# The History of Urea and Its Use in the Modern Fertilizer Industry

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Abstract: From the common name of the organic compound "urea", it can be inferred that urea is a major component of urine. Urea naturally occurs in most mammals and is crucial for removing toxic waste products from the human body. This work investigates the history of urea, including the discovery of the "urea cycle" in humans. Moreover, urea was the first organic compound to be synthesized from inorganic compounds, bringing about a new definition of organic chemistry. This work examines the specific mechanism behind Fredrich Wohler's synthesis of urea from inorganic compounds. Furthermore, urea is now synthesized on a large scale for nitrogen-based crop fertilizers, and such modern processes have great implications on the environment.

## 1 INTRODUCTION

Urea is composed of a carbamide--- a carbonyl group attached to two amide groups (see Figure 1). Its molecular formula is $CH_4N_2O$, and its exact mass is 60.06g. Due to the carbonyl group in the compound, urea is polar. Furthermore, it is highly soluble in water and has a neutral charge overall (National Center for Biotechnology Information, 2021).

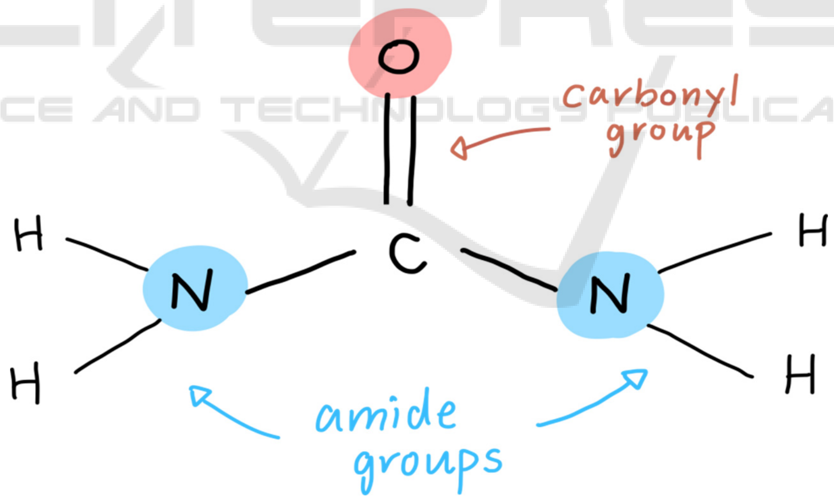


Figure 1: Urea Molecular Diagram.

## 2 HISTORY OF UREA DISCOVERIES

The first known description of urea is by Belgian chemist Jean Batiste von Helmont in 1664, who realised that there was a natural salt in urine (Raine, 1973). In 1732, Dutch chemist Hermann Boerhaave published his chemistry textbook Ementa Chemiae, which included the purification method of urea from urine (Raine, 1973). Almost 50 years after Boerhaave, French chemist Hilaire Rouelle found the same method as his (Eknoyan, 2017). Despite Boerhaave's earlier work, Rouelle is frequently attributed for the discovery and isolation of urea from urine (Raine, 1973).



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## 2.1 Wöhler's Synthesis of Urea from Inorganic Compounds

Nearly 100 years after Boerhaave's findings were published, German chemist Fredrich Wöhler made the groundbreaking achievement of synthesizing urea in a lab. Previously, scientists had believed that naturally occurring organic compounds only originated from living organisms from other organic compounds (Rabinovich, 2007). This idea, known as the "vital force theory", expresses that a hypothetical "vital force" in living organisms was necessary for the formation of an organic compound (Friedmann, 1997). Upon this discovery, Wöhler wrote to his mentor, "I can no longer, as it were, hold back my chemical urine; and I have to let out that I can make urea without needing a kidney, whether of man or dog." (Friedmann, 1997). The popularity of the "vital force theory" declined as Wöhler's synthesis put an emphasis on chemical structures in compounds. Since Wöhler's discovery almost two centuries ago, thorough studies continue to be conducted on structural chemistry to further understand the intricacy of organic compounds (Heitmann, 1989).

Wöhler's original intention had not been to create synthetic urea. Rather, this unanticipated discovery came when he combined lead cyanate with ammonia and water to form ammonium cyanate and lead hydroxide.

$$Pb(OCN)_2 + 2NH_3 + 2H_2O \rightarrow Pb(OH)_2 + 2NH_4(OCN)$$

Wöhler's original experiment (Carr, 2018)

When Wöhler heated ammonium cyanate, he realised that its properties aligned entirely with the properties of urea. This, as he later found, was due to an isomerization that had taken place after the ammonium cyanate was formed. As Figure 2 shows, the cyanate was the nucleophile that attacked the hydrogen attached to ammonium. This resulted in ammonium cyanate decomposing into ammonia and cyanic acid and forming a reactive carbonyl. From there, the ammonia attacked the carbonyl, leading to the final planar urea molecule after proton transfers.

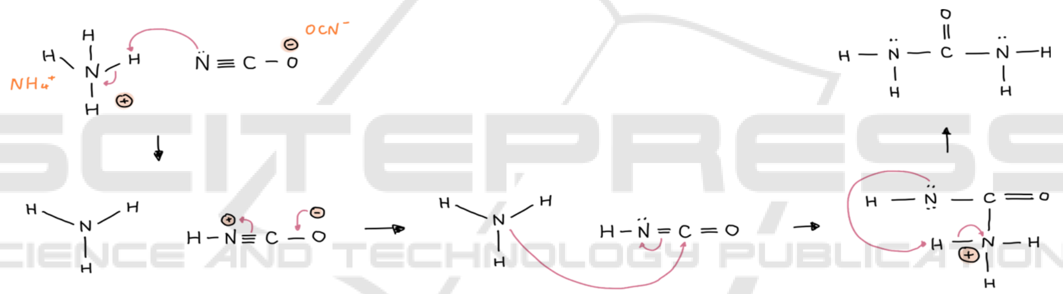

Figure 2: Reversible isomerization reaction from ammonium cyanate into urea.

## 2.2 Discovery of the Human Urea Cycle

This synthesis opened up a new possibility for organic chemistry: the mass production of organic materials. Scientists worked to find ways to synthesize organic compounds from inorganic ones. Amongst these included new methods of synthesizing urea from other compounds. Further research was also conducted on naturally occurring urea.

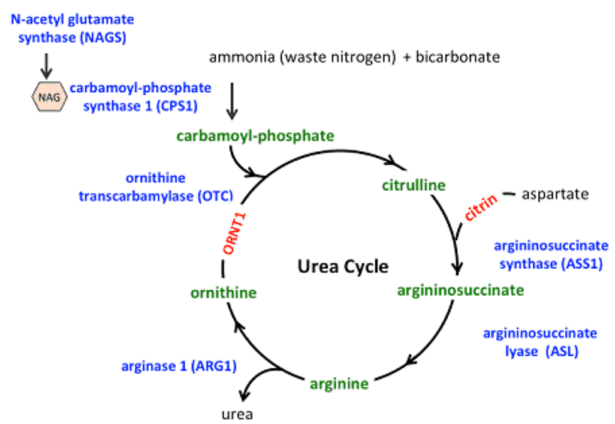


Figure 3: Overview of Urea Cycle (Ah Mew, 2003).

In 1932, Hans Krebs and Kurt Heinselet discovered the natural “urea cycle” in the human body (see Figure 3). It was the first metabolic cycle to be proposed, and it details the formation and excretion of urea. When toxic ammonia is naturally formed in digestive processes, the body relies on the cycle to remove it safely. Specifically, ammonia is converted into urea in the liver’s mitochondria and cytoplasm, with the help of enzyme catalysts like ornithine transcarbamylase and argininosuccinate synthetase (Barmore, 2021).

$$2NH_3 + CO_2 + 3ATP \rightarrow H_2N(CO)NH_2 + H_2O + 3ADP$$

Overall reaction from ammonia to urea (Cheriyedath, 2019)

# 3 MODERN PROCESSES OF SYNTHESIZING UREA AND ITS IMPLICATIONS

On the other hand, synthetic urea is found in various products, such as instant cold packs, skin care products and resins, but it is most used in nitrogen-based fertilizers. This is because urea has the highest nitrogen content amongst solid nitrogen fertilizers (Bradley, 2018). In fact, due to its properties, more than 90% of urea production is used for agricultural purposes (American Chemical Society, 2021).

## 3.1 Employment of Haber-Bosch Process to Synthesize Urea from Ammonia

To facilitate global production of urea, a specific process known as the Haber-Bosch process is employed. As seen in Figure 4, hydrogen is first formed by reacting methane or other natural gases with steam. Under high temperatures, the hydrogen is synthesized with gaseous nitrogen to make ammonia. Ammonia is subsequently combined with carbon dioxide to form ammonium carbamate, which then decomposes into urea and water (Copplestone, 2017). Though this synthesis equation was always known, German chemists Fritz Haber and Carl Bosch found ideal conditions for it to happen with much higher yield than before: high temperatures, high pressures and typically an iron-based catalyst. The process also removes substances such as carbon monoxide, water, and other carbon oxides during synthesis (Copplestone, 2017). This developed industrial process is key to the global output of 220 million tons of urea per year (American Chemical Society, 2021).

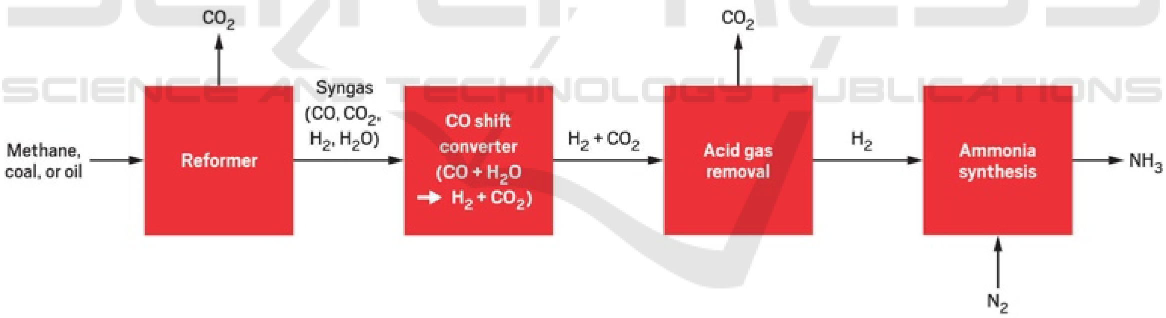


Figure 4: Overview of the Haber-Basch process (Boerner, 2019).

$$CO + H_2O \rightarrow CO_2 + H_2$$

Hydrogen synthesis in industrial processes (Copplestone, 2017)

$$N_2 + 3H_2 \rightleftharpoons 2NH_3$$

Ammonia synthesis in industrial processes (Copplestone, 2017)

$$2NH_3 + CO_2 \rightleftharpoons NH_2COONH_4 \text{ (ammonium carbamate)}$$

$$NH_2COONH_4 \rightleftharpoons H_2O + NH_2CONH_2 \text{ (urea)}$$

Urea synthesis in industrial processes (Copplestone, 2017)

## 3.2 Existing Issues with Mass Production of Synthetic Urea and a Possible New Method

Such a wide-scale level of production comes at a global cost, though. The multitude of problems begins from the compound itself and extends all the way to its industrial process. For instance, Christer Aakeröy from Kansas State University explains that urea is highly soluble in water, offering an unfavorable property for storage and transport (Sandhu, 2018). Farmers therefore tend to overuse urea fertilizer to compensate for potential losses, leading to inefficiencies and increased nitrogen concentration in the air (Bradley, 2018). The most pressing issue, however, is the copious amounts of energy needed to produce urea. 80% of ammonia produced globally is used specifically for urea synthesis (Chen, 2020), yet ammonia production through the Haber-Bosch process accounts for 1-2% of worldwide energy consumption and 1.44% of $CO_2$ emissions (Kyriakou, 2020). This makes it the industrial process that emits the most $CO_2$ worldwide (American Chemical Society, 2021).

The harsh impacts of the process on the environment have propelled scientists to investigate more energy-efficient methods of urea synthesis.

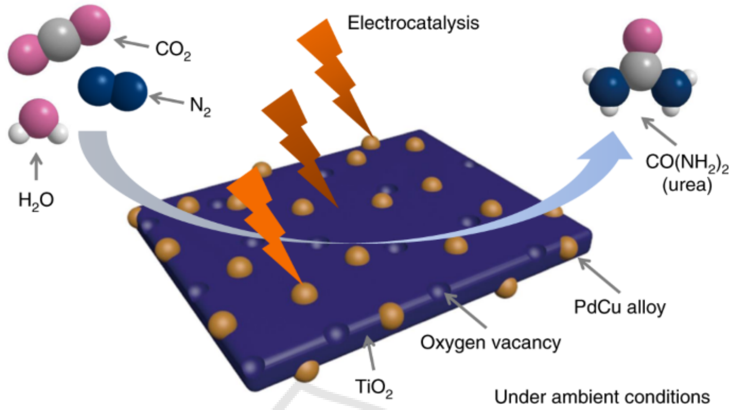


Figure 5: Electrocatalysis to synthesize urea (Chen, 2020).

In 2018, chemical engineer Shaungyin Wang and his colleagues from Hunan University in Changsha, China used an electrochemical reaction to develop a method of urea synthesis. Its synthetic route, as shown in Figure 5, directly combines nitrogen, $CO_2$, and water to form urea at ambient temperature and pressure (American Chemical Society, 2021). While this process is still in its preliminary stage, it offers a possibility of producing urea fertilizers with lower energy consumption rates and higher yields.

## 4 CONCLUSION

The simple organic compound urea has had an unbelievable impact on the scientific community. The urea cycle was also the first metabolic cycle discovered by Krebs and Henseleit, which was even earlier than their renowned Krebs (tricarboxylic) cycle. As French chemist Louis Pasteur once said, “Chance favors only the prepared mind” (Gibbons, 2013). In such a vast field of organic chemistry, serendipitous discoveries happen when one is ready to recognize. Wöhler was able to identify the isomerization of ammonia to urea because he was familiar with the compound from studying medicine before (Shampo, 1985). Without Wöhler’s synthesis, the idea of producing organic compounds from inorganic ones would not even exist.

The transformative understanding of urea synthesis now seeps into people’s everyday lives, most prominently in fertilizers that pillar the agricultural system worldwide. What may the next step be? Perhaps a more resource and energy efficient form of synthesis may be witnessed and fully developed in the near future.

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