THE American Society of Pharmacognosy News Letter

Volume 18, No. 1

EDITORIAL

You will note from the cover illustration that we are still using line drawings of medicinal and/or economic plants. The response to the call for contributions for illustrations for the cover was not overwhelming, in fact we received only two. Thankfully Dr. Robert Perdue not only provided the line drawing but he also included a contribution on the native use of the plant and the development of it as a source of maytansine. I would encourage other readers to submit the drawings of useful plants and/or microorganisms and if they desire a short discussion of the folklore use and/or development of the isolation of useful phytochemical constituents.

There is still a crying need for input from the membership to contribute to the categories listed below into which the *Newsletter* is divided. Please contribute to any or all.

(1) EDITORIALS - By the Editor, President and selected guest editors. These editorials will hopefully reflect concerns of pharmacognosists which need to be aired and discussed.

(2) COMMENTARY SECTION - To provide a forum for areas of concern for which an editorial is not the proper forum: teaching improvements; suggestions, with discussion, to the Society which can air major concerns; and news and views from the President and Executive Committee to allow dialog with the membership.

(3) LETTERS TO THE EDITOR - To provide a forum for the membership to reflect their concerns with Society policy, to respond to opinions expressed in the Editorial section, or to allow members the chance to provide commentary on subjects that they feel should be aired to the reading audience.

(4) MEETING REPORTS - Brief reports on meetings to provide a synopsis of interesting invited speakers and presented papers that have a bearing on interests of some segment of the membership. These reports will hopefully capture novel developments and new trends surfacing at such meetings, particularly in workshops or invited symposia to which only a limited number of members have access.

(5) ARTICLES OF INTEREST - These are to be short of formal journal papers and should make either informative or amusing reading for pharmacognosists. These could be short technical papers (alerting the membership to, or describing newer techniques) or simply broad interest articles.

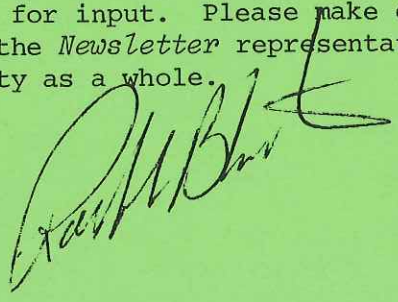
(6) SOCIETY NEWS - A section where decisions of the Executive Committee can be presented, matters dealing with the Society's journal, future meeting plans, calls for papers and the like.

(7) REVIEW ALERTS - Reviews of major review articles that have been published and should serve to aid the membership, particularly if they were published in a language other than English.

(8) NEW EQUIPMENT - A section that will include brief descriptions, prices, manufacturer and pertinent data that will bring to the attention of the membership new equipment that the respondent has found useful in his/her work.

(9) NEWS AND NOTES - This will be very much like the old format and will include; new appointments, promotions, sabbaticals, deaths, new products, grants funded and other personal news, *i.e.* recent and upcoming activities of members.

Please note that with the expanded format, we are extremely dependant on the MEMBERSHIP **(YOU)** for input. Please make every effort to make the *Newsletter* representative of the Society as a whole.



COMMENTARY

Expanded Report of Past President, James E. Robbers. The original was presented at the Annual Business Meeting, July 11, 1980, Faculté de Médecine, Strasbourg.

Since the attendance was sparse at the annual business meeting in Strasbourg, I welcome this opportunity to inform the membership of some of the business that was conducted by the Executive Committee and the appointed Committees on behalf of the Society over the past year (1979-80). My remarks in Strasbourg were brief; however, at this time I would like to elaborate on some of them and give you an expanded version, since there are some important issues facing the Society.

It is fair to say that the Society is prospering. Full memberships have increased by approximately 130 over the last 2 years. The balance in the treasury has remained stable with total assets of $56,000 as of June 24, 1980 compared to $54,850 for June 30, 1979.

The Journal of Natural Products is an endeavor of the Society of which we can continually be proud. In my opinion it is the high caliber of our Journal which is the single most important factor in our dramatic increase in membership. In this regard in keeping with the hard work and dedication that is required of the Editor, the Executive Committee has increased the Editor's honorarium to $3,000. This amount is still meager when compared to what is awarded to other journal editors; however, it does represent a tangible gesture on the part of the Society to show Editor Beal that we appreciate his efforts.

The planning for future meetings is well in hand. We will meet jointly with the Society for Economic Botany in Boston, July 12-17, 1981. A symposium entitled: "Plants and Their Products in the Service of Man" has been arranged and all of the speakers have made firm commitments to participate. The pharmacognosists at the University of Pittsburgh have offered to host the 1982 meeting on August 1 through August 7 at the Seven Springs Mountain Resort just outside Pittsburgh. It appears the local arrangements will be on somewhat the same order as the 1976 Telemark meeting. The Scientific Program Committee for this meeting is tentatively planning a symposium on "Aspects of Biotransformation".

As a result of the discussion at the 197 annual meeting at Purdue concerning screening new members, the Membership Committee has provided a reasonable solution to this problem which will require a change in the Constitution as well as the By-Laws. These changes will be on this year's mail ballot and will represent a fair means of selecting new members while still protecting the integrity of the Society.

Perhaps the most pressing business we dealt with this year concerns fiscal problems associated with the *Journal of Natural Products*. Last year the treasurer of the Society alerted the Executive Committee to the fact that due primarily to inflation the financial picture for the Journal has been slowly eroding over the last few years. In order to appraise the seriousness of the problem and to recommend what steps should be taken to remedy the situation, I appointed an Ad Hoc Committee to Review the Fiscal Problems of the Journal. The Committee, chaired by Lynn Brady, has provided a comprehensive report. Some of the Committee's recommendations have already been instituted by Executive Committee action while others will require membership approval.

A startling figure that surfaced in the Committee's report was that the Society contributed approximately $50 per member to cover the expenses of the Journal for volume-year 1979. Needless to say, if some of this cost is not borne by those who directly benefit, namely the members, the Society will be in dire financial straits; consequently, the Executive Committee recommends a dues increase of $10 to a total of $35 per annum. An amendment to the By-Laws to effect this increase will be on this year's mail ballot and passage of the Amendment will be crucial to the continued financial stability of the Society.

Other measures which have been instituted by the Executive Committee are as follows: 1) Increased non-member (commercial) subscription rates from $40 to $60 domestic and $50 to $70 foreign; 2) Increased airmail distribution charge from $10 to $18

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which more accurately reflects actual cost; 3) Increased reprint charges to twice the actual printing costs; 4) A decrease of alteration charges by the printer, through more careful editorial monitoring of galley proofs; 5) A discontinuance of printing in the Journal of the abstracts of papers presented at the annual meeting; and 6) A recommendation that the Editor establish an annual limitation on the number of pages per volume in order to budget funds more accurately.

In closing I would like to thank my fellow officers and Executive Committee members for the support and cooperation they have provided during my term in office. Most importantly I would like to convey a very special thanks to the many individuals who served on committees this past year. It is important to remind ourselves that these dedicated workers are what keep the wheels of the Society turning.

Dr. David G.I. Kingston (Virginia Polytechnic Institute and State University) has prepared the following Book Reviews and list of Books Received for Review.

HERBAL DRUGS IN INDIAN PHARMACEUTICAL INDUSTRY. S.L. Kapoor and R. Mitra, Natural Botanical Research Institute, Lucknow 226001, India. 1979. 85 pp. 21.5x27.5cm RS 14. (Approx. $4.00)

This volume contains a listing of the herbal ingredients of the pharmaceutical preparations produced by 160 Indian pharmaceutical companies. Also included are indices listing the drugs most commonly used, the botanical equivalents of the common names employed in these listings, the common neames of the botanical names, and the pharmaceutical concerns listed in the publication. In all, some 600 different plants are listed, attesting to the importance of herbal ingredients in Indian medicine. Regrettably, however, there is no listing of the biological activity of any of these plants, so it is not possible to judge the effectiveness of the various ingredients listed.

GUIDE TO BASIC INFORMATION SOURCES IN CHEMISTRY. Arthur Anthony, Science-Engineering Library, University of California, Santa Barbara. Jeffrey Norton Publishers, Inc., distributed by Halsted Press, 605 Third Avenue, New York, NY, 10016. 1979. vii + 219 pp. 14x21.5cm. $14.95.

This useful book summarizes a large amount of information in compact form. The bulk of the book consists of annotated lists of publications under headings such as Bibliographies, Nomenclature, Specialized Data Compilations, Guides to Techniques, etc., with a slightly more extensive treatment of such major subjects as Chemical Abstracts and Beilstein. There are also short chapters on Bibliographic searching by computer (almost out of date before it was written, thanks to rapid advances in this area) and Non-print media. All libraries involved with chemistry will want to have available this handy guide to the riches they contain.

New Journal - CURRENT RESEARCH ON MEDICINAL AND AROMATIC PLANTS. Published quarterly by the Central Institute of Medicinal and Aromatic Plants, 474/6, Sitapur Road, Lucknow 226007, India. Volume I (1979). Subscription rates: Individuals $8.50, institutions $10.00.

The contents of the first issue of this new journal consists of a section devoted to abstracts of work on medicinal and aromatic plants ranging from agronomy through chemistry to processing technology, sections on economic and industrial news, meeting announcements, and new book announcements, and a review article on colchicine and related compounds with 193 references.

Books Received, Jan. 1, 1980 - June 30, 1980.

(1) Biological/Biomedical Applications of Liquid Chromatography. II. Edited by Gerald L. Hawk, Waters Associates, Inc. Marcel Dekker, Inc., 270 Madison Avenue, New York, NY, 10016. 1979. xiii + 504 pp. 16x23.5cm. $45.00. ISBN: 0-8247-6915-5.

(2) Bailey's Industrial Oil and Fat Products. 4th Edition. Volume I. Edited by Daniel Swern, Fels Research Institute and Temple University. Wiley-Interscience, 605 Third Avenue, New York, NY, 10016. 1979. xii + 841 pp. 16x23.5cm. $45.95. ISBN: 0471-83957-4.

(3) Organic Stereochemistry. Henri Kagan, Université de Paris-Sud. Halsted Press, 605 Third Avenue, New York, NY, 10016. 1979. vii + 166 pp. 13.5x21.5cm. $14.95. ISBN: 0470-26725-9.

(4) Studies in Organic Chemistry I. Complex

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Hydrides and Related Reducing Agents in Organic Synthesis. Andor Hajós, Research Institute for Pharmaceutical Chemistry, Budapest. Elsevier Scientific Publishing Company, P.O. Box 211, Amsterdam, The Netherlands, and 52, Vanderbilt Avenue, New York, NY, 10017. 1979. 398 pp. 17x 25cm. $76.00. ISBN: 0-444-99791-1.

(5) Aspects of Cancer Research 1971-1978: Editorials from The Journal of the Natural Cancer Institute. John C. Bailar III, Editor in Chief, National Cancer Institute, Bethesda, MD. NIH Publication No. 79-1863. U.S. Public Health Service, National Cancer Institute, Bethesda, MD, 20205. 1979. 531 pp. 22x28.5cm. $13.00. GPO Stock. No. 017-042-00140-4

(6) Synthetic Aspects of Biologically Active Cyclic Peptides - Gramicidin S and Tyrocidines. N. Izumiya, T. Kato, H. Aoyagi, M. Wake, Laboratory of Biochemistry, Kyushu University, and M. Kondo, Department of Chemistry, Saga University. Halsted Press, John Wiley and Sons, Inc., 605 Third Avenue, New York, NY 10016. 15.5x23cm. 1979. $24.95. ISBN: 470-26863-8.

(7) Rodd's Chemistry of Carbon Compounds. 2nd Edition. Volume IV. Heterocyclic Compounds. Part I. Edited by S. Coffey. Elsevier Scientific Publishing Company, P.O. Box 211, Amsterdam, The Netherlands, and 52 Vanderbilt Avenue, New York, NY 10017. 1980. xviii + 506 pp. 16x23cm. $126.76. ISBN: 0-444-41768-0.

(8) Encyclopedia of Antibiotics, 2nd Edition. John S. Glasby, ICI (Organics) Ltd., Manchester. Wiley-Interscience, John Wiley and Sons, Inc., 605 Third Avenue, New York, 10016. 1979. 467 pp. 25.5x18.5cm. $66.00. ISBN: 0-471-00722-6.

(9) The Biosynthesis of Aromatic Compounds. Ulrich Weiss, National Institutes of Health, Bethesda, MD., and J. Michael Edwards, The University of Connecticut, Storrs. Wiley-Interscience, John Wiley and Sons, Inc., 605 Third Avenue, New York, NY 10016. 1980. viii + 729 pp. 16x23.5cm. $29.50. ISBN: 0-471-926 90-6.

LETTERS TO THE EDITOR

GRADE INFLATION AND ITS POSSIBLE EFFECTS ON STUDENTS

Dear Editor:

At a recent Administrative Council meeting of our College I was shocked to find that the overall grade distribution for the Kentucky College of Pharmacy included an amazing 34% of A grades (A=34%, B=39.2%, C=16.4%, D=2.3%, E=0.2%, other grades=7.3%). Equally disturbing to me was the lack of any visible reaction from my colleagues when I expressed my surprise at these figures.

My first reaction was to use this as an excuse for my "not so outstanding" student evaluations, since the percent of overall A's that I give is approximately one-half of the College average. (I thought I was being generous!!) However, a more serious consequence of this grade inflation hit me later. What about the effect on our students? The not-so-outstanding students that are given A's are led to believe they are doing outstanding work (a completely erroneous conception in my opinion). Even more damaging is the possible effect on the truly outstanding students. Their honor is so diluted that they are cheated out of true recognition. This is somewhat reminiscent of our honors banquet in which half the class receive awards. I suspect this grade inflation is not peculiar to Kentucky but is common to most colleges of pharmacy in the U.S.

Sincerely,
Laurence H. Hurley, Ph.D.
Assoc. Prof. of Med. Chem.
Pharmacognosy

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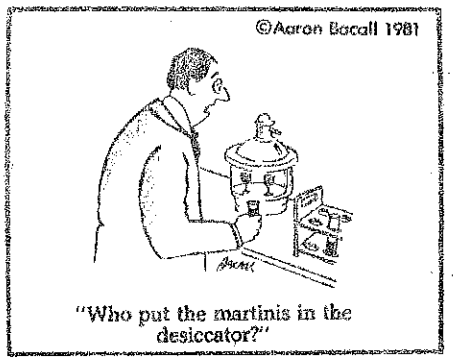

"Who put the martinis in the desiccator?"

MEETING REPORTS

Joint Meeting of the Society for Medicinal Plant Research, the American Society for Pharmacognosy, the Phytochemical Society of Europe and the Association Francaise des Enseignants de Matiére Medicale.

Reporters: Dr. E. Leistner, Münster, FRG
Dr. R.P. Labadie, Utrecht, The Netherlands

From July 6th to 11th the four societies held a joint meeting at the University of Strasbourg. The location for this meeting was well chosen and approximately 600 participants enjoyed not only the scientific program but also the ancient city of Strasbourg and the special kind of food and wine for which the Alsace is famous. The scientific program comprised poster sessions, plenary lectures and a panel discussion. Abstracts of the posters have already been published in Planta Medica, No. 3, Vol. 39 (1980). The 207 posters were grouped together under the following headings: Microbiol. Natural Products, Natural Products of Higher Plants, Biologically Active Natural Products, Ethnopharmacology and Future Production of Medicinal Agents. The plenary lectures of this meeting will be published by the Hippokrates Verlag, P.O. Box 593, D-7000 Stuttgart 1 (West Germany). The title of the book will be "Natural Products as Medicinal Agents". Since most of the scientific program has been or will be published, the reporters will confine themselves to certain aspects of this meeting only.

The first lecture was presented by Dr. G. Ourisson. He talked about compounds isolated from Chinese and Russian drugs some of which were of strange origin, *e.g.* fungi infecting worms and insects or silk worm faeces. Dr. Ourisson presented a range of new natural products. In most cases no relation between these compounds and the therapeutic use of the drugs was evident. This might have been due to the fact that he and his coworker had concentrated on terpenoids and steroids only. Some of the compounds, however, exhibited cytotoxic effects including a terpenoid from Curcuma or a phytosterol causing deregulation of cholesterol synthesis. In conclusion Dr. Ourisson said that he found it more useful to screen a taxonomic group for new compounds with physiological activity rather than investigating ancient drugs. He also said that in almost all organisms, compounds are found which have physiological activity including food plants. Subsequently Dr. T. Salzman from Merck, Sharp and Dohme presented recent results on the chemistry and biology of thienamycin. This remarkable antibiotic belongs to the β-lactam antibiotics. It is stable against β-lactamase and is the most potent and most broadly applicable antibiotic known. It is also active against Pseudomonads. Methods for the synthesis of this compound have been worked out.

Dr. Keller-Schierlein (Zürich) talked about sideramines and developed new ideas about the potential use of these compounds in therapy. Sideramines may be used as compounds carrying therapeutic agents which are normally not taken up by pathogenic microorganisms into these organisms.

Dr. Luckner from Halle (GDR) presented results in which he delineated recent progress in his *Penicillium cyclopium* system. The organism produces alkaloids. It is the aim of Dr. Luckner and his group to discover some of the principles underlying secondary product formation and to investigate the relationship between developmental stage of the organisms, primary and secondary metabolism. *Penicillium cyclopium* is used as a model system. Dr. Luckner pointed out that the production of alkaloids is an aspect of cell differentation and that secondary product formation is a strictly controlled process.

Dr. Milne from the NIH in Bethesda discussed the application of computers for compound identification. He showed that a computer can assist in the identification of a natural product which had previously been described or that a computer can propose structural formulae when it is fed with physical data of structurally known compounds. The application is limited, however, to compounds not exceeding 30 C-atoms, because the amount of possible combinations increases tremendously with every extra C-atom. In the discussion following Dr. Milne's presentation he said that the computer would be accessible also to other scientists wishing to use it.

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The reporters especially enjoyed the lecture given by Dr. D.M.X. Donelly from Dublin. She talked about secondary metabolites and insects. She showed that natural plant products can function as compounds warding off insects or their larvae but that larvae also can accumulate natural plant products after ingestion and use them to ward off their enemies.

Dr. Hostettmann from Zürich discussed the applicability of the droplet counter current chromatography (DCCC), a method which has been developed in Japan. The method seems to give good results although its use is limited to certain combinations of solvents only.

In the subsequent presentation Dr. Cassady from Lafayette presented results on the antileukemic activity of plant extracts and the methods employed to test the fractions obtained from these extracts. Dr. Cassady also discussed structure-activity relationships as did Dr. Potier (Paris) and Dr. Wall in their lectures. The future production of medicinal agents was one of the topics of the meeting which attracted much attention. Dr. Goebel from Würzburg (FRG) and Dr. Fraser from Kalamazoo (USA) delineated the recently developed methods and perspectives for recombination of DNA molecules and the microbial production of animal proteins. The steps to recombinant DNA-products are 1) to identify the desired gene, 2) clone the gene, 3) express the gene and 4) isolate the product. For cloning of the gene *E. coli* is most convenient because it grows fast and a lot of the biochemistry of this organism is known.

The talk presented by Dr. Xiao Peigen (Beijing, China) was interesting in two respects in particular. Firstly, novel Chinese scientific results in the field of drug research, not accessible to everyone, were discussed. Secondly, the approach practiced in China in the search for novel effective drugs from traditionally used ancient Chinese herb medicines is in a sense unique. As a rule the data collected from ancient medical records, folkloristic and clinical practices of traditional medicines are studied and integrated with modern multidisciplinary research. Dr. Xiao Peigen reviewed both biological active principles as such and their therapeutic preparations which are in clinical use now in China.

The last two lectures dealt with plant tissue culture and its potential in the production of medicinal agents. Dr. Petiard from Tours (France) presented an impressive number of different strains isolated from *Catharanthus* tissue cultures. The strains differed in the pigments produced (red, green, yellow) and in the cytostatic activity. The different strains were stable when kept under constant conditions. Dimeric alkaloids were not detectable. The reason for the variability of different strains is unknown. The last lecture of the meeting was presented by Dr. Barz (Münster). Plant cell cultures have often been compared with microbial systems. Dr. Barz pointed out that there are common characteristics of both systems. *e.g.* today plant cells can be plated, selected and cultivated in large tanks like microorganisms, however, as opposed to microorganisms the doubling time of plant cells is worse, the media required are more expensive and plant cells are sensitive to sheer stress in tanks. Plant cell cultures are therefore only useful if specific plant compounds are produced. The potential use of cell cultures is evident from the following observations: 1) Accumulation of compounds in tissue cultures is sometimes higher than in the intact plant; 2) Cell cultures may contain novel compounds; 3) Cell cultures may be useful for isolating enzymes because they are rich in easily extractable protein as compared to the intact plant; 4) The enzymes or cells may be immobilized; and 5) Cell cultures may be used for biotransformations.

There were many more lectures presented at this meeting. The reporters, however, were unable to attend all of them. They have been told that especially the lecture of Dean Tyler created a lot of fun because the speaker took off his coat in front of the audience and dressed up like a hippie before he presented his talk about hallucinogenic drug hoaxes of the American hippies.

Panel discussion: The panel discussion on "Future biological production of medicinal agents", was conducted by Dr. H.G. Floss,

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and Dr. W. Barz, Dr. T. Fraser, Dr. A.W. Alfermann and Dr. V. Petiard being panel members.

The following topics were viewed: 1) uses of existing capabilities of plant cells, 2) uses of existing capabilities of microorganisms, 3) uses of new capabilities of microorganisms or plant cells acquired by gene transfers, 4) impacts of patentability of genetically altered organisms. Concerning the capabilities of plant cells, it was stressed again that cultures of plant cells will in particular be important for the production of new specific plant compounds. It is no use competing with products from microorganisms.

Manipulations with microorganisms through selection of strains will be of particular importance for single step and multi-step conversions of useful molecules. In addition microorganisms might be useful as metabolic models to gain information on metabolic conversions, for example, in the liver. As for the transfer of genes it was expected (Dr. Fraser) to be possible within the foreseeable future to transfer any chromosome fraction of any organism. The question of whether it will be possible to transfer genetic information for a complete biosynthesis was put forward. Dr. Fraser answered that this will be difficult because the genes for a total biosynthesis are spread over different chromosomes. However, he hoped this would be possible in a similar manner as in the case of the biosynthesis of ovalbumin, which proceeds by recombination of relevant chromosome fractions. Dr. Fraser also confirmed that to his view it will be possible to synthesize proteins *in vitro*. He explained that "gene cloning" and "gene libraries" are existing practices and realities, and are cheap. The problem is how to select a specific procedure or conversion out of these gene clones. However, this development will be important in the future for the manufacture of vaccines, and useful and new proteins. The panel discussion was closed with the statement that patented microorganisms will be available for university researchers, which is regarded as a positive development.

The meeting can be considered a success also because of the social program. The reporters especially enjoyed the alsation buffet in the Bishop's Mint in Molsheim.

Additional notes on meeting in Strasbourg:

Reporter: Dr. David G.I. Kingston, Virginia Polytechnic Institute and State University

Tuesday, July 8 - "Natural Products of Higher Plants": The lectures on the second day of the conference were centered on the theme of "Natural Products of Higher Plants", although there was some inevitable overlap with the theme of the third day, "Biologically Active Natural Products", and the first two lectures dealt more with techniques than with natural products as such. In the opening lecture, Dr. G.W.A. Milne (N.I.H., Bethesda, MD, USA), discussed recent advances in the use of computers for compound identification. He briefly described methods applicable to previously characterized compounds, and then went on to discuss the more useful, but much more difficult, task of using the computer to make structural conclusions when the compound is not in the library. Initial approaches to this problem include the Cornell STIRS system and a pattern recognition program developed at NIH. Finally, a number of methods based on exhaustive generation of all structures corresponding to a given molecular formula were described. Algorithms now exist for this process, and the number of possible structures for even simple molecules is surprisingly high - over 200 for C_6H_6, for example, over 300 million for a moderately complex molecule such as $C_{15}H_{26}O$. The addition of constraints derived from spectroscopic data rapidly reduces this number, however, so that for example a relatively small number of fairly simple conclusion from spectroscopic data reduces the number of possibilities to manageable proportions, at least for molecules smaller than C_{20}. Two conclusions that follow from this talk are that the human brain has a truly remarkable ability to compete with the computer, and that exhaustive generation of structures may not in fact be the best way to solve the structure elucidation problem. It is also noteworthy that while extensive use is made of IR, PMR, CMR, and MS, little use is made of UV spectroscopy in this approach, because of the relative lack of documentation in this area. Perhaps this is a challenge that will be taken up by some reader of this report?

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In the second lecture Dr. K. Hostettmann (ETH Zürich, Switzerland) gave a lucid account of the principles and practice of droplet counter-current chromatography and its application to the isolation of natural products. Because this subject has recently been reviewed by Dr. Hostettmann (Planta Medica 39, 1-18 (1980), no further discussion of the lecture is necessary except to point out that while the technique appears to be a valuable complement to the more classical chromatographic procedures, it is unlikely to displace these procedures.

In the concluding paper of the morning session, Dr. D.M.X. Donnelly (University College Dublin, Ireland) gave us a fascinating glimpse into the world of the ecological interactions between plants and insects. She discussed two problems in detail: the relationship between the Pine sawfly (*Neodiprion sertifer*) and the *Pinus* species on which it feeds, and the compounds produced by the fungus *Fomes annosus*. In the first case it has been found that resin acids in the leaves serve as antifeedants; since new growth has a higher proportion of these acids than old growth, the new growth is not attacked by the insect. The insect is nevertheless very destructive, since it uses compounds from the twigs in its defense and thus causes considerable damage to the tree. Dr. Donnelly described the isolation of various compounds from *P. contorta*, and discussed their possible roles as antifeedants. In the second part of her talk, dealing with the active compounds of *F. annosus*, she showed that the more active toxic compound is in fact fomannoxin, and not fomannosin. The absolute stereochemistry of this compound was elucidated and its biosynthesis discussed.

The afternoon session was devoted to natural products with anticancer activity. Dr. O. Potier (CNRS, Gif/Yvette, France) gave a comprehensive account of the antitumor alkaloids of the Madagascan periwinkle, including the history of the plant itself (*Catharanthus roseus*) and of the discovery of the antitumor alkaloids vinblastine and viscristine. He described in detail his elegant work on the synthesis of anhydro vinblastine by a coupling involving a modified Polonovskii reaction, and described some more recent work in which anhydro vinblastine could be converted to either leurosidine or vinblastine by hydrogenation followed by a second Polonovskii reaction to yield an isomeric anhydro compound, which could then be converted by oxidation-reduction to either of the desired bisindole alkaloids. He spectulated that the "natural dimer" might even be anhydro vinblastine, which could then be oxidized to vinblastine and other products. In conclusion, he discussed the action of vinblastine in inhibiting mitosis, and described the fairly simple test that is used at Gif to assay samples for antimitotic activity.

Dr. J.M. Cassady (Purdue University, West Lafayette, Indiana, USA) described some recent advances in the isolation and structure elucidation of natural products with anticancer activity from higher plants. A large number of sesquiterpene lactones are known to have cytotoxic activity, and some have modest *in vivo* activity. Three of the most promising compounds, elephantopin, eriofertin and eriofertopin have been selected for testing in the NIC animal tumor panel, and it is encouraging to note that eriofertopin shows significant activity in the B16 tumor system. New compounds described included some novel germacranolide sesquiterpene lactones from *Piptocarpha chontalensis*, some compounds related to the physalins from *Capsicum fuscoviolaceum*, an anthrone from *Psorospermum febrifugum*, and three new diterpenoid dilactones from *Podocarpus milanjianus*. Some structure activity relationships in the xanthone field were also discussed in connection with the compound psorospermin; it was concluded that the molecules require an active functionality (epoxide, double bond, etc.) located in a fairly precise manner with respect to the xanthone ring system.

The concluding paper of the day was given by Dr. M.E. Wall (Research Triangle Institute, North Carolina, USA), who described some structure-activity relationships of plant antitumor agents related to camptothecin and the quassinoids. The work clearly involved a large amount of synthetic chemistry, and in the camptothecin area it yielded an improved route to hydroxycamptothecin, which is a better drug than campthothecin, and occurs only in trace amounts in *C. acuminata*.

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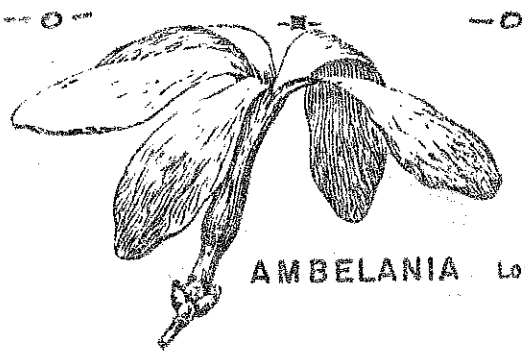
In addition, this work showed that there are two basic requirements for activity - the planar aromatic ring system required for binding to DNA, and the acylating lactone function. In the quassinoid area, which was reviewed more briefly, a number of compounds were tested and some structure-activity correlations were made - for example, the α,β-unsaturated keto group and all of the hydroxyl functions were shown to be necessary for activity. It is encouraging that bruceantin, the most promising member of this group of compounds, is entering clinical trial in the near future.

Joint Meeting of the American Society of Plant Physiology and the Plant Society of North America

A joint meeting of the American Society of Plant Physiology and the Plant Society of North America held in Pullman, Washington attracted nearly 1,200 whose interests in plant science superceded their fears of another eruption from Mount St. Helens. The meeting, which was held from August 3-7, 1980, was highlighted by special symposia on cell recognition, and the molecular biology of chloroplasts. Special workshops were also held in the areas of glycoproteina, molecular biology of the chloroplast, hormone action, stress physiology, and high energy constituents of plants. Over 914 papers and posters were presented. Abstracts of the presentations can be found in Voleme 65, number 6, June, 1980, of Plant Physiology. A special session on the Mount St. Helen's eruption and its aftermath attracted an audience of 1,000. Steve Harris, author of "Fire and Ice, The Story of the Cascade Volcanos" was the featured speaker. A special video film from Seattle highlighted his talk.

Reporter: Dr. Gary Meadows, Washington State University, Pullman, Washington.



AMBELANIA Lopezii Woods

ARTICLES OF INTEREST

Maytenus Buchananii, SOURCE OF MAYTANSINE
ROBERT E. PERDUE, JR., PH.D., CHIEF, PLANT TAXONOMY LABORATORY, BELTSVILLE AGRICULTURAL RESEARCH CENTER, BELTSVILLE, MD 20705.

Isolation of maytansine by the late S. Morris Kupschan was prompted by antitumor activity of crude extracts of *Maytenus ovatus (Celastraceae)* collected in Ethiopia by US Department of Agriculture Botanist F. G. Meyer in November, 1961 and January, 1962. The extracts were active against the KB Cell Culture assay, but inactive *in vivo*.

According to the current concept of Norman Robson (British Museum), authority on taxonomy of African Celastraceae, the extracts represented two closely related species, *M. obscura* and *M. serrata*. True *M. ovatus* is native to India. These plants are known to the Galla people of Ethiopia as "atat" because the wood crackles when burned: "atat-tat-tat."

Maytansine was concentrated in the fruit, probably in the seed. Kupchan's isolation of the compound required a large quantity of fruit. Yield of maytansine was extremely low, about 0.25ppm. To obtain fruit for isolation of sufficient maytansine for preclinical and clinical evaluation would have been a formidable and probably impossible task. While *M. obscura* and *M. serrata* are fairly common in Ethiopia and can produce heavy yields, fruits are small and light, crops are erratic, and seeds are commonly destroyed by insects.

By the early 1970's it became evident that plants in several families were unusually good sources of antitumor activity. The capacity for fractionation to isolate active agents was far greater than the number of active plants available. The USDA, with the concurrence of the National Cancer Institute, subsequently initiated a "Families of Special Interest" (FOSI) Program. Plants in selected families would be collected in substantial amounts and these samples would be treated like any other "confirmed active." That is, preliminary extraction and screening would be bypassed; fractionation would be initiated based on presumed activity. The Celastraceae were included among the FOSI families. We hoped this would lead to new antitumor agents,

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and better sources of others. The philosophy was vindicated by the discovery of triptolide and tripdiolide, also isolated by Kupchan, from *Tripterygium wilfordii (Celastraceae)*, and by the discovery of far superior sources of maytansine.

The FOSI philosophy prompted the collection of *Maytenus buchananii* in the Shimba Hills of southeastern Kenya near the Indian Ocean. This is a rambling, scadent, twisted, vine-like shrub, known to the local Digo tribe as "mudziadzyah." The stem wood proved to be a good source of maytansine, more than three times better than fruit of the Ethiopian species. The FOSI Program thus set the stage for procurement of an adequate supply of raw material when the NCI decided to develop maytansine as a potential anticancer drug.

Judging from specimens in the East African Herbarium and Kew Herbarium, the plant is widely distributed in tropical Africa but not common at any one site. When 10 tons of *M. buchananii* were needed in 1972, we logically turned to the Shimba Hills. Forwarned of our need, the Kenya Forest Department's Shimba Hills Station assigned Ali Bandari, a Digo knowledgeable about local plants, to a reconnaissance. By the time I arrived, Bandari had located the plant in three areas. It was abundant in none. It was clearly evident, however, that the usual habitat was along forest margins. The plant required light but also other vegetation for support. It would not be in deep forests. It was not likely to be abundant in sunny open areas except where it persisted after forest was removed. The ideal area most likely would be an open forest, from which larger trees had been removed for timber, yet one which was protected so the plant would not be destroyed by fire-wood cutters. Study of a topographic map of the area revealed an isolated forest of about 100 acres that seemed ideal. *M. buchananii* was found there in abundance.

Collecting such a large quantity of one plant requires a large labor crew which cannot be completely depended upon to avoid contamination with similar plants. However, *M. buchananii* stems are distinct and quite unlike other species in this forest. The inner bark is red, with a thin bright-yellow layer, just under the outer gray surface. A crew of 50 local laborers was recruited; 10 tons of stems were assembled in 4 days.

This on-the-ground experience provided a good concept of the type of area where *M. buchananii* would be most abundant. In 1976, when an additional supply was needed, reconnaissance with a light aircraft identified other areas where the plant is common. While it could not be observed from the air, a keen observer could select areas where the plant was likely to be present. Its presence was later confirmed by ground reconnaissance. An additional 15 tons were collected in 1976.

To assure future supplies, the conservation-minded Kenya Forest Department certified *M. buchananii* as a protected species.

M. buchananii is readily adapted to cultivation in the tropics. It is easily propagated from seed or cuttings and has been grown at the Shimba Hills Forest Station and in a nursery at Bamburi near Mombassa, Kenya.

The FOSI program ultimately led to sources of maytansine superior to *M. buchananii*. These are *Putterlickia verrucosa* of South Africa and *Maytenus rothiana* of Southern India.

The folklore record of *Maytenus* in cancer treatment....? These quotations are from an account of an interview with a Kenya herbalist, National Magazine, Nairobi, July 28, 1972, in reference to *M. buchananii*: "The American scientist hasn't discovered anything. ...I have been using this plant for ages and I knew right from the beginning this plant could cure cancer." ..."How did he start and where did he learn his herbal skill?" "I started way back in 1939 when there was an outbreak of chicken disease...in Kikuyuland." "He went into the bush and gathered some herbs, mixed them with roots of some other trees and fed the medicine to his chickens." "They were cured almost immediately."

This amusing anecdote aside, another species of *Maytenus* has been used in southern Africa for treating cancer. The phloem of *M. heterophylla*, another source of maytansine, was a major component of a mixture recommended for this purpose, the "Davis herbal remedy." This "remedy" also includes *Sansevieria hyacinthoides* and *Scutia myrtina*. An extract of this *Sansevieria* was assayed

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in 1976 and was active against KB Cell Culture. An extract of *Scutia myrtina* was active against P388 leukemia (*in vivo*) in 1977. It may be just a remarkable coincidence but *Scutia* is a genus of Rhamnaceae, and antitumor maytansinoids have been isolated from another plant in the same family, the American *Colubrina texensis*.

There is no questions that the Davis herbal remedy is a valid folk record of the use of *Maytensus* in cancer treatment. It is clearly not an effort by an herbalist to capitalize on the discovery of maytansine. The remedy is said to have been first used in South Africa in 1945 for treatment of "carcinoma and sarcoma." Although I cannot vouch for its use at that early date there is a record of its use as early as October, 1969. At that time the identity of all components was not known but the 1969 record shows the remedy did indeed include *Maytenus buchanophylla*. Kupchan's isolation of maytansine from *M. ovatus* was published in 1972.

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SOCIETY NEWS

The research group at the University of Illinois, Department of Pharmacognosy and Pharmacology is again making available plants from their cancer contract which are of no further interest. If you are interested in acquiring any of the material please contact Dr. Geoggrey A. Cordell, College of Pharmacy, Department of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Chicago, PO Box 6998, Chicago, IL 60680.

Also, Drs. A. Douglas Kinghorn, Djaja D. Soejarto, Philip J. Medon of the department and Dr. S.K. Kamath of the Department of Medical Dietetics have been awarded a contract from the NIH of Dental Research ($318,208 over 3 years) for "Studies to Identify, Isolate, Develop and Test Naturally Occurring Noncarcinogen Sweeteners That May Be Used As Dietary Sucrose Substitutes.

1981 Annual Meeting: Joint Meeting of THE AMERICAN SOCIETY OF PHARMACOGNOSY AND THE SOCIETY FOR ECONOMIC BOTANY

The meeting will be held at the Massachusetts College of Pharmacy in Boston, MA from July 12th through July 17, 1981. The scientific program will consist of a symposium and contributed papers. A Symposium entitled, PLANTS AND THEIR PRODUCTS IN THE SERVICE OF MAN, has been arranged to provide an overview of some useful medicinal and economic products which can be obtained from plants. Plenary lectures will be as follows:

1) Herbaria as Resource Centers, Peter Ashton, Harvard University

2) Medicinal Plants in Third World Countries, Edward Ayensu, Smithsonian Institute

3) Plants, Insects and Man - Their Interrelationships, Martin Jacobson, USDA, Beltsville

4) Plants as Renewable Resources, Lambertus Princen, USDA, Peoria

5) Current Status of the NCI Plant and Animal Product Program, Mathew Suffness, National Cancer Institute

6) New Techniques in the Separation and Identification of Natural Products, Koji Nakanishi, Columbia University

7) Chemistry of Alkaloids of Pharmacologic Significance, Maurice Shamma, Pennsylvania State University

8) Biosynthesis of Natural Products - An Overview of Current Problems, Richard Hutchinson, University of Wisconsin, Steven Gould, University of Connecticut

9) New Areas for Plant Product Research, Norman Farnsworth, University of Illinois

For information concerning the local arrangements, contact Dr. Robert F. Raffauf, College of Pharmacy, Northeastern University, Boston, MA 02115. Information concerning the scientific program is available from Dr. Geoffrey A. Cordell, College of Pharmacy, University of Illinois, PO Box 6998, Chicago, IL 60680.

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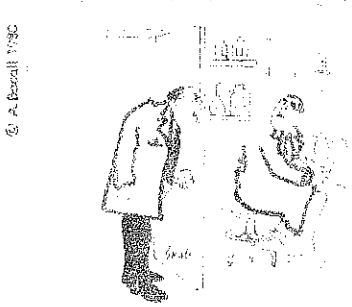

"Let's hear more Eurekas and less Damn-its from this lab!"

THE AMERICAN SOCIETY OF PHARMACOGNOSY

The American Society of Pharmacognosy was founded in 1959 to promote the growth and development of pharmacognosy, to provide the opportunity for association among the workers in that science and in related sciences, to provide opportunities for presentation of research achievements, and to promote the publication of meritorious research.

Active membership in the Society is open to scientists of all nations with an interest in pharmacognosy and natural products chemistry. Active members receive the *Journal of Natural Products* and the *ASP Newsletter*; associate members receive the *ASP Newsletter*. The current dues structure is as follows. Members residing in U.S.A., Canada, and Mexico: active membership, $25.00; symposium contribution (voluntary), $3.00. Members residing in other countries: active membership, $25.00; symposium contribution (voluntary) $3.00; airmail delivery *Journal of Natural Products*, $10.00 (if this airmail delivery supplement is not paid, members residing outside U.S.A., Canada and Mexico will receive *Journal of Natural Products* via sea-mail). Associate membership (students): $2.00. Honorary members are selected by the Executive Committee on the basis of meritorious service to pharmacognosy. Any person or organization may become a patron by contributing $100, a sustaining member by contributing $500, or a benefactor by contributing $1,000 for the support of the Society. Such membership is renewable annually.

All correspondence concerning active or associate membership should be addressed to the Vice President. Inquiries regarding patron membership and notice of address change should be sent to the Treasurer.

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COVER ILLUSTRATION: *Maytenus buchananii* (LOES.) WILCZEK COURTESY: U.S. DEPT. OF AGRICULTURE