Invitational ONR Lecture

The Two-Faced Microbiologist:
Contributions of Pure and Applied Microbiology to Good Research

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INTRODUCTION

“There is no such thing as Pure or Applied science,” said a British industrialist recently, “there is only Good or Bad science.” The occasion was a meeting of the British Mycological Society dedicated to the proposition that traditionally minded academic mycologists could learn a lot by applying the techniques of submerged culture and the chemostat, and his remark has given me the theme for my own talk. As an academic, it would hardly be proper for me to lecture to the Society for Industrial Microbiology on—say—the manufacture of cephalosporins from activated sludge, and I have never yet been in a position to persuade anyone of the economic importance of my latest discovery. To an audience of fellow-academics it might be worthwhile for me to argue the importance of a proper attitude toward economic, social, and political problems, and to consider how to steer a middle course between selling oneself to the highest bidder and locking oneself in the ivory tower, though I should think that most of us have already been pretty well exposed to those arguments. However, the present occasion gives me a welcome opportunity to look at the reverse process and to acknowledge how much the pursuit of seemingly academic problems owes to the discoveries made in industrial and technological laboratories.

This task of highlighting the origins of a piece of “pure” science has its dangers. It might make me very unpopular with my peers if I were to argue at length how much their latest and most elegant papers owed to some industrial innovation of which they were in fact quite unaware. I can only expose, therefore, the roots of my own researches, and hope to do so with as little tedium as possible. If the resulting account is too much like a scientific autobiography please excuse me, there must be something I have done which will interest some of you; otherwise, I should never have been honored by your collective invitation!

DISCUSSION

Basidiomycete Polycetylenes

The polycetylenes are a large group of natural products which today must be numbered in their hundreds, but 20 yr ago they were still rare curiosities. Many have been produced by basidiomycete fungi, and some of these are antibiotics of no clinical interest; the group as a whole has passed through most of the stages of scientific exploration in a relatively short span of years. Their study was, in fact, the problem to which I was first assigned on arrival at Manchester, and we looked at them, on and off, for about 16 yr.

Polycetylenes in the plural first emerged as curiosities of the plant kingdom,
particularly from the work of the Sørenseins (1958) in Norway, and simultaneously some very apposite new chemistry had been developing in E. R. H. Jones' school at Manchester. The historical roots of that chemical work are themselves of great interest, but I cannot pursue them here; one outcome was that the very distinctive UV absorption spectra of some basidiomycete metabolites described by Anchel (1952) and her co-workers at the New York Botanical Garden (NYBG) had been recognized as polyacetylenic. The New York work came out of a screening program for antibiotic activity, and so it had obvious "applied" origins; moreover, the NYBG had concentrated upon the Basidiomycetes because of their well-established and very practically oriented expertise with these important tree pathogens and timber destroyers.

For similar reasons, since I knew literally nothing about any kind of microbiology when I was assigned the job of growing these organisms, I soon found myself taking a crash course at a comparable British laboratory, that of Forest Products Research at Princes Risborough, where I learned the rudiments of technique and also had my first sight of the chemical problems which a close study of these pathogens and saprophytes might reveal (Cartwright and Findlay 1958). For the remainder of my hasty mycological education I was almost totally indebted to a book by one of the great pioneers of modern mycology, a man to whom "pure" and "applied" science were indistinguishable and who was an intellectual leader both in industry and outside. I refer of course to Jackson W. Foster and his book "Chemical Activities of Fungi" (1949).

In due course, Anchel's fungi grew for us and their polyacetylenes were characterized (Bu'Lock 1956) more or less simultaneously with the antibiotic mycomycin which emerged from the Pfizer Laboratories (Celmer and Solomons 1952, 1953a,b) with its remarkable structure fully worked out and the parent organism wrongly identified (but that is another story). The Jones research group moved to Oxford; the number of polyacetylene structures grew monthly, with an explosion of new plant polyacetylenes from Boehm and more modest additions from our fungi. At Manchester, the accumulating structures threatened to become boring and we started to look for some meaningful pattern in them, the first steps toward elucidating their biosynthesis (Bu'Lock et al. 1957). At the same time, the quite nonchemical job of growing the cultures gave us a real interest in questions of when, and how much, and even why, our metabolites were being produced — the beginnings of an interest in regulation. At the time, the theories of metabolic regulation were in their infancy, even for primary processes, and yet out of the severely practical experience of the people who were busy making antibiotics the ideas about secondary metabolite regulation were already emerging, and indeed their origins are all in the book by Foster (1949).

Of course, with the arrival of Arthur Birch at Manchester our own first steps toward biosynthetic experimentation had a tremendous boost, and we also acquired practical experience as a service laboratory with a much bigger range of fungi. And for this phase there is no doubt in my mind that the biggest generators of interest in natural product biosynthesis were our industrial colleagues, who in effect promoted, by their reception of the results, as much as by direct backing, the establishment of what is now a well-recognized and self-sustaining discipline of chemical biology.

For me, one of the nicest things about the natural polyacetylenes is that by 1966, when the series as a whole was just about to become too big and too miscellaneous to comprehend, I found myself able to rationalize all the known structures — and incidentally, most of those that have since been found — in terms of a relatively small number of biochemical transformations and a unified overall origin; moreover, within a