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The Life and Work of Thudichum - The Father of Neurochemistry

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B S Sridhara Rama Rao, - *Department of Neurochemistry, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Abstract

The various applications of chemistry and biochemistry to the study of the nervous system forms a large part of the now well established scientific discipline of 'Neurochemistry'. As a separate discipline, neurochemistry came into existence only in the early part of this century. It is surprising that for a long time the sister discipline of chemistry was not recognized by the other disciplines involved in the study of the nervous system such as physiology, pathology, histology, among others. It is indeed amazing that, in this background, studies were carried out by the Thudichum during the eighteenth century. The present paper briefly describes the life and work of this genius, Thudichum, who is rightly called as 'the Father of Neurochemistry'.

Key words -
Thudichum ,
Neurochemistry,
Physiological chemistry,
Biochemistry

Johann Ludwig Wilhelm Thudichum was born on the 27th August 1828 in Budingen, Grand Duchy of Hesse, Germany. His parents and close relatives were known for their scholarly background. During his early childhood and adolescence, there was absolute peace and security in Germany. When he was 18 years of age, Thudicum accompanied his father who went to consult the famous chemist, Justus Van Leibig, about the analysis of mineral water from a newly discovered pond. The visit made a formidable impact on the young mind and from that time onwards Thudichum developed a great interest in chemistry. The early life and work of Thudichum has been described by McIlwain [1].

Based on Leibig's advise, Thudichum's father enrolled him as a medical student at the University of Giessen in 1847. Thudichum got his MD degree in Medicine in 1851. The topic for his MD thesis was an anatomical subject viz., "Fractures of the upper end of the humerus". During his stay at the University (1847-1851), Thudichum found time to work in the laboratory of Leibig and throughout his life he expressed his pride as a student of the famous Leibig.

After his MD degree, Thudichum started practicing as a physician and built a good practice. But this was shortlived since Germany became politically unstable from 1850 onwards. Moreover, Thudichum found it difficult to work in Germany since he had joined in the army of Schlesweg-Holstein to fight against Denmark. Emotionally Thudichum found it somewhat risky to stay any longer in Germany!

Fortunately Thudichum knew a family who had migrated from Germany and settled well at London. Thudichum decided to leave his country of birth and migrate to England to stay with the family he knew. One of the members of the family, Dr. Augustus Dupre, who was working as a Lecturer in Chemistry at the Westminister Hospital medical school helped Thudichum to make his academic career at London. Later Thudichum married Charlotte Dupre who was the sister of Dr.

Augustus Dupre. The stay at London from the beginning till his death was full of extraordinary curiosity, adventure pursuit and scientific productivity.

Thudichum worked at the Westminister Hospital and got his MRCS degrees in 1854. He was appointed as a physician at the St. Pancras's Hospital and he also set up a busy practice. His specialty was otology and rhinology. Based on his clinical observations he published several papers. He devised a special speculum subsequently named after him as, "Thudichum's nasal speculum". He attempted the use of electrocautery for nasal surgery. He published a book entitled "A treatise on nasal polyps".

From 1858-1865, he worked as a Lecturer in Chemistry at the Grosvenor Medical School. Later he was appointed at the St. Thomas's Hospital, first as a Lecturer and subsequently as the Director of the Pathology and Chemistry Laboratory. With this latter appointment, Thudichum became the first medical chemist involved in teaching and research at a medical school in Britain.

At St. Thomas's Hospital, Thudichum was busy in making some reforms in teaching chemistry to medical students. During the early 1800's medical students were taught the same chemistry as was taught to science students with no reference to the living system. There was also a lot of inorganic chemistry taught to medical students much of which was quite irrelevant for subsequent medical practice. Thudichum prepared a new syllabus and succeeded in obtaining permission to introduce it in the medical curricula. Thus, for the first time the concept of medical biochemistry originated in Britain as a result of the efforts of Thudichum. Later this was called physiological chemistry and became an accepted subject of study for medical students in Britain. Thudichum's concept was tried out in USA at the Yale University.

Based on his research work he was able to publish in 1858 a book entitled "A treatise on the pathology of the urine" [2]. This book gave an account of the chemical constituents in urine and the method of analysis of these. This book did not discuss about kidney function nor gave any idea of the origin of substances from blood. A second edition of this book entitled "A treatise on the pathology of the urine including a complete guide to its analysis" was published in 1877 [2]. This book had fifty chapters and stressed two important aspects viz., that urine was free of protein and so testing was relatively easier and that urine examination indicated a relationship between the living system and chemical testing. This book for the first time gave a review of some important tests described for analysing the constituents in urine such as for example: analysis of sugar (Trommen, 1850); Quantitation of sugar (Fehling 1850); acetone(Peters, 1857); albumin (1812); Bence-Jones Protein (1848) and bile salts (Peterkofers, 1844). This book gave a clear example of the utility of medical biochemistry and gained popularity in UK and also in USA.

Thudichum made investigations to understand the nature of gall stones. This work made him work not only as a chemist but also as a microscopist. He found that casts of bile duct were seen in the centre of gall stones. He published his findings in a book entitled "A treatise on the gall stones, their chemistry, pathology and treatment" [1]. This book was a great success and several copies were sold in UK and USA. Leibig, on seeing this publication, wrote to Thudichum and queried how he was able to accomplish so much in a big city and wondered how he did it.

Till 1866 Thudichum was spending money earned from his medical practice for his research work. A turning point in his career came on the 7th of August 1866 when the medical officer to the Privy Council, Sir John Simon, asked Thudichum to study the discharges and the diseased bodies of typhus and cholera victims. Sir John gave generous financial assistance after obtaining the approval of parliament for this purpose. Thudichum made extensive investigations on blood, urine, feces and tissues and used only chemical tests but also spectroscopic tests. For nearly 16 years Thudichum worked without rest and published his findings in the annual reports which had limited circulation. Unfortunately many of the significant findings were published in scientific journals long after their discovery so much so that there was a delayed recognition of Thudichum's industrious work and salient findings.

In 1874, the medical officer recommended that Thudichum be given financial assistance from the local government board without having to go to parliament for approval. This was the first time in the history of medical research that funds were made available on the basis of the merit of research. In the first annual report Thudichum stated the object of his research as follows: "by investigation of the choleric discharges and of the diseased body after death and by such auxiliary observations of the sick as may be needful; to ascertain what successive chemical changes are undergone by the body in the progress of cholera and what relation subsists between those changes and the symptoms presented by the patient

during life".

It was in this spirit and background that Thudichum carried out his major original work on the chemical constituents of brain [3], [4], [5]. This was started in 1876 and from then for almost 16 years he carried out his work relentlessly. During the 1860's, fevers with their prominent distressing mental symptoms were the major medical problems of the day. Bacteriology was not known nor was the microscopic appearance of brain understood. Thudichum felt that, if urine could show chemical changes in a certain disease there is no reason why brain should not show chemical changes during disorders of the nervous system. He wrote that "there was a great complexity in the brain and unforeseen complications arose during investigations". One could understand when one realizes that since brain has plenty of lipid material, ordinary analytical techniques cannot be used easily with brain tissue. Thudichum isolated and characterized about 140 chemicals from brain. These were preserved well by his children till the second world war when they handed them over to scientists for preservation and safe custody. These are now kept at the National Institute of Mill Hill, UK and NINDS, USA.

During 1884 he published his monumental work on brain entitled "A treatise on the chemical constitution of the brain (Bailliere, Tindall & Cox, London)". In 1901 this was revised and published in German. This was the first time an attempt was made to understand the chemistry of the brain and much of what Thudichum reported is of eternal value since the analytical techniques used by him were of excellent quality. In 1884 he wrote "if chemistry of brain is well known, pathological derangemenrts could be easily understood and this would enable us in devising models of medical treatment". Thudichum, true to his education, gave euphoneous names of Greek derivatives to substances isolated by him such as cephalin, phrenosin, sphingomyelin, sphingosine, cerebronic acid. Sphingosine particularly defied analysis and so he named it after the enigmatic 'Sphinx'. It was only decades later that it was found to be having a very long fatty acid chain [3]. At the time the book was to be released George Buchanan, the then medical officer wrote about Thudichum as follows: "his researchers have shown the brain to be the most diversified chemical laboratory of the animal body; all other organs being much more simple and very much less specific in their chemical constitution than the organs producing and conducting nerve power".

From 1870 onwards Thudichum's interests varied and he carried out extensive tests on urochromes and other pigments using spectroscopy. These came to be known as lipochromes or luteins and carotenoids (and one of them carotene, being the precursor of vitamin A). An interesting sidelight on Thudichum's spectral analysis was that, once when he was demonstrating the abilities of the spectroscope to medical scientists, he used cylinders of compressed oxygen and hydrogen for his source of light. This was observed by Charles James Fox who was seeking a way to make nitrous oxide manageable for anaesthesia. Fox persuaded the firm of Coxeter to compress nitrous oxide for anaesthetic use and from 1870 was using it widely in the Dental Hospital, London. This appealed to the spirit of Thudichum as a patriot and humanitarian and so during the Franco-Prussian war he made an urgent appeal in the newspapers for obtaining nitrous oxide for military surgery. About pound sterling 180 were collected for the nitrous oxide fund and Coxeter supplied over 5000 gallons of the gas free for this purpose. Thudichum volunteered to go to the war theatre to see its use.

After 1884 Thudichum stopped his active research work. By then he was 56 years old and had a family of five children (one son and four daughters) but he was still busy with his medical practice. From 1870 onwards he way carrying out analysis of wines for the Pure Wine Society of London and published a paper with an intriguing title "On wines, origin, nature, analysis and uses with special reference to a new alcoholic drink made from tea [1], [2]". Next Thudichum undertook the task of providing firm scientific underpinnings for hedonism. His book entitled "The spirit of cookery" which appeared in 1895 is praised even today by epicureans and by those whose interest in food is of a more scientific nature. This work was followed closely by "A treatise on urines" in 1896 [1], [2].

Thudichum was a chemist by training and believed in it so much that he proved he was no paragon of scientific virtue when he criticised Gangee in UK, Hopee-Seyler and Kuhne in Germany. He misunderstood them and felt that they were not appreciating the contributions made by him. Possibly the busy medical practice in an area different from his research work and lack of proper assistants might have made Thudichum speak ill of some honest workers. Perhaps Thudichum would have fared better in the atmosphere of an University where he would have had better infrastructure for his research work.

In 1901 Thudichum died of cerebral hemorrhage. Many scientific and medical workers in Europe, UK and USA wrote

fitting obituaries. Unfortunately for the next twenty years his work lay buried without any recognition. Round about this time i.e., in the early half of the century rapid advances were made in physiology, pathology and histology of brain. Many of them did not consider the sister discipline of chemistry as relevant. By 1907 reputed anatomy centres were started by brilliant workers like Cajal, Feschig, Monakow, Edinger, Vogt and Donaldson [1], [2], [3].

Minor achievements in chemical discoveries did not gain much attention such as the release of adrenaline after sympathetic nerve stimulation [4] (Elliott, 1905) and the release of 'Vagustoff' after stimulation of vagus nerve [5] (Loewi, 1921). It was the isolation and characterization of acetylcholine by Dale and Dudley in 1921 [3] which made workers realize the significance of chemistry in understanding the function of the nervous system. This was a great land mark. By this time the formation of a department of brain chemistry at the Kaiser Wilhelm Institute in Munich, Germany and work at Cardiff in England testified to atleast local re-awakening of interest. Decades later the area of neurochemistry became firmly established and is now populated by a highly competent group of able investigators [3], [4], [5].

Considering that Thudichum worked at a time when scientific and analytical investigations were tedious and time consuming it should be appreciated that great achievements were made by him much of which have stood the test of time. Reminding ourselves about the life and work of Thudichum in this 'Decade of Brain' is a fitting tribute to him.

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