Nitya Anand

A Tribute

Nitya Anand, a legendary figure on the Indian Drug-Research scene, known as Nityanand to his friends and colleagues, was born on 1st January 1925, at Layallpur, West Punjab, now in Pakistan. His father (the late) Shri Bhai Balmukund was a Professor of Physics and Mathematics at the Agriculture College at Lyallpur, while his mother was honorary Principal of an institution for imparting training in handicrafts to widows and destitute women. Both his parents were actively involved in social work and the national freedom movement. Nityanand had his early education (upto Class X) at Dhanpatmal Anglo-Sanskrit High School, Intermediate Science (1941) from Government Inter College, Lyallpur, B.Sc. (1941-43) from Govt. College, Lahore, now in Pakistan. He then moved to Delhi for an M.Sc. in Chemistry (1943-45) from St. Stephen's College and then to the University Department of Chemical Technology (UDCT), Bombay for research in organic chemistry with Prof. K. Venkataraman where he was awarded a Ph. D degree in 1948 on "Synthesis of Gentisin and other Experiments in the Pyrone Group". It was Dr. Venkataraman who rechristened Nityanand to Nitya Anand for his scientific publications to bring the name in line with Sanskrit traditions, and this duality in name still persists. This was followed by yet another Ph. D from St. John's College, Cambridge University under Prof. Alexander (later Lord) Todd where he worked on "Synthesis of Isoguanine and Certain Nucleotides". After this he returned to India in late 1950 and after a short stay at Delhi University, he joined the Medicinal Chemistry Division of the newly inaugurated Central Drug Research Institute in March 1951 and continued there until his retirement in 1984.

His stay in CDRI first as a Scientist, then as Head of the Medicinal Chemistry Division (1963-1974) and later as a director (1974-1984) has been of great significance in shaping and

directing the Institute. Although he is now a retired scientist he is still involved in drug discovery research and also in advising many R&D institutions and industries. In order to sharpen his skills in drug research and gain broader and deeper insights into biological sciences, he undertook post-doctoral training under a Rockfeller Foundation Fellowship in 1958 with Prof. Bernard D. Davis at Harvard Medical School, Boston, USA. A significant observation made by him during his work at Harvard was that damage to *E. Coli* by streptomycin results in the induction of bidirectional leakiness in its membrane. Although the importance of this membrane damage was overshadowed by the subsequent discovery of the block of protein synthesis by binding to ribosomes as the site of action of streptomycin Decades later the knowledge regarding the misreading rather than blockage of protein synthesis by sublethal doses of streptomycin at membrane-bound ribosomes provided a link between the pioneering observations of Nitya Anand and Davis and the mechanism of action of streptomycin. It also explained the known synergism between the bacterial action of в- lactam and aminoglycoside antibiotics – an effect of considerable clinical value. In the words of Davis "*Our first breakthrough came from the work of Nitya Anand, an exceptionally idealistic person and an excellent pharmaceutical chemist from India who joined us for a year to broaden his background for drug development*". Anand thus left his mark also in Bacteriology.

Dr. Anand started his research work at CDRI with the design and synthesis of sulphones and sulphonamides for leprosy. In this pioneering work, he made full use of the understanding of crucial factors in drug design such as transport across membranes, biology of the parasite and pathology of the disease through a multidisciplinary approach. The drug development studies of the candidate molecules included a study of their absorption, metabolism and distribution even at that early stage.

The most creative phase of Dr. Nitya Anand's career, however, started in the early sixties, when he became the guiding spirit behind the synthetic drug development program of the Institute after his exposure to recent developments in molecular biology and bacterial genetics during his stay at the Department of Bacteriology & Immunology at Harvard Medical School. Under his leadership, the Division of Medicinal Chemistry became the leading school in the field and achieved international recognition. He was first to initiate the era of synthetic peptides in the country and synthesized muramyl-peptide analogs as cell wall antagonists and a number of nucleosides as potential purine antagonists.

The synthesis of potential drugs in his group came to be guided more and more by the concepts of drug design and consideration of the factors like drug-receptor interaction, metabolism and pharmacokinetics. Synthesis of the designed molecules required stringent planning and execution of the synthetic schemes and Dr. Anand pioneered the synthesis of a wide variety of heterocycles including several new prototypes of chromenes, chromans, isochromans, diazabicyclo-octanes, bridged-piperazines, quinazolines, pyrazinoquinazolines, imidazopyrimidines, oxazolines, thiazalines, thiazolidenes, aminopyridines, imadizopyridines, polymethylenequinolines, benzocycloheptenes, benzapines, pyrazinobenzapines, pyrazino[1,2-a]quinolines, triazobicyclo(4,4,0)decan-2-ones, secosteroids, aza-prostagladins, pyridobenzoxazine, pyrazinopyridoindoles, pyrazinoisoquinolines, diazapinoquinolines, cyclazines, diazepinoindoles, and oxazoles. Dr Anand also retained his passion for basic organic chemistry and organic synthesis of special relevance to medicinal chemistry and made significant contribututions in the areas of Diels-Alder reactions, and the use of activated lactams such as lactam acetals for creating molecular diversity.

It was always fascinating to discuss our future plans of work with Dr. Anand. He would give

us information about the likely topography of the binding sites (receptors) involved in drug action, and his understanding of agonist, partial agonist and antagonist activities and the structure-activity relationship involved. In the light of these ideas molecular structures started to have a more dynamic meaning and we could visualize molecules permeating across membranes, wandering through biological systems and interacting with 3 receptors, with an ability to evoke response or otherwise, which could then be imagined intuitively and explored experimentally. Each part of the molecule began toi have a different meaning and the idea of substructural analysis through SAR became very vivid.

Dr. Anand was among the first to propose and use with much success the concept of designing prototype molecules in which the likely active conformation of the lead molecule with its pharmacophore(s) is frozen by incorporating it in a structure with constrained or fixed geometry. This not only provided drugs having selective and specific action, but also led to a better understanding of the 3D topography of the receptors involved in their action at a time when receptors had still not been isolated. These basic ideas were used extensively by Dr. Anand's group in the design and synthesis of agents for CNS and CVS disorders, fertility regulation (estrogen receptor modulators: SERMs), parasitic and infectious diseases. Apart from the discovery of a number of NCEs which provided candidate molecules for drug development, these studies also provided valuable information about the ligand receptor binding site. The 5-site binding model, thus proposed for the estrogenntiestrogen binding site in the early 1980s has been upheld after estrogen receptor cloning studies. Some of the molecules thus discovered and marketed, include Centchroman (contraceptive, INN: Ormeloxifene), Centbutidole (neuroleptic, INN: Biriperone), Centbucridine (local anesthetic, INN: Bucricaine) and Gugulipid a hypolipidimic agent (trade name Guglip). In his post-retirement period his keen interest and efforts in drug research led to discovery of some more drug candidates under clinical development which include an б1A-antagonist for BPH and a FXR antagonist for hyperlipidemia.

He has published more than 400 research papers, been granted about 130 national and international patents, and jointly authored two books on "Art in Organic Synthesis" 1969, Holden Day Inc. California; 200 Edition, 1996 John Wiley & Sons, New York; He has also edited two books: "Chemotherapy and Immunology in the control of Malaria, Filariasis and Leishmaniasis", eds Anand and Sen, 1984, Tata McGrew Hill, New Delhi; "Approaches to Design and Synthesis of Antiparasitic Drugs", Ed. Anand 1999 Elsevier, Amsterdam and published around 30 book chapters in medicinal chemistry textbooks, and many review articles.

An important outcome of Dr. Anand's scientific contribution was creation of trained medicinal chemists. He has supervised about 90 students for their Ph.D. degree, the last one in June 2003, and many post-docs. Many of these now occupy senior research positions in R&D Labs of Academia and the Pharmaceutical Industry.

Dr. Anand's contribution to the growth and development of the Central Drug Research Institute has been monumental. He propelled its advancement to a world-class center for drug discovery and development especially for tropical diseases (malaria, filaria), contraception and drugs from medicinal plants, areas of special national relevance. The Institute became a hot destination for joint or funded research in these areas with many national and international agencies, which has continued ever since. The Institute greatly encouraged interaction with academia and industry. Dr. Anand is deeply committed to the utilization of science for social benefits, and he took Drug Research because of the direct benefits it could provide to society. He has been a great champion of self-reliance and self-sufficiency of the Indian Pharmaceutical

Industry, and has supported this cause in the Drug Policy Committees of the Government of India and nongovernmental bodies of which he was a member for many years. He has also been a great supporter of spreading the message of scientific temper and of science as a way of life in schools.

He was associated with different drug policy formulating bodies of the Government of India for almost four decades. He has been an adviser and consultant to many scientific bodies and institutions. He was a member of the Scientific Advisory Committee to the Cabinet of GOI (1981-83), a Member & Chairman of the Steering Committee for Chemotherapy of Malaria of W.H.O., a Member of the Scientific and Technical Advisory Committee for Tropical Diseases and for Human Reproduction of the W.H.O., and a Consultant to UNCTAD and UN1DO He has been the Chairman of the Indian Pharmacopoeia Committee of the Govt. of India since 1978. He is a member of the Board of Directors and Chairman, Academic Board of the National Institute of Pharmaceutical Education and Research, Chandigarh. He has been a member of the Board of Directors and R&D Adviser to some of the leading Pharmaceutical companies of the country.

He has received many honours and awards. He is a Fellow of the Indian National Science Academy, New Delhi, the National Academy of Science, and the Allahabad and Indian Academy of Sciences, Bangalore. He has been a President of the Indian Pharmaceutical Congress. He received the Amrut Mody Research Award (1971), the K.G. Nayak Gold Medal, Baroda University (1972), the Vishwakarma Medal, INSA (1982), the J.B. Chatterji Gold Medal, Tropical School of Medicine, Calcutta (1982), the Acharya P.C. Ray (1972) and Sir J.C. Ghosh (1976), Medals, Indian Chemical Society, the National Nehru Science Award of MP, CST (1996) and the Vigyan Gaurav Award of UPCST (2000). Endowed orations include Bawa Kartar Lectures, Punjab University, Bhatnagar Medal Lecture, I.I.C.T., Hyderabad, R.C. Shah Memorial Lecture, Institute of Science, Bombay, Sokhey Memorial Lecture, New Delhi, Platinum Jubilee Lecture of Science Congress, TR Seshadri Memorial Lecture, Delhi University, Raj Kristo Dutt Memorial Award Lecture ISC, Darshan Ranganathan Memorial Oration of Society, Biorganic Chemists of India (2001) and Prof. Rama Krishna Memorial Oration, I.I.T., Delhi (2002).

Apart from being a visionary, an outstanding, scientist and an able science administrator; Dr. Anand is also a great humanitarian. He has set an example in modesty, hard work, devotion and dedication, which have motivated almost all who have come into contact with him, particularly his students. It is because of these human qualities that he commands outstanding respect among his colleagues, students and friends. In his personal life, he has been supported by Dr. (Mrs.) Swarn Nityanand, his children Mr. Neeraj Nityanand, Dr. Naveen Nitya Anand and Dr. Sonia Nityanand and their families, who are flourishing in their choosen careers. We are privileged to salute and honor such a unique personality, a connoisseur of science and human values, a young man of 80 years with great personal charm – for his contributions in drug research, in shaping the Central Drug Research Institute as a center of excellence and in the growth of the Indian pharmaceutical industry.

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Selected Publications

1. Anand, N.; Venkataraman, K. *Proc. Indian Acad. Sci. Sect. A*. **1947**, *25*, 438. Synthetical experiments in the chromone group. Part XXI. Synthesis of gentisin, the colouring matter of gentian root.
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