The First Modern Drug Discovered in India

History of modern drug discovery and development testifies that Indian Scientist Dr. U N Brahmacari's research acumen was comparable to Paul Ehrlich. This comparison emanates from the fact that as Paul Ehrlich discovered and developed organic arsenical salvarsan/arshphenamine for the treatment of syphilis, Brahmacari discovered and developed organic antimony compound urea stibamine for the treatment of kala-azar. Both worked in the field of chemotherapy. Ehrich’s formula continued in use until penicillin became commercially available for treatment of syphilis. However, Brahmacari’s formula continues in market even now or for over 96 years in many countries in a modified form.

During 1915-1921 Brahmacari discovered Urea Stibamine after a systematic research as a therapy for visceral leishmaniasis. Visceral leishmaniasis was a severe health burden during the early part of the 20th century in Eastern India. In 1923 it was used on an experimental basis in Assam (India). The therapeutic success of the new drug favoured its use on a mass scale from 1928. The life saving attributes of the drug can be judged from the fact that by 1933, it saved about 3.25 lakh lives in Assam alone. The medicine has also been used successfully in Greece, France and China. Moreover, it was never patented.

Urea Stibamine became a life saving drug for a large section of the population. Historically, it was the second safe drug developed against an infectious disease after Salversan (against Syphilis) and well before penicillin or sulfa drugs. Like Paul Ehrlich, Brahmacari had also conducted systematic search for an effective therapy for kala-azar. Brahmacari had the advantage that he was both a medical doctor having M.D. and Ph. D. degrees and a Chemist of high caliber having obtained M. Sc. from Presidency College, Calcutta as student of Sir Alexander Pedler and Acharya Prafulla Chandra Ray, the legendary Indian Chemist and founder of Bengal Chemical and Pharmaceutical Works, the first Indian Pharma venture.

In the beginning of 20th century modern drug discovery was in nascent stage. There were only few specific drugs like, quinine for malaria, iron for anemia, digitalis for heart diseases and arsenic for syphilis. To this arsenal entry of urea stibamine was a great contribution from India.

The background of Brahmacari’s research was that in 1913 Gaspar Vianna, a Brazilian doctor reported to have cured the South American form of Kala-azar by the intravenous administration of tartar emetic (potassium salt of antimony tartrate). Subsequently, in 1915 Christina and Cortina of Sicily also reported successful use of tartar emetic in infantile Kala-azar. In the same year Rogers also obtained favourable results in Calcutta, by the intravenous use of tartar emetic. Unfortunately, there were serious disadvantages after prolonged use of tartar emetic intravenously, which was a matter of great concern. This background indicated knowledge gap. Brahmacari decided to fill this knowledge gap. First, he selected the sodium salt of antimony tartrate instead of the potassium salt. The principle behind the use of sodium salt was that it would avoid the depressant action of potassium and give better results. Brahmacari later found that prolonged use of the sodium salt also had disadvantages. Brahmacari started using metallic antimony—first as fine powder and then as colloidal antimony. Both forms of antimony used by Brahmacari gave good results but they were also associated with disadvantages like,

i. not readily available.

ii. could not be stored for a long time i.e. stability problem. Had to be prepared afresh every time.
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iii. The method of their preparation was tedious.
iv. The technique of their intravenous administration was quite complicated.

In view of these disadvantages Brahmachari extended his search for a more efficient means for treatment of Kala-azar. Thus in those days also Brahmachari was conscious about safety and efficacy of drugs, the soul of drug laws.

Around the same time Ehrlich was successful in treating sleeping sickness by using atoxyl or sodium salt of para-arsanilic acid. Brahmachari applied his sound knowledge of chemistry and decided to replace arsenic of atoxyl by antimony as both arsenic and antimony belong to the same group in the Periodic Table. He used his new compound for treatment of Kala-azar. Towards the end of 1919 Brahmachari received a grant from the Indian Research Fund Association for conducting further research into the treatment of Kala-azar. He carried out his research work in the Campbell Hospital (now N.R.S. Medical College, Kolkata). He did not even have a gas burner, a water tap or an electric bulb. Working under such adverse conditions Brahmachari discovered a potent agent against Kala-azar, which he named Urea Stibamine. Recalling the moment of his important discovery he later wrote: “I recall with joy that memorable night in the banished from India and other parts of the world where it occurs. That will be happiest and proudest day of my life if it falls to my lot to see it.”

Urea Stibamine was a great success in treating Kala-azar. In 1932, Col. H. E. Short, Director, Kala-azar Commission, appointed by the Government of India stated: “We found Urea Stibamine an eminently safe and reliable drug and in seven years we treated some thousands of cases of Kala-azar and saw thousands more treated in treatment centers. The acute fulminating type characteristic of the peak period of an epidemic responds to treatment extraordinarily promptly and with an almost dramatic cessation of fever, diminution in the size of spleen and return to normal condition of health.”

REFERENCE


About Dr. U. N. Brahmachari

Upendranath Brahmachari was born on December 19, 1873 in Jamalpur, District Monghyr of Bihar. The title Brahmachari has a little history. A person who lives a life of celibacy is called Brahmachari. His father Nilmony Brahmachari was a physician in East Indian Railways. His mother’s name was Saurabh Sundari Devi.

Upendranath completed his early education from Eastern Railways Boys High School, Jamalpur. In 1893, he passed B.A. Degree from Hooghly Mohsin College with Honours in Mathematics and Chemistry. In those days, it was possible for a student to appear in two honours subjects. Brahmachari stood first in order of merit in Mathematics in his B.A. examination and awarded the Thwyates Medal. Though, Brahmachari had keen interest in Mathematics and shown great proficiency in the subject, he decided to join the Calcutta Medical College and the Presidency College at Calcutta for studying Medicine and Chemistry respectively. He passed his Masters degree with first class in Chemistry from the Presidency College, Calcutta in 1884. Sir Alexander Pedler and Acharya Prafulla Chandra Ray taught him chemistry. Brahmachari was greatly influenced by Acharya Ray. Brahmachari also pursued his medical career with equal diligence. He obtained his L.M.S. degree in 1899 and in the next year, he took the MB degree. In MB Examination of 1900 of the University of Calcutta, he stood first in Medicine and in Surgery for which he received Goodeve and Macleod awards. In 1902, he obtained the M.D. degree of the Calcutta University. In those days, it was a rare distinction. He also obtained PhD degree of the Calcutta University for his researches in physiology. His thesis was titled studies in Haemolysis, a work which even today is considered an important piece of work on Physiological and physiochemical properties of the Red Blood Cells. He married Nani Bala devi.

After a firm grounding in Mathematics, Chemistry, Physiology, and modern Medicine, Upendranath joined the Provincial Medical service in September 1899. For a brief period, he worked as the House Physician in the Ward of the First Physician Sir Gerald Bomford’s. Sir Bomford was highly impressed with young Brahmachari’s urge for carrying out research and his strong sense of duties. Bomford got Brahmachari appointed as Teacher of Physiology and Materia Medica and Physician in Dacca Medical School in November 1901. He spent about four years at Dacca.

In 1905, he was appointed as a teacher in Medicine and Physician at the Campbell Medical School, now renamed as Nil Ratan Sarkar Medical College and Hospital, Calcutta, where he carried out most of his work on Kala-Azar and made his monumental discovery of Urea Stibamine. Upendra Nath Brahmachari was a leading medical practitioner of India of his time. His monumental discovery of Urea Stibamine, an organic antimonial compound, played a crucial role in the treatment of and campaign
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against Kala-Azar. His “Treatise on Kala-Azar” is a premier work on the subject. As a teacher and educationist, his work was of a high order. He was associated with almost all the known scientific and literary organizations at Kolkata. He had an insatiable thirst for knowledge. He had large private collection of books, which included not only scientific works but also literary works.

In 1923, he joined as Additional Physician in the Medical College Hospital. He retired from the Government service as a Physician in 1927. After retirement from the Government service Brahmachari joined the Carmichael Medical College as Professor of Tropical Diseases. He also served the National Medical Institute as In-charge of its Tropical Disease Ward. He was also the Head of the Department of Biochemistry and Honorary Professor of Biochemistry at the University College of Science, Calcutta.

Brahmachari died on February 06, 1946. The Kolkata Municipal Corporation renamed Loudon Street as Dr. U.N. Brahmachari Street.

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