of them, and established the configurations of the sixteen possible stereoisomers of glucose. Fischer utilized the method of Heinrich Kiliani to convert pentoses into hexoses, the latter into heptoses, etc., thereby synthesizing sugars with as many as nine carbon atoms. Starting with glyceraldehyde, he built up molecules step by step to synthesize several pentoses and hexoses, including glucose, fructose, and mannose, using the Kiliani method. Fischer achieved his first synthesis of a sugar in 1887. Fischer found that glucose, fructose, and mannose form the same osazone and, therefore that the three sugars have the same configuration below the second carbon atom. He subsequently found that upon hydrolysis with hydrochloric acid, the phenylhydrazine is eliminated from osazones to form osones, a new type of glucose derivative possessing adjacent carbonyl groups. By reducing these, he obtained sugars, although with the conversion of aldoses into ketoses. Through differential reduction and oxidation reactions, Fischer could transfer the carbonyl group from one end of the chain to the other, and by testing the products for their properties and the optical rotation of the plane of light polarization that they induced, he could elucidate the structures of the compounds. Fischer