Nervous Hawaiian plants

A new, fast and effective screening technique that can screen tissue without the need to extract the chemical components first has been developed by US scientists. The method could accelerate the search for novel neuroactive compounds with pharmaceutical potential from plant species, according to the researchers.

Nature has acted as a rich source of medicines; many drugs, from aspirin to Taxol (paclitaxel), have their derivations in plants, moulds and bacteria. The rainforests and the seas have been the focus of much research. According to Professor Garry Rechnitz, a chemist at the University of Hawaii in Honolulu, Hawaiian plants in particular represent an especially rich and untapped source of potential novel pharmaceutical agents because many of the native species grow nowhere else. "Conventional analytical techniques are of limited utility", he says, "because the demonstration of the desired medicinal activity must precede the identification and isolation of the responsible agent." Rechnitz and his team in the University's Biosensor Laboratory have turned the traditional approach on its head and developed a sensor system that can screen a plant tissue sample for particular activity first and, if a positive result is obtained, allows the researchers to then isolate the compound or compounds responsible [*Anal. Chim. Acta* (1997) 337, 297]. Thus, numerous plants could be screened without the usual expense and time incurred in analysis.

To demonstrate the power of the technique, the researchers have incorporated neuronal tissue from a crayfish into a sensor probe. When the neuronal tissue is stimulated it produces a measurable signal in the probe. Tissue from the plant of interest is simply crushed into solution or, if the suspected components are insoluble in water, lipid vesicles are added to act as carriers for the hydrophobic components. Dipping the probe into the solution then either gives a signal or not depending on the presence or absence of a neuroactive component.

The team first tested the approach on various local anaesthetics, such as lidocaine, which all rewarded the scientists with a fast and reversible response in the neuronal tissue. They then turned to Hawaiian plant species, such as the awa plant (*Piper methysticum*) and the Tahitian hutu tree (*Barringtonia asiatica*), which were already known to contain neuroactive compounds; the early Polynesians used the plants in medicinal and in religious ceremonies. For instance, extracts from the awa plant were used to cause temporary paralysis to allow the medicine man to treat ailments, and preparations from the hutu tree were used to stun tidal pool fish temporarily, so that they could be gathered without toxic effects on the people eating them.

The team has identified several neuroactive compounds in this way from awa root, such as kawain and dihydromethysticin. Rechnitz points out that there is a rich folklore describing the use of plants in Hawaiian medicine and religion, and this history should allow the team to make a more educated guess as to which plants to screen first for neuroactive properties.

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Book reviews

Molecular Diversity and Combinatorial Chemistry: Libraries and Drug Discovery edited by I.M. Chaiken and K.D. Janda, American Chemical Society, 1996. $109.95 (ix + 328 pages) ISBN 0 8412 3450 7

Interest in the creation of vast numbers of chemical entities has exploded over the past five years. Whatever you call this area of science – and here the book title covers all bases – there hasn't been this much hype in chemistry since molecular modelling was claimed by some in the 1970s to be on the verge of calculating its way to magic bullets. While molecular modelling now has an established role in drug discovery, it is too soon to say precisely what impact molecular diversity technology will have, but currently its future looks bright. It is notable that this book contains chiefly methodology and descriptions of the potential and promise of the technology; presumably, if these are to be fulfilled, a similar book in five years time will be full of examples of the part molecular diversity has played in the discovery of new drug candidates.

Molecular Diversity and Combinatorial Chemistry: Libraries and Drug Discovery is published in the ACS Symposium Series, which aims at providing a snapshot in time of research in the field. This the book certainly achieves, although as it is based on presentations made at two conferences in early 1996 (CHI, 28 January–2 February 1996, Coronado, California) there is little that will be new to most practitioners of the art. However, the format does have the virtue of collecting a range of literature pertinent to the area, including some material that one might not pick up in a narrow literature search.

For example, it was interesting to see contributions covering molecular diversity derived from 'natural' sources given space in the book, as natural products are sometimes thought to be 'in competition' with purely synthetic molecules. In a chapter on gene transfer, Thompson puts forward a powerful case that only 1% of microbes and plants have so far been used as natural sources of molecular diversity because only that small proportion can be cultured or cultivated. The chapter suggests that using molecular biology techniques to extract genes from these organisms, to clone them into appropriate expression systems, should allow us to access a large part of the remaining 99%, delivering a richness of chemical structures as yet untapped. A complementary