

# **MOTI LAL DHAR**

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*M. S. Swaminathan*



# MOTI LAL DHAR

(1914-2002)

Elected Fellow 1960

## EARLY LIFE AND EDUCATION

**M**OTI LAL DHAR was born to Pandit Dina Nath and Smt. Posh-I-Kuj Dhar on 29<sup>th</sup> October 1914 at Srinagar (Kashmir). He received his early education (upto Intermediate Science) in Srinagar and then moved to Lahore (now in Pakistan) and joined the Forman Christian College, to do his M.Sc in Chemistry from the University Chemical Laboratories, Punjab University, at that time one of the most reputed Chemistry Departments in India. Moti Lal had a brilliant academic career, securing a first division and first position in both the B.Sc. (Hons) (1936) and M.Sc.(Chemistry) (1937) examinations and received the special Alumni Gold Medal and a university scholarship for research in the University Chemical Laboratories (1937-38). He then moved on to UK for higher studies on a scholarship sponsored by the Jammu and Kashmir State Government and joined the Sir William Ramsay and Ralph Forster Laboratories, University College, London in 1938 where he worked under the supervision of Professor CK Ingold, FRS, the doyen of Physical Organic Chemistry, in his classic work on the kinetics of olefin elimination in the uni- and bi-molecular substitution reactions of alkyl halides. Some of the research papers published by Ingold jointly with Dr Dhar are considered to be amongst the classic papers of Ingold. After being awarded the Ph.D. degree of London University in 1940; Dr. Dhar returned to India. Much later, in 1957, Dr. Dhar was a Visiting Scientist in the laboratory of Prof. Linus Pauling, NL at California Institute of Technology, USA on a Rockefeller Foundation Fellowship, when he worked on the structure and function of proteins. Thus, Dr. Dhar had the privilege of being associated with both the stalwarts of structure-function relationship studies of organic molecules.

## FAMILY

Dr Dhar was married to Mohini, an unusually kind & gentle house-wife, who pre-deceased him in 2000. Dr. Dhar is survived by his two sons. The elder son, Dr Jawahar Lal Dhar, Ph.D. (Physics), retired as Advisor, Department of Science and Technology, Government of India, his wife Renu Dhar is an illustrious IAS Officer, with a daughter, Isha who gave Dr. Dhar much comfort and company in the last years of his life. The younger son, Dr. Naveen Dhar is a Cardiac Surgeon, settled in U.S.A. with his physician wife Usha, a practising physician and a daughter, Arunima.

## PROFESSIONAL CAREER

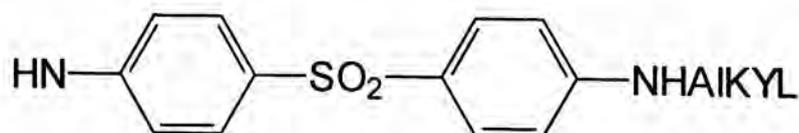
On his return from England in 1940 Dr. Dhar joined the Drug Research Laboratory (DRL) of the Jammu & Kashmir State at Jammu, taken over later by the Council of Scientific and



Industrial Research and renamed as Regional Research Laboratory (Jammu). He was deputed by the State government to the School of Tropical Medicine, Calcutta (now Kolkata) for one year for training in the development of new drugs from Indian medicinal plants. He served the DRL for about 10 years in the capacity of Chemist and Works Manager during which he helped to organize the production of drugs which were in short supply because of the Second World War.

In May 1950, Dr. Dhar joined the newly established Central Drug Research Institute at Lucknow (a constituent laboratory of the Council of Scientific & Industrial Research) as scientific Officer, in the Medicinal Chemistry Division, becoming Assistant Director and first Head of the Division in December, 1950.

The modern era of drug discovery research with its emphasis on synthetic drugs had become well established in the western world by 1950. However, drug research in India was still mainly confined to investigation of medicinal plants used in traditional systems of medicine and even this work was carried out in a non-collaborative mode with each discipline group working more or less independently of the others, which was not conducive to development of new drugs. Further, research on chemotherapy was insignificant. Recognizing these lacunae, Dr. Dhar initiated research programs which would overcome these shortcomings. He initiated projects for the synthesis of new chemotherapeutic agents for the treatment of mycobacterial infections, (tuberculosis, leprosy), filariasis and amoebiasis, three major health problems of particular relevance to India at that time. In the design of synthetic drugs Dr Dhar, with his background of physical organic chemistry, applied the principles of mechanistic organic chemistry to the functioning of biological systems and to the design of chemotherapeutic agents. Thus, all the projects on new drug discovery research were based on some distinct rationale, which laid a sound foundation of medicinal chemistry research. In the design of new drugs for leprosy and tuberculosis, the lipid-rich character of the causative organisms and the role of lipid solubility of drugs in their transport across biological membranes, were taken into consideration. At that time diaminodiphenylsulfones were emerging as suitable antimycobacterial agents. Dr. Dhar and his group designed analogs of 4,4'-diaminodiphenylsulfone (DDS) of type 1, which carried an alkyl chain on one of the amino groups to impart a lipophilic character, while a galactose residue on the other to impart a balance of hydrophilicity, which would be hydrolysed in the biophase to provide one free amino group essential for the antibacterial activity of sulfones.

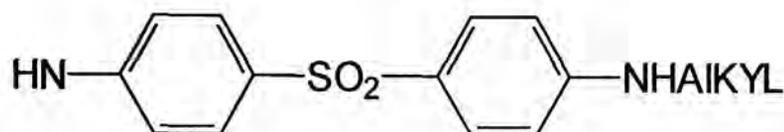


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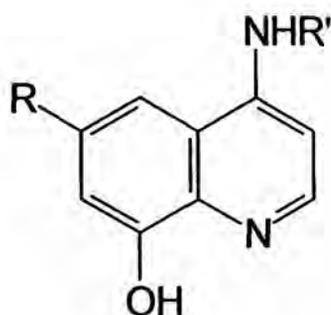


Some of these compounds exhibited a high order of anti-mycobacterial activity.

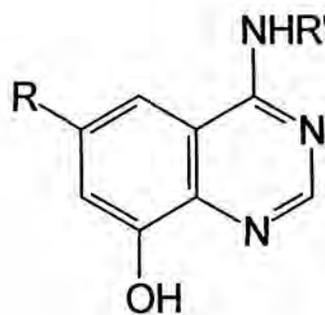
Similarly, the early work on the design of antiamebic agents based on 8-hydroxyquinolines and quinazolines, took into consideration the contribution of various substituents to the stereo-electronic factors affecting the chelating property of the 8-hydroxyquinolines and related molecules. A large number of molecules of type 2 and 3 were investigated, some of which showed promising antiamebic activity.



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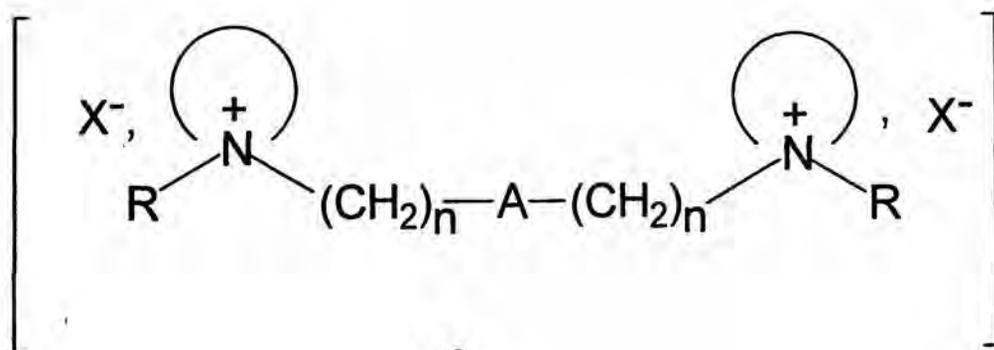


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Again in the design of bis-onium compounds of type 4 as neuromuscular blocking and muscle relaxing agents, he applied the principles of stereo-electronic fit of the molecules at the receptor site considering the charge at the onium heads, the steric fit around it and the flexibility of the connecting bridgehead. Some of the compounds showed promising neuromuscular blocking activity with minimal muscarinic and nicotinic effects.



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Dr Dhar thus laid the foundation of mechanism and structure based drug design and discovery research at CDRI, which grew into a very active school of medicinal chemistry research and attracted much attention for its contributions.

At that time the approach to development of drugs from plant resources was based on selecting plants reputed in traditional medicine texts or in folk medicine and subjecting these plants to detailed chemical investigation, followed by pharmacological evaluation of the pure isolated products. Although following this conventional approach at CDRI in its early day did lead to the development of a few drugs, including *Bacopa monniera* (Brahmi) as a memory enhancer and *Picrorhiza kurrooa* (Kutki) for treatment of liver disorders, the approach was not cost-effective and very productive. A different approach was required. Dr. Dhar, therefore, initiated in early 1960s a programme of broad-spectrum biological screening of extracts of plants identified and collected systematically by CDRI botanists from different ecological regions of the country. Plants showing biological activity in the screening were followed up by bioassay-based chemical fractionation and detailed chemical and pharmacological evaluation, followed by preclinical tests and clinical trials. This still continuing programme has provided much useful data on Indian flora. More than 4000 plants have been collected, extracted and screened till date and the data analysed. This data base of plants collected and screened and of extracts available for future screening is a very valuable national asset. This biological screening programme helped not only to discover new drugs from plants, many of which were not even mentioned in traditional medicine texts, but also provided leads for the design of new biodynamic agents. Later the extracts of marine flora fauna were also included in the screening project and many useful leads emerged from this work.

This screening programme attracted much attention, it led to a long-term collaborative project between the CDRI and the National Institutes of Health, Bethesda, U.S.A. for the anticancer screening of plant extracts by the latter, providing many useful leads.

Dr. Dhar was promoted to Deputy Director in 1962 and selected as the Director of the Institute in 1963. In this enlarged sphere of responsibility, his management capabilities now found full scope. He not only consolidated the foundation laid down by his predecessors but gave a new direction to the organization of R&D work. Understanding the need of a multidisciplinary working in drug research, and after much discussion with his senior colleagues, he integrated different disciplines together into collaborative mode of working through project-based re-organisation of the scientific work of the Institute, while maintaining the discipline-oriented basic frame work of the Institute. All the R&D work of the Institute was assigned to project teams whose members were drawn from different disciplines. Each project team had well defined objectives and time-schedules. Each project team would meet frequently, at least once in 8 weeks. This orientation gave considerable impetus and speed to the new drug development programme of the Institute. In the formulation of the work programmes. Dr. Dhar also gave due emphasis to oriented basic research which he considered was the scaffolding on which the superstructure of applied research should be built. This basic organisational structure of the Institute has been maintained to this day.



By the time Dr Dhar became the Director, some of the compounds/products developed by the Institute had reached the stage of toxicology and preclinical studies, Dr Dhar created such a facility as a component of the Division of Experimental Medicine. The Institute thus established the complete infrastructure for new drug discovery and development from initial Lab. studies to Phase 1 clinical studies.

Dr. Dhar was a strong advocate of cooperation with other scientific organizations. As a first step in this direction, the latest micro-analytical and spectroscopy facilities of the CDRI were made available to university laboratories. This nucleus ultimately became the present Regional Sophisticated Instrumentation Centre which is supported by the Department of Science & Technology of the Government of India. He was also responsible for establishing linkages between CDRI and other government and non-government agencies involved in chemical research and particularly the pharmaceutical industry, both Indian and foreign, through collaborative and sponsored projects on development of processes and products, including custom synthesis of new compounds for biological screening. A collaborating foreign organisation provided gifts of special chemicals and sophisticated instruments which would have been almost impossible to procure because of the acute shortage of foreign exchange for many years. This "barter" deal enabled the CDRI to build up its infrastructure and the availability of special/rare chemicals greatly accelerated the research output. In fact the Institute's first NMR spectrometer was a gift from a foreign collaborator. The first research fellowships in CDRI were provided by an collaborating Indian pharma company.

### PERSONAL TRAITS

Dr Dhar possessed leadership qualities of a very high order. Although a person of strong convictions, he was always open to suggestions. He was essentially a person who believed in compromise and consensus, but could be quite firm when a principle was involved. Above all he was a good judge of talent; he could pick up a talented scientist, give him full responsibility and also full credit for his performance. He was among the few scientists of his time who did not allow his name to be included in a research paper unless he was directly involved in the work. He gracefully withdrew from many project teams when his managerial duties increased and he could not contribute to the project. These qualities earned him the respect, regard and admiration of his colleagues.

### ON THE NATIONAL SCENE

As a member of the Governing Body of CSIR, Chairman of the Coordination Council of the Biological Group of CSIR Laboratories and Chairman of the Pay and Core Committee of the CSIR. Dr Dhar played an important role in the formulation of CSIR plans and policies of that time. It was on his initiative that CSIR introduced the system of promoting its outstanding scientists to the grade of Director, who did not want to be (or should not be) burdened with Director's administrative responsibilities. This innovative rule helped CSIR to retain its senior scientists during its formative years, and also give due recognition to those who were not interested in administration.



Even outside the CSIR Dr Dhar was actively associated with many institutions and committees of U.P. Government and Government of India, especially those connected with supporting R&D and with those connected with the growth and development of the Indian Pharmaceutical industry. He was instrumental in the creation of UP Council of Science and Technology and was a member of its first Executive Council and taking UPCST off the ground. He was a member of the Executive Council of Lucknow University, and of the Board of Governors of Moti Lal Nehru Engineering College, Allahabad. He was a member of the Scientific Advisory Board and of the Governing Body of ICMR.

Dr Dhar was a member of many of the Government Drug Policy committees. He was a member of the Development Council for Drugs and Pharmaceuticals, Committee for Fixation of Prices of Bulk Drugs and of the Hathi Committee for Drugs & Pharmaceuticals. He was a great believer in self-reliance and in development of self-sufficiency by the Indian Pharmaceutical industry, and in whatever committee he worked he promoted this view. He played an important role during the discussions which resulted in the change in Indian Patent Law in 1971 limiting it to only process patents for pharmaceutical products. This change to only process patent has been the major driving force for the growth of the Indian pharma industry in the last three decades. Dr Dhar was a member of the Board of Directors of Indian Drugs & Pharmaceuticals Ltd., Hyderabad and Hindustan Antibiotics Ltd., Pune, the two largest public sector pharma companies. Dr Dhar was also a member/leader of many Government/Science Academy delegations sent abroad. He visited the USSR in 1963 and 1967 as a member of a Government of India delegation to identify areas of scientific and technological collaboration and again in 1968 and 1973 to attend Indo-Soviet Symposia on Natural Products. He led the Indian delegation to the Fifth Commonwealth Scientific Committee meeting in Pakistan in 1968. Following this at the request of the Committee and of the Pakistan Government, he prepared a comprehensive project report for the establishment of a Drug Research laboratory at Chittagong. In 1970, Dr Dhar headed the Indian delegation to West Germany to study the working of the pharmaceutical industry and the status of drug research in that country. The same year he participated in the first meeting of the International Science Foundation at Stockholm, Sweden, as a delegate from India.

Dr Dhar superannuated from CDRI in October 1974 after an illustrious tenure of 24 years with 12 years as Director, the longest held by any Director of CDRI.

#### **AFTER SUPERANNUATION**

Even after his retirement from CDRI, his association with educational and scientific institutions continued. He was appointed Chairman, Board of Governors, Indian Institute of Technology, Kanpur (1974-76). Thereafter he served as Vice-Chancellor, Banaras Hindu University, Varanasi (1977-79), after which he settled down in Delhi. He was invited to be a member of the Institute Body of the All India Institute of Medical Sciences, New Delhi, and was made Chairman of its Academic Council and of its Finance Committee. A committee headed by him, often referred to as Dhar Committee, submitted a landmark report, the recommendations of which greatly improved the career prospects of the AIIMSc and PGI faculty. Dr Dhar also served as Chairman of the Scientific Advisory Committee of the Institute of Microbial Technology of CSIR at Chandigarh in its formative years.



## HONOURS AND AWARDS

Dr Dhar received many honours and awards. He was an elected Fellow of the Indian National Science Academy (INSA), New Delhi of the National Academy of Sciences, Allahabad and of the Indian Academy of Sciences, Bangalore. He served on the Council of INSA (1970-72) and was its Treasurer for a brief period in 1977. He was President of National Academy of Sciences (1971-1972). In recognition of his valuable contribution to drug research and development and outstanding leadership as a science administrator, Dr. Dhar was awarded the Padma Shri in 1971 by the President of India.

Dr Dhar passed away on 20<sup>th</sup> January, 2002 after a protracted illness at the All India Institute of Medical Sciences, New Delhi.

## PERSONAL NOTE

I had the privilege of being associated with Dr. Dhar for almost 52 years, of which 24 years were as his colleague at CDRI, and this association was an enriching experience. What I have written above is based on my perception of him as a person, as a scientist and as a science administrator. However, the best judge of as a person are his family members who see all the aspects of a person's character at much closer quarters. I am reproducing below a few lines spoken by his grand-daughter Isha on the occasion of a memorial service for Dr. Dhar after his death on Jan. 31<sup>st</sup>, 2002 at Delhi. "Moti Lalji was a many-splendored personality, extremely well-read and informed on a variety of subjects, the spectrum covered books on literature, fine arts, philosophy, metaphysics and religion. The ethereal beauty and composite Sufi culture of Kashmir touched him profoundly ..... Moti Lalji was Tathiaji, the Beloved-One, to his family and friends. A towering personality, a father figure to many, he was also great fun to be with despite his short fuse and sharp tongue..... At a personal level, he was a kind, warm, generous loving and caring grandfather who has inspired us to dream of a wonderful future for mankind, where man will help man to fulfill his DHARMA in life. Let us pray for his eternal peace and may his spirit guide us for a happier, less-troubled world".

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