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Nobel Prize in Chemistry 1937


Walter Norman Haworth


Paul Karrer

The Nobel Prize in Chemistry 1937 was divided equally between Walter Norman Haworth *"for his investigations on carbohydrates and vitamin C"* and Paul Karrer *"for his investigations on carotenoids, flavins and vitamins A and B2"*.

RESEARCH INFORMATION:

To the most important chemical compounds belongs a group of substances named carbohydrates. They have been so called because of their composition, which is such that they may be considered as built up by a combination of carbon and water - *hydrates* is the common terminology for chemical compounds in which water is a constituent. The least complicated forms of carbohydrates are the so-called monosaccharides, among which belongs grape-sugar, so designated because of its presence in the juice of grapes. The Latin name of sugar is *saccharum;* hence, the various types of sugar are also named saccharides. By a combination of particles - molecules - from the monosaccharides under separation from part of the water, complex saccharides are obtained, in the first place disaccharides, among which may be mentioned the well-known cane-sugar, and also milk-sugar and maltose. By continued combination more complex carbohydrates may be obtained, which have too been called polysaccharides, even though they have lost the properties of sweet

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taste and easy solubility in water. To these compounds belong, i.a., all kinds of starch, which constitute such an important part of our food, and also *cellulose*, the building material of the plants, which represents the most complicated form of the carbohydrates. While one molecule of grape-sugar is built up by 6 atoms of carbon, 12 of hydrogen, and 6 of oxygen, the number of atoms in one molecule of cellulose probably exceeds two thousand.

When the Nobel Prize in Chemistry was distributed for the second time, in the year 1902, it was awarded to the scientist of genius Emil Fischer, in recognition of his investigations partly concerning sugars and partly relating to caffeine and substances allied thereto.

This year the Royal Academy of Sciences has decided to attribute one half of the Nobel Prize in Chemistry to Professor W.N. Haworth of Birmingham in recognition of his researches concerning carbohydrates and vitamin C.

One may perhaps question if there remained much to be done within the domain of chemistry of the carbohydrates after the classical works of Emil Fischer. This question must, however, be answered in the affirmative. To take only the case of monosaccharides of the type of grape-sugar, no less than 32 different forms are possible, all having the same chemical composition and containing an equal number of atoms in the molecule, but still differing from each other, this difference depending on the different arrangement of the atoms within the molecule. The possibilities are still more diverse when complex saccharides - the disaccharides - are considered, to say nothing of starch and cellulose, and these differences, in the case of the saccharides alone, small as they may appear, are yet of great interest, not only from a theoretical point of view, but also for the comprehension of the central role of the sugars in metabolism, as well as in their technical applications.

It is true that Haworth is not alone in having effected progress within this domain. He commenced his researches with his countryman Irvine, who has also produced eminent works relating to carbohydrates. Others, too, among them the Nobel Laureate in Chemistry this year, Professor Karrer, have made highly meritorious contributions. Among the works of Haworth, his researches regarding the different forms of grape-sugar and on the

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arrangement of the atoms in cane-sugar, maltose and milk-sugar, starch and cellulose, ought to be given special prominence.

Among the motives for the awarding of the prize are also mentioned, however, the researches upon vitamin C which have been made by this scientist and which stand in close relation to his work on the monosaccharides.

The vitamins represent substances which have lately attracted the greatest interest and about which, up till very few years ago, the public knew just as much - or as little - as the chemists. It had been found that certain mysterious substances were necessary, though only in very diminutive quantities, in connection with the foodstuffs proper - i.e. carbohydrates, fats, and proteins - together with certain mineral salts, for the growth and normal development of the animal body, and that a lack of these substances caused diseases of various kinds. The animal body itself, in general, is lacking in the capacity to produce these substances, which must therefore be supplied in a ready form from vegetables, or else be prepared within the body from other more complicated substances contained in the vegetable foodstuffs.

The discovery of the vitamins has already been honoured by the awarding of Nobel Prize in Medicine. In 1929 one half of such a prize was awarded to the Dutchman Eijkman in recognition of his discovery that the eating of polished or peeled rice produced the severe, chiefly tropical, disease called beri-beri, while people eating unpeeled rice remained quite sound. Hence he reached the conclusion that a substance of the kind aforesaid, now described as the antineuritic vitamin, or vitamin B_1, was contained in the husk or peel of the rice. The other half of the Nobel Prize in Medicine was awarded in the same year to Hopkins in recognition of his discovery of the vitamins of growth, that is, the substances necessary for the growth of the animal body - contained for instance in milk - and of which one of the most important has now been identified with vitamin A. And today the Nobel Laureate in Medicine is awarded his prize, i.a., for his discovery in connection with the very same vitamin which had been made the subject of investigation by Haworth.

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What has Haworth then accomplished within this domain? The answer may be thus formulated that he has, above all, made clear the chemical structure of vitamin C.

The chemical structure of substances is expressed by the so-called chemical formulas. By chemical analysis the percentage of the different elements - in this case of carbon, hydrogen, and oxygen - which enter into a compound may be ascertained. Further, the weight of the atoms of the different elements, expressed for instance in relation to the atom of hydrogen, has long been known, the hydrogen atom being the lightest of all the elements. It is likewise possible to determine the weight of a particle, or molecule, of a compound, expressed in the same measure. It is hence possible to indicate how many atoms of the different elements are entering into one molecule of the compound. Thus, the gross formula of the compound is obtained. This formula, in the case of vitamin C, is quite simple, considering that it represents a vitamin, viz.: $C_6H_8O_6$. This formula tells us that one molecule of vitamin C consists of 6 atoms of carbon, 8 of hydrogen, and 6 of oxygen. It also indicates that vitamin C may be conceived as having originated through the elimination of 4 atoms of hydrogen from one molecule of grape-sugar.

But it is possible to advance still further. By ingenious adjustment or speculation, reminding us somewhat of the play of a puzzle, only perhaps a little more intricate, a firm conception has been formed about the order in which the atoms combine. If we conceive an ultra-enlarged model of a molecule, taken at a certain moment - because the atoms are not at a standstill within the molecule - and place a white screen on the one side of the model, while the other is exposed to light, a shadow-figure, also called a projection, of the molecule is obtained on the screen, showing the position of the atoms in their relation to each other. A formula which is intended to reproduce this situation, under the assumption that the atoms were placed on the same plane, is called a structural formula. Such formulas have proved capable of explaining with a high degree of clarity the properties of the compound, and the puzzle thus may be considered as having been solved.

In reality it is, however, hardly correct to suppose that all the atoms within a molecule should be placed on the same plane; if that were the case, even the largest molecules would have the shape of a leaf of paper, which is less than probable. There remains then their dispersion in space, the so-called configuration, which also may be expressed by a formula.

Such a formula for vitamin C has been proposed by Haworth and Hirst, as well as by von Euler and has been subsequently proved to be correct by Haworth.

Before entering upon the practical significance of knowing the chemical structure of a vitamin, I ought to say a word about the notable properties which characterize vitamin C - the terminology does not, of course, give any indication in this regard. But this vitamin was previously called the antiscorbutic vitamin on the ground that the lack there of caused the disease of scurvy, so much dreaded by the polar explorers of earlier times. This disease appeared during periods when the members of these expeditions were compelled to live on badly preserved foodstuffs, whereas the danger has been obviated by the introduction of better food preservation and a supply of fresh vegetables. The chemical name is ascorbic acid. This indicates on the one hand that the substance is an acid, on the other hand that it has a counteracting effect on scurvy, the medical name of which is *scorbutus*; thus the word ascorbic acid is equivalent to anti-scurvy acid.

The knowledge regarding the constitution of a vitamin does not only possess a theoretical interest but is also of very great practical importance. On the one hand it may be found possible, by minor changes in the known composition which may be brought about in an artificial way, to produce compounds which in some cases may prove to be more suitable as medicine. And above all, it opens the way to the artificial production of the compound, a thing of very great importance in the case of vitamins which do occur in nature only in a state of very great dilution. Thus vitamin C is already produced on a technical scale and at a price very much lower than that of the natural product.

The Royal Academy of Sciences has decided also to award to Professor Paul Karrer in Zurich one half of the Nobel Prize in Chemistry this year in recognition of his researches concerning carotenoids and flavins, and the vitamins A and B_2.

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Thus these two scientists have both worked on another common field of research, the vitamins. As I have already endeavoured to elucidate at some length the importance of making clear the chemical structure of the vitamins, taking vitamin C as an example, I may be somewhat brief regarding the brilliant discoveries made by Professor Karrer.

The carotenoids form a group of yellowish-red colouring matters, widely dispersed within the vegetable kingdom, which have obtained their name from the carrot in which they were first observed. The French name of the carrot is known to be *carotte*, while *Karotte* is one of the German names thereof. Carotenoids occur in various other red or yellow parts of vegetables, such as tomatoes, hips, turnips. The examination of these numerous substances was commenced by Karrer ten years ago, and he has succeeded in making clear their chemical structure. The mother substance is in itself a hydrocarbon of very complicated composition, i.e. a chemical compound consisting only of carbon and hydrogen. Its molecule consists of no less than 40 atoms of carbon and 56 of hydrogen. Other carotenoids also contain oxygen, as is the case, for instance, with astacene, which gives the red colour to boiled crayfish and to the "cardinal of the sea", the lobster. The colour of saffron and of paprica is likewise due to carotenoids.

The splendid research concerning the carotenoids, made by Karrer, received its coronation, when it led to the isolation, the production in a pure form and the determination of the chemical structure of vitamin A. This vitamin, which had been known to exist from its biological effects already since 1906 and the synthesis of which in a pure form had been tried in vain in many laboratories all over the world, was successfully isolated by Karrer in 1931 from cod-liver oil, and it was the first of the vitamins of which the chemical structure was clarified. It forms a growth factor, i.e. a substance necessary for the growth of the body. In 1929 von Euler found the same property existing in the carotine itself, and it has been proved since then that this is dependent on the circumstance that carotine, that is the dyestuff of the carrot, is a substance from which the animal body can in itself produce the vitamin A, which has a somewhat less complicated structure. It is also a

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medicine, as it prevents the serious disease of the eye called "dry eye" or xerophthalmia. Hence vitamin A has received the name of axerophthol.

Some words now regarding Karrer's researches on flavins and on vitamin B_2, which were commenced in 1933. Flavins are natural substances of a light yellow colour which often glisten, or fluoresce to the green. One of them is vitamin B_2, also called factoflavin, which was discovered by Warburg and Christian in the yellow respiratory ferment, and which has also been disentangled in regard to its chemical structure by Karrer. It constitutes likewise a growth factor, and Karrer's method of producing this compound has led to a technical production of the substance, which is of great biological importance. It contains, besides carbon, hydrogen and oxygen and also nitrogen.

Karrer has thus succeeded in elucidating completely the nature of two of the vitamins, hitherto considered as so mysterious, and one of them is now produced artificially. A characteristic of this scientist is his open eye to the great and important problems as well as to their kernels, and the independent way in which he attacks the problems and pursues his new departures with the aid of his own methods.

There remain many questions to be studied regarding the way in which the vitamins cooperate in such processes of life as cannot be started without their presence.

A vitamin does certainly not produce the effect alone, however. The lactoflavin, for instance, combines, with the aid of phosphoric acid, with an albuminous substance, and only in this way the yellow respiratory ferment is formed. Its molecule contains about 200 times as many atoms as that of the vitamin itself. The yellow ferment is reckoned as belonging to the catalyzers, i.e. substances capable to accelerate a chemical reaction without undergoing any change themselves. Their action may be compared to that of a lubricating oil on a rusty machine. In this case the oxidation of certain substances present in the body is taking place, thus a kind of combustion, although of course much slower than for instance the burning of wood in a stove. We may perhaps compare the very effect of the vitamin to that of a key. A heavy door may thus resist the strongest blows and knocks, but can easily be opened by the aid of a small key - always provided that the right key is found.

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The discoveries, which have now engaged our attention, touch upon the domain of Physiology as well as that of Chemistry, a circumstance which has found its expression in that they have been awarded Nobel Prizes in Medicine as well as in Chemistry. Often it is just within the borderland between two sciences, where efforts have been frequently made to establish demarcatory lines (although mostly in vain), that the important discoveries are to be found. In such cases it is evidently of small avail, generally speaking, to try to decide, even with the aid of the greatest acuteness, to which field of science such discovery should be properly attributed. The principal thing is, however, that the discoveries are recognized, if such be their value, and the classification of the prize awarded is a question of minor importance. In the present case it may be said, nevertheless, that the discoveries which have been awarded a prize in Chemistry are on the whole more chemically accentuated in their character than those which have received the prize in Medicine. In all the cases, however, such discoveries may be said to have "conferred the greatest benefit on mankind" in accordance with the intentions expressed in the will of Alfred Nobel.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1937/press.html