KRISHNAMURTHI GANAPATHI

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(1911-2004)

Elected Fellow 1946

KRISHNAMURTHI GANAPATHI was born on August 18, 1911 in Tiruvarur, Tamil Nadu. His father S Krishnamurthi Iyer, a wealthy landowner, had to cut short his education to take on family responsibilities at a very young age. He was progressive and advanced in his thinking, always willing to try out new strains of seeds and methods of cultivation. He was much respected by the whole village. His mother Rajalakshmi, died very young leaving him and his siblings to be brought up by their paternal grandmother, Meenakshi. His grandmother, a remarkable woman, had a strong influence on him, instilling in him a sense of fairness and generosity. Originally named Subramanian his name was changed to Ganapathi after his mother discovered a Ganapathi idol in a nearby pond. Later on his father built a permanent temple in the village to install and consecrate the idol.

Ganapathi had a very happy and carefree childhood, first attending the village school in Sendakottai and later matriculating from the High School in Pattukottai in 1927, when he was awarded the Chokalingam Gold Medal for standing first in the class. In 1927 he joined Kumbakonam College for his intermediate, being the first in his family to enter college. In 1929 he enrolled at St. Joseph's College in Trichinopoly. He graduated in 1931 with a B.A. in Chemistry, obtaining a first class, with first rank in the Presidency. It was during this period that he first began to sympathise with the civil disobedience movement that was spreading through the country. Fortunately he did not suffer, only being watched and warned. He also gave up wearing foreign clothes and took to wearing *khadi*.

At first he had not planned to take up scientific research, which was regarded as an esoteric activity in his village, but his father encouraged and stood by him. In 1932 he was accepted at Annamalai University (Chidambaram) as a research student for an M.Sc. in Organic Chemistry. He esteemed his supervisor Dr. SN Chakravarti, who inspired him with his high sense of idealism. This was just an initiation into what research was really like, and he spent a lot of time reading the journals in the library and obtaining a specialised understanding of the Electronic Theories of Robinson, Ingold and others. Dr. Chakravarti regarded him as a pleasant and hardworking student, who had extensively studied the theoretical problems in chemistry, for which he had a definite flair.

On June 13, 1933 Ganapathi married Jampakam, daughter of Physics Professor KC Subramania Iyer, then a Lecturer of Physics in Kumbakonam College, and later

its Principal. His wife, proved to be a tower of strength who managed all the household affairs leaving him free to pursue his research. In later years Ganapathi would often remark that without her support he would not have been able to achieve all that he did. They had a long and happy married life and were fond parents to three daughters and a son.

In 1934 Ganapathi was admitted to the Indian Institute of Science, Bangalore, at that time the premier research institute in India. He joined the department of Organic Chemistry under Professor PC Guha. Here he received a much wider exposure to scientific research and its practices that was to equip him well for the future. The library was excellent and he made full use of it. He distinguished himself by his work and the ability to give good colloquia. In 1935 he was awarded the prestigious Sudborough medal as the best researcher. At this time, he attempted to work under Sir Robert Robinson in the UK and Professor Richard Kuhn in Germany, but due to the impending war they did not materialise. Nevertheless, he continued to regard them as his intellectual gurus, finally meeting them much later on in his life. In 1937 he was awarded the prestigious Lady Tata Memorial Scholarship to pursue research on the Chemotherapy of Tuberculosis. He started studying bacteriology working initially on gold salts of alloxazines then on sulpha drugs. In a couple of years he was an independent researcher, reading a paper at the Indian Science Congress at Hyderabad. The work at the Institute, on Synthetic Investigations in Pinane and Decalin Groups and the Chemotherapy of Bacterial Infections, led to the granting of a D.Sc. by Madras University in 1941.Though this work was completed two years earlier it was delayed by his not having an official diploma for the M.Sc. as yet! He often recalled the four years he spent in Bangalore as among the happiest overall.

Towards the end of the second year of his scholarship, he had to start looking for a job. He even applied for a third year for the scholarship with no hope of its being extended. In April 1939 he received a letter from Colonel SS Sokhey, Director of the Haffkine Institute in Bombay, who showed interest in his work on sulpha drugs and enquired as to whether he would come and work at the Institute. In what he later regarded as the most crucial event in his life Ganapathi visited Sokhey at the Haffkine Institute in June 1939 and accepted his offer. Thus began a lifelong symbiosis, almost a father and son like relationship, with Sokhey, that lasted till the latter's death.

In July 1939 Ganapathi moved to the Haffkine Institute and his scholarship was extended for an unprecedented third year. He was assigned to the Biochemistry Department. Initially, there was not much facility for work but as time went on he got the best equipment and chemicals. His work proved so promising and impressed Sokhey so very much that a new Department of Chemotherapy was established under him in 1940 first as Senior Chemist and then expanded in 1944 with him as

Assistant Director for the Institute in the Bombay Medical Service. This was in keeping with Sokhey's philosophy of creating a department around people rather than finding people to fill a created department. The Haffkine Institute further enlarged his vision; he got exposure to more advanced medical subjects by observing how things were done, and eventually moving into a new building with the best equipment. In 1946 he attended the Empire Scientific Conference in England, arranged by the Royal Society of London where he met many of the leading Indian scientists. He later spent much time in Europe, Canada and the United States, becoming acquainted with the latest research that was going on, and meeting many of the leading scientists in his field. The 13 years he spent at the Haffkine Institute proved to be one of his most productive periods in research.

In 1942-1943 he fell seriously ill due to glandular tuberculosis and pleurisy and had to spend time at the Madanapalli Sanatorium to recover. Here he picked up a regimen of good eating habits and exercise that he adhered to for the rest of his life. Under medical advice he gave up work in Organic Chemistry and took to Biochemistry and Microbial Chemistry.

In 1953, he spent a period of 5 months as a fellow of the WHO, and then with the permission of the Bombay Government his services were granted to the newly created Penicillin Factory at Pimpri, which later came to be known as Hindustan Antibiotics. He was appointed the Research Superintendent in charge of the Antibiotics Research Centre, which he personally designed and equipped to world class standards. From the beginning he took a leading part in the production work in the factory and organised from scratch the Quality Control Section and was personally in-charge of it for quite some time. He also designed a very nice animal house, which for instance was equipped to breed Swiss mice and rabbits. In 1955 he had the opportunity to visit the USSR and acquaint himself with the latest advances there. From April 1958 to January 1959 he served as the Works Manager of the factory in-charge of the plant.

In January 1959 Ganapathi returned to the Haffkine Institute as the seniormost Assistant Director in-charge of Medical Administration, and would officiate on several occasions as the Director. The Diamond Jubilee Celebrations led to the establishment of Scholarships with a grant of Rs. 5 lakhs for research in Bacteriology, Virology and Immunology. He was in-charge of these Diamond Jubilee Scholarships, as they were known, and enabled several researchers to work in his lab. Once again, he equipped the laboratory well with spectrometers, centrifuges, etc. to do the latest in radioactive work. He headed up research in bacterial metabolism and some good work was done. At this time he studied Molecular Biology and took a prominent part in the Critics Club meetings. In May 1959 he toured Prague, presiding over a section at the International Symposium on Antibiotics.

In April 1964, he was offered the Directorship of the Regional Research Laboratory in Jammu. Having spent a quarter of century in the Bombay area he was unwilling at first to accept the post. He later did at the insistence of Dr. Hussain Zaheer, then Director General of the CSIR. This was a very challenging venture which later gave him tremendous job satisfaction and earned him the respect of those around him. The following year he also took charge of the Drug Factories and Farms of CIMPO. In July 1964 he attended the meeting of the International Biology Organization in Prague and Paris, where plans for a National Biological Laboratory were presented. During the hostilities with Pakistan in 1965, he along with his wife and daughters chose to remain in Jammu despite the obvious danger of being so close to the border. After what was his peak period of 7 years he retired from RRL in November 1971.

From 1972 to 1977 he resided in Bombay and worked as a Consultant for drug manufacture. He variously worked for CIPLA, Kothari Plantation Industries and the Tamil Nadu Agro Industries Corp. Among other activities, for Kothari he proposed a plant at Madurai for manufacturing drugs from medicinal plants. From 1977 to 1980 he was a consultant for various projects in Kerala. Following a stay in the United States he returned to Bangalore in 1983 where Dr. Akthar Hussain and Dr. Siddhu set him up as a Consultant for Bangalore Zonal Centrem, CIMAP. Though initially intended for only a couple of years it ended up lasting for four years. Here he undertook the comprehensive project of writing up a history of the Universe from the Big Bang to the Evolution of Man. This work was never published, but the manuscript revealed his extensive knowledge of various branches of science, history and philosophy.

In 1987 after his wife passed away in Bangalore he moved to the United States to reside with his daughter and son-in-law. Except for brief stays with the other members of his family this was to be his home for the rest of his life. He led a quiet life, reading extensively on various subjects and broadly keeping up to date with the progress in various branches of science. He enjoyed his daily walks and the company of relatives and friends. He passed away peacefully on October 15, 2004 in Bethesda, Maryland having been physically active and mentally alert to the very end.

SCIENTIFIC WORK

What stands out in his work is his tremendous vision that enabled him to plunge into the unknown without trepidation, blazing new trails and meeting both success and failures with a philosophical outlook. Relishing challenges, undeterred by difficulties and by always keeping his eye focused on the goal he came out successful with great job satisfaction. His was not a one-track mind, but broad-based and forward thinking. He did experimental work in the laboratory, had a fairly good

grasp of the theoretical problems and translated the laboratory work into pilot plant and regular industrial production. He thus brought into being the Chemotherapy Department in Haffkine Institute, the Penicillin Factory at Hindustan Antibiotics and renovating and energizing the Research Laboratories and Production Facilities in Jammu and Kashmir. He earned a DSc, FNA, FASc, and was the Director of two Laboratories for the CSIR thus gaining a good reputation.

At Annamalai University he worked on chemical investigations of Indian medicinal plants. He also published papers on synthetic investigations in alkaloids such as quinoline, isoquinoline and paraberine. At the Indian Institute of Science he made a good study of the terpenes, mastering the two volumes of JL Simonsen. *The Terpenes* and all the literature. After some initial work he was assigned to work on synthesis in the pinane group, something he regarded as a happy choice. He also started using atomic models and following closely the work of Linus Pauling.

(a) Chemistry of Pinene Derivatives: Pinic acid, a degradation product of *alpha* pinene was presumed to have the *cis* configuration. It was proved to have the *trans* configuration on the other hand by synthesising it from *cis* norpinic acid and making a comparison (1937c). Starting from *cis* norpinic acid, pinononic acid, homopinic acid and diketonorpinane were synthesised. However efforts to synthesise pinocamphone were fruitless. A good method of preparing ketonopinone was worked out. The stereochemistry of the bicyclic pinane system was studied to elucidate the various isomeric compounds previously reported, and also to explain the Meerwin-Wagner transformation and the types of monocyclic compounds produced by fission of the bicyclic ring (1939a). On the basis of the study of the relative abundance of various terpenes in the essential oils in which alpha pinene predominates, a scheme of biogenesis of the mono and the bicyclic terpenes were proposed postulating linalool as having the suitable structure to serve as the basic terpene.

(b) Trans Decalin Derivatives and Suggestion of Projection Representation: 2:3 *trans* Diketodecalin was synthesised from *trans beta* decalone by selenium dioxide oxidation; its structure was proved and the report in the literature found to be in error. By various methods three 2:3-dihydroxy *trans* decalins were synthesised and their reactions established. Configurations were assigned to them based on the old forms of *cis* and *trans* decalins. The projection formulae were used for the first time in this, these being now known as Herman projections (1939b). This work was published in the Berichte and the entire article was reproduced in the Chemical Abstracts.

(c) Synthesis of Alloxazine, Isoalloxazine and Pteridine Compounds, as Possible Therapeutic Agents: Beginning in 1937 a very elaborate scheme of research on the chemotherapy of tuberculosis was undertaken. The various possible methods of synthesis of alloxazine and lumazine derivatives were explored and many compounds of the

group were synthesised. These compounds were very valuable as starting materials for the preparation of pyrazine and quinoxaline derivatives of the sulphonamide group.

(d) Studies in Sulpha Drugs: Following Gerhardt Domagk's sensational discovery announced in 1935 of the red dye Prontosil's remarkable curative properties, he started work on the derivatives of sulphonamides. Upon his arrival at the Hafffkine Institute he started preparing many heterocyclic substituted derivatives of sulphanilamide. It was then that for the first time, 2-sulphanilamidethiazole (now known as sulphathiazole), independently discovered, was established to give protection against plague infections in mice far superior to sulphapyridine. Enough of this drug was produced and tried in human plague infections in the field in comprehensive clinical trials, and the therapeutic effect confirmed (1941c). Thus the dreaded plague infection could be cured by sulpha drugs. This work created a sensation when reported at the 1940 Indian Science Congress in Benares. All told about 400 sulphanilamide derivatives of numerous types were synthesised, and a selected group was tested for protection against *Streptococcal, Pneumococcal* and *Pasteurella pestis* (and some other) infections in mice (1951g). Among about a dozen compounds discovered with outstanding protective effects were sulphaguanidine, sulphamethazine and sulphamerazine, compounds still in use today. This work has been referred to in the monograph of EH Northey, (1948), *Sulfonamides.*

(e) Chemotherapy of Malaria and Investigations on Synthetic Antimalarials: In search of possible antimalarials which will have effect on the exoerythrocytic forms of the malaria parasite, about 200 compounds of quinoline, thiazole, guanidine, biguanides, uracil, thiouracil and pteridines were synthesised for studies in *Plasmodium berghii* infections in mice.

A well known, comprehensive review of the subject covering all aspects, as the cycle of the malaria parasite between man and the mosquito, the various stages of the parasite and their implications in therapeutic control, as the sporozoites, exoerythrocytic forms, erythrocytic forms, gametocytes, the various methods of testing the drugs, was published. All the work done in the United States during the war was nicely summarised (1947a, b).

(f) Chemistry of Thiazoles: In 1945, he launched as fundamental work the study of the chemistry of thiazoles. This was undertaken to explore different methods of production of sulphathiazole and also the thiazole moiety of the vitamin, thiamine. Methods of production of 2-amino, 4-amino and 5-aminothiazoles were established, also to produce sulphanilamide derivatives from these. A simplified and very efficient method of producing 2-chlorothiazole and 2-halageno thiazoles was worked out and also patented (1945d). The parent compound thiazole, a curiosity so far, was prepared in quantity and its reactions studied. 2-acetamido-5-nitrothiazole was synthesised which was discovered by others to have good antiprotozoal activity. The

orientation in the thiazole nucleus by nitration and bromination of various thiazole derivatives was studied; marshalling all the evidence so far, the fine structure of the thiazole ring was clarified to explain the various types of reactions the thiazole compounds undergo (1953d). A critical review of the chemistry of the thiazoles prepared was not published due to the appearance of a book, but was incorporated into the thesis of a colleague. This work is referred to in the book of EH Rodd, (1957), *Chemistry of Carbon Compounds*, Vol. 4A, pages 386-400. He was very happy about this work.

(g) Laboratory Scale and Pilot Plant Production of Sulpha Drugs and Antimalarials: In 1940, he undertook investigations, necessitated by national needs, for the large scale production of Sulpha Drugs and Synthetic Antimalarials. A new method of producing sulphathiazole was worked out wherein acetsuphanilyl chloride (ASC) could be used in a wet condition and the condensation with 2-aminothiazole were effected in aqueous media, with great practical advantages. For this process (1943c, Indian Patent 29093) along with several others Indian patents were taken out because they did not conflict with those of foreign firms. These patents about 10 in number were assigned to the Bombay Government. Two patents related to the manufacture of sulphadiazine and its derivatives were the master patents in the country.

Following an initial interest in the antimalarial compound atebrine attention turned to paludrine which showed great promise as an antimalarial with special properties, as action against nonerythrocytic, tissue forms of the malaria parasite. The details of the methods of its manufacture in pilot plant worked out, at an estimated price of Rs. 20/lb from basic raw materials. This figure was questioned by the DG, Delhi; the cost accountant deputed to study the details came up with a figure of Rs. 18/lb. This gave the Haffkine Institute a lot of confidence in their methods. Finally methods of manufacture of atebrine (which went out of use), chloroquin (which took the place of atebrine) and paludrine were standardised.

This work on the synthesis of sulpha drugs and antimalarial drugs proved so successful that he designed and equipped a chemical pilot plant, the first of its kind in India. The Department of Chemotherapy was organised and equipped from scratch to such a level that any type of work could be undertaken there from small scale laboratory work to pilot plant operations. The pilot plant was fitted up with reaction kettles of capacities up to 200 gallons, with glass lined kettles, big centrifuges, filter press etc. This pilot plant was eulogised as the only one of its kind in the country by the Russian delegation which visited the country in their report.

This pilot plant produced about 8000 lbs of sulphathiazole per year which was compounded into a good paste to be applied topically to treat wounds and burns. This was the first instance of a modern and important synthetic drug being produced in the country from raw materials. Sulphathiazole manufactured as per

the new process was sold at Rs. 15/lb and it broke the monopoly of foreign firms and enabled Haffkine Institute to manufacture and sell it. This brought down the market prices of sulphathiazole a great deal and had a very good sale.

Paludrine was produced in good yields in the pilot plant in about 50 lb lots of the final product at about Rs. 20/lb with imported material, while the material marketed in the country by a foreign firm was costing even in bulk around Rs. 160/lb.

(h) Manufacture of Vitamin A Tablets: The Bombay Government wanted Vitamin A to be administered to children in their nutritional programme. The drug companies wanted a lot of money. Then it occurred to the Haffkine Institute as to why not they do it? The Bombay Government Fisheries Department was producing good neat Shark Liver Oil, a rich source with 20,000 units of vitamin A/gm. From the unsaponified fraction by solvent extraction they prepared vitamin A concentrate. After trying many methods of putting this into some vehicle, ultimately incorporating these into tablets was deciding on. The tablets were prepared with 2000 units of vitamin A plus 400 units of vitamin D, using dried milk powder and chocolate as fillers. These tablets became very attractive and so a new tabletting section was established capable of manufacturing 4-5 million tablets a month. This grew up to be a big source of revenue for the Institute, bringing down the market price of vitamin tablets. Other tablets were also prepared and sold at a low price to the public. This was a great service.

There was work on the freeze drying of blood plasma, a new technique of value and setting up the Blood Bank in Haffkine Institute. Of vital interest during the Second World War was the work on freeze dried antivenin for snake bites used extensively in the Burma campaign and the suggestion of using a detergent for the rapid dissolution of the crystals in the field.

Phenyl mercuric nitrate was prepared as an antiseptic compound, being used as a preservative in vaccines in place of phenol. Then the method of manufacture was worked out for the antiseptic phenyl mercuric acetate and nitrate which was used extensively by Haffkine Institute. With this as the base the preparation of an antiseptic solution called 'pemon', was standardised which for so many years completely replaced the commercial preparation 'dettol'.

(i) Laboratory Scale Penicillin Production: In 1943 following the publication of the paper by H Florey and EB Chain on penicillin, which by then seemed established as a miracle drug, he dared to take up the study of its production. This was a new venture for an organic chemist, but Sokhey gave his blessings.

During 1943-1945 there were attempts at increase in titres. Many cultures of *Penicillium notatum* and *Penicillium chrysogenum* were obtained and surface cultures tried in the liquid medium. This was switched to a new method of using wheat bran

as solid support, and soaking it in a Czapek-Dox with unrefined sugar *'gud'* as the sugar source. Thousands of glass bottles were used, a special 24 degree room was put up and penicillin was extracted from the squeezed fluids. The extraction was conducted with counter current glass columns which was designed and locally fabricated and worked in the cold room. The final concentrated solution was freeze dried. Dr. Baliga tried this on one of his patients! The cup method of assay was worked out with help from Dr. Wagle in growing the *Staphylococcus*. This (cup-plate) assay was a spectacular method. A fraction insoluble in chloroform was also found, this indeed being the enigmatic penicillin X, but was missed by relying on information contained in the literature!

Many visitors came to Haffkine to see the mould, the plate assay, and the crude penicillin being produced. The official photographer took beautiful pictures of the laboratory and production methods. These were published in the central pages of the *Illustrated Weekly of India* and became well known. One of the pictures was also included in the book *India Today* published by Hindu. In December 1944 a lecture was given on Penicillin to the Pharmaceutical Association, and published as a review (1943d)

Notes on the manufacture of Penicillin, Sulpha Drugs and Antimalarials in the country were submitted to the Planning Department of the Government of India (1944-5). The Government constituted a committee with Col. Chopra as Chairman to study the possibilities of manufacture of drugs in the country, which came to be known as the "Panel on Drugs". This was the first committee constituted and Ganapathi was co-opted a member. The three notes with the claim that it can take care of about 80 % of infections in country were submitted by Sokhey and him and based on the decision of the committee were incorporated as appendices. This was called by Dr. B Mukherji "the last word on the subject".

This work of utmost importance to the country led to Sokhey along with him being deputed abroad in 1946 and they submitted a project report for the establishment of this industry in January 1947. Though this report was approved by the Cabinet, yet due to conditions prevailing at that time in the country it could not be implemented. So they were deputed again in 1948 to bring the project up-to-date. After visiting many reputable manufacturing units and research laboratories in West Germany, Sweden, Denmark, England, Canada and the United States a very comprehensive project report, with flow sheets and blue prints was submitted to the Government in October 1948. This report was again approved by the Cabinet but it was not implemented. Ultimately the Penicillin part of the project was opted by the World Health Organization and the UNICEF who employed Ganapathi as their consultant to finalise the project and Hindustan Antibiotics was constructed with the financial assistance of the WHO and the UNICEF on the basis of the technical data furnished by him, arrived at by studying the various plants in the United States.

included designs of the equipment set up and the whole complex, which was incorporated into the basic designs of the Hindustan Antibiotics Factory, although this fact is not recognised.

In 1946 there was also work on the production of Streptomycin on a laboratory scale.

In 1955 with General Sokhey and another colleague he visited Soviet Russia to investigate their processes for chemical manufacture, and under the leadership of Sokhey submitted to the Government of India the integrated drug project for the country. They made plans for what came to be known as the Indian Drugs and Pharmaceuticals Ltd. (IDPL) comprising an antibiotic plant, a synthetic drug unit, one for the manufacture of intermediates and another for the plant drugs.

(j) Penicillin Factory at Pimpri: He was associated with Hindustan Antibiotics from its very inception being connected with the planning, organising and execution of the penicillin plant. He also conducted research on various Microbiological and Biochemical aspects of the Penicillin mould.

Working in collaboration with Dr. NN Chari, Dr. Kunjitapadam and others, several innovations were introduced in the production of penicillin in the plant. This work enabled the imported raw materials to be replaced with indigenous ones. The seed was made in the laboratory, this inoculated into the seed tanks and this in turn used to inoculate the 5000 gallon fermentors. A number of modifications in the medium were introduced, like the use of peanut meal partly replacing corn steep extracts, periodic addition of sucrose in place of imported lactose. Penicillin V, the 'oral penicillin' was produced using phenoxy acetic acid as the precursor in place of phenyl acetic acid. Crude Potassium Penicillin was obtained which was very white and even the first batch gave a good product, with recrystallisation done from butanol. A routine for the conversion to Sodium Penicillin was worked out. There was also work on Procaine Penicillin.

(k) Mechanism of Biosynthesis of Penicillin: Marshalling all the apparently disconnected facts available, a mechanism of the biosynthesis of penicillin by the mould *Pencillium chrysogenum* was suggested as a diversion from protein synthesis from the available amino acids when the growth phase of the mould had stopped (1957a).The disintegrated mycelium did not produce penicillin in shaken cultures, the integrity of the mycelium was essential. An experimental system was established in which the washed cells were suspended in a suitable synthetic medium and the cultures shaken. The materials to be investigated were added to the medium and the penicillin production measured. Penicillin synthesis was stimulated by a variety of carbohydrates, inositol, glycerol, fatty acids, fatty oils and many amino acids, while the Krebs' cycle intermediates did not cause any stimulation. The biosynthesis was inhibited by dinitrophenol, cyanide and arsenite, implicating the electron transport

system in the biosynthesis. It was postulated that the compounds that caused stimulation were serving as sources of continuous production of ATP molecules required to form the peptide bonds and the removal of two hydrogen atoms, dehydrogenation, was postulated to be mediated by the cytochromes in the respiratory chain. This work attracted wide interest.

(l) Cellular Components of Penicillium chrysogenum: The constituents of the mycelium as obtained in the Pencillin Factory were analysed. Chitin was detected by the presence of acetylaminglucose in the hydrolysate. The lipid fraction contained the usual fatty acids. Mannitol (two percent) and tiglic acid were isolated. The sterol content was less than 0.1 percent, with ergosterol probably predominating.

(k) Carbohydrate Metabolism of Penicillium chrysogenum: Studied in shaken cultures, Penicillium chrysogenum utilises a variety of carbohydrates (18 in number were studied) and convert them all into glucose which seemed to polymerise into glucan. There was a difference between the 'seed mycelium' which does not produce penicillin and the 'mature mycelium' which does so. The mature mycelium contained about 10 to 20% of free reducing sugars in the cold water extract, called the 'free sugar pool'; this was depleted in the seed mycelium. In the mature mycelium, irrespective of the sugar used for growth promotion, the free sugar pool contained mostly glucose, with more sugars detected by paper chromatography; free ribose was present. The seed mycelium contained in the aqueous extract fructose and ribose with small amount of glucose. Hydrolysate of the extract yielded galactose. Thus it appeared that numerous pathways involving the carbohydrates function in the mould explaining the vast adaptabilities of the moulds to varying environmental conditions (1960b, c).

In the course of this work techniques were developed to work with 25 to 50 micrograms of the mycelia, and identify the various pentoses and hexoses by paper chromatography and recorcinol-sulphuric reactions which give characteristic spectra for each sugar. They were able to differentiate glucose from galactose so very closely related. Taking advantage of the differences found between riboses and deoxyriboses, a method for differential assays of DNA and RNA was also worked out (1965d). This technique attracted attention with lots of requests for reprints.

A review on the Chemical Pathways in Carbohydrate Metabolism (1960a) and another on Regulatory Mechanisms in Microorganisms involving feed back inhibitions (1961c) were published. In a note there was a suggestion of a scheme for the biosynthesis of ascorbic acid that looked attractive but was not correct! The actual course is more complex, but an interesting suggestion that serine is the aminated product of hydroxypyruvic acid drew attention.

(n) Biochemistry of Pasteurella pestis, Vibrio cholerae, Bordetella petrussis: Starting in 1959 at the Haffkine Institute a comparative study of the biochemistries of the pathogenic

bacteria, was undertaken by using C^{14} labeled sugars, amino acids, purines and pyrimidines, and their incorporation into the cellular constituents. Shaken cultures were used; the bacterial mass obtained was fractionated into ether soluble, water soluble and hydrolysed fractions. Presence of radioactivity was detected by the usual counting methods. There was interest in sialic acids in microorganisms as possible connection with antigenic fractions. Sialic acid was detected in the cells of *Pasteurella pestis* and in many gram positive and gram negative bacteria (1959d).

(o) Citric Acid Production by Submerged Fermentation using Aspergillus niger: Suitable strains of *Aspergillus niger* were selected which could convert in shaken cultures and in one gallon stirred fermentors, convert sucrose into citric acid in high yields. The system was not sensitive to iron. Use of molasses in the place of sucrose gave erratic results because of the varying compositions of the molasses from different sources (1971a).This work was a great breakthrough.

Several of his collaborators earned their doctorates under his direction.

DIRECTOR OF REGIONAL RESEARCH LABORATORY AND CIMPO

The Regional Research Laboratory is an applied science lab whose main aim is to aid in the industrial development of the North-West Himalayan region, particularly the state of Jammu and Kashmir. Among the activities of the Laboratory was research on medicinal plants, with its sister organization, CIMPO, consisting of farms in Jammu and Kashmir and two factories, one in Jammu and another in Srinagar all functioning under the CSIR.

When he took over as the director of RRL in June 1964, the facility was desperately in need of renovation and modernisation. About a year later, he took over the CIMPO Drug Manufacture and finally the Drug Farms in the Jammu and Srinagar regions. The Drug Farms and Factories had run into considerable difficulties in the late 1950's and were transferred to the CSIR for revival as there was collaboration between RRL and CIMPO. He was responsible for the conversion of a rather primitive facility into a modern one. This work was full of considerable challenges. He threw himself into the task with his usual vision, energy and determination. In the end it gave him tremendous job satisfaction. After an initial period he gave up working in the lab, published his last research paper, and devoted himself to the task of running the Laboratory, Farms and Factories.

The management and control of the research work was organised on the principle of 'project- oriented research' adapting the spirit and philosophy of the 'Zuckerman Report'. Every scientist was encouraged to formulate research projects with definite objectives, specific plan of action, target dates, staff requirements, expenditures etc., with full freedom to the project leaders in the achievement of their goals.

Land around the laboratory was acquired on lease. Considerable construction work was done including the establishment of power lines, transformers, tube wells and facilities for the staff. A beautiful technology block was built with pilot plant facilities, which, when complete included fermentors, freeze driers and equipment for food technology. Considerable land was set aside for terraced cultivation of various medicinal plants. The condition of the animal house was considerably improved. The library was modernised and expanded, and a routine of weekly seminars was set up.

The Research Laboratory and the Drug Manufacturing Facility were amalgamated into one. The drug manufacturing areas were modernised with new wiring, and for working tables and benches were set up rather than having to sit on the floor. A new extractor was designed and installed as was a new cold room where mint oil could be cooled and menthol extracted. A big steriliser like the one used at the Haffkine Institute was fabricated in Bombay and installed. This was used in the preparations of large amounts of spore suspensions for ergot work. Inoculation boards were fabricated for the inoculation of rye in the field on a large scale.

Workers who were on a temporary basis were put on a regular salary with CSIR benefits. When he took over in 1964-1965 production stood at Rs. 8.39 lakhs, it went up to Rs. 30.35 lakhs by the time he left in 1970-1971. It was on the way to being profitably run, with qualified staff to run the facilities.

Equally notable was the construction of a branch laboratory in Srinagar. It was beautiful in its settings and functional in its design. Much attention was paid to the landscaping around the building with flowering plants that Kashmir was justly famous for. This facility brought the praise of many. Its inauguration in June 1971 was the culminating moment of satisfaction for him. During the inaugural addresses his work was praised, especially commending the rapid progress the laboratories had made in the few years under his directorship.

Cultivation of *Pyrethrum* in the farms in Kashmir was expanded along with the extraction of the valuable insecticide, *pyrethin*, from its flowers. This extract is ideal for household use and the preservation of food grains.

The process of the isolation of *belladonna* alkaloids from *belladonna* leaves and roots was worked out and production was stepped up to meet demands of the country. Prior to this the total alkaloids were imported. A much improved *belladonna* plaster was also produced. Of importance is the isolation of hyoscyamine which is easily converted to atropine and its commercial scale production. Also hyoscine (scopolamine), in great demand, was produced from the seeds of the *Datura stramonium* species.

Diosgenin was manufactured from *Diascorea deltoidea*. The roots were pulverised, acid hydrolysed, the plant material washed and dried, and extracted

with solvent oil; diosgenin in good yields and fairly good purity was obtained that could be utilised for the production of steroid hormones such as progesterone, cortisone and prednisolone. Previously, the state had sold the tubers to outside firms but now diosgenin could be sold instead.

The Japanese mint plant, *Mentha arvensis* was introduced in Jammu. The steam distillation of this herb yields mint oil which contains about 70% menthol. It is useful in confectionary and pain balms. It was cultivated in about 200 acres in the farm in Jammu producing about 1.5 tonnes of the oil. Also *Mentha piperita* was grown to replace import.

The highlight was the production of ergot of good quality on a large scale for the first time in India. Ergot is a fungal mass which is produced by infecting the rye plant. As a result of the intense work carried out for over 6 years, details of the method were successfully worked out to produce ergot on a large scale. Infected rye with fungus grown in the laboratory to produce a mass called sclerotia on the ear heads of rye and harvested when ready. About 3.5 tonnes of good quality ergot were produced in 1970-71. There was the isolation of ergotamine with the technique worked out in the laboratory. The ergot had very high alkaloid content. The stuff was grown in the farms at Chakrohi and Manasbal.

Ganapathi had the good fortune to work for most of his life for superiors who valued his vision, appreciated his work, respected and sought his views and had complete trust in him. As a result he rarely lacked for facilities to carry out his endeavours. He had the confidence of Dr. Hussain Zaheer and Shri. MS Chagla. He became very good friends with Shri. Bhagwan Sahay, the former Governor of Jammu and Kashmir, enjoying conversations about varied topics.

In his turn he was generous and fair in dealing with his researchers, staff and workers. Willing to give encouragement, support and guidance when needed and always credit whenever due. He firmly believed in the future and had great faith in the younger generations.

MEMBERSHIPS AND WORK ON COMMITTEES

He was a fellow of the following: National Institute of Sciences (elected 1946), Indian Academy of Sciences (elected 1951), The Chemical Society, London (1946-1958) and The Society of General Microbiology, England (1953-70).

He served as a member of the Board of Governors of Indian Institute of Technology, Kanpur; Pharmaceuticals and Drug Research Committee (CSIR); Minerals Advisory Board of J&K State; Development Council for Sugar Industry, Kanpur; The Central Council of J&K University and on the Panel of Drugs & Pharmaceuticals (Government of India). He was assessor to the Tariff Commission Enquiry into the Cost of Drugs.

He was fully conversant with the working and enforcement of the Drug Act and served as a member of the Indian Pharmacopeal Committee. He possessed a good knowledge of the Indian and Foreign Patent law and took an active part in the Patent Enquiry Committee and was instrumental with General Sokhey in changing Sections 22 and 23 of the Indian Patent Law.

Since its inception he was keenly associated with the scientific workers movement in the country and had served in various capacities in furthering the movement through the Association of Scientific Workers of India. He participated in the drafting of the original constitution and was President of the Bombay and Poona units for many years.

THE MAN

He was a man of wide interests, a scholar in the true sense of the word. In science he had a broad knowledge of subjects ranging from physics and cosmology to biology and geology. He had a deep interest in evolution of life on the planet. He continued to think about these to the very end of his life, revising his ideas as more facts became available. He had a very extensive knowledge of the history of science. For him science was not a dry collection of facts but an evolving process that was a human creation. He had a very detailed knowledge of the personalities in science, reading almost every biography of famous scientists that was published. He studied both Indian and Western Philosophy. He took a keen interest in current and world affairs. He could converse with people of all generations on a wide range of topics.

He read extensively the classics in English and Indian Literature. Among his favourites were Charles Dickens, George Eliot and Sir Walter Scott. He was a Sanskrit scholar and read many of the works in the original, his very favourite being Kalidasa.

He had a very deep appreciation of Indian Karnatic music and studied its intricacies in great detail, with a truly scientific approach. He served as a music critic for the newspaper Hindu. He wrote numerous reviews of books and also wrote articles of a popular nature on the role of science and medicine. He had written numerous articles in dailies and weeklies under various pen names; and also articles for Scholar, Vijnankarme, and Science Reporter publications.

He was held in high esteem by the labour union at the Hindustan Antibiotics and by the workers in Bombay and Jammu who knew him to be fair and sympathetic. He had a good reputation in his official career, being known for his sense of justice, honesty and fair play. On many occasions he helped a number of his staff members.

Like most of his generation he was motivated by Nationalistic ideals, striving to make his work of use to the country. He did not financially benefit from his patents

stating that he would never profit from the suffering of others. Throughout his life he never lost sight of the common good.

Above all, it was his sense of boundless optimism that never left him till the end. The belief that there is a better future ahead, and everything could be made better.

As a young man he was very active physically, participating in many sports and being especially good at badminton. At Kumbakonam College he did a lot of boating on the Cauvery River. Throughout his life he was very meticulous about getting an adequate amount of physical exercise, being moderate in his habits and keeping mentally alert till the end.

Ganapathi always mentioned the tremendous influence that General Sokhey had on his outlook, specially his belief that one learns by doing things; that knowledge is for achieving ends not for safe keeping; that excess of theorizing is futile; and above all - what we do and should do must be relevant for our country and society as a whole. He attributed his interest to subjects like philosophy, economics and political science to the guidance of Sokhey. He held the view that science and research should be exercised to solve problems by rational methods. He wrote Sokhey's Biographical Memoir for the Indian National Science Academy.

Another scientist whom he held in great esteem was Dr. Zaheer who was instrumental in bringing him to the CSIR. When Zaheer retired he wrote an article about him in Vijnankarme entitled, "A Modest Cough" which was commended by many.

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