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Peter Howard Elworthy (1933–1995): a Biographical Note

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Peter Elworthy had a considerable influence on pharmaceutical science, education and practice, in the UK. He died in December 1995 at the early age of 62, but he had retired from full time academic work from his post as Professor of Pharmacy and Head of the Department of Pharmacy in the University of Manchester twelve years earlier. Concerned about his health but also not a little disillusioned by the multiple pressures placed even then on senior academics, he foresaw the era of cuts and the central oversight and restrictions. His heart was elsewhere. In his 1976 Harrison Memorial Lecture (reproduced in this issue) he said: "Looking back, I have the feeling of having been very lucky. 'Much have I travell'd in the realms of gold, and many goodly states and kingdoms seen.' My main interest has been in the phenomenon of micellization. The subject has been of absorbing interest, and continually shows new bright facets which lead to new scientific advances. Travelling in the realms of gold has nothing to do with gold, but to me it means travelling in sunlight, which illuminates things brightly, and makes visible new facts, which have been invisible before. Occasionally dark clouds form; they are the disappointments and frustrations, but we need them in order to be able to recognize the sunlight by contrast."

Career

The son of a pharmacist, Peter was educated at Mercers' School in London. He spent a year at South East Essex Technical College before becoming an undergraduate at the School of Pharmacy of the University of London (then in Bloomsbury Square). In 1953 he graduated BPharm with first-class honours. With the aid of a Pharmaceutical Society scholarship and a Wellcome Pharmaceutical research scholarship he began research under the direction of Professor Leonard ('Giles') Saunders and obtained his PhD in 1956 with a thesis entitled 'Some Physico-Chemical Properties of Lecithin Sols'. A period of national service in the RAF intervened, but he was discharged on medical grounds. In 1957 he became an assistant lecturer in pharmaceutical chemistry at the School of Pharmacy. Within two years he was appointed to a lectureship in pharmaceutical chemistry in the School of Pharmacy at the Royal College of Science and Technology in Glasgow. Here he was responsible for the development of a physical pharmacy unit within the School, which at that time was headed by Professor James P. Todd. Todd was shortly to retire and be replaced as Professor of Pharmacy by the senior lecturer in pharmaceutical chemistry, John Stenlake.

It was in Glasgow that Peter took on his first research students. His first two postgraduates, Calum Macfarlane and Donald McIntosh were joined by Tom George and Charlie McDonald. I joined the group in 1962. Several strands of Peter's interests were pursued in that small group including phospholipid behaviour in aqueous and non-aqueous systems, properties of macromolecular solutions and non-ionic surfactant synthesis and characterization. With Moira Buchanan (McCubbin), who as Peter's research technician kept this group of postgraduates in order, work on the solution properties of a variety of small molecules was pursued. Having gone straight into research, to join the Pharmaceutical Society register Peter had to sit the Society's law and practice exam; he became a member of the Society only in 1961. In 1982 he was elected a Fellow of the Society.

Between 1961 and 1962 leave of absence at Glaxo and at Allen and Hanbury enabled study of the application of physical chemistry to problems of pharmaceutical formulation. In 1964, armed with a Fulbright Grant, he spent six months with Professor Karol Mysels at the University of Southern California. Returning to Glasgow he was promoted to a senior lectureship in pharmaceutical chemistry. One year later he was awarded the degree of Doctor of Science by the University of London for his published work in the field of physical chemistry. He was by then only 32.

The Royal College of Science and Technology, long affiliated to Glasgow University, was, under its Principal Sir Samuel Curran FRS, soon to enjoy its own degree-awarding powers and university status. So emerged the University of Strathclyde and a newly established chair of Pharmaceutical Technology to which Peter Elworthy was appointed. He had made the transition from pharmaceutical chemistry to pharmaceutics, proving that traditional subject boundaries can be breached. I became a lecturer in pharmaceutical chemistry in 1966 a few months after David Attwood had also been appointed to a lectureship. Although both David and I were part of the Department of Pharmaceutical Chemistry we continued to collaborate with Peter. Sometimes we felt our more natural home was in pharmaceutical technology, although John Stenlake gave us freedom to pursue our interests in physical pharmaceutical chemistry. David Ganderton and Harry Worthington were among those recruited by Peter into pharmaceutical technology in Strathclyde.

In 1970, Peter was approached to head the Department of Pharmacy at the University of Manchester. He left Scotland to return to England and to begin again the task of building up a strong research activity and providing leadership to the department. He devoted 13 years to Manchester.

Conferences

His first British Pharmaceutical Conference had been in Aberdeen in 1955; he drove there in a hired Ford Anglia with Norman Brudney, whom he describes as a "virtual elder brother". The Chairman at Aberdeen was J. P. Todd. Todd, Peter observed, was of the generation of Berry and Brindle who worked hard to bring Schools of Pharmacy into academic respectability. They were key players at an important time in the history of pharmaceutical education and research. At that conference, the young Mr Elworthy had agreed to help the reporter of the Chemist and Druggist by writing notes of the discussions at the science sessions, in the hope of getting paid, which he did not. When Norman Brudney gave his paper and no one asked a question, Peter did, as part of an agreement between the pair, "and [it] was so obviously a plant that we felt a pair of idiots". He was impressed by Brudney's ease with people in contrast with his own shyness, although he remarked that at later conferences it was he who had to avoid all those who wanted to speak to him. It was his turn to assume the key conference role. In 1971 as the Science Chairman of the Conference in Glasgow he delivered a memorable address with the even more memorable title 'Dehydrated Elephants and other Matters', reproduced in part in this special issue. The surreal in Peter manifested itself not only, for a period, in his Daliesque oil paintings, but also in other lecture titles. One to the hospital pharmacy group of the Pharmaceutical Society was called 'The Quest for Green Plastic Ears'. I have been unable to trace an explanation for this. Dehydrated elephants, at least, he explained.

Pharmacy Practice and Manpower Matters

His interest in the wider aspects of pharmacy no doubt stemmed from the family involvement in pharmacy. His 1973 Merck, Sharp and Dohme lecture alluded to the "unrecognized potential of the pharmacist". Peter's concern for the profession was expressed, too, in founder membership, governorship and later chairmanship of the board of examiners of the College of Pharmacy Practice. Significantly, during his retirement he conducted valuable research on manpower requirements in pharmacy. His findings were published in 1986 in the Pharmaceutical Journal, which considered his paper to be 'significant' although it objected to the author's 'polemic'. What was this polemic? His quite reasonable assertion that the Society's manpower report six years earlier which had concluded that fewer graduates were needed fell 'like manna from heaven' into the hands of the University Grants Committee and was pivotal in the events which led to 15% resource cuts in Schools of Pharmacy and the closure of one (Heriot–Watt). He concluded: "One of the main objectives of the Pharmaceutical Society under its Royal Charter is to promote pharmaceutical education. It is difficult to think of a more curious way of pursuing that objective than by over-reaction which has destroyed a significant part of the profession's resources for higher education".

Peter Elworthy's expertise was put to use in membership of Committee 17 of the British Pharmacopoeia Commission from 1973–1979. For many years he was a member of the Committee on Safety of Medicines (CSM) and of its subcommittee on chemistry, pharmacy and standards (CPS), which he chaired with precision and firmness from 1980–1988, after John Stenlake's retirement from the position.

Retirement

His retirement from Manchester at so early an age surprised many. What is not so surprising to those of us who knew him is to find that he meticulously weighed up the reasons for going. On Monday 15 November 1982 he sat down and wrote out 12 reasons. One of these was that retiring would lessen the impact of growing ill-health, but underlying it all his notes reveal a feeling of disenchantment; his research had been taking second place to administration in a University where he felt he did not have the Vice-Chancellor's confidence. He, who was the teacher who had certainly inspired me (and others) to do research, was losing interest in teaching and students. In fact, he had lost his confidence and writes, "I may need a holiday and a break more than usual".

Many, I am sure, do not appreciate the pressures laid on heads of academic departments. Not only do we have to be good managers, we have to perform well in research and to be good teachers. It is exacerbated now when everything is reviewed by some group or other which always has some superior knowledge of how things should be done. Peter with his innate intelligence and feel for how things should be done would bridle at what we have been turned into.

Professors are human, and one certainly sees this in the notes that Peter wrote after retirement. We all knew he was human, of course, but hadn't realized that behind the great success at an early age he sometimes felt insecure. Photographs of him bear a characteristic look, not of impatience, but perhaps of some work demon? At Strathclyde he arrived early each day, left punctually in the evening, to begin work at home. There he had two evenings off, not including the Thursday "working late evening" in the department which frequently ended up however in discussion of life in general. After retiring he recalled that "my health improved dramatically, the ulcer cleared and hasn't bothered me since". His enthusiasm for teaching returned and as a visiting professor at both the King's College Department of Pharmacy and the Square he gave a good deal of support to staff also.

For a period after retirement he ran Vick's research laboratories in the UK while the company was seeking a permanent head. He had long been a consultant for Vick, Norman Brudney being a Vice-President of the company.

A family tragedy darkened his and Mary's later years. Their son Andrew was killed while climbing on July 21st 1985, a blow from which he never really recovered. David and Julie lost a brother, but their love and support was crucial and their careers an interest. Major work, though, still occupied him. Membership of the CSM lasted until the end of 1989, by which time he had served in this capacity for 12 years. He would have liked to have served another term as chairman of its CPS subcommittee and was a little disappointed that this was not to be, feeling "unwanted" with the cessation of a number of such activities. Then he says, he got his notebook out with its list of 21 retirement projects and made a start, completing three, but so like him, adding two new ones to the list! His alma mater,

the School of Pharmacy made him a Fellow in 1992 which he said gave him much pleasure, writing that this was the last honour and "perhaps, now, I'll get somewhat nearer to serenity. I'm working on it".

The Science

Peter Elworthy's complete list of publications is appended to this biographical note. It is appropriate that the *Journal of Pharmacy and Pharmacology* is publishing this commemorative issue, for a good deal of Peter Elworthy's work was published in its pages. Only a brief account of the range of his work can be provided here.

The first paper was not on any of his later topics of research but on assay processes involving the use of ion-exchange resins. It was published in the *Journal of Pharmacy and Pharmacology* in 1954 with Leonard Saunders and Robert (Bobby) Fleming (Saunders et al 1954). His PhD work with Saunders led to two papers (Elworthy & Saunders 1955, 1957) and a review on the physical chemistry of lecithin (Elworthy & Saunders 1956). Writing on the move of the Society and School from Bloomsbury Square, he said "They cannot pack my memories and cast them off to Lambeth. "In the little basement laboratory" with the old fireplace full of the Goüy diffusometer....' he worked with Norman Brudney and 'Uncle' (Giles Saunders) "very dark and cuddly as a teddy bear". In his Harrison memorial lecture Peter reminisced how he and Saunders had probably seen liposomes in their lecithin–cholesterol mixtures but had not recognized them as such. Saunders himself did know of the liposome-like aggregates but was convinced that they were not closed systems but Swiss roll structures and argued strongly that this was so. It was A. D. Bangham who rightly received the credit for discovering the closed bilayer structures which have since had such an impact on drug delivery.

Papers entitled 'A test of Perrin's relationships for small molecules in solution' (Elworthy 1962b) and 'Estimations of deviations from Stoke's Law for small molecules' (Elworthy 1963a) laid the foundation for later work on neuromuscular blocking agents in solution (Elworthy 1963b, 1964). Perrin's equations relate frictional coefficients to the shape of non-spherical molecules. In representing non-spherical molecules, ellipsoids with three unequal semi-axes (a, b and c) were considered and he adapted Perrin's equations to give the relationship between ellipsoidal shape and the limiting ionic conductance as a function of a, b and c.

Stokes and Robinson had suggested that the conductances of symmetrical tetraalkylammonium ions could be used to calculate the Stokes' radius whereas the true radius could be obtained from molar volumes. Early studies on the surface activity of hexadecane disodium sulphate (Elworthy 1959b) and the conductance and diffusion coefficients of the dicarboxylic salts of sebacic acid, dodecane carboxylic acid and hexadecane carboxylic acid (Elworthy 1962a) led to the conclusion that the dicarboxylic acids were not fully extended in solution, although the trimethylammonium derivatives were less extended and monocarboxylic acid anions and dodecylsulphate anions least extended, their hydrocarbon chains being 'curled' in solution (Fig. 1).

In Glasgow, John Stenlake and J. J. Lewis (University of Glasgow) were working on neuromolecular blocking agents, research that was to lead much later to the discovery of atracurium by Stenlake's group. The inter-onium distance was thought to be an important parameter that had earlier been estimated by Gill. Again using conductance techniques Elworthy calculated the inter-onium distance of hexamethonium to be 6·3 Å (compared with Gill's 6·9 Å). For decamethonium the N^+–N^+ distance of 9·5 Å was in accord with estimates of 9–10 Å (Elworthy 1963b). This work was followed up (Elworthy 1964) in studies on the effect on the inter-nitrogen distances of altering the onium substituents.

Papers on micelle formation by lecithin in non-aqueous systems such as benzene (Elworthy 1959a) indicated the formation of small micelles (MW 3200) at low concentrations and larger aggregates (MW 55 000) at higher concentrations. The size and shape of the micelles was deduced from measurements of viscosity, osmotic pressure and diffusion coefficients (Elworthy 1959b); a spherical configuration was ruled out in favour of a laminar model. Large amounts of dibasic fatty

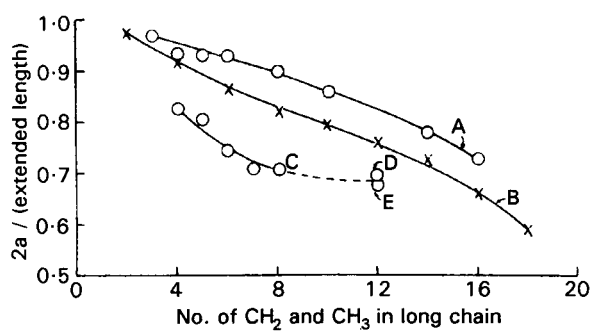

FIG. 1. The extension of various molecules in aqueous solution determined from conductance measurements and plotted as a function of their hydrocarbon chain length: (A) dicarboxylates, (B) alkyltrimethylammonium compounds, (C) monocarboxylates, (D) sodium dodecylsulphate and (E) dodecylamine (Elworthy 1963a).

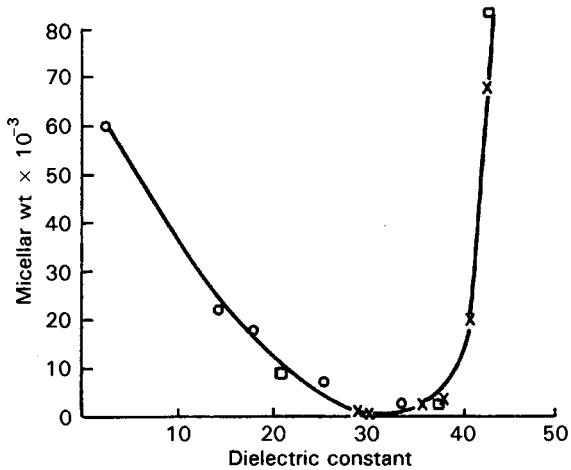

FIG. 2. The effect of dielectric constant, ε, of the solvent on the micellar weight of lecithin in single solvents (○), in mixed solvents (×). □ Represents data from diffusion–viscosity experiments (Elworthy & McIntosh 1964b).

acids could be solubilized in these inverse micelles (Elworthy 1960a), acids containing an odd number of carbon atoms being taken up to a larger extent than those containing an even number. In this series of papers precise experimental measurements are tested against several theoretical models to provide the most logical physical explanation of the data. The interaction of water with the lecithin micelles in benzene up to a maximum of 0·33 g water (g lecithin)$^{-1}$ converted the micelles into spheres (Elworthy & McIntosh 1964a). A paper on the effect of dielectric constant on micellization by lecithin (Elworthy & McIntosh 1964b; Fig. 2) concluded the publications on phosphatides. Some of these papers are still cited today. With Karol Mysels in the USA, he tackled the problem of the surface-tension–concentration behaviour of sodium dodecylsulphate (Elworthy & Mysels 1966), demonstrating experimentally, using highly purified samples, the theoretically expected decreasing surface tension above the critical micelle concentration (Fig. 3), a result often masked by impurities.

Aqueous non-ionic surfactant systems and their micelle-forming properties occupied much of the 60s and 70s. Calum Macfarlane (later Senior Vice-President, Syntex Research Centre, Edinburgh) synthesized a series of pure hexadecyl polyoxyethylene ethers and performed a comprehensive study of micellar properties using the raft of techniques discussed above (Elworthy & Macfarlane 1962a, b, 1963, 1964). Charlie McDonald investigated the growth of these micelles as a function of temperature and their changing hydration states (Elworthy & McDonald 1964). The very hydrophobic surfactants $C_{16}E_6$ and $C_{16}E_7$ formed very large micelles. We now know that these can, under certain conditions, form vesicular structures or 'niosomes'. My own work was to investigate the influence of branching of the hydrocarbon chain on micellar properties. This involved the synthesis of a series of non-ionic surfactants based on the structure:

$$\begin{matrix} CH_3(CH_2)_x \diagdown \\ CH_3(CH_2)_x \diagup \end{matrix} CH.CH_2(OCH_2CH_2)_yH$$

which formed small micelles when x ranged from 0 to 3 and y from 6 to 9 (Elworthy & Florence 1963, 1964, 1965). Their generally high critical micelle concentrations, however, proved a bonus as it was possible to investigate solutions above and below the CMC. In particular, by using a large home-made vapour pressure apparatus we were able to determine the activity coefficient of several surfactants above and below the CMC. Fig. 4 shows the data on the measured activities of several surfactant systems (Elworthy & Florence 1966).

Work on non-ionic surfactants with David Attwood (Attwood et al 1969, 1970, 1971a, b), Walter Guthrie (Elworthy &

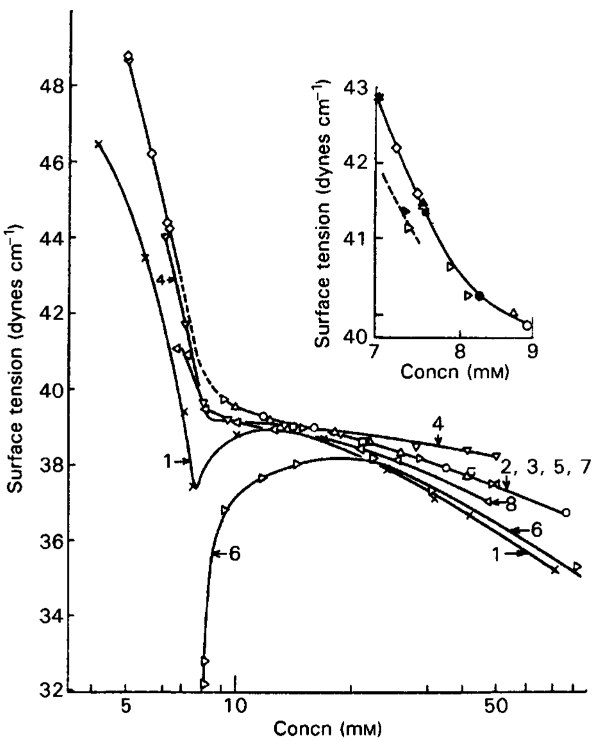

FIG. 3. Plots of surface tension, γ, (dynes cm^{-1} [mN m^{-1}]) against log concentration for impure and pure samples of sodium dodecylsulphate around the CMC, showing in purified samples the decrease in activity above the CMC. The insert gives the detail around the CMC of purified systems obtained by foaming and removal of breakdown of dodecyl alcohol and the recombination of pure and impure fractions to show the return to original values. Solid symbols show the data at the end of extensive foaming, open symbols the data at the end of the experiments. The line labelled '6' shows the data for an impure (and commonly encountered state of) sodium dodecylsulphate. Note, of course, the large scale used to depict surface tension values. The other numbers (2–9) refer to experimental runs in which the sodium dodecylsulphate solution is being purified (Elworthy & Mysels 1966).

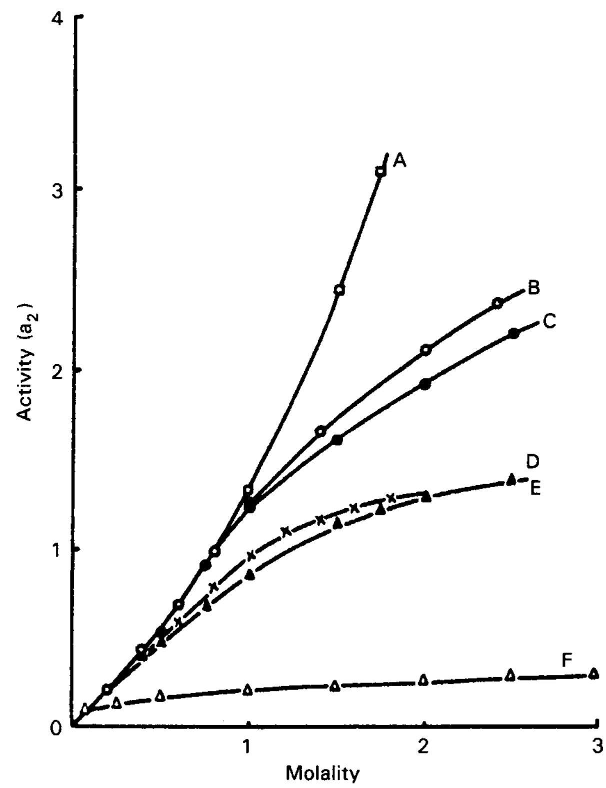

FIG. 4. A plot of solute activity (a_2) as a function of concentration for several surfactants, with high CMC values, synthesized in the laboratory at Strathclyde: (A); C_2E_6 at 20°C, (B) C_4E_6 at 20°C; (C) Me_2E_6 at 20°C, (D) C_4E_6 at 30°C, (E) Me_2E_6 at 30°C, (F) Et_2E_6 at 20°C (Elworthy & Florence 1966).

Guthrie 1970) and on non-ionic-stabilized emulsions with me and Jim Rogers (Elworthy & Florence 1969b, c, Elworthy et al 1971a, b) grew from these early studies.

Solubilization

Work on solubilization was systematically pursued in Strathclyde (Corby & Elworthy 1971a, b), confirming the relatively low capacity of the micelles of available surfactants. In Manchester, the question posed was would it be possible to increase the capacity of the micelle by increasing the size and hydrophobicity of the monomers sufficiently to increase the amount of lipophilic solubilizate taken up into the micellar interior? Arnarson synthesized a series of very long (C_{22}) alkyl surfactants (Arnarson & Elworthy 1980, 1981, 1982), and the work on customizing micelles was continued by Patel (Patel et al 1981, Elworthy & Patel 1982a, b, 1984) and then by Peter's last PhD student, Jayne Lawrence (now at King's College, London) in association with David Attwood (Attwood et al 1986, 1989, 1990), who had moved to Manchester from Strathclyde. Attention was turning for a time to microemulsions (which often are difficult to distinguish from swollen micelles), investigated in some detail in collaboration with David Attwood (Attwood et al 1974a, b, c).

Research on the properties of lecithin, non-ionic surfactants and the shape of small molecules in solution was complemented at various periods by investigation of the properties of ghatti-gum (Elworthy & George 1963, 1964) the obstruction effect (Elworthy et al 1972) and the internal viscosity (Elworthy 1971) of polymer solutions, studies on dissolution and solubilization (Elworthy & Lipscomb 1968a, b, 1969; Corby & Elworthy 1971a, b) and crystallization (Elworthy & Worthington 1968, 1971). With Ray Rowe and David Ganderton the pore structure of plastic matrix tablets was investigated (Rowe et al 1972, 1973a, b) and a variety of physicochemical features of tablet formulations were pursued in collaboration with industry (Cole et al 1974, 1977; Pickard et al 1975; Chalmers & Elworthy 1976a, b, c).

End note

Peter Elworthy's publications spanned 30 years, his last being on the work patterns of pharmacists (Elworthy 1986, 1988, 1989) where his scientific method was applied to a manpower problem which required hard data. Peter liked precision. He was drawn to solution chemistry possibly because of the precision possible in measurements, such as with the Goüy diffusometer. A replica of the London instrument was built in the basement of the Royal College in Strathclyde. When no commercial instruments were available, workshops were commandeered and apparatus appeared–light scatterers of varying degrees of sophistication, vapour-pressure instruments, diffusometers and Langmuir troughs. Araldite was as important an ingredient in the laboratory as distilled water.

What gave Peter the greatest pleasure was the testing of hypothetical molecular structures against the evidence of the experiment. He enthused his research students, introducing us to the art of lecturing, the presentation of results and the writing of papers. Had he continued his science for longer who knows what areas he would have explored. Those of us who were trained by him hope that we have taken on the mantle and are continuing the work that he began. The papers published in this special issue of the *Journal of Pharmacy and Pharmacology* show not only the diversity of work that continues, but also the central themes with which we grew up-of surfactants and solutions.

A group photograph (circa 1963) in the basement workshop of the Royal College of Science and Technology (left to right): Geoffrey Wood, Donald McIntosh, Calum Macfarlane, Moira Buchanan (McCubbin), Sandy Florence, Peter Elworthy, Charlie McDonald, George Cochrane. (Chief Workshop Technician to whom all had to be kind), Tom George.

Acknowledgements

I wish to thank Mrs Mary Elworthy for allowing me access to photographs and notes made by Peter before and after retirement, Dr Joseph Chamberlain who encouraged the idea of this commemorative issue and the library staff of the School of Pharmacy for their literature searches and the collection of original papers.

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