Peter P. T. Sah and the Synthesis of Vitamin C in China and Europe

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The synthesis of vitamin C was one of the main scientific achievements in the 1930s. Many scientists in Europe made contributions to this field, especially Albert Szent-Györgyi (1893-1986) from Hungary and Sir Walter Norman Haworth (1883-1950) from England, both of whom won the Nobel Prize in 1937. In the same period, a Chinese chemist, Sa Bentie 薩本鐵 (1900-1986), better known outside China as Peter P. T. Sah, was also studying vitamin C. Although he suggested several methods of synthesis, he did not bring his work to fruition. In this paper, I provide an outline of research done in the 1930s for the synthesis of vitamin C in Europe and China, and raise some questions that appear to be crucial for understanding Sah's contribution and its meaning from both a scientific and a social point of view.
Ascorbic Acid and Vitamin C

Several scholars have traced the history of scurvy from its earliest accounts in fifteenth-century sources. The disease was prevalent in times of famine and war and was frequently associated with long voyages. Sailors and explorers have known the relation of diet to scurvy since the eighteenth century because the disease was found to be preventable and curable by eating fresh vegetables and fruits. The efficacy of lemon juice and orange juice was known at an early time so that the incidence of scurvy decreased to a remarkable extent.

In 1895, Theobald Smith in the United States reported a peculiar hemorrhagic condition in guinea pigs restricted to a diet containing cereal but no grass, clover, or succulent. A few years later, two Norwegian scientists, Axel Holst and Alfred Fröhlich, pointed out the similarity between this disease in guinea pigs and human scurvy. The discovery was remarkable: a diet that causes scurvy in humans also produces it in the guinea pigs, and the substances that exert a curative effect in humans are equally efficacious against the scurvy of guinea pigs. However, the idea that scurvy might also be a deficiency disease caused by some form of avitaminosis did not, initially, gain much attention. The convincing observations of Harriette Chick and her colleagues in London were necessary before it was finally accepted. In 1919, Sir Jack Drummond designated the antiscorbutic substance as vitamin C.

The work that followed had multiple objectives, including the development of methods of standardization and assay, the understanding of the vitamin's distribution in plant and animal tissue, its requirements and role in nutrition, its significance in certain physiological processes, the pathological changes resulting from its deficiency, and finally the processes of its isolation, identification, and synthesis.

The Synthesis of Vitamin C in Europe

In 1928, Szent-Györgyi, then a research fellow at the Rockefeller Foundation, was working with Sir Frederick Gowland Hopkins on the oxidation and reduction of life processes. He isolated a reducing substance from various plant sources (including orange, lemon, and cabbage) and from the suprarenal cortex and recognized it to be hexuronic acid \((C_6H_8O_6)\). As a result of a series of investigations, Joseph Tillmans in Germany discovered a correlation between the reducing potential of various foods and their vitamin C content. Glen King and associates at the University of Pittsburgh were working independently on preparing vitamin C concentrates from lemon juice and they observed the strong reducing action of

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1 See, for instance, Harris 1935; Keevil 1957-63, vols. 1 and 2; Carpenter 1986.
the physiologically active material. In 1932, W. A. Waugh and King finally succeeded in isolating a crystalline substance which remained constant in its antiscorbutic activity on repeated recrystallization. The substance was proved to be identical with the hexuronic acid first isolated by Szent-Györgyi from the adrenals and other sources.

Around the same time, J. Svirbely, another Hungarian, and Szent-Györgyi also recognized the antiscorbutic property of hexuronic acid. Pursuing the problem further and employing red pepper as a source, they obtained 450 gr of the acid in crystalline form. To prove its identity with vitamin C, they prepared the monoacetone derivative, recrystallized it, and then recovered the hexuronic acid. The final product possessed the same activity as the original material, and in agreement with the observations in King's laboratory, 0.5 mg was found to be the daily protective antiscorbutic dose for guinea pigs. The name, ascorbic acid, was suggested by Haworth at the University of Birmingham and by Szent-Györgyi. In the meantime, researchers in several laboratories were actively engaged in an attempt to determine the chemical constitution of this substance. Haworth and his team finally discovered its chemical structure in 1933.²

It is noteworthy that Tadeus Reichstein and his co-workers accomplished the synthesis of the vitamin in Paul Karrer's laboratory in Switzerland before its constitution was definitely established.³ Later, Reichstein developed a method of synthesizing the vitamin on a commercial scale. Meanwhile, the Birmingham group also reported that they had achieved the synthesis of ascorbic acid.⁴ In 1937, Szent-Györgyi received the Nobel Prize for Physiology or Medicine for his discoveries concerning the biological oxidation processes with special reference to vitamin C and the fumaric acid catalyst, and Haworth was awarded the Nobel Prize in Chemistry for his work on carbohydrates and vitamin C.

The Chemical Study of Vitamin C in China

Peter P. T. Sah was born in 1900 to a wealthy and learned family. He earned his doctorate at Wisconsin in 1926, after which he returned to China to take a position in the Department of Chemistry at the Tsinghua University. He produced many research articles (by far more than any other Chinese chemist of that time) and trained dozens of students in modern laboratory techniques. In the mid-1930s, he worked in the laboratory of Adolf Windaus, a German organic chemist who won the Nobel Prize for Chemistry in 1928 for his study of vitamin D. During the Second World War, Sah left China and completed his career at the University of California at Davis.

² Herbert, Hirst, et al. 1933.
³ Reichstein, Grüssner, and Oppenheimer 1933.
⁴ Haworth and Hirst 1933.
While doing postdoctoral work at Yale, he investigated the vitamin content of Chinese litchi nuts (*Litchi chinensis*). After returning to China, Sah continued this work, concentrating on the vitamin C content of fruits and vegetables available in the Peiping (Beijing) market and on the dietary needs of the local population. In a paper published in 1933, he wrote:

> Although the methods employed by the Swiss and the English workers in the synthesis of ascorbic acid are clever and brilliant in serving to prove the structure of the compound, they cannot be considered as practical because much time and energy are required to gather the base materials. Besides this, the synthetic product comes from hydrocyanic acid or potassium cyanide, both of which are the most poisonous substances known in chemistry. Even if the method could be employed to produce a large quantity of ascorbic acid, who is willing to risk the danger of ingesting a compound derived from HCN or KCN when lemon and orange juices are so safe and inviting, and red pepper and other vegetables rich in vitamin C can so readily and cheaply be bought at the market?  

In the same paper, Sah also stated that L-ascorbic acid has the same origin as the sugars to which it is structurally related and that it may be formed in any of the following four ways:

1. Through the aldol condensation of glyoxalic acid with L-threose
2. Through the aldol condensation of glycolic aldehyde with L-threose, followed by oxidation
3. Through the rearrangement of inosite to L-gulose or L-sorbose, followed by oxidation
4. Through the rearrangement of inosite to L-galactose, followed by oxidation

On the basis of the above theory, Sah suggested a number of methods of synthesis of L-ascorbic acid in the laboratory, using as base materials compounds easily available in large quantities: (a) glyoxalic acid and L-threose, (b) D-glucose, (c) starch, and (d) peels of citrus fruits. Sah’s paper was published on December 15, 1933. Then he continued to make experiments in order to find proof of the theory in the laboratory, but the results do not appear to have ever been published.

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5 See, for instance, Sah 1934c; Sah 1934a.
6 Sah 1933, 183.
Peter P. T. Sah’s Contribution

The synthesis of a new compound is one of the major and most exciting challenges in organic chemistry, and the synthesis of vitamin C was the first of any vitamin. On the other hand, between the late 1920s and the early 1930s, investigating the nutrition situation of China and the nutritional composition of Chinese staples was one of major occupations of Chinese chemists and biologists, as this could help the government in establishing nutritional standards.7 Sah himself analyzed the contents of Chinese vegetables and fruits and compared them with imported foods. He published nearly twenty articles on this subject between 1927 and 1936. However, as a professionally trained chemist, Sah had qualities for scientific research and a keen insight into academic problems. Therefore, as other organic chemists around the world, he chose to focus his studies on the synthesis of vitamin C.

In spite of this, Sah did not accomplish the experimental synthesis of vitamin C but only suggested several procedures in theory. In a paper published in 1934, he wrote:

These experimental results [achieved in Europe] are apparently identical in principle with the theoretical synthesis proposed by the [present] author. While we wish to extend our hearty congratulations to the Swiss chemists for their excellent performance, regrets must be expressed that due to lack of materials and expenses, the Chinese laboratories can only wish to compete in experimental work with our foreign friends, especially at the present time when the general atmosphere in this country is totally political and far from being scientific.8

In these sentences, Sah not only admitted that he had done no more than suggesting theoretical methods of synthesis, but also expressed his bitter disappointment toward the government. In his view, a scientist’s success depends mainly on the economical and social conditions. Shortly later, Sah left China and went to Germany to study sterols and sex hormones with Windaus.

Another point requires attention. In every article he published on the structure and the synthesis of vitamin C, Sah reviewed or cited the recent achievements of European scientists. However, a review of European articles published during the same years reveals that Sah’s own work was ignored outside China. This seems to mean that, at least as far as research on the synthesis of vitamin C is con-

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7 For instance, Wu Xian 吳 懷 (1893-1959), regarded as the father of biochemistry in China, also published several articles on the nutrition of Chinese people during the same period.
8 Sah 1934b, 289.
cerned, academic communication between Chinese and European scholars worked only in one direction. Two explanations are possible for this fact. First, most Chinese scientists who were active at that time, like Sah himself, had just returned to China from abroad. Continuing work they had begun elsewhere, they engaged themselves in new research projects. However, owed to their limited number and to the conditions current then in China, these scientists were unable to establish research groups that would be more competitive and could become part of the international scientific mainstream. Second, Sah’s articles on the structure and synthesis of vitamin C, like those of several other Chinese researchers, were written in English and were published in Chinese journals. Most of these journals, however, had been newly founded; one example is the Journal of the Chinese Chemical Society, established in 1933. As these journals enjoyed a limited circulation and had little impact on the international academic circles, it was difficult for a Chinese scientist to gain enough attention from abroad.9

At the end of the 1940s, Sah decided to move again to the United States. In his career, he obtained most of his scientific achievements while working at the Tsinghua University, and was one of several scientists who, between the 1920s and the 1940s, contributed to the establishment and the institutionalization of modern science in China. However, because of the isolation in which Chinese scientists were bound to work, and because of the particular social conditions of China at that time, the research done by Chinese scientists did not enjoy enough attention from their foreign colleagues. For the same reasons, the work of Chinese scientists was bound to consists mostly in supplements to, and verification of, discoveries or theories first made by Western scientists. Sah’s work on vitamin C, therefore, helps us to understand the reasons of the lack of creativity of Chinese scientific work at his time.

References


9 In 1934, Sah’s article on the theory of the formation of vitamin C (Sah 1933) was abstracted in Chemistry Abstracts by William Adolph, who had been working at the Yenching University (Yanjing daxue 燕京大学) as a chemist for a long time. However, I have been unable to find the abstract of another paper of Sah’s on the experimental verification of the synthesis of vitamin C (Sah 1934b).


Sah, Peter P. T. 1933. “Structure of Vitamin C (Ascorbic Acid) and a Theory of its Formation.” Science Reports of National Tsing Hua University 2: 167-90.

