

## GUEST EDITORIAL

### KEEPING UP WITH THE TIMES

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The village where I live in the UK was only connected to mains electricity in 1962. It is hard to imagine life without electricity, but that is just one thing among many which has changed. Progress has occurred at a much faster rate than most people can keep up with, particularly those of my generation and older. Although I find it difficult that some people of my age are still illiterate as far as computers are concerned, I provide much amusement to my great-nephews and great-nieces with my ignorance of how to use an iPhone, Twitter and the like.

In the same way I am all too conscious of changes in my lifetime in natural product research, particularly that with a medical or pharmaceutical dimension. Although I stopped active research over 7 years ago, I still read some journals and referee submitted articles, but it is frustrating how many authors use approaches and methods which belong to a former generation; so it is not surprising that they find it difficult to get their papers published, especially in internationally-respected journals.

Let me highlight some changes which need to be taken into account.

#### **Lists are not enough!**

Too often a paper might provide list of plants growing in a particular area, either gleaned from the existing literature or from a botanical or ethnographic survey. Similar instances are chemicals found in a genus or plant family.

Sometimes it is difficult to see any order in these lists, but even when they are put into some sort of logical order, e.g. by botanical family or by use, the information given is not well-referenced and a lot of important details are omitted, e.g. part of plant used, time and method of harvesting, method of preparation, dose given (if the use is pharmaceutical).

#### **Reviews should be critical**

Not all research, even if it is published in an international journal, is of equal quality. This particularly applies in interdisciplinary work, where authors or referees may not have much knowledge about one of the topics investigated. This is notoriously true where botanists or pharmacologists may have little phytochemical expertise, or where clinical or pharmacological scientists do not realise the importance of defining botanically and chemically the material they are using, not appreciating the wide variation that occurs in chemistry and therefore activity even in a single species.

Very often reviews consist of a summary of work that has been done and no comment is made on seemingly contradictory results or discussion written about factors such as techniques used, doses given, numbers used and statistics applied.

#### **Chemical compound isolation on its own is of limited interest**

The advent of chromatography and advanced spectroscopic methods in the mid-twentieth century resulted in an explosion of the numbers of novel natural products being reported. Sometimes these were small variations of known classes, but novel structural types were sometimes described. This enabled chemosystematics to develop as well as providing large libraries of compounds for small-scale biological testing.

Although it is quite possible that nature may still surprise us with novel compounds and compound types, particularly as far as plants and perhaps fungi are concerned, novel chemical structures alone no longer excite much interest. Much more attention is paid to novel compounds linked with an interesting property, especially a biological activity which can be applied to a

pesticidal or pharmaceutical use.

Indeed much research of this type now commences with testing for the activity and not doing any chemical investigation or structural elucidation until significant activity has been found. This approach has yielded several useful and interesting lead molecules in recent times. However, the large input of effort has little value when a known compound with that activity is identified. Too often this is not addressed in papers, either by dereplication being carried out by linked techniques such as LC–MS, or by a lack of thorough searching of the literature. In the past this was partly excusable in parts of the world where economic considerations militated against access to a good library, but the introduction and availability of online databases and ability to download electronic versions of papers almost anywhere in the world now makes such lack of rigour inexcusable.

### **The use of animal experiments is increasingly unacceptable**

A strong case can be made scientifically for whole animal experiments or living tissue obtained from animals rather than in-vitro assays to investigate the reputed treatment of plant extract for treating a disease state.

However, ethical considerations over animal rights, are making such research increasingly difficult in most parts of the world. In many countries those who do such work have to be trained and licensed and considerable costs are incurred.

There are, however, more directly scientific problems with the use of animals, particularly in research seeking to identify active constituents in extracts. The most common approach is to use bioassay-guided fractionation, consisting of a repeated cycle of fractionation and testing of fractions until a pure compound is obtained.

If whole animals are used, numbers have to be high to make results statistically valid, and the consequent costs and ethics involved make such a project unlikely to be viewed favourably.

### **Quantitation and statistics are important**

As mentioned above, too often surveys consist merely of lists. Quantitation gives an increased value to data, e.g. the numbers of users of a species listed, together with numerical information of

its occurrence, can give information about its importance and availability.

With increasing use of biological and clinical experiments in much research on natural products, it is vital that those planning experiments and processing results obtained, consult with statisticians before the projects are finally executed. The response of any biological system to the same dose of the same substance is notoriously variable, and this must be borne in mind so that an accurate view can be taken of the validity and usefulness of results.

### **Conclusions**

A thorough, well-planned and well-executed piece of research in most cases is costly, especially if advanced scientific equipment and skilled operators have to be used. Many countries have limited resources and difficult decisions have to be made about how or whether natural product work can be carried on.

A partial answer also applies to researchers in more fortunate places as far as resources are concerned, namely cooperation, either between different countries, or between different disciplines in the same country. Although there are many examples of successful working together, it also has to be said that, even in the same university, individuals resist sharing their facilities and expertise work with anyone else.

Personal ambition, historical rivalry and suspicions about allocation of funds are some of the many factors that stop or stunt collaboration and obtaining worthwhile results.

However, to return to the topic first mentioned, it is also true that lack of time or inclination to keep abreast of new development, as well as an innate desire to stay with familiar approaches has no small part to play in the fact that too much natural product research carried out and published is of inferior quality. Let's change that!

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