Asima Chatterjee, one of the brightest stars in the galaxy of organic chemistry

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Asima Chatterjee was one of the few Indian women scientists who have been duly recognized during their lifetime for their brilliance. She isolated a significant number of natural products from several plant species indigenous to the Indian subcontinent and unravelled the mystery of their structures by simple chemical transformations, spectroscopic and degradative procedures. The development of new synthetic methodologies, discovery of reaction mechanisms and study of chemotaxonomy and medicinal applications of isolated molecules deserve praise keeping in mind the infrastructure available in an Indian university in those days. The article aims to portray the life and research of Chatterjee in a brief manner to the young minds of all branches of science.

'I wish to work as long as I live.'

Asima Chatterjee

Since time immemorial, India has been famous for its rich and valued contributions to the field of science. India’s rich history is replete with examples of several distinguished women scientists who have brought immense pride and glory to the nation. There was a time in India when scientific research was only meant for men and the social and cultural prohibitions kept women away from research. It is quite important for students to understand how these women scientists overcame socio-cultural barriers to pursue their scientific or academic career. In this article, we shall discuss the life of a scientist who was the first Indian woman to receive the ‘Doctorate of Science’ by an Indian University and the Shanti Swarup Bhatnagar Award (recognition of an Indian researcher for his/her outstanding contribution in science and technology given annually by the Council of Scientific and Industrial Research (CSIR)). She was the first Indian woman to occupy the prestigious Chair known as the Khaira Professor of Chemistry (in the University of Calcutta) and be known as the Khaira Professor of Chemistry specialising with Organic Chemistry in India and remain as such till date. In 1934, she obtained her MSc degree with chemistry as the subject of research and joined the University of Calcutta to pursue her MSc degree. In 1938, she obtained her MSc degree with organic chemistry specialization along with a silver medal from the University of Calcutta for securing second rank. She started her research work in the University of Calcutta under the supervision of Pratibha Kumari Bose, one of the pathfinders of natural product chemistry in India. The support, encouragement, inspiration and affection she received from the legendary Acharya Pratibha Chandra Ray during her university days were remarkable. In 1940, she joined Lady Brabourne College, Calcutta as the founder head of the Department of Chemistry. In 1944, she became the first Indian woman to receive DSc degree from an Indian University (University of Calcutta) for her research on ‘Naturally Occurring Indole Alkaloids and Coumarins’1-6. In 1944, she was appointed Honorary Lecturer in the Department of Chemistry, University of Calcutta (Supplementary Information 2).

Matrimony and post-doctoral research abroad

Asima Mukherjee tied the knot with Baradananda Chatterjee in 1945 (Supplementary Information 3). The academic mindset of Baradananda Chatterjee along with his open-minded nature motivated Asima Chatterjee (née Mukherjee) to pursue higher education after her doctoral research. She left for the USA in 1947 taking her eleven month old daughter and her governness along with her. This was a remarkable feat as in 1947, when India was still under British rule, a young, middle class Indian lady from a conservative Bengali family showed her courage to pursue higher education and went abroad with her nursing. Asima Chatterjee worked with L. M. Parks at the University of Wisconsin, Madison, on naturally occurring glycosides and with L. Zechmeister at the California Institute of Technology, Pasadena, USA on carotenoids and pro-vitamins. She was awarded the coveted Watumull Fellowship in recognition of her research work in the USA. Asima Chatterjee moved to University of Zurich in 1949 to work with Nobel laureate Paul Karrer on ‘biologically active alkaloids’. She was so fascinated while working with biologically active alkaloids that she dedicated the rest of her research career to the field of natural product chemistry1,5,6.

Homecoming and journey forward with chemistry

In 1950, Asima Chatterjee returned to India and re-joined her service at Lady Brabourne College, and also resumed her research on alkaloids and coumarins. In 1954, a big recognition came her way when she was appointed the Reader in the
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Asima Chatterjee and her favourite plants (Source: Wikipedia).

Scheme 1. Representative structures of yohimbine, rauwolscine, piperlongumine, flexicorine, halopine, piperlonguminine, aegeline, atalaphyllidine, edgeworthin and corynantheine.

Department of Chemistry at the University of Calcutta. Consequently, she grew popular both as a teacher and as a research guide amongst the academic peers. Her charismatic and unique style of delivering lectures became popular among her students. She always believed that merely conveying the facts of chemistry would not be enough to learn the subject; rather, she always tried to inculcate and cultivate the significance of the subject among her students. Her tenacity, perseverance and communication skills were something noteworthy as compared to the other faculty members. In 1962, she became the first woman scientist to adorn a Chair of any university in India. Kumar Guruprasad Singh Khaira Professor of Chemistry was one of the most coveted Chairs of Calcutta University, which she adorned till 1982, the year she retired. She remained the departmental Head, University of Calcutta, from 1969 to 1979. Her good relationship with fellow faculty members, liaison with the industry, student friendly attitude and above all, her dynamic leadership ability allowed her department to garner nationwide acclaim in research and academics.

In 1967, the untimely passing of her father and husband within a span of just four months left Asima Chatterjee devastated. The sincere support and care of her well wishers helped her to recover from her grief within few months. In 1968, she was actively involved and readily agreed to be the principal witness in the legal battle over infringement of a patent right involving a ‘sulphonamide derivative’ between Bengal Chemical and Pharmaceutical Works Ltd, Kolkata, a brainchild of Acharya Prafulla Chandra Ray and Hoechst Co Ltd. Nothing could be a better homage to her mentor Acharya Prafulla Chandra Ray than this (Supplementary Information 5).

A brief discussion on her research

Asima Chatterjee contributed substantially in the research fields of alkaloids, polyphenolics and terpenoids along with the structural and mechanistic aspects of organic chemistry. In 1938, while working...
with *Rauwolfia canescens*, she developed an interest in indole based alkaloids. She isolated Rauwolscine (structurally similar to Yohimbine), a potent anaesthetic, aphrodisiac and central nervous system stimulant (Scheme 1)\(^9\). She also isolated several alkaloids in the forms of flexicornine from *Rauwolfia reflexa*, piperlongumine and piperlongumine from *Piper longum*, an acridine based alkaloid, atalaphyllidine from *Atalantia monophylla*, aegeline, aegeleneine and halopine from *Aegle marmelos* and many others (Scheme 1)\(^9\)–\(^12\). The derivation of structures of the monoterpene, diterpene and steroidal alkaloids isolated from natural sources was performed by Chatterjee through some fundamental studies related to chemical transformations with the help of UV–Vis, IR, NMR and mass spectroscopic techniques. High resolution Nuclear Overhauser Effect (NMR), use of shift reagents, Nuclear Overhauser Effect (NOE) and deuterium exchange procedures became available to her only in the latter part of her career.

Chatterjee’s interest in coumarin skeleton developed with the structural elucidation of luvangetin isolated from *Luvanga scandens*, marmesin (a chemical precursor in psoralen and linear furanocoumarins biosynthesis) from *Aegle marmelos* and many others from *Prangos pabularia* (Scheme 2)\(^12,13\). The isolation and determination of structures of edgeworthin, a bis-coumarin from *Edgeworthia gardneri* and trimethylgallic acid from *Euphorbia tirucalli* were of high importance in those times (Scheme 2)\(^14,15\). Isolation and structure determination of lupenyl acetate from the leaves of *Leuconotis eugenifolia*, walsurenol from *Walsura tabulana*, aphanamixin, aphanamixinin and aphananin from *Aphanamixis polystachia*, calliterpenone and calliterpenone monoacetate from *Callicarpa macrophylla*, crotoacaudin and isocrotoacaudin from *Croton caudatus* are her other noteworthy research contributions (Scheme 2)\(^1–5\).

Chatterjee deduced the structures of various triterpenes, diterpene alkaloids and sesquiterpenoid coumarins from several medicinal plants like *Leuconatis eugenifolia*, *Dillenia indica*, *Callicarpa polystachia*, *Alstonia neriifolia* and *Ferula assafoetida* based on fundamental chemical degradation and spectroscopic studies. Twenty new alkaloids were isolated from *Alstonia venenata*. She also isolated echitamine (quaternary alkaloid) from *Alstonia scholaris* having pyrrolidino-indole moiety possessing important pharmacological activities (Scheme 3). Her research on *Alstonia macrophylla* gained importance...
Chatterjee developed a methodology to obtain 'diazoketone intermediates' to synthesize several alkaloids based on isoquinoline and indole skeleton along with (+,−)-2,3-dimethoxy berbine, (+,−)-norcoralydine, derivatives of gambirtanine and yohimbanes. Among many significant contributions, conformational analyses of yohimbine isomers and novel chemical transformations of ajmaline and ajmalicine deserve special mention (Scheme 4).17,18

Her significant contribution to the chemistry of indole and its alkaloids deserve special mention. For example, she predicted and subsequently vindicated the formation of a dimer when indole is treated with acetone in presence of a Lewis-acid (Scheme 5).1–5

Chatterjee also isolated and determined the structures of murrayatin (7-methoxy-8-(2-isovaleryloxy-3'-hydroxy-3'-methylbutyl) coumarin) from Murruya exotica L., saradaferin (sesquiterpenoid coumarin) from gum resin of Ferula assafoetida Regel (famous in folklore medicine and locally called 'Hing')19 and sparsiflorine, an alkaloid from the leaves of the shrub Croton sparsiflorus Morong (Scheme 6).1–5

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Scheme 7. Representative structures of grandifoline, crotocaudin, teucvidin, taraxerone, taraxerol, taraxeryl acetate and cleogynol.

Scheme 8. Synthetic strategy of (+, −) rauwolscine.
Scheme 9. Synthetic strategy of (+, −) decarbomethoxy dihydrogambirtannine, (+, −) 2,3-dimethoxy berbine and (+, −) 2,3-dimethoxy berbine hydrochloride.

Scheme 10. Synthetic strategy of (+, −) norcoralydine.
as ent-8S,10S-15,16-epoxy-19-norcleroda-4,11,13(16), 14-tetraene-18,6S:20, 12-diolactone along with the congener teucvidin as ent-10S-15,16-epoxy-19-norcleroda-4,13(16), 14-triene-18,6S:20,12R-diolactone. Other triterpenoids that were isolated were taraxerone, taraxerol and taraxeryl acetate. She even isolated cleogynol, a hemiketal from Cleome gynandra, useful in the Indian system of medicine (Scheme 1).

Chatterjee considered tryptamine, an indolamine metabolite of tryptophan and derivatives of isochromanone (obtained by Bayer Villiger oxidation of indanone system) as starting molecules to synthesize Rauwolscine, a plant alkaloid with alpha-triene (S-C) as a key intermediate in the synthesis of several alkaloids (having protoberberine skeleton) along with the concept of condensation of an amine with a lactone (Scheme 10).

She also developed synthetic route to coumarins from cinnamic acid derivatives using the Baeyer–Villiger oxidation of 1-indanone with m-chloroperbenzoic acid (Scheme 11).

She isolated and synthesized several 4-phenyl coumarins (dalbergin, nordalbergin, isodalbergin and methyl dalbergin) that possessed insect and termite repellent properties from the heartwood of Dalbergia sissoo. Dalberginone and Dalbergichrome were the two other additionally reported compounds (Scheme 12).

Vanillin, under the condition of Dakin reaction yielded o-methoxyhydroquinone which, on condensation with freshly distilled ethyl benzoylacetate produced dalbergin which in turn on demethylation with BBr₃ produced nordalbergin (Scheme 13).

Total synthesis of Yohimbone was another important research work from Chatterjee’s laboratory (Scheme 14).

Chatterjee isolated harmine, harmaline and deoxyvascetine from Peganum harmala. She developed a new synthetic route of deoxyvascetine using anthranilic acid and γ-aminobutyric acid, though she obtained two side products ‘X’ (thermal trimerization of anthranilic acid) and ‘Y’ (heating of ‘X’ with anthranilic acid) (Scheme 15).

She developed a novel route to anticonvulsant imesatins using solution phase dielectric heating of isatin and aromatic amines and diamines without using any catalyst and also made an approach to cryptolepine skeleton from one of the imesatins (Scheme 16).

Even her study of medical applications of natural products was also noteworthy (Supplementary Information 7).

Words fall short to describe Asima Chatterjee

The academic and social contributions of Asima Chatterjee is vaster than what has been mentioned in this article. Her lifelong discipline, dedication and sincerity are an example to young academicians worldwide (Supplementary Information 7). Chatterjee supervised 59 Ph.D. and 3 D.Sc students and published 328 research papers in reputed national and international journals.

More than 20 review articles were published under her credentials in reputed serial volumes. Over the years, many of her research works have been included in several text books. She edited and revised the six-volume Bharatiya Banoushodhi published by the University of Calcutta. She was the Chief Editor of the six-volume series, The Treatise of Indian Medicinal Plants published by CSIR.

In 1960, she was elected a Fellow of the Indian National Science Academy, New Delhi. In the following year, she received the Shanti Swarup Bhatnagar Award. She was awarded Padma Bhushan in 1975 (Supplementary Information 8).
Scheme 13. Synthetic strategy of dalbergin and nordalbergin.

Scheme 14. Synthetic strategy of yohimbine.
Genuine dedication, discipline, an unquenchable thirst for knowledge, eagerness to learn (even from her students) and above all, her hard work were responsible for the accolades she received throughout her career. Just a week before she slipped into coma, the then Mayor of Kolkata (formerly Calcutta), India conferred on her the award of 'Honoured Citizen of Kolkata'.

The maestro of natural product chemistry left us on 22 November 2006. Her death was undoubtedly a terrible loss to the chemistry community.

**Summary**

Asima Chatterjee isolated and characterized several molecules of immense biological significance. She made significant contributions in the field of medicinal chemistry with special reference to alkaloids, coumarins and terpenoids. Her research in mechanistic organic chemistry and the development of several drugs including anti-epileptic, anti-convulsive and chemotherapy deserve special mention. A perfect blend of innate mastery on the subject, competence, perspective towards the
molecular architecture of an organic molecule, use of diverse spectroscopic techniques and methodical approach towards research helped her reach a high position in the chemistry fraternity.

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