Glycoconj J (2006) 23: 269–271
DOI 10.1007/s10719-006-8287-6

OBITUARY

Academician Nikolay Konstantinovich Kochetkov: 1915–2005

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Nikolay K. Kochetkov was born on May 18th, 1915, in Moscow. His father, Konstantin Alexandrovich Kochetkov, a chemical engineer, nurtured a strong interest in chemistry in his son. After having received his primary education in an elementary school in Moscow (1929) and the Moscow Technical School on Silicates (1932), Nikolay worked for two years as a technician in the central laboratory of the Dorogomilovo chemical plant before admission to the M.V. Lomonosov Moscow Institute of Fine Chemical Technology in 1934. Following graduation from the Institute in 1939, he was drafted and served with the army during the Great Patriotic War of the USSR.

On his return to Moscow in late 1945, Kochetkov joined the Laboratory of Organoelement Chemistry headed by Academician A.N. Nesmeyanov at the M.V. Lomonosov Moscow State University as Lecture Assistant. In 1948, he completed his Ph.D. studies and began exploration of the synthetic potential of β-chlorovinyl ketones as convenient sources of various classes of organic substances, especially heterocyclic compounds. This work culminated in awarding him a D.Sc. degree in 1953, and Kochetkov then continued his association with the University as Docent (Associate Professor) and, since 1955, as full Professor. Since 1954 until 1960, he headed the Department of Organic Synthesis at the Institute of Pharmacology and Chemotherapy of the USSR Academy of Medical Sciences, where antihistamines, anticonvulsants, antibiotics, including anti-tuberculosis drugs, and pyrrolizidine alkaloids were synthesized.

From 1956–1957, Kochetkov spent six months working with Sir Alexander Todd, the Nobel Prize winner (1957), at the Chemical Laboratory of the Cambridge University (U.K.). The interest in carbohydrates and nucleotides kindled at that time remained with him for the rest of his career. In 1959, he took part in the founding of the Institute of Chemistry of Natural Compounds in Moscow as Deputy Director and the head of the Laboratory of Carbohydrates and Nucleotides. Here, Kochetkov and his co-workers began structural analysis and synthesis of these compounds.

In 1966, Professor Kochetkov was appointed as Director of the N.D. Zelinsky Institute of Organic Chemistry of the USSR Academy of Sciences and held this office for the next 22 years. During this period, he played a significant role in the modernisation of the Institute and initiated studies in new fields of organic and bioorganic chemistry. Up until his last days, he remained Honorary Director of the Institute.

Along with the co-workers who moved with him to the Zelinsky Institute, Kochetkov continued his investigations in the Laboratory of Carbohydrate Chemistry, which enlarged

and strengthened in a short while and became a world-class centre of research in the structure, chemical synthesis and biosynthesis of carbohydrates and glycoconjugates. His scientific enthusiasm and creativity, reputation and ability to have a far-reaching vision made him an internationally acknowledged scientific leader.

In-depth penetration of Kochetkov into the field of heterocyclic compounds predetermined his success in the chemistry of nucleotides and nucleic acids (1962–1970). In an effort to develop efficient methods for structural analysis of these compounds, new reagents were proposed for modification of nucleic bases, including cytosine-specific *O*-methylhydroxylamine (1963). Later, chloroacetaldehyde was used to obtain fluorescent derivatives of adenine and cytidine (1971–1978).

The early 1960's were the beginning of Kochetkov's introduction to carbohydrate chemistry, too. An approach to access halodeoxy, deoxy and amino sugars was elaborated. The Wittig reaction was employed as a method for the synthesis of higher sugars (1962–1970), including 3-deoxy-D-*manno*-oct-2-ulosonic acid. A number of model compounds, *e.g.*, *O*-glycosides of hydroxy amino acids, were synthesised and their hydrolytic stability examined in connection with structural analysis of glycoproteins. Studies in radiation chemistry of carbohydrates (1964–1977) revealed hitherto unknown radiolysis pathways, *e.g.*, epimerization and redox processes leading to deoxyhexoses and 6-aldohexoses.

Since his early work in the field of carbohydrates, the major concern of Kochetkov was development of new methods for formation of the glycosidic bond. The discovery of the highly stereoselective orthoester method of 1,2-*trans*-glycosylation (1963) was an important breakthrough in the field. Later, more efficient procedures were proposed for stereospecific 1,2-*trans*- and 1,2-*cis*-glycosylation (1975–1998).

Pioneering chemical syntheses of oligosaccharide derivatives related to the O-antigens of *Salmonella* and some other bacteria (1974–1981) and their co-polymerisation with acrylamide led to neoglycoconjugates useful as artificial antigens in serodiagnostics of salmonellosis (1979–1992). In search for an approach to glycopolymers, in which sugar units are linked by phosphodiester bonds, the so-called glycosyl-H-phosphonate method was elaborated (1987–1990) and employed in synthesis of oligomers by stepwise chain elongation.

The longstanding challenge for Kochetkov was synthesis of regular polysaccharides, and the problem was solved using the specially designed trityl-cyanoethylidene polycondensation. Following unprecedented stereospecific syntheses of homopolysaccharides (β-D-glucan, β-D-galactan, α-D-mannans, α-L-arabinofuranans), several heteropolysaccharides were prepared (1980–1987) with structures of linear O-antigens of *Salmonella newington* and *Shigella flexneri* and a branched streptococcal capsular polysaccharide. These achievements remain unsurpassed in the synthetic polysaccharide chemistry. Subsequent syntheses of cyclooligosaccharides and regular polysaccharides as glycosides with functionalised aglycones for conversion into neoglycoconjugates also deserve mentioning.

Kochetkov and co-workers carried out extensive investigations into the use of accessible monosaccharide synthons, *e.g.*, levoglucosan, as chiral precursors of aglycones of macrolide antibiotics (1977–1991). This work culminated in the total syntheses of erythronolide A, erythronolide B and oleandonolide having 10 chiral centres.

Elucidation of structures of polysaccharides and glycoconjugates was in the centre of Kochetkov's research, too. He was among those scientists who had early realised the importance of modern physicochemical methods. His pioneering work on electron-impact mass spectrometry (1962–1971) resulted in elucidation of the major fragmentation pathways of various monosaccharide and disaccharide derivatives. Later, an efficient computer-assisted ^{13}C NMR-based approach to structural analysis of regular polysaccharides was designed (1987–1993). It exploits the discovery of a distinct dependence of ^{13}C NMR chemical shifts of disaccharides on the glycosidic bond type and absolute configurations of the constituent monosaccharides, which was rationalised by conformational studies (1981–1984).

Kochetkov and co-workers elaborated efficient methods for chemical fragmentation and modification of glycopolymers. These include selective cleavage of uronans (1970) and hexosaminoglycans (1973) as well as solvolytic depolymerisation of various heteropolysaccharides with hydrogen fluoride (1982) or trifluoromethanesulfonic acid (2000). Based on selective splitting of amide bonds leaving *O*-glycosidic bonds intact, a useful approach was developed for isolation of glycopeptides from glycoproteins (1976–2002). A mild solvolytic method was proposed for desulfation of gel-forming sulfated polysaccharides of red seaweeds (1967–1976).

Saponins from Far-Eastern medicinal plants, including ginseng, were the subject of structural studies of Kochetkov in 1960–1967. For the first time, the structures of triterpene glycosides comprising up to 10 monosaccharide residues were established. A significant progress was made in structural analysis of sphingoglycolipids of echinoderms, which started in 1961. Gangliosides from starfish and sea urchins were characterised in detail and found to differ from mammalian gangliosides in sugar constituents (*O*-sulfated and *O*-methylated sialic acids, arabinofuranose) and types of carbohydrate chains (internal sialic acid residues).

Investigations into blood group-specific glycoproteins from stomach mucosa enabled isolation and structural elucidation of the largest by that time oligosaccharide fragments containing up to 11 monosaccharide residues

(1976–1982). These data and mapping of the highly heterogeneous *O*-linked carbohydrate chains by 'two-dimensional' HPLC allowed formulation of a general concept of the glycoprotein structure. Later, carbohydrate chains of haemagglutinins from different influenza virus strains were analysed and compared (1983–1990).

The leading position of Kochetkov's scientific school in structural elucidation of lipopolysaccharides of Gram-negative bacteria is generally recognised. Structures of O-antigenic polysaccharides of numerous medically important microorganisms, including acute pathogens, and phytopathogenic bacteria were established (1973–2004). In these polymers, several classes of unusual monosaccharide components, such as new sugar ethers with lactic acid, 2,3-diamino-2,3-dideoxyhexuronic acids and 5,7-diamino-3,5,7,9-tetradeoxynon-2-ulosonic acids, were discovered and their structures confirmed by chemical syntheses (1975–1987). In certain cases, the structural data of polysaccharides necessitated revision of the existing serological classification schemes of the bacteria.

Kochetkov paid considerable attention to studies of carbohydrate biosynthesis. Numerous nucleoside diphosphate hexoses with modified nucleoside and sugar residues were chemically synthesised and assayed in enzymatic reactions (1961–1975). Efficient chemical syntheses of highly labile polyprenyl diphosphate oligosaccharides were developed, and heteropolysaccharides having the structures of bacterial O-antigens were obtained by enzymatic polymerisation of these biosynthetic precursors (1982–1988).

Experimental research of Kochetkov was described in more than 1000 scientific publications. He wrote 60 review articles, book chapters and books, including *Chemistry of Natural Products* (1961), *Chemistry of Carbohydrates* (1967), *Organic Chemistry of Nucleic Acids* (1970), *Radiation Chemistry of Carbohydrates* (1978), *Carbohydrates in the Synthesis of Natural Products* (1984), and *Synthesis of Polysaccharides* (1994).

It is also worth emphasizing the activity of Kochetkov in the teaching and training of young researchers. In the late 1950's, at the Moscow State University he taught the first class in the USSR on the chemistry of sugars and nucleotides as well as on the basic organic chemistry. In the scientific school he created, more than 100 Ph.D. and 30 D.Sc. dissertations were successfully defended. Many of his former students are world-renowned leaders in various fields of chemistry and biology, both in Russia and abroad.

Kochetkov represented the USSR at the International and European Carbohydrate Organisations from the beginning of their founding until 1989. He organised and was Chairman of a number of national and international scientific meetings. Being a Regional Editor of the journals of the *Tetrahedron* series for many years, Kochetkov served as a bridge between Russian chemists and these prestigious publications. He was a member of Editorial Boards of many other international and Russian scientific journals.

Professor Kochetkov was distinguished by election as Corresponding Member (1960) and then Full Member (1979) of the USSR Academy of Sciences, Corresponding Member of the USSR Academy of Medical Sciences (1957), and Foreign Member of the Polish Academy of Sciences (1988). During his life, he garnered numerous awards and prizes in recognition of his outstanding scientific contributions. Among them were Hero of Socialist Labour (1985), Lenin Prize (1988), three Orders of Lenin, Demidov Foundation National Prize (1993), M.V. Lomonosov Great Gold Medal of the Russian Academy of Sciences (1994), Gold Medal of the Slovak Academy of Sciences (1986) and Haworth Memorial Medal of the Royal Society of Chemistry (1989).

For 60 years Nikolay Kochetkov was married to Vera Sergeevna Volodina. They raised a daughter Maria and a son Sergei, enjoyed three grandchildren and one great-granddaughter. In May of 2005, he celebrated his 90th birthday among his family members, friends, co-workers and colleagues. With great sadness, but also with great appreciation for his extraordinary contributions to chemistry, the scientific community learned of his passing away the same year on December 21st. Among the many individuals who had great happiness working with him and learning from him, Academician N.K. Kochetkov, an outstanding Russian chemist of the 20th century, will always be remembered as a true Scientist and a true Teacher.

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