István Hannus

The Analysis of Vitamin C in Szeged

Albert Szent-Györgyi was awarded the Noble prize at the age of 44 in 1937. On the front side of the Noble medal, which is made of 23-carat gold and weighs approximately 200 grams, you can see the portrait of Alfred Nobel, while on the reverse side you can find a symbolic image: a woman is healing another woman with the water of life springing from a piece of rock. The medal, which has a rather adventurous past, is now in the Hungarian National Museum in Budapest. There is a copy of the medal in the Szent-Györgyi memorial room at 103. Tisza Lajos Street, Szeged. *(Illustration 1. The Nobel medal)*

Illustration 1. The Noble Prize

Leaves of the „pepper tree"

The justification on the Nobel Diploma written in sophisticated Swedish language says "for the discoveries in the field of biological burning processes, in particular vitamin C and fumaric acid catalysis". As previous presenters, László Dux, János Wölfling and Gábor Tóth also emphasized, the discovery is about biological oxidation. As Professor Dux described, Albert Szent-Györgyi was the first to suspect the existence of the citric acid cycle (which was discovered and described by Krebs) and the role of four-carbon-atom carbonic acids, including fumaric acid, in the oxidation cycle. In his presentation at the Nobel award gala Szent-Györgyi illustrated the process as a half circle. He suspected that there was a cycle, which is known today as Krebs' cycle, therefore in Hungary and Szeged we can rightly call it Szent-Györgyi - Krebs cycle.

The Swedish graphic designer of the Nobel Diploma drew a slightly strange image of the pepper plant and it looks like a "pepper tree". He also created images of cities that played an important role in Szent-Györgyi's career: Budapest, where he was born and where he studied; the Dutch cities of Groningen and Leiden; Cambridge in England and, of course, Szeged. (*Illustration 2. The Nobel Diploma*)

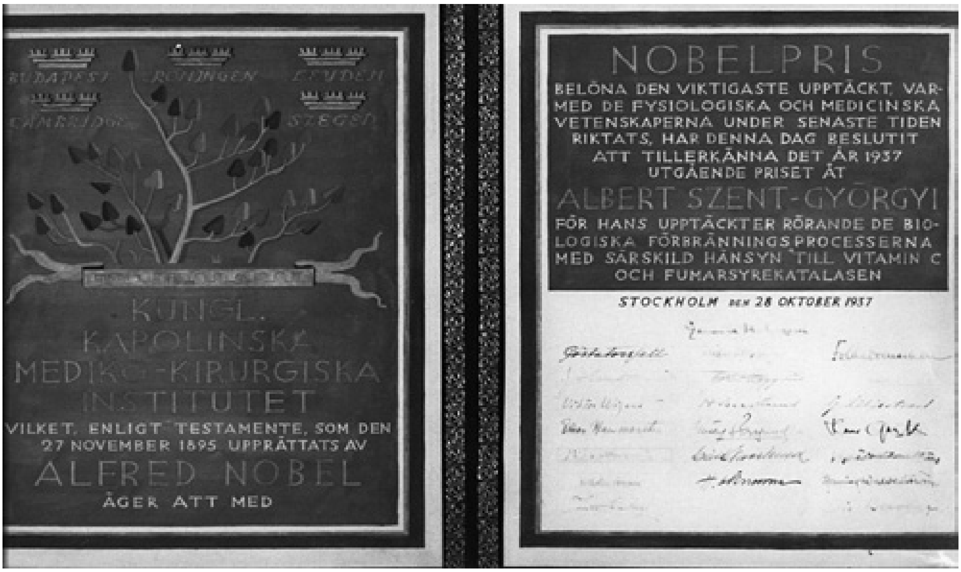


Illustration 2. The Noble Diploma

Before I move on to the topic of vitamin C research in Szeged, I will outline the important milestones in Szent-Györgyi's life. He was attending the medical university in Budapest, when World War I broke out and he was ordered to the Ukrainian front. Because of his tremendous physical and mental sufferings he was desperate to come home. He deliberately wounded himself by shooting into his own arm. Self-mutilation is a capital offence in the military, but his action remained unveiled and he was sent back to Hungary for medical treatment. He could complete his medical studies, he was awarded his diploma and he got married. However, the war had not ended by then and he was sent to the Italian front where he survived the terrors of the Isonzo-Piave swamps before the war ended and he could return home.

The years after the war were turbulent for the whole country, including the Szent-Györgyi family. He had many jobs, he took his family to Hamburg, then he received a job in Leiden, the Netherlands. The next milestone is Groningen, where he focused on biological oxidation. His research settled the dispute between Wartburg and Wieland, an important scientific controversy of that time, as it was described by László Dux in his presentation about the basics of biochemistry. Interestingly, following the principle of "Nomen est omen", O. Wartburg said that active oxygen (O) plays an important role in oxidation, whereas H. Wieland said it was active hydrogen (H). Then came Albert Szent-Györgyi, a young scientist, who conducted experiments using potato and found that both of them are right: they examined two different sides of the same process, in which active oxygen oxidises active hydrogen. Szent-Györgyi published a series of five articles on the topic bringing him international reputation in the field of biological oxidation.

At the end of 1920s in Groningen he used the adrenal cortex to isolate a highly reactive anti-oxidant, similar to the substance found in citrus fruits, orange, lemon, as well as pickled cabbage. Then he moved to Cambridge, the town he later considered as his scientific home. We, chemists are proud of the fact that in 1927 he was awarded his PhD title in the field of chemistry. By that time he was able to isolate one gram of clear crystallic substance from the adrenal cortex. His doctoral thesis described the results of these experiments.

In order to obtain their PhD titles, researchers were also required to publish articles, although not as many as today, and describe their results. The interesting anti-oxidant Szent-Györgyi discovered was simply called "Szent-Györgyi's substance" by his colleagues in Cambridge, but this name was not suitable for publication. Having analysed the substance they found that it was a sugar-like substance, an acidic carbohydrate whose formula was $C_6H_8O_6$.

They wondered what name to give to the substance. Szent-Györgyi recommended Ignose (unknown sugar), based on the Latin word 'ignosco', 'do not know' and the ending '–ose' which refers to the fact that it is a kind of sugar. The editor of the journal did not have a good sense of humour, neither was he so poetic as Szent-Györgyi, so he refused the name. Then Szent-Györgyi came up with 'Godnose' (God knows what kind of sugar). The editor did not like this name either, and because the substance contained six carbon atoms and it was acidic, he called it hexuronic acid. From then on Szent-Györgyi's substance, which later was found to be vitamin C itself, was called hexuronic acid.

Key components: the place, the colleague, the guinea pig

In 1928, when Szent-Györgyi had already gained international reputation, Minister of Education, Kuno Klebelsberg invited him to Szeged to fill the vacant post of Chairman of the Department of Medical Chemistry. Szent-Györgyi accepted the invitation, but since the construction of the university was still in progress, he asked for and received a two-year unpaid holiday to work at the Mayo Clinic in the USA. It took one year to isolate 25 grams of hexuronic acid from adrenal glands of cows from a slaughterhouse near Chicago. He sent 10 grams of hexuronic acid to Professor Haworth in Birmingham, who was an acknowledged researcher of carbohydrates, so that he could determine the structure of the new substance. He brought the rest of the substance to Szeged.

He started to work in Szeged as a professor in 1930. He had a flat and a lab on Kálvária Square. Although he was not even 40 years old when he came to Szeged, he was internationally acknowledged due to his research into biological oxidation. The common belief that Szent-Györgyi is the only Hungarian scientist to be awarded the Nobel prize for research conducted in Hungary is not entirely true. Even so I would not like to dismiss his merits, I am too much of a Szent-Györgyi fan.

Illustration 3. The building with Szent-Györgyi's first laboratory in Szeged

Where is *the building* in which vitamin C research was conducted? It is situated on Kálvária Square and today it houses Miksa Déri Technical Secondary School. The building, which was originally designed to be a school building, was completed in 1914. When World War I broke out the building which had wide corridors and large windows was found to be ideal for military hospital. After the war it gave shelter to refugees from Transylvania. In 1921 when the University of Kolozsvár moved to Szeged, university hospitals, including the department of surgery, were also moved to the building. The building was also home to various academic departments, such as the Department of Medical Chemistry where Szent-Györgyi worked. In the side wing there were flats for the academic staff, including the Szent-Györgyi family: his wife, his daughter and his mother, Jozefina Lenhossék. *(Illustration 4. Female family members*)

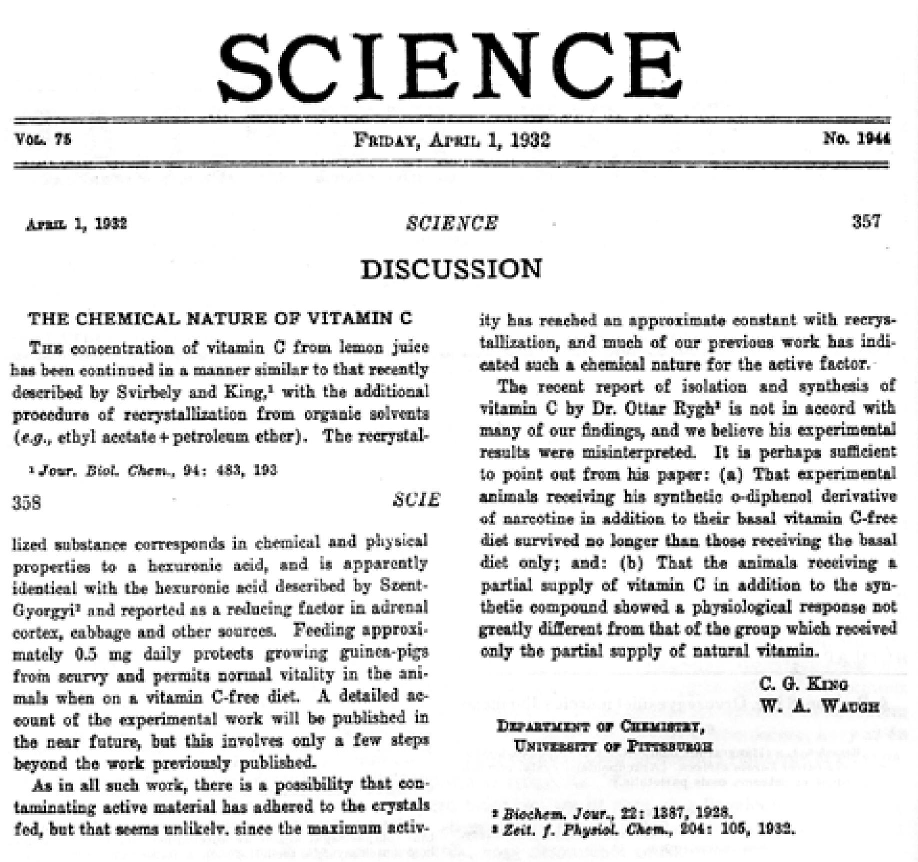
Illustration 4. Female family members

The second key component of vitamin C research was the colleague. In the autumn of 1931 Joseph Svirbely, a young American scientist of Hungarian origin, came to Szeged with the intention to work with Szent-Györgyi. His parents were Hungarian, and after obtaining his doctoral title he felt obliged to visit his parents' home country. He visited the most well-known biochemist, Szent-Györgyi. Szent-Györgyi asked him what he was involved in and what he was good at. He explained that he had been involved in vitamin C research with Professor King and with the help of guinea pig tests he was able to tell if a substance was effective against scurvy, that is it has the properties of vitamin C. (Similarly to man, guinea pigs are not able to synthetise vitamin C, they should take it with food. That is why they are suitable for research.) Szent-Györgyi gave him a few grams of the substance he brought from America. He explained him that in his opinion it was vitamin C. He told the young man to conduct the guinea pig experiment using the substance. So the third key component of vitamin C research was the guinea pig.

Priority debate

It had been known for a long time that there was a substance that could prevent scurvy and researchers called it vitamin C. However, researchers had not been able to tell exactly what this substance was until the early 1930s. József Svirbely came to Szeged in the autumn of 1931 and in the winter of 1931-32 he conducted a successful experiment. He was euphoric to tell Szent-Györgyi "Sir, your substance, hexuronic acid is vitamin C indeed". They were enthusiastic, however, they were aware of the fact that the experiment was not entirely accurate (they used few animals and fed them differently than described in literature) and one experiment was not enough, it should be repeated. The second experiment proved to be successful. József Svirbely then asked Szent-Györgyi if he could write to Professor King in Pittsburgh and tell him that they had identified vitamin C, it was hexuronic acid. Szent-Györgyi answered that "if you had been working with me and you had found something we had been searching for working with some one else and you had not report this fact to me, I would say you are a lousy, lousy fellow. Of course, you should write to Professor King."

Svirbely sent a letter to Pittsburg by sea. At the same time Professor King sent a letter to him saying that they had failed to identify vitamin C. The two letters crossed each other. When Professor King received Svirbely's letter, they quickly published an article on the discovery of vitamin C in Science, America's leading scientific journal, which started a priority debate between King and Szent-Györgyi. King and his colleagues published the article on April 1. In their article they described that they continued the experiment they had started with Svirbely and through crystalisation they managed to produce the same substance from lemon as Szent-Györgyi from adrenal cortex, namely hexuronic acid. *(Illustration 5. The article in Science magazine)*



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DISCUSSION

THE CHEMICAL NATURE OF VITAMIN C

The concentration of vitamin C from lemon juice has been continued in a manner similar to that recently described by Svirbely and King,[1] with the additional procedure of recrystallization from organic solvents (*e.g.*, ethyl acetate + petroleum ether). The recrystal-

[1] *Jour. Biol. Chem.*, 94: 483, 193

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lized substance corresponds in chemical and physical properties to a hexuronic acid, and is apparently identical with the hexuronic acid described by Szent-Gyorgyi[2] and reported as a reducing factor in adrenal cortex, cabbage and other sources. Feeding approximately 0.5 mg daily protects growing guinea-pigs from scurvy and permits normal vitality in the animals when on a vitamin C-free diet. A detailed account of the experimental work will be published in the near future, but this involves only a few steps beyond the work previously published.

As in all such work, there is a possibility that contaminating active material has adhered to the crystals fed, but that seems unlikely, since the maximum activity has reached an approximate constant with recrystallization, and much of our previous work has indicated such a chemical nature for the active factor.

The recent report of isolation and synthesis of vitamin C by Dr. Ottar Rygh[3] is not in accord with many of our findings, and we believe his experimental results were misinterpreted. It is perhaps sufficient to point out from his paper: (a) That experimental animals receiving his synthetic o-diphenol derivative of narcotine in addition to their basal vitamin C-free diet survived no longer than those receiving the basal diet only; and: (b) That the animals receiving a partial supply of vitamin C in addition to the synthetic compound showed a physiological response not greatly different from that of the group which received only the partial supply of natural vitamin.

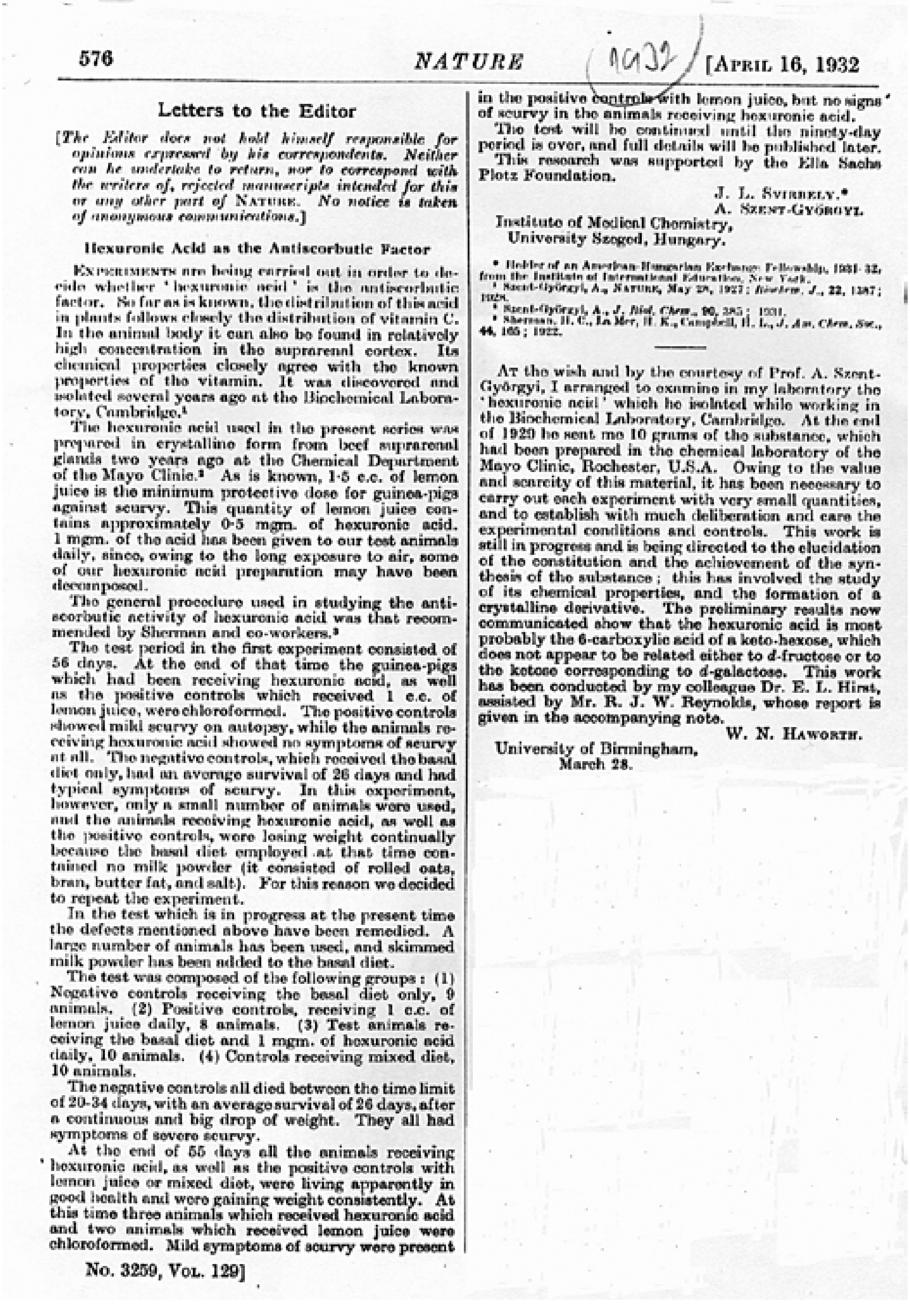
C. G. King
W. A. Waugh

Department of Chemistry,
University of Pittsburgh

[2] *Biochem. Jour.*, 22: 1387, 1928.
[3] *Zeit. f. Physiol. Chem.*, 204: 105, 1932.

Illustration 5. King's article in Science magazine

After completing the animal tests Szent-Györgyi published their article in Nature magazine, Europe's leading scientific journal, on April 16 only. In the article they described the experiment in detail. Each group included 8-10 subjects. The diet of the control group included powdered milk, rye flakes, bran, cream and salt. Animals in the control group had a mean survival rate of 26 days, they were losing weight steadily and finally died of scurvy. Animals in the positive control group were also administered 1.5 ml of lemon juice, whereas the test animals received 1 mg of hexuronic acid. They were still alive after 56 days without developing any symptoms of scurvy. So they published their article and added that they will continue the experiment until day 90. There was another article in Nature by Haworth in Birmingham describing that they were still working on determining the structure of vitamin C using the substance they had been given by Szent-Györgyi. *(Illustration 6. The article in Nature magazine)*



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Letters to the Editor

[The Editor does not hold himself responsible for opinions expressed by his correspondents. Neither can he undertake to return, nor to correspond with the writers of, rejected manuscripts intended for this or any other part of NATURE. *No notice is taken of anonymous communications.]*

Hexuronic Acid as the Antiscorbutic Factor

EXPERIMENTS are being carried out in order to decide whether 'hexuronic acid' is the antiscorbutic factor. So far as is known, the distribution of this acid in plants follows closely the distribution of vitamin C. In the animal body it can also be found in relatively high concentration in the suprarenal cortex. Its chemical properties closely agree with the known properties of the vitamin. It was discovered and isolated several years ago at the Biochemical Laboratory, Cambridge.[1]

The hexuronic acid used in the present series was prepared in crystalline form from beef suprarenal glands two years ago at the Chemical Department of the Mayo Clinic.[2] As is known, 1·5 c.c. of lemon juice is the minimum protective dose for guinea-pigs against scurvy. This quantity of lemon juice contains approximately 0·5 mgm. of hexuronic acid. 1 mgm. of the acid has been given to our test animals daily, since, owing to the long exposure to air, some of our hexuronic acid preparation may have been decomposed.

The general procedure used in studying the antiscorbutic activity of hexuronic acid was that recommended by Sherman and co-workers.[3]

The test period in the first experiment consisted of 56 days. At the end of that time the guinea-pigs which had been receiving hexuronic acid, as well as the positive controls which received 1 c.c. of lemon juice, were chloroformed. The positive controls showed mild scurvy on autopsy, while the animals receiving hexuronic acid showed no symptoms of scurvy at all. The negative controls, which received the basal diet only, had an average survival of 26 days and had typical symptoms of scurvy. In this experiment, however, only a small number of animals were used, and the animals receiving hexuronic acid, as well as the positive controls, were losing weight continually because the basal diet employed at that time contained no milk powder (it consisted of rolled oats, bran, butter fat, and salt). For this reason we decided to repeat the experiment.

In the test which is in progress at the present time the defects mentioned above have been remedied. A large number of animals has been used, and skimmed milk powder has been added to the basal diet.

The test was composed of the following groups: (1) Negative controls receiving the basal diet only, 9 animals. (2) Positive controls, receiving 1 c.c. of lemon juice daily, 8 animals. (3) Test animals receiving the basal diet and 1 mgm. of hexuronic acid daily, 10 animals. (4) Controls receiving mixed diet, 10 animals.

The negative controls all died between the time limit of 20-34 days, with an average survival of 26 days, after a continuous and big drop of weight. They all had symptoms of severe scurvy.

At the end of 55 days all the animals receiving hexuronic acid, as well as the positive controls with lemon juice or mixed diet, were living apparently in good health and were gaining weight consistently. At this time three animals which received hexuronic acid and two animals which received lemon juice were chloroformed. Mild symptoms of scurvy were present in the positive controls with lemon juice, but no signs of scurvy in the animals receiving hexuronic acid.

The test will be continued until the ninety-day period is over, and full details will be published later.

This research was supported by the Ella Sachs Plotz Foundation.

J. L. SVIRBELY.*
A. SZENT-GYÖRGYI.

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* Holder of an American-Hungarian Exchange Fellowship, 1931-32, from the Institute of International Education, New York.
[1] Szent-Györgyi, A., NATURE, May 28, 1927; *Biochem. J.*, 22, 1387; 1928.
[2] Szent-Györgyi, A., *J. Biol. Chem.*, 90, 385; 1931.
[3] Sherman, H. C., La Mer, V. K., Campbell, H. L., *J. Am. Chem. Soc.*, 44, 165; 1922.

AT the wish and by the courtesy of Prof. A. Szent-Györgyi, I arranged to examine in my laboratory the 'hexuronic acid' which he isolated while working in the Biochemical Laboratory, Cambridge. At the end of 1929 he sent me 10 grams of the substance, which had been prepared in the chemical laboratory of the Mayo Clinic, Rochester, U.S.A. Owing to the value and scarcity of this material, it has been necessary to carry out each experiment with very small quantities, and to establish with much deliberation and care the experimental conditions and controls. This work is still in progress and is being directed to the elucidation of the constitution and the achievement of the synthesis of the substance; this has involved the study of its chemical properties, and the formation of a crystalline derivative. The preliminary results now communicated show that the hexuronic acid is most probably the 6-carboxylic acid of a keto-hexose, which does not appear to be related either to *d*-fructose or to the ketose corresponding to *d*-galactose. This work has been conducted by my colleague Dr. E. L. Hirst, assisted by Mr. R. J. W. Reynolds, whose report is given in the accompanying note.

W. N. HAWORTH.

University of Birmingham,
March 28.

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Illustration 6. The article in Nature magazine

What was the result of the priority debate? Historians of science have found out that Szent-Györgyi and his colleagues should be given priority. Szent-Györgyi announced their results at a conference in Budapest and the discovery was published in an article in Hungarian in the Hungarian Medical Weekly on March 26. This article was adopted and published in a German journal in March. So it was as early as March that Szent-Györgyi announced that hexuronic acid is identical to vitamin C. When the 90-day experiment was over, they published another article in Nature in May, announcing that the animals had not developed scurvy. The animals who survived were euthanized and dissected to see if they had signs of scurvy in their internal organs. All results were normal proving that hexuronic acid could prevent scurvy. In the same article Szent-Györgyi hinted at the fact that King failed to give detailed description of the experiment and analysis of hexuronic acid, and until they did this it was not proved that they had produced vitamin C. Later, in a figure included in an article published in Biochemical Journal in 1933, we can see that the animals in the control group who did not receive vitamin C lost weight and died within a short period of time, whereas the animals who were given lemon juice or ascorbic acid (as vitamin C was called by that time) lived happily until they died natural death. Then they performed other experiments with various derivatives and found out that acetone derivatives, for example, were less effective than clear substance. So Szent-Györgyi and his colleagues published detailed description of their experiments they conducted in spring 1932. *(Illustration 7. The article in Biochemical Journal)*

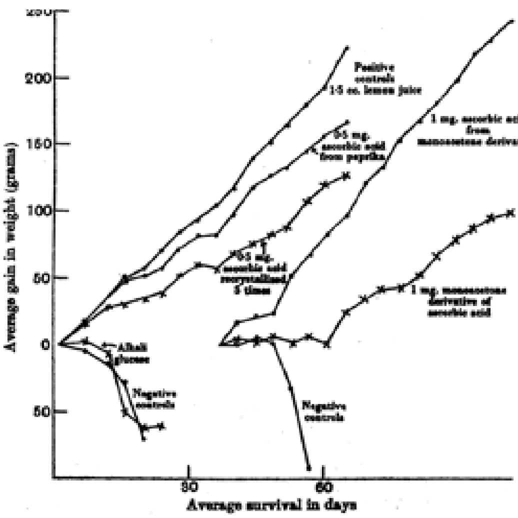


Illustration 7.
The article in Biochemical Journal: The effect of vitamin C on the weight of guinea pigs

The fortune of the cowardly husband: pepper

A real breakthrough was achieved on the first days of October 1932, when great amounts of pepper was available. They could extract one and a half kilograms within one week. Earlier they only had a maximum of 25 grams. Szent-Györgyi recalled the story and it has entered the history of science as *a husband's cowardice resulted in revolutionary discovery*. The story is as follows: Szent-Györgyi invited a new colleague to his home in the Déry Miksa building. His wife served cold dinner with pepper. Szent-Györgyi did not like pepper, but he did not have the courage to tell it to his wife. Instead he said that he had not examined pepper to see if it contained vitamin C and he should do it right away. With this he left behind the guest, which was rather impolite of him, and went to his laboratory to do the test. Soon he discovered that pepper was "the fountain of vitamin C", as he called it. From this huge amount he could send further samples to Birmingham, where they managed to determine the structure of vitamin C. He sent samples to other researchers all over the world who were involved in vitamin C research. He sent it to everyone so that they could carry on further tests. That is how he became the moral winner of the priority debate.

The amount they had was enough for detailed chemical analysis. Haworth and Szent-Györgyi decided to change the name hexuronic acid to ascorbic acid and they announced it in an article in Nature stating that ascorbic acid is an anti-scurvy factor. So they had discovered a substance against scurvy.

In 1937 two Nobel prizes were awarded for research into vitamin C. Szent-Györgyi was awarded the medical Nobel prize, while Norman Haworth and Paul Karrer received a joint Nobel prize in Chemistry for vitamin research. Haworth's prize was awarded for vitamin C research. *(Illustration 8. The structure and reaction of vitamin C)*

The formula is the former and contemporary illustration of the ring structure. We could learn from János Wölfling's presentation that a carbon atom with four different substituents forms a chiral carbon atom which has two optically active isomers. This is the case with ascorbic acid, and L-ascorbic acid is vitamin C itself. The chemical equation at the bottom represents the antioxidant reaction of vitamin C. Szent-Györgyi noticed that when certain fruits are cut into pieces, the cutting surface turns brownish, while with other fruits this process is less prominent. They contain a substance that prevents oxidisation. Vitamin C can prevent oxidation of its environment, because it can easily oxidise. The two hydroxyl groups on the covalent bonds turn into two ketone groups by releasing two hydrogens. The process is easily reversible. Due to heavy oxidation vitamin C yields to oxalic acid and threonic acid.

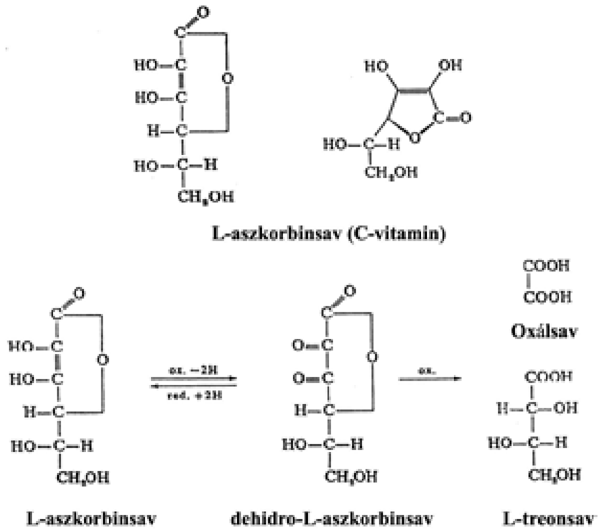


Illustration 8. The structure of vitamin C

Returning to the place, in this photo you can see the inner courtyard of Déri Miksa building. There was the entrance of Szent-Györgyi's flat and he took these stairs to get to his laboratory, where he examined the pepper for vitamin content. Today these stairs are called Szent-Györgyi stairs. *(Illustration 9. The Szent-Györgyi stairs)*

Illustration 9. The „Szent-Györgyi stairs" in Déri Miksa building

Several photos were taken at that time. This arch still exists today. The volleyball court where he and his colleagues played volleyball was situated in this courtyard. The woman next to Szent-Györgyi is clearly identified as his nearest colleague, Ilona Banga. *(Illustration 10. Albert Szent-Györgyi and his colleagues)*

Illustration 10. Albert Szent-Györgyi and his colleagues.

In the next photo you can see the famous pepper spin, which was used to extract the juice from the plant. The floor tiles are still there in the Déri Miksa building, so we can say without doubt that the equipment was used here. *(Illustration 11. Albert Szent-Györgyi and Brunó F. Straub with the pepper spin)*

Illustration 11. Albert Szent-Györgyi és Brunó Straub F. with the pepper spin

The question arises: what kind of pepper did Szent-Györgyi use to extract vitamin C? An article in the December 4, 1932 issue of Új Nemzedék (New Generation), a newspaper in Szeged, says that "Albert Szent-Györgyi has been looking for plants that contain plenty of vitamin C. Therefore in October this year he started determining the chemical composition of a special fleshy sweet pepper grown around Szeged." From this article it is clear that it was the so called 'tomato pepper'. I found another clue in Ralph Moss' book on Szent-Györgyi, which is the best biography of the researcher, that "Szent-Györgyi sent students to the market for 'tomato pepper' because tests revealed that it contained five-six times as much vitamin C as orange juice." These sources confirm that first they tried to acquire large amounts of this pepper. However, they could not have enough of it, so they tried other types of pepper, including hot spice peppers. It has also been described that Szent-Györgyi hired women to process spice pepper, and when the seeds of the hot spice pepper got into someone's eyes, he used his medical knowledge to give first aid. The first type he tested, the one he received for dinner, was probably 'tomato pepper', and later they used various types as well.

Publications show that the key figure was József Svirbely. He became a tragic character, the victim of the debate between King and Szent-Györgyi. (Here is a photo of him, which can be found in Somogyi Library, Szeged.) *(Illustration 12. József Svirbely)*

Illustration 12. Joseph Svirbely

In the USA he was accused of stealing the secret of vitamin C from his boss, Professor King, and bringing it to Hungary to Szent-Györgyi. In Szeged he was blamed for writing to King and revealing that hexuronic acid is identical to vitamin C. After returning to the USA later on, he had to explain himself. His friends told him to withdraw and keep away from the debate. He stopped vitamin C research. There is no proof of his cooperation with Szent-Györgyi later on when Szent-Györgyi was living in the USA. In the 2012 August issue of Szeged Journal László Péter wrote an article with the title "The real Svirbely" in which he tried to redress the researcher, who had an important role in vitamin C research. Due to the unjust accusations we fail to acknowledge his merits.

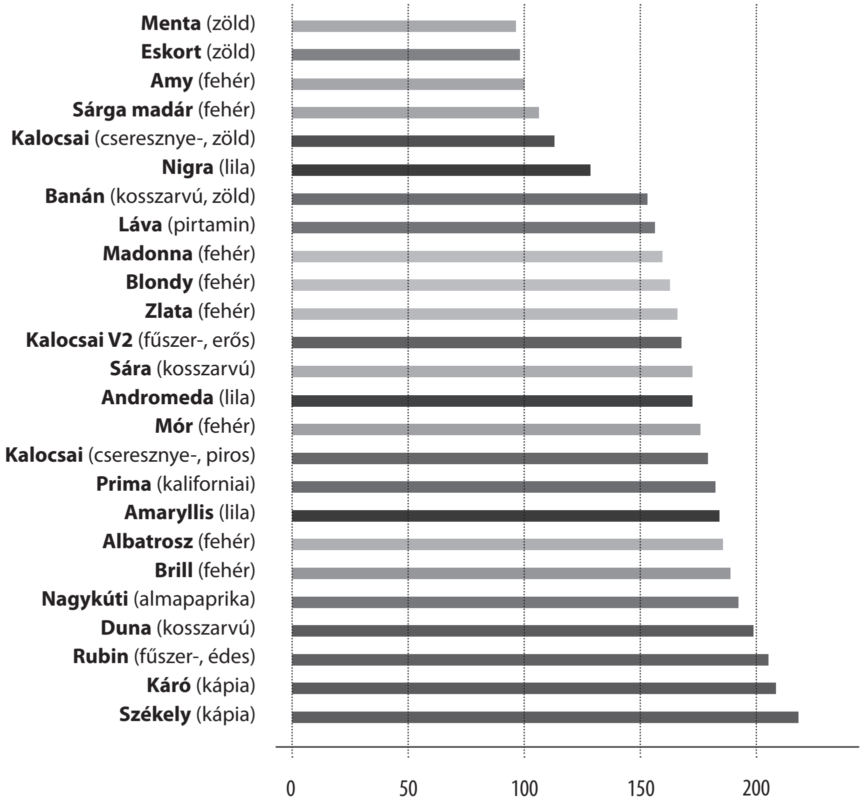
Here you can see the results of a comprehensive examination of the vitamin content of various fruits and vegetables initiated by HVG (a Hungarian weekly magazine on global economics). Now let us focus on vitamin C. Official data can be seen in the top row. We can see that pepper contains the highest amount of vitamin C. They usually bought pepper from various producers at the market. Pepper bought in discount stores contains the smallest amount of vitamin C, but even this small amount is as high as 100-200 mg. If 100 g of pepper contains 200 mg of vitamin C, the vitamin content of the pepper is 0.2 %. The study compared various types of peppers, the colours indicate the colour of the pepper. Green and white stuffing pepper from Cece (a Hungarian town) and red peppers, including the spice pepper from Kalocsa, all contain 150-200 mg of vitamin C per 100 g. Capia pepper is at the top of the list, and 'tomato pepper' is also near the top. So pepper is a "fountain of vitaminC', just as Szent-Györgyi noticed it 80 years ago.

(Illustration 13. The vitamin C content of various fruits, vegetables and peppers)

	PAPRIKA	PARADICSOM	SÁRGARÉPA	KÁPOSZTA	ALMA	SZILVA	SZŐLŐ
C-vitamin (mg/100 g)							
Hivatalos	**120**	**25**	**3**	**50**	**5**	**6**	**5**
Termelő 1	239	25	12	14	10	18	29
Termelő 2	259	32	11	18	10	35	27
Piac	157	36	17	11	20	27	22
Diszkont	102	33	Ő	20	11	40	23
B1-vitamin (mikrogramm/100g)							
Hivatalos	**50**	**100**	**50**	**40**	**50**	**50**	**50**
Termelő 1	101	59	79	75	23	34	55
Termelő 2	62	35	59	87	21	82	60
Piac	63	55	53	73	23	76	56
Diszkont	95	55	56	75	21	58	83
B2-vitamin (mikrogramm/100g)							
Hivatalos	**30**	**60**	**50**	**60**	**50**	**20**	**50**
Termelő 1	8	9	9	21	4	8	23
Termelő 2	24	5	11	6	3	17	21
Piac	9	6	14	21	8	12	19
Diszkont	25	5	10	13	7	8	22
B6-vitamin (mikrogramm/100g)							
Hivatalos	**240**	**70**	**200**	**310**	**70**	**40**	**70**
Termelő 1	776	66	166	160	44	35	103
Termelő 2	688	67	110	47	9	34	96
Piac	620	72	110	99	8	35	76
Diszkont	355	72	165	88	15	35	103

Illustration 13. The vitamin content of various fruits, vegetables and peppers

Vitamin C content of different Hungarian peppers (mg/100 g)



Forrás: *Semmelweis Egyetem egészségtudományi kar dietetikai és táplálkozástudományi tanszék 2004-es vizsgálata*

Szent-Györgyi tried to make some profit from his discovery. He obtained a patent for producing durable food products rich in vitamin C, such as Erős Pista or Édes Anna (concentrated spice pepper pastes). Szent-Györgyi had an anti-German, anti-war attitude, but ironically, most of his products were used to supply vitamin C to German submarine crews to prevent them from developing scurvy. Interestingly, his product marketed with the brand name 'vitaprik' was not really popular in England and the USA. Ralph Moss wrote in his book that Szent-Györgyi did not speak English well enough to know slang expressions. He was told that 'prick' is a vulgar word for penis. They quickly re-named the product pritamin, since then 'tomato pepper' has also been known as pritamin pepper.

Szent-Györgyi and his colleagues discovered another vitamin, vitamin P. Gábor Tóth told us in his presentation that the definition of vitamin is not clear. There are 13 real vitamins, which have physiological effects, the body needs small amounts of them and they have an impact on certain enzyme mediated cycles. So vitamins are substances our body needs, or else we die. Vitamin P is controversial, because it does not meet this last criterion. They discovered vitamin P when they were trying to treat certain conditions with vitamin C. In some cases the permeability of capillary walls increased. When pure ascorbic acid was used, this effect was not observed, however, when they used pepper extract, they could achieve this effect. They realised that this is not due to vitamin C, but another substance in pepper, a flavonoid. Szent-Györgyi named this flavonoid vitamin P.

Szent-Györgyi should not have used 'P' to name this vitamin if he had followed the alphabetical order, but we can recall his creativity from the 'ignose-godnose' story. He followed a similar trait of thought: P should stand for permeability and pepper. Mihály Beck, author of the book Humour in Science, said that Szent-Györgyi "added another argument to support his choice, namely that the best thing in the world starts with the letter 'p' in Hungarian". Is it pipe? Flavonoids may fail to meet all criteria to be vitamins, but they have important physiological effects.

Effects of free radicals

Now let me finish my presentation by summarising the legacy of Szent-Györgyi and vitamin C. I have already referred to Ralph Moss's book which was published in the USA in 1988. This thorough book is worthy commemoration of Albert Szent-Györgyi. The author has Hungarian origins and is involved in cancer research, and these two facts motivated him to write the book. In the USA he talked to Szent-Györgyi many times, he made several interviews and visited Hungary to collect materials for his book. When he visited Szeged, he was guided by Szent-Györgyi's former student and the founding director of Biological Research Centre of the Hungarian Academy of Science, Brunó F. Straub. He took Moss to Miksa Déri school building where they visited the former location of the research laboratory. It was not until Moss's visit in the 1980s that the leaders of the school realised how famous events had happened in the building. The English title of Moss's book is 'Free Radical, Albert Szent-Györgyi and the Battle over Vitamin C'. Free radical is a chemical term which refres to an atom or a group of atoms that has only one, unpaired electron. It is therefore highly reactive, it needs another electron, because a chemical bond requires a pair of electrons. After the book was published, László Péter wrote an article about it in Szeged's daily newspaper, Délmagyarország. In his article he suggested that the title 'Free Radical' also refers to Szent-Györgyi's independent, radical character, personality. His suggestion induced heated debate in the newspaper. I agree with László Péter, even so certain chapters in the book have ambiguous titles. 'Muscle Man' can refer to muscle research and Szent-Györgyi's versatility as a sportsman. In spite of the fact that this book is the most complete biography of Szent-Györgyi, it took a long time to translate it into Hungarian. When it was published in Hungary 15 years later, its title was 'Albert Szent-Györgyi' in order to avoid ambiguous interpretations. Those who have read it probably think that it was worth reading, but I would recommend it to everyone, I am sure they will find Szent-Györgyi's adventurous life and his remarkable scientific work intriguing.

People often ask about the daily dose of vitamin C, how much you should take. The recommended daily dose is 60 mg, although some people say it is 75 mg. Anyhow, it is less than 100 mg. Szent-Györgyi thought that (my apologies to doctors) veterinary surgeons are more humane to monkeys than human doctors to people, because the determined daily dose in monkeys is higher than that in humans. He said that 60-70 mg is enough to prevent scurvy. However, if we take more vitamin C, we can strengthen our immune system, the resistance of our body. After isolating the vitamin in pepper, he took 1000 mg daily. The forerunner of today's megavitamin therapy and multivitamin theory is Linus Pauling, who was awarded the Nobel Prize twice (Chemistry Nobel Prize in 1954, Peace Nobel Prize in 1962, both individually). In an attempt to promote his approach in the USA he visited Szent-Györgyi, who supported the idea of consuming higher amounts of vitamin C. Opponents of the idea say that excessive doses of vitamin C can cause kidney stones. The oxidisation equation of vitamin C shows that one of its break-down products is oxalic acid. There are three types of kidney stones: carbonate, phosphate and oxalate stones. If you are prone to oxalate stones, you should avoid high doses of vitamin C. Similarly, if you have a sensitive stomach, avoid consuming vitamin C, since it is ascorbic acid, it has acidic pH. Those who have a cast-iron stomach can take in 1000-2000 mg. Gábor Tóth told us that fat soluble vitamins can cause hypervitaminosis, which means that an excess of such vitamins can be harmful. Apart from indigestion and kidney stones, water soluble vitamins are not harmful. Since these vitamins dissolve in fluids, excess amounts leave the body unabsorbed with urine.

Returning to free radicals, when Szent-Györgyi was researching vitamin C, little was known about free radicals. Today we know that various external factors can produce free radicals which have highly reactive oxygen atoms with unpaired electrons and form strong oxidising substances. In this illustration we can see that certain external factors, such as ozone, nitrogen oxide, radioactive radiation, UV light, heavy metal ions, diseases, medicines, smoking, or even strenuous training can increase the amount of free radicals in the body. Last time someone asked if you do a lot of sports, is it recommended to take high amounts of vitamin C. If the amount of free radicals is increased due to any reasons, an increased intake of vitamins (E, A or particularly C) can fight these free radicals. PUFA stands for polyunsaturated fatty acid. PUFAs, especially omega 3 fatty acids, are said to be beneficial for our body. This table shows that increased intake of PUFAs can increase the amount of free radicals, therefore more vitamin C is recommended. What impact does it all have on your body? Free radicals can lead to diseases and accelerate ageing. We cannot arrest the latter, we can only slow it down by consuming more vitamin C. *(Illustration 14. The causes of free radicals and their harmful effects)*

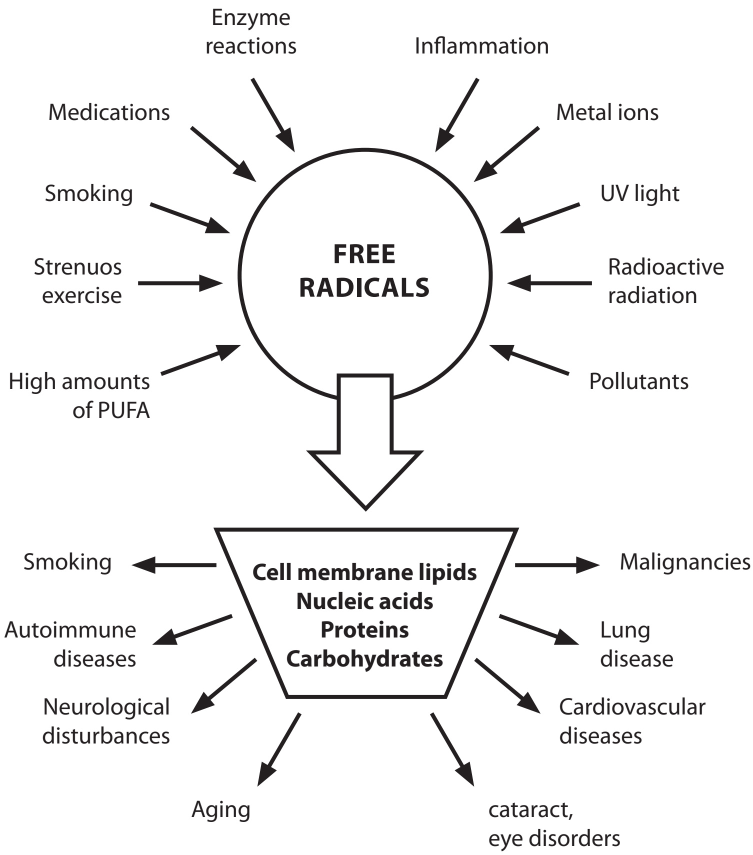


Illustration 14. The sources and harmful effects of free radicals

To sum up, I am not a doctor or an expert in vitamins, so I avoid making suggestions. All I can say is that my daily dose is 1000 mg. When Moss's book about Szent-Györgyi was published 25 years ago I was in the USA and I bought it right away. Since then I have been taking 1000 mg, my stomach is healthy, I do not have kidney stones and I am less prone to diseases. Some people say though, if you take such high amounts of vitamin C, you should be careful not to stop it, because your body is used to this higher intake. If you discontinue taking vitamin C regularly, you will be more prone to diseases.
In 2007 the University established a Memorial Room to Szent-Györgyi in the building of the Dean's Office of the Faculty of Medicine (109. Tisza Lajos street). There you can see, for example, a copy of the Nobel Prize or photos illustrating Szent-Györgyi's work. In 2012 another memorial room was established in the building of Miksa Déri Technical Secondary School on Kálvária Square, Szent-Györgyi's former work place in 1930-1935, the site of vitamin C discoveries.

In September 2013 on the 120 anniversary of Albert Szent-Györgyi's birthday the Csongrád County Division of the Society of Hungarian Chemists adopted guinea pigs as part of the adoption program of the Szeged Zoo.

References

- Ralph W. Moss, Free Radical, Albert Szent-Györgyi and the Battle over Vitamin C, Paragon House Publishers (1988)
- Ralph W. Moss, Albert Szent-Györgyi, Tipotex Publishing Company, 2003 (in Hungarian)
- C.G. King, W.A. Waugh, Science, 357, 75 (1932)
- J.L. Svirbely, A. Szent-Györgyi, Nature, 576, 129 (1932)
- J.L. Svirbely, A. Szent-Györgyi, Biochemical Journal, 279, 27 (1933)
- Mihály Beck, Humour inScience, Academy Publishing Company, 108 (2010 (in Hungarian))