

## Jeffrey B. Harborne (1928–2002) – An appreciation

### 1. History of Jeffrey's career and highlights of his research

Jeffrey Harborne (Photo 1) was born in 1928 in Bristol, where he lived until 1953, apart from the war years when his family was evacuated to Gloucestershire. In 1946, he won an open entrance scholarship to Bristol University, where he studied chemistry with physics and maths, and specialised in biological chemistry in his 3rd year. It is a matter of luck that Jeffrey studied chemistry at all, as the emphasis in Wycliffe College, the grammar school he attended, was on the Arts rather than on Science, and Jeffrey was not introduced to chemistry until he was in the sixth form. From 1949 to 1952, he did postgraduate research at Bristol University under Prof. Wilson Baker FRS and Dr. David Ollis. During this time among other things he developed a new method of synthesising isoflavones using ethoxalylchloride, which was published in *Nature*. He confirmed the structure of the isoflavone in soyabeans as genistein by synthesis (this was the days before NMR spectroscopy was available) and developed a new chemical reagent for detecting aromatic amines on paper chromatograms. From 1952 to 1953, he was an assistant chemistry lecturer at Bristol and in July 1953 he was awarded his PhD in chemistry (the Nobel Laureate, Sir Derek Barton, was his external examiner).

In the same year, Jeffrey received an Eli Lilly grant to do postdoctoral research at the University of California (Los Angeles) under the guidance of Prof. Theodore Geissman. Here Jeffrey worked on the pigment genetics of *Antirrhinum majus* (snapdragon) employing paper chromatography and UV/Vis absorption spectra, newly developed methods in the early 1950s (Harborne, 1957). Phytochemists now often frown on paper chromatography but at that time this technique opened up a whole new world, as before it had been almost impossible to separate mixtures of water soluble plant phenolics. UV spectroscopy of phenolics was still an elaborate and time-consuming technique, since scanning UV spectrometers were yet to become available and the UV absorption of each compound had to be measured at each wavelength, plotted on graph paper and the spectrum drawn by hand. Using these new techniques, Jeffrey completely characterised the flavonoids present in known geno-

types of a range of garden plants such as *Antirrhinum* cultivars. The results not only indicated the pathway of biosynthesis, but also the biochemical steps catalysed by the enzymes involved, thus laying the basis for later investigations by other workers of the enzymology of flavonoid production. For example, the recognition that hydroxycinnamic acid esters accumulated in the albino mutant of *Antirrhinum majus* showed unambiguously that the first step in the biosynthesis required hydroxycinnamic acids as precursors (Harborne, 1955).

Jeffrey also worked extensively on a rare class of floral pigment, the aurones, which were first discovered by Geissman. Jeffrey synthesised a range of substituted aurones and studied their UV/Visible spectra (Harborne and Geissman, 1956).

In 1955, Jeffrey was appointed as a biochemist at the John Innes Institute, where he continued and extended his research programme on pigment genetics, studying phenotypic variation in *Solanum tuberosum* (potato) and in *Primula sinensis*. Here he established the structures of many anthocyanins and other flavonoids and worked extensively on low molecular weight phenolics in plants and their metabolism. The discovery of the activity of the pleiotropic gene *Ac* in cultivated potato showed that methylation, acylation and glycosylation of anthocyanins



Photo 1. Jeffrey Harborne (1928–2002).

occur at the final stages in pigment synthesis (Harborne, 1960). Jeffrey described many new anthocyanins and other flavonoid pigments (e.g. rare flavones in the petals of primroses), and discovered six new aglycones of anthocyanins (anthocyanidins). This work he admirably summarised in a review on pigment genetics (Harborne, 1962), and his research on anthocyanins and flavonoids was the subject of the monograph *The Comparative Biochemistry of the Flavonoids* (Harborne, 1967), which is still largely relevant today, especially for the study of anthocyanins and for the distribution of flavonoids in the angiosperms.

While working at the John Innes Institute, Jeffrey came to know well 'EC' Bate-Smith and Tony Swain at the Low Temperature Station in Cambridge, whose work on plant polyphenols was along similar lines. EC was the expert on paper chromatography and the distribution of phenolics in plants. He surveyed the flavonoids in the Dicotyledoneae and started on the Monocotyledoneae, a study that Jeffrey and, later, his research associate Christine Williams, continued.

Jeffrey was soon involved in the Plant Phenolics Group, founded by EC and Tony Swain. He was an early proponent of enlarging the interests of the Group, proposing that it changed to the Phytochemical Society in 1963 (the motion was defeated but passed in 1964 as the Phytochemical Group), which later became the Phytochemical Society of Europe.

Tony Swain set Jeffrey off into the field of scientific editing, and arranged for him to edit his first scientific book, *The Biochemistry of Phenolic Compounds* (Harborne, 1964), the proceedings of the PPG meeting in January 1962. Tony Swain also introduced Jeffrey to the editing of the journal *Phytochemistry* which Pergamon had founded in 1962 with Tony as the first Editor. Jeffrey took over the editorship of the journal in 1972 when Tony became a professor in the USA.

In 1965, Jeffrey was appointed a senior research associate of the Science Research Council to work on a multivariate approach to the systematics of the plant family Umbelliferae, which was established by Prof. Vernon H. Heywood in the Hartley Botanical Laboratories of the University of Liverpool. Jeffrey studied the leaf, flower and fruit flavonoids of the Umbelliferae grown at the Botanical Garden at Ness, and also their essential oils, coumarins, polyacetylenes and phenylpropenes. Protein and enzyme patterns of the seeds were determined in collaboration with French scientists. In 1968, Prof. Heywood was appointed to the Chair of Botany at the University of Reading, and the Umbelliferae research programme and Jeffrey moved with him. In that year Christine Williams became his research associate and worked with him right until the end of his career. Publications on the Umbelliferae work include Harborne et al. (1969) and Crowden et al. (1969). By 1967, Jeffrey had written more than a hundred publications and was awarded a DSc by the University of Bristol.

The Phytochemical Unit established by Jeffrey at the University of Reading, which was initially funded by the SRC, was taken over by the University in 1971, and Jeffrey became Reader in plant physiology and biochemistry. His undergraduate teaching included chemistry for botanists, plant biochemistry and biochemical plant pathology, and based on his lectures and practical classes he wrote the teaching publication *Phytochemical Methods, a Guide to Modern Techniques of Plant Analysis* (Harborne, 1973), which sold well and appeared in 3 editions. This phase of Jeffrey's research was devoted to the general distribution of flavonoid pigments in plants, their contribution to flower colour and the systematic and evolutionary significance of anthocyanins and other flavonoids. For example, surveys of blue-flowered plants in the Polemoniaceae with Prof. Dale Smith from Australia showed that natural selection for a bee-preferred colour led to gain mutation and the synthesis of pigments based on delphinidin, which have an additional hydroxyl group in the B-ring in comparison with the more common cyanidin pigments (Harborne, 1978). On the other hand, in bird-pollinated flowers the natural selection is towards orange-red pigments, e.g. a loss mutation of the 3-hydroxyl group in the anthocyanins of the New World Gesneriaceae (Harborne, 1966) or the loss of a B-ring hydroxyl in anthocyanins based on pelargonidin. These were examples that Jeffrey included in his newly developed course 'Introduction to Ecological Biochemistry', which was offered to all biology undergraduates at Reading University. Based on this course he wrote the first textbook on ecological biochemistry (Harborne, 1977). Four editions have appeared of this book, which has been translated into Japanese, Russian, German, Spanish and other languages.

Much of the anthocyanin and flavonoid research in the 1970s was devoted to determining the bound form in which flavonoids occurred, both in the flower and in other tissues. Paper chromatographic surveys showed that flavonoids and anthocyanins were present as complex mixtures of glycosides. However, in ca. 20 families sulphate conjugates of flavonoids were found and ca. 50 structures characterised (Harborne, 1977). Those flavonoid sulphates were found mostly in aquatic plants and halophytes. They were identified by electrophoresis, HPLC and FAB-MS (Harborne and Boardley, 1984). In the palm family, a correlation was found between the presence of sulphates and anther structure (Williams et al., 1973).

Jeffrey had been active in the field of chemosystematics since 1962 when he presented a paper in a NATO-organised meeting in Paris on "Chemical Plant Taxonomy", which was the first major symposium covering this rapidly burgeoning field. In 1973, he was invited to the prestigious Nobel Symposium "Chemistry in Botanical Classification" in Stockholm, Sweden, at which all the leading figures in the subject presented papers. One of Jeffrey's contacts in the field was Prof. Robert Hegnauer from The Netherlands, who is the author of the 11 volume series "Chemo-taxonomie der Pflanzen". Robert was the external



Photo 2. Jeffrey (right) with Prof. Robert Hegnauer (left) at a PhD examination in the Netherlands.

examiner at the PhD viva of Jeffrey's associate Christine Williams, and in turn, Jeffrey was the external examiner during the PhD examination of Robert's student Renée Grayer at the University of Leiden (Photo 2). Apart from doing chemosystematic research, Jeffrey also gave lectures and practical courses in chemosystematics of plants to MSc students in plant taxonomy at Reading University. His lectures and contributions to plant chemosystematics are summarised in a textbook (Harborne and Turner, 1984).

In later years Jeffrey became more interested in the *raison d'être* of secondary metabolites and their ecological importance. Research into the antifungal activity of secondary metabolites centred on the comparative biochemistry of the phytoalexin response to fungal infections (Harborne, 1999). The phytoalexin induction appeared to vary chemically according to the systematic position of the plant (Ingham and Harborne, 1976). Much research was devoted to the Leguminosae, especially by Jeffrey's postdoc John Ingham. The major phytoalexins in this family appeared to be isoflavonoids, but some legume genera produced other compound classes such as chromones and furanoacetylenes as phytoalexins (Robeson et al., 1980; Robeson and Harborne, 1980). Other families studied for their phytoalexin response were the Asteraceae (Marshall et al., 1987), Rosaceae (e.g. Kokubun and Harborne, 1995) and Poaceae (e.g. Dillon et al., 1997). The main purpose of this research was to discover new types of natural antifungal activity and resistance mechanisms in plants against pathogenic fungi.

The chemical basis of resistance of plants to herbivory was also studied. Three sesquiterpene lactones and the coumarin cichoriin were shown to be feeding deterrents to locusts in the chicory plant (Rees and Harborne, 1985). Slug or larval feeding induced an increase in alkaloid synthesis (186%) in *Atropa acuminata* (Khan and Harborne, 1991). Condensed tannins appeared to be responsible for the resis-

tance of the groundnut plant to the aphid *Aphis craccivora* (Grayer et al., 1992).

## 2. Visiting professorships, honours and medals

Jeffrey was a visiting professor at the University of Rio de Janeiro (summer 1973); at the University of Texas, Austin, in 1976; at the University of California at Santa Barbara, in 1977 and at the University of Illinois at Urbana-Champaign, 1981. Jeffrey met Dr. Miriam Rothschild FRS at a conference in Santa Barbara. She was a pioneering figure in the field of Chemical Ecology and she encouraged him to develop a number of ecological research projects with his students (Harborne, 1977).

Honours and medals that Jeffrey received include the Gold Medal in Botany of the Linnean Society of London (1985); the first Silver Medal of the Phytochemical Society of Europe (1986); Life Achievement Award from the Phytochemical Society of North America and Phytochemical Society of Europe (1992); the Silver Medal of the International Society of Chemical Ecology (1993); and the Pergamon Phytochemistry Prize for Creativity in Plant Biochemistry (1993). He received the greatest honour of his career when he was elected a Fellow of the Royal Society in 1995.

## 3. Editorships

In 1972, Jeffrey became the executive editor of the journal *Phytochemistry*, and after Tony Swain's death in 1986, the Editor-in-Chief. During his time as an editor of this journal something like 20,000–30,000 papers were submitted to *Phytochemistry*. The journal also received many books for review, about half of which he reviewed himself. Apart from being an editor for *Phytochemistry*, he was on the Editorial Board of *Biochemical Systematics and Ecology* from the start of the journal in 1973 until his death in 2002, and he was a founder of the journal *Phytochemical Analysis*.

Jeffrey was also an editor of several book series, including the series "Methods in Plant Biochemistry" (with P.M. Dey as co-editor) (e.g. Harborne, 1989) and the famous series "The Flavonoids", which appeared in four volumes (Harborne et al., 1975; Harborne and Mabry, 1982; Harborne, 1988, 1993).

## 4. Publication statistics

Jeffrey was the author, co-author or editor of ca. 420 phytochemical publications. These included sole author of three books, senior author of a fourth book, editor or co-editor of another 24 books and author or co-author of more than 390 research and review papers or chapters of books. He published 132 of his papers in the journal *Phytochemistry*, right from volume 1 in 1962 until his death in 2002. Actually, the majority of these papers were published in the earlier years of his career, before he became editor of



the journal, so he cannot be blamed for pushing his own papers in his journal. The years 1969 and 1971 were especially prolific for Jeffrey in this respect, with 11 and 13 publications, respectively, published in *Phytochemistry*. When his friend Tony Swain started the sister journal *Biochemical Systematics* in 1973, renamed *Biochemical Systematics and Ecology* in the next year, Jeffrey published the first of his 34 papers in this journal; the 34th paper was published posthumously this year. Other journals in which Jeffrey published more than ten papers are the *Biochemical Journal* (14 publications between 1956 and 1962), *Zeitschrift für Naturforschung* (13 papers between 1966 and 1996) and *Nature* (12 papers between 1952 and 1976).

## 5. Collaborators

Many of the research papers written after 1974 were co-authored by one or more of Jeffrey's 24 postgraduate students (nine from the UK and 15 from abroad) or his postdoctoral fellows, including John Ingham (phytoalexins of the Leguminosae), Mick Richardson (flavonoids of the Caryophyllales) and Renée Grayer (various projects) and especially by his research fellow Christine Williams (chemotaxonomic surveys of Monocot families, the Compositae and other families) (Photo 3). Other co-authors included visitors from abroad who were invited to do research in the phytochemical unit at Reading, including Prof. Norio Saito and Prof. Kosaku Takeda from Japan, who worked on the anthocyanin pigments in blue flowers, Prof. Raymond Brouillard from Strasburg, another

famous anthocyanin chemist, and the flavonoid chemists, Prof. Nabil Saleh from Egypt, Dr. Ken Markham from New Zealand, Dr. Paco Tomás-Barberán and Dr. Mabel Gil, from Spain, Prof. Louis Sequiera from the USA and Dr. Bill Glennie from Canada.

Other collaborations were with his colleagues at Liverpool and Reading Universities (especially the plant taxonomists) and plant taxonomists at Kew. He also had interactions with other members of the Phytochemical Society of Europe (Jeffrey was Secretary for 5 years, organising 3 symposia a year during this time, mainly in the UK but also in Europe), with the editorial board members of the journal *Phytochemistry* and with the referees and authors through his post as executive editor of this journal.

## 6. Conclusions and personal attributes

Perhaps the greatest contribution that Jeffrey Harborne made to the field of Phytochemistry is that he made the subject accessible to biologists and other non-chemists. His books, papers and lectures, both at Reading and at International Symposia, were inspirational to many students and researchers in Britain and abroad.

Despite his fame as a phytochemist, Jeffrey was a shy, modest and religious man, who would go for long walks in the countryside or visit stately homes on Sunday afternoons. He also liked classical music and played the clarinet. Despite the fact that he had to spend long hours in his office for his departmental work, writing his papers and books and doing editorial work for *Phytochemistry*,



Photo 3. Staff and visitors of the Phytochemical Unit at Reading University in 1979. From left to right: Renée Grayer, Jean Harborne, Jeffrey Harborne, Syed Housein, John Ingham, Ken Markham and Christine Williams.

as often as possible he would do some work in the laboratory, often using some brightly coloured flowers, which he extracted and analysed by paper chromatography, HPLC and electrophoresis. Anthocyanin and flavonoid chemistry remained among his major passions right until the end.

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Available online 7 November 2007