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In Memoriam
Professor Udo Gräfe, 1941–2003

Professor Dr Udo Gräfe died of acute heart failure on 14 February 2003 at the age of only 61. His death is a loss deeply felt by all who have been involved in antibiotic research.

For nearly two decades he was very active in the development of natural antibiotics at the Central Institute for Microbiology and Experimental Therapy, later the Hans-Knöll Institute for Natural Product Research.

Udo Gräfe was born on 8 May 1941 in Jena and received his primary and secondary school education there. At an early age he developed a keen interest in science. After studying chemistry at the University of Jena from 1961 to 1966 he worked as a research assistant at the Institute of Organic Chemistry and Biochemistry. He received his PhD degree from the University of Jena in 1969 for his studies on the synthesis of bicyclononane. His career in natural product research began in 1970 at the Jena Institute of Microbiology and Experimental Therapy, which was under the auspices of the German Democratic Republic (GDR) Academy of Sciences. Gräfe became a key member of the group working on theoretical and applied aspects of directed manipulations of control mechanisms governing the expression of microbial secondary metabolism. He isolated two new autoregulators (the so called L-factors) affecting the cyto-differentiation of the anthracyclin-producing *Streptomyces griseus*, and was closely associated with the industrial development of the leucomycin-type macrolide antibiotic turimycin, and of the anthracyclines daunorubicin, adriamycin and aclacinomycin. He also isolated nitrogen-free glycosides of platenolides as precursors of turimycin from the industrial strain *S. hygroscopicus*.

In 1985 Gräfe became Professor of Microbial Chemistry at the GDR Academy of Sciences and Head of the Division of Antibiotic Research.

Following German re-unification in 1990 a tremendous change in all aspects of life took place in East Germany. In 1991 the Beutenberg-Campus in

Jena, one of the largest science communities in the old GDR, was revitalized. The Hans-Knöll Institute of Natural Products Research was founded in 1992 as a non-profit organization. With its roots in the former GDR Academy Institute, the Institute had to find its own way in this process of continuity and restart. Building on its strengths in microbiology, chemistry and biotechnology new disciplines of the modern life sciences have been added in the past few years.

In 1992 Gräfe was appointed Head of Division Chemistry, later the Department of Biostructure Chemistry. In this position he was closely associated with the isolation and structural elucidation of new bioactive natural products by screening strains and the chemical modification of bioactive structures

to uncover new structure–activity relationships. He was especially interested in new antibacterial and antifungal antibiotics. Moreover, he was engaged in the buildup of physical-chemical methods of structural assignment, such as high-field NMR and modern MS methods. Emphasis was also put in the development of coupled methods such as LC-NMS and LC-NMR.

During the period 1990–2001 he determined the structures of many newly discovered antibiotics with highly unusual chemical features and biological properties. These included: deoxyxylerythrin; cantharellic acid; *N*- methylniphimycin; apidiothricin (a chlorine-containing macrolide); the cervimycin complex (from a *Streptomyces* strain isolated from the Grotta de Cervi, Italy); a siderophore-type asterobactin; and queenslandon (mycotoxin). From fungi he isolated a series of new structures such as the illudanes, hexacyclinol, lignoren, agrocybolacton, acremonol, acremodiol, cerrenatriol, tubarialacton and cerrenatriolacton.

From endophytic actinomycetes isolated from maytansin-producing plants, he isolated the new structures celastramycins A and B. He characterized microbial metabolites of different structure as membrane active agents: cyclopeptides (aurantimycins), linear peptides (helioferins, peptaibolins, roseoferins, ampullosporins, chrysospermins, lipohexin) and macrolides. The interesting neuroleptic and morphogenic effects of ampullosporin A, a 15-membered peptaibol, led him to continue in the study of peptaibol-type microbial peptides and structure–activity relationship.

A second basic line of research concerned the synthesis and partial synthesis of analogues of natural products acting as antibiotics. Recently, antibiotic structures such as macrocyclic lactones (macrolide) and siderophore-type molecules were the subject of his investigations.

Gräfe had over 200 publications and 50 patents covering many areas of antibiotic research and had given many invited lectures on various aspects of natural products throughout the world. He was the author of the well known volume *Biochemistry of Antibiotics* (1992).

Promoted full Professor of Natural Product Chemistry at the University of Jena in 1993, he still taught at the Faculty of Biology and Pharmacy, and mentored many pre- and postdoctoral fellows.

He was a member of the Editorial Board of the *Journal of Basic Microbiology* from 1985, and was a thoughtful and well-disposed reviewer of many papers in antibiotic research.

Gräfe made many research visits to Japan, Great Britain, USA, Vietnam, China, Russia and other countries where he had good friends and associates.

For Gräfe's many friends and colleagues it is unforgettable that he chaired the workshop 'Peptaibols: Biosynthesis, Structural Diversity, Bioactivity, and Mode of Action' on 9–11 October 2002 in Jena.

All of us who knew him admired his profound knowledge of science and his keen interest in many fields of research.

The scientific community will wish to express their sympathy to Mrs Gräfe and the Gräfe family.

In the name of all his colleagues
Brigitte Schlegel
Klaus Jürgen Dornberger