



Review

David J. Triggle: Medicinal chemistry, to pharmacology, calcium channels, and beyond



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ABSTRACT

David Triggle's scientific career began as a chemist, went through medicinal chemistry into pharmacology, and finally on to somewhat more philosophical interests in later years. It was a career marked by many contributions to all of those aspects of science. Chief amongst his many contributions, in addition to those in medicinal chemistry, was his work on the drugs known as calcium ion channel blockers or (calcium antagonists). In the calcium ion channel field he was a particularly instrumental figure in sorting out the mechanisms, actions and roles of the class of calcium channel blockers, known chemical and pharmacologically as the dihydropyridines (DHPs) in particular, as well as other calcium blockers of diverse structures. During the course of a long career, and extensive journeys into medicinal chemistry and pharmacology, he published voluminously in terms of papers, reviews, conference proceedings and books. Notably, many of his papers often had limited authorship where, as senior author it reflected his deep involvement in all aspects of the reported work. His work always helped clarify the field while his incisive reviews, together with his role in coordinating and running scientific meetings, were a great help in clarifying and organizing various fields of study. He has had a long and illustrious career, and is wellknown in the world of biomedical science; his contributions are appreciated, and well recognized everywhere. The following article attempts to chart a path through his work and contributions to medicinal chemistry, pharmacology, science, academia and students.

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1. Introduction

Any attempt to summarize the contributions, scientific or otherwise, as part of a *Festschrift* for a colleague requires a certain amount of juggling of perceptions, both scientific and humanitarian. After all, the colleague has to be seen both as a scientist and as a person, as well as in terms of the interaction between the two. The human as a scientist, and the scientist as a human, are equally of interest, as is their interplay. A *Festschrift* therefore requires a somewhat different approach from that used for purely scientific discussions. The question of what to write, what to discuss, and what are the important points to consider is not easily answered, but it is worth trying for an answer for David, even if only as a record of some of his many achievements. It has been told to me, but I cannot vouch for the truth of the story, that David has had connections with the British satirical magazine “*Private Eye*” (https://en.wikipedia.org/wiki/Private_Eye). If this is true, all one can say is, “good for him”, but conscious satire on my part has been removed from the following although any unintentional satire is just that – unintentional. Thus, I apologize beforehand for all errors, assumptions, suppositions and omissions – all made unintentionally. However, for those wishing to quickly review David’s scientific career there is a very useful transcript of an interview with him, published in 2004, in which he briefly, but fascinatingly, describes his intellectual journey through chemistry, medicinal chemistry and pharmacology [1].

2. An historical outline

The central theme of this section is, of course, David’s contribution to science. This contribution will be viewed mainly through the writer’s eyes which are those of ‘an old and old-fashioned, pharmacologist’. Much of what follows therefore relates to what David has given to the discipline of pharmacology in general, as well as to particular topics and aspects of pharmacology. However, his scientific ‘mother’s milk’ was chemistry, as studied at two different English universities but, like many a good

chemist before him, he eventually wandered from the bright uplands of the more exact science of chemistry into the darker more obscure valleys of the science known as pharmacology. Possibly, he was led there by intriguing questions of just how medicinal chemistry translates into the magic of drug effects in pharmacology, especially in the area of autonomic pharmacology. There is no question he began his academic career with contributions to chemistry and medicinal chemistry. The latter is an area peripheral to my own interests, and one in which I claim little expertise, therefore, this article mainly concentrates on David’s contributions to pharmacology. He has spoken about his drift from chemistry to pharmacology but on a personal level, over many years of academic life, one encounters quite a few organic and medicinal chemists who slowly, and almost inexorably, drift from the magic of alchemy (in its modern form of chemistry) into the far more imprecise magic of potions (drugs and their actions). Far from suggesting this was the case for David, it does, however, cross one’s mind when noticing, as will be shown later, that he has in recent years drifted somewhat into more ill-defined areas that whisper of philosophy more than science. Perhaps I am being unfair in this matter, but look at the titles of his most recent publications; “*Nous sommes tous des bactéries . . .*” [2]; “The chemist as astronaut . . .” [3]; or “Treating desires not diseases: a pill for every ill and an ill for every pill?” [4]. Of course I am being unfair since it is the prerogative of the elderly scientist to indulge in a little philosophy as a relief from the struggle of dealing with what may be the harsher realities of science. In this respect many an elderly scientist has to plead, ‘*mea culpa*’, and so one should not accuse others of similar ‘sins’.

What follows is a personal view of David’s work, as it impinged on those areas of my own pharmacological interest, and how he has contributed to my own understanding of that area. However, that said, we cannot just leave the views of aging scientists, as they mutate and grow old with time and approach the end of a long career, without a few extra comments. For some, age brings an impulse to enter into and explore philosophical aspects of science; an impulse that grows stronger with time. Since David has

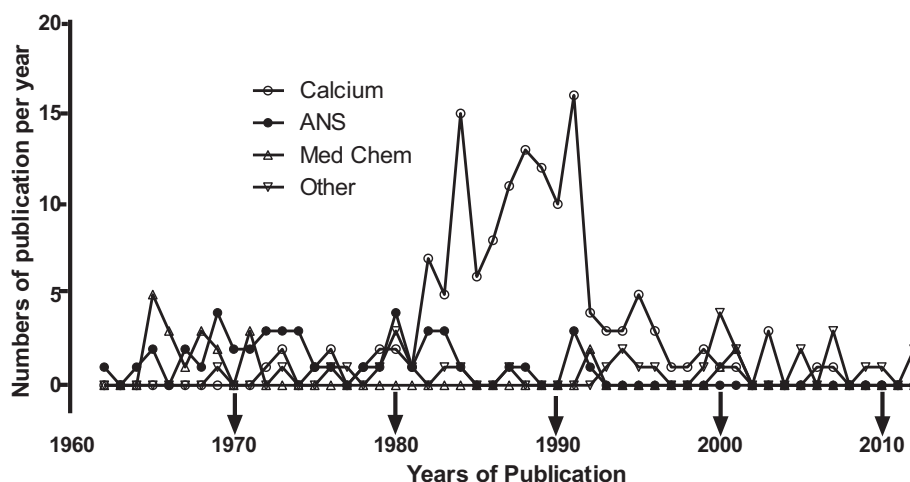


Fig. 1. Journal Publications by D. Triggle over the decades.

A count of journal publications over David’s career was made on the basis of the usual search procedures with publication subjects categorized under four headings. The four categories chosen were calcium and calcium channel drugs (Calcium), autonomic nervous system drugs (ANS), medicinal chemistry (Med. Chem.) and other subjects outside of those categories (Other). This approach is somewhat subjective and does not necessarily offer the most precise analysis of what David has achieved during the course of his career. Instead it is intended to give a qualitative impression of what were his research interests during the course of a long and illustrious career. The most notable feature is the peak of publications on calcium, and drugs acting on calcium ion channels that covers a 20 year period, the peak of which is centred in an almost Gaussian-like manner around 1986/87.

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