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LETTER TO THE EDITOR

Letter to the Editor regarding the publication of studies on extracts/complex mixtures from natural products

There is a continuing discussion in the natural products research community regarding the quality of publications and impact factor of journals. This debate is tending, in my judgment, to tip the balance unfairly against publication of investigations involving medicinal plant extracts/complex mixtures which do not include purification and characterization of "active" compounds or marker compounds. I feel this reflects an infatuation within the community with the tools of our trade - analytical methodology (HPLC and other separation technologies), various spectroscopic/spectrometric methods (high field NMR technologies, various mass spectrometry technologies, etc.), coupled (or hyphenated) methodologies, and so on - rather than recognition that these are tools useful to research and understanding the role that natural product compounds play in the grand scheme of Nature.

The exploratory work done in those programs examining preparations of plants used in traditional practices, especially those located in resource-poor countries (i.e., "developing countries"), which pursue validation of their biological activities, are certainly appropriate for publication in this Journal. Successful validation of the potential therapeutic activity of these traditionally used preparations can provide immense benefit to the health and well-being of the populace of these countries. That the research is done with complex mixtures/crude extracts is also appropriate, since that is usually the manner in which the materials are used traditionally. We need to pay close attention to the methodology of the experimentation: is the biomass correctly authenticated?; collected at the appropriate time consistent with traditional practices and the correct plant part used?; are the methods of extract preparation consistent with traditional use or connected in some logical fashion to traditional use (not a chloroform extract when a decoction is the usual dosage form)?; is the preparation being evaluated for the appropriate indication?; is the biological assay consistent with the expected application and dosing appropriate (not the equivalent of grams per kg as is often the case in *in vitro* assays)?; are the statistics sufficient?; is the documentation of the work recorded in sufficient detail that subsequent work can build from it?; etc.

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It is the quality of the science we need to maintain, not holding researchers to some arbitrary, largely analytical chemistry-based requirements. I would point out the increasing evidence in support of the synergistic activities found in these complex mixtures and the increasing acceptance of the concept of Botanical Drugs/ Phytomedicines, even at the historically conservative US FDA. Our usual single-chemical-entity approach being applied by the pharmaceutical industry is increasingly less productive, as attested by the paucity of new drug approvals in recent years. I think we all recognize that Nature operates via complex signal transduction networks (the "new" Systems Biology), so why is it any surprise that the concept of a Magic Bullet (i.e., THE "active principle" of natural product preparations) may be outmoded in the discovery of new leads for the development of pharmaceuticals, agrochemicals, and other useful materials?

The exploratory work being reported in this Journal holds great value to lead to new treatments for our increasingly prevalent complex disorders for which current approaches are not yielding leads. Indeed, it is my expectation that complex mixtures derived from plants (Botanical Drugs) will be the next wave of "new" and effective therapeutics. We as reviewers need only demand good science in the research methodology.

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