

Nobel Prize in Chemistry 1955



Vincent du Vigneaud

The Nobel Prize in Chemistry 1955 was awarded to Vincent du Vigneaud *"for his work on biochemically important sulphur compounds, especially for the first synthesis of a polypeptide hormone"*.

RESEARCH INFORMATION:

The word sulphur may give rise to rather disparate sensations; to most people it has not a very pleasing ring. Also many chemists are inclined to keep their distance; they know that organic sulphur compounds may infect the atmosphere around wood pulp mills and that they form part of the chemical weapon of the common skunk. In spite of that, the element sulphur is of vital importance, and it has many functions in the living organism.

Professor du Vigneaud once defined true exploratory research as "the working out of a winding trail into the unknown". He himself has followed the trail of sulphur in metabolism.

The story starts in the nineteen-twenties with insulin, a substance whose importance is now well-known. As to its chemical nature, it is a protein with a remarkably high percentage of sulphur. The proteins are built up from so-called amino acids, and their sulphur is due to the presence of one or two sulphur-containing amino acids: cystine and

methionine. Considering the special properties of insulin, one could perhaps expect to find its sulphur in quite a new combination, but it turned out that it was present in cystine. The result may seem to be of little significance, but the trail pointed in a definite direction; the sulphur-containing amino acids must be more closely investigated.

It would lead too far to give an account of Professor du Vigneaud's numerous works on cystine, methionine, and related compounds. They led, *inter alia*, to the discovery of the biological importance of the methyl group and of its migrations in the organism. I must also leave aside the distinguished works on biotin, also known as vitamin H, and coenzyme R, and the important contributions to the chemistry of penicillin.

Underneath the brain, there is a small, well-protected gland, the pituitary gland. In man it is about as big as a bean. There are secreted several hormones, that is, substances which regulate important physiological functions. spite of its small size, the pituitary gland is made up of several distinct parts with different functions. We are interested here in the posterior lobe, which contains two substances called oxytocin and vasopressin. The former stimulates the contractions of the uterus and also the lactation, the latter raises the blood pressure and regulates the function of the kidneys. As early as in 1933, when rather impure preparations from the posterior lobe were used in experiments, du Vigneaud found a high percentage of sulphur, which seemed to be correlated to the physiological activity.

Using the experimental methods, which the development of science has put at his disposal and making the best of his own intimate knowledge of the organic chemistry of sulphur, du Vigneaud has step by step forced his way. Both hormones were isolated in a state of purity, and it was found that they are built up from amino acids in the same way as proteins, but with a far lower molecular weight. Such compounds are, as distinguished from real proteins, called polypeptides. The nature of the amino acids and their positions in the molecule could be determined. The sulphur is present in cystine. The two hormones have a very similar structure; both contain eight amino acids, connected to a chain, which at one point is closed to a ring. The molecule has some resemblance to a figure six or nine,

where the loop contains five amino acids and the "tail" three. Two sulphur atoms, linked to each other, form a part of the ring.

The design of the molecule was thus known. It remained to build it up by synthesis and check the correctness of the design. That was perhaps the most difficult part of the work. The interest was first concentrated on the synthesis of oxytocin. Step by step the amino-acid chain was built up with the two sulphur atoms in the proper positions, one at the end of the chain and the other near the middle. At last the ring was closed by formation of a bond between the sulphur atoms. Now followed the most thrilling moment, the testing of the chemical properties and the physiological activity; perhaps there had been some mistake after all. It turned out, however, that the synthetic polypeptide was identical with the natural product.

A biologically important substance of complicated structure had been investigated and synthesized with eminent skill. However, more important still are the far-reaching consequences of this achievement. It is the first synthesis of a polypeptide hormone. It also shows, that such substances with very important physiological properties may be built up from well-known amino acids according to well-known principles. The eight amino acids must, however, be combined in a special sequence; it may not be out of place to draw attention to the principle of the combination lock. The result may also be of importance for revealing the secrets of the real proteins.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1955/press.html