

J. E. Robbers

THE American

Society of Pharmacognosy

News Letter



Volume 16, No. 1

EDITORIAL

THE PANGS OF BIRTH ARE DIFFICULT

With this issue of the Newsletter (Vol. 16, No. 1) we hope to continue the new format, but, as with any new enterprise, birthing of a new offspring is not as easy as its conception. For a myriad of reasons Volume 15 consisted of only one issue. With this issue of the Newsletter it is hoped that the normal three times yearly publication will commence (April, August and December).

I am greatly heartened by the responses of our members who have agreed to serve as correspondents and am thankful to those of you who have written for news and comments.

I would solicit any input into any of these areas that our members would care to make. In this issue the Article of Interest by Professor Farnsworth particularly when read in conjunction with the Commentary by Professor Floss, from the last issue, should generate some deep thought. If you wish to comment in Letters to the Editor, please feel free to do so.

Listed below you will find the categories into which the Newsletter will be divided.

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) BOOK REVIEWS - Very brief reviews of major books published that may be of interest.

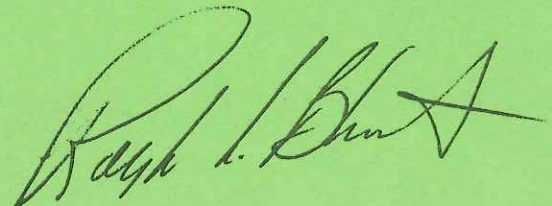
7) SOCIETY NEWS - A section where decisions of the Executive Committee can be presented, matters dealing with the Society's journal, future meeting plans, calls for papers and the like.

8) 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.

9) 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.

10) NEWS AND NOTES - This will be very much like the current format and will include: new appointments, promotions, sabbaticals, deaths, new products, grants funded and other personnel news, i.e. recent and upcoming activities of members.

It is hoped that the Newsletter will benefit by these changes. You will note that with the expanded format we are still very much dependent on the membership for input, I am looking forward to your comments, pro and con on these changes.



LETTERS TO THE EDITOR

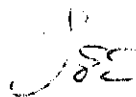
A NOTE FROM THE TREASURER, LEE C. SCHRAMM:

"I would like to thank the membership for their confidence in me as demonstrated by the recent election. I shall continue to work for the best interests of the Society, and am presently in the process of transferring the membership list to computer storage. Hopefully, this will be a help to many and will eliminate some of the past problems of missed issues of Lloydia (now the Journal of Natural Products), and the Newsletter. To make the system work, I must be informed of changes of address as soon as possible.

To our members residing outside the US, Canada or Mexico, I must remind you that, unfortunately, we cannot guarantee shipment of the Journal via surface mail. The postal system of various countries and the shipment of mail by boat involves so many variables that surface shipment is a risky situation. We have had very little problem with deliveries in Europe and Japan, but air mail is the safest way to insure timely receipt of the Journal.

One problem that has plagued previous treasurers, and causes headaches for the present treasurer, is associated with the collection of foreign checks. If the check you send to the treasurer is not collectible at a bank which is a member of the Federal Reserve System (USA), a charge is made by our bank for the collection of funds. The charge is in addition to any charges associated with collection of non-US currency. If you are in doubt as to the collectability of the check you send, ask your banker. To give two specific examples, all Eurocheques and checks on personal accounts in Canadian Banks require the payment of a collection charge. A recent Eurocheque that I received was written for US\$ 38. The collection charges amounted to US\$ 8.36, over 32% of the original amount! Unfortunately, the Society cannot stand losses like that for long. I would urge all the members living outside of the US to make certain that the funds sent to me are collectible with no added charges. Items that must be sent for collection will be returned to the remitter.

Sincerely,



TO THE EDITOR ASP NEWSLETTER:

Dear Ralph:

I would appreciate it if you could include the following statements in the Newsletter:

Books Received. Beginning with the January-February 1979 issue, the Journal of Natural Products (Lloydia) will be publishing book reviews. The book review editor is Dr. David G.I. Kingston, Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061. The books listed below have been received for review, and reviews of many of them will appear in the Journal of Natural Products during the next year. Books marked with an asterisk (*) have not yet been assigned to reviewers: any member of the Society who wishes to review one of these books should contact David Kingston.

1. WALTER H. LEWIS and MEMORY P.F. ELVIN-LEWIS. "Medical Botany, Plants Affecting Man's Health" Wiley-Interscience, John Wiley and Sons, Inc., 605 Third Ave., New York, N.Y., 10016. 1977. xv + 515 pp. \$27.50.
2. W.W. SIMONS, ed. "The Sadtler Handbook of Infrared Spectra." Sadtler Research Laboratories, Inc., Philadelphia, Pa. 1978. vi + 1089 pp. \$150.00.
3. J.F.K. HUBER, ed. "Instrumentation for High-Performance Liquid Chromatography." Elsevier Scientific Publishing Company, 52 Vanderbilt Avenue, New York, N.Y., 10017. 1978. xii + 204 pp. \$34.75.
4. MARVIN J. WEINSTEIN and GERALD H. WAGMAN, "Antibiotics, Isolation, Separation, and Purification." Elsevier Scientific Publishing Company, 52 Vanderbilt Avenue, New York, N.Y., 10017. 1978. x + 752 pp. \$84.75
- *5. S. TUCEK, "Acetylcholine Synthesis in Neurons", Chapman and Hall Ltd., 11 New Fetter Lane, London EC4P 4EE (distributed in the U.S.A. by Halsted Press, a Division of John Wiley and Sons, Inc., New York). 1978. xiii + 259 pp. \$37.50.
6. ERIC REID, ed. "Blood Drugs and Other Analytical Challenges." Ellis Horwood, Ltd., 1 Cooper St., Chichester, England; (Distributed in the U.S.A. by Halsted Press, a Division of John Wiley and Sons, Inc., New York). 1978. xi + 355 pp. \$47.50.

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LETTERS (Continued from previous page)

7. ICHIRO CHIBATA, ed. "Immobilized Enzymes. Research and Development." A Halsted Press Book, John Wiley and Sons, Inc., New York. 1978. viii + 284 pp. \$35.00.

* 8. J. VESELY, D. WEISS, and K. STULIK. "Analysis with Ion-Selective Electrodes." Ellis Horwood, Ltd., 1 Cooper St., Chichester, England; (distributed in the U.S.A. by Halsted Press, a division of John Wiley and Sons, Inc., New York). 1978. 245 pp. \$40.00.

9. J.T. BAKER and V. MURPHY. "Handbook of Marine Science. Compounds from Marine Organisms. Volume I." CRC Press, Inc., 18901 Cranwood Parkway, Cleveland, Ohio 44128. 1976. 226 pp. \$36.50.

10. HAROLD A. HANSEN. "The Witch's Garden" Unity Press-Michael Kesend, Santa Cruz, CA 95060. 1978. 129 pp. \$4.95.

11. JOSEPH C. TOUCHSTONE and MURRELL F. DOBBINS. "Practice of Thin Layer Chromatography" Wiley-Interscience, New York, N.Y. 1978. xxiii + 38 pp. \$21.50.

12. EDWARD S. PERRY and ARNOLD WEISSBERGER, eds. "Separation and Purification" 3rd edition. Volume XII in "Techniques of Chemistry" (ed. A. Weissberger) Wiley-Interscience, New York, N.Y. 1978. x + 438 pp. \$30.00.

13. R.O.C. NORMAN. "Principles of Organic Synthesis" Second edition. Halsted Press, a division of John Wiley and Sons, Inc., New York, N.Y. 1978. xiii + 800 pp. \$19.95.

14. GEORGE R. PETTIT and GORDON M. CRAGG. "Biosynthetic Products for Cancer Chemotherapy" Volume 2. Plenum Press, New York, N.Y. 1978. ix + 150 pp. \$29.50.

15. W. KLYNE and J. BUCKINGHAM. "Atlas of Stereochemistry" Volumes 1 and 2. Oxford University Press, Inc., New York, N.Y. 1978. Vol. 1, xix + 236 pp; Vol. 2, xi + 241 pp. 21.5 x 30.5 cm \$49.50 each volume.

16. EDWARD S. AYENSU. "Medicinal Plants of West Africa" Reference Publications, Inc., Box 344, 218 St. Clair River Drive, Algonac, MI. 48001. 1978. 330 pp. 15.5 x 23.5 cm \$29.95.

17. R.J. HAMILTON and P.A. SEWELL. Liverpool Polytechnic, England, "Introduction to High Performance Liquid Chromatography" Halsted Press, a division of John Wiley and Sons, Inc., New York, N.Y. 1977. xii + 183 pp. 16 x 24 cm \$20.00.

18. P.G. SAMMES, ed., "Topics in Antibiotic Chemistry. Volume 2", Halsted Press, a division of John Wiley and Sons, Inc., 605 Third Avenue, New York, N.Y. 10016. 1978. 283 pp. 15.5 x 23.5 cm \$42.50.

19. J.F. MORTON, "Major Medicinal Plants. Botany, Culture, and Uses." Charles C Thomas, Publisher, 301-327 East Lawrence Avenue, Springfield, Illinois, 62717. 1977. xix + 431 pp. 17.5 x 25.5 cm \$57.00.

20. G.L. HAZELBAUER, ed. "Taxis and Behavior. Elementary Sensory Systems in Biology" (Receptors and Recognition, Series B, Volume 5). Halsted Press, John Wiley and Sons, Inc., 605 Third Avenue, New York, N.Y. 10016. 1979. x + 341 pp. 16 x 24 cm \$45.00.

21. F. BIANCHINI and F. CORBETTA. "Health Plants of the World" Newsweek Books, Inc., 444 Madison Avenue, New York, N.Y. 10022. 1977. 242 pp. 11 x 30 cm \$19.95.

22. F. KORTE and M. GOTO, editors, "Methodicum Chemicum. Volume 11 Natural Compounds Part 1. Nucleic Acids, Proteins, and Carbohydrates" Academic Press, Inc., 111 Fifth Avenue, New York, N.Y. 10003. 1977. viii + 231 pp. 19.5 x 27.5 cm \$39.50.

23. F. KORTE and M. GOTO, editors, "Methodicum Chemicum Volume 11. Natural Compounds. Part 2. Antibiotics, Vitamins, and Hormones." Academic Press, Inc., 111 Fifth Avenue, New York, N.Y. 10003. 1977. ix + 304 pp. 19.5 x 27.5 cm \$49.50.

24. F. KORTE and M. GOTO, editors, "Methodicum Chemicum Volume 11. Natural Compounds. Part 3. Steroids, Terpenes, and Alkaloids." Academic Press, Inc., 111 Fifth Avenue, New York, N.Y. 10003. 1978. viii + 244 pp. 19.5 x 27.5 cm \$49.50.

25. W.A. REMERS. "The Chemistry of Antitumor Antibiotics" Wiley-Interscience, John Wiley and Sons, Inc., 605 Third Avenue, New York, N.Y. 10016. 1979. viii + 289 pp. 16 x 23.5 cm \$29.00.

26. A. PRYDE and M.T. GILBERT. "Applications of High Performance Liquid Chromatography." Halsted Press, John Wiley and Sons, Inc., 605 Third Avenue, New York, N.Y. 10016. 1979. xii + 244 pp. 16 x 24 cm \$25.00

*27. M.A. MEHLMAN, R.E. SHAPIRO, and H. BLUMEN-THAL. "New Concepts in Safety Evaluation." Halsted Press, John Wiley and Sons, Inc., 605 Third Avenue, New York, N.Y. 10016. 1979. xi + 191 pp. 16 x 23.5 cm \$24.50.

Dr. David G. I. Kingston
Professor of Chemistry

ARTICLE OF INTEREST

THE FOLLOWING THOUGHT PROVOKING ARTICLE REPRESENTS THE TEXT OF THE PRESENTATION BY DR. NORMAN R. FARNSWORTH, ON RECEIPT OF AN HONORARY DOCTORATE IN PARIS IN DECEMBER.

THE PRESENT AND FUTURE OF PHARMACOGNOSY - Norman R. Farnsworth, Ph.D., University of Illinois, at the Medical Center Chicago, Ill. 60680

Half way across the Atlantic Ocean three days ago on Air France Flight 70, an announcement was made over the loudspeaker "This is your captain speaking. I have some good news and I have some bad news. The good news is that we have a favorable tailwind, and our arrival time in Paris is now scheduled at 8:00 a.m., one hour ahead of schedule." Loud cheers arose from virtually all of the 325 sleepy passengers. The captain continued by saying "The bad news is that we do not have enough fuel to reach Paris."

Even as the captain of Air France flight 70 brought good and bad news to his passengers, so shall I, bring you good and bad news.

THE PAST AND PRESENT - All is not well with Pharmacognosy in the United States. Undoubtedly most of you already know this, and you may also feel that the same situation exists here in France. There are undoubtedly some among you who will cheer over this news. On the other hand, if you are an audience of true scholars, which I suspect is the case, you may share my concern. Before going further, I shall point out that although things are not well with Pharmacognosy, they are worse for Medicinal or Pharmaceutical Chemistry. If I am any judge of the future, most of the basic sciences that have been the foundation of pharmaceutical education for two centuries, are destined for deemphasis in the near future.

It is hoped that my remarks and comments will serve to answer the obvious question going through your mind, "what is the reason for this deemphasis in some science areas of the pharmaceutical curriculum in the United States?"

Twenty years ago, every College of Pharmacy in the United States was required to teach a course entitled "Pharmacognosy", and most of the 65 or so Colleges had a Department of Pharmacognosy with one or two trained faculty

members responsible for teaching this subject. At the present time, in 1978, there are 71 accredited Colleges of Pharmacy. Of these, only about 14 have Departments of Pharmacognosy, or Pharmacognosy combined with either Pharmacology or Medicinal Chemistry. Pharmacognosy, as an identifiable subject, is now a required course for students in less than 15 Colleges of Pharmacy (*ca* 25 per cent). Twenty of the 71 Colleges of Pharmacy have approved Ph.D. programs in Pharmacognosy, but only nine of these are productive. Some have not produced a Ph.D. graduate in over 30 years. The decline of pharmacognosy and pharmacognosists has been alarmingly rapid. For example, in 1971 (1) there were 116 academic pharmacognosy faculty positions in 66 of the 71 Colleges of Pharmacy. Seven years later, in 1978, there are only 77 academic pharmacognosy faculty positions in 42 of the 71 colleges.

Speaking in modern day pharmaceutical terminology, and based on a two-compartment pharmacokinetic model, Pharmacognosy appears to have a predictable half-life of about one year in the United States, and a final half-life of no more than five or six years. Stated more simply, about 90 per cent of the Pharmacognosy courses being taught at present in the United States, will cease to exist before the year 1983, and most likely about 95 per cent of those currently in existence, will disappear before the year 1987.

Even though it is theoretically possible to prevent this predictable death of pharmacognosy, by the simple application of pharmacokinetic principles, it is my personal opinion that in practical terms, we have waited too long to administer the antidote, at least in the United States.

It is not with great joy that I stand before you and make these statements. Indeed, it is ironic that you have selected a person to be the recipient of the highest academic honor, who represents a scientific discipline that is destined for extinction in the United States in the predictable near future. However, you may recall that I indicated that the "bad" news would come first. There will eventually be "good" news, but I should like to first present some historical facts that have led to the decline of Pharmacognosy. The reason for this, is that I am personally convinced, that the future of Pharmacognosy

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has never been brighter, in fact, I would even say exciting. It is unfortunate that in the United States this discipline is now so weak, that recovery to join in the reaping of the harvest, cannot be expected.

Although I am sure that you are fully aware that the symptoms of this decline of Pharmacognosy are clearly evident here in France, indeed, throughout Europe; nevertheless, I believe that recovery here is still distinctly possible. It is my hope that by briefly relating the events that have led to the demise of Pharmacognosy in the United States, you may be better prepared to cope with this same problem here in France.

Since I have related this problem to drug metabolism, I should like to remind you that there are means available to increase the half-life of a drug, and hence to extend its duration of action, or even its existence. So also are there ways to increase the half-life of a scientific discipline such as Pharmacognosy, and my intent is to conclude this lecture by presenting these means.

We all know that Pharmacognosy is a science unique to Pharmacy, and that no two people define this science in the same way. For the past 20 years, most pharmacognosists have argued that courses in pharmacognosy were necessary on the grounds that 25 per cent of all useful drugs in the United States are still derived from plants. Any discipline arguing relevance based primarily on the origin of drugs, i.e. organic vs. inorganic; natural vs. synthetic, is on weak grounds. Administrators and colleagues have not been impressed with such arguments, and being a relatively small force in terms of voting numbers, pharmacognosy has lost virtually all of its battles to exist.

The term Pharmacognosy was introduced in the year 1815 by Seydler, and at that time all drug knowledge was considered within this discipline. Fifty years later, Schleiden discovered that various types of sarsaparilla root could be differentiated by microscopic analysis. At this point, Pharmacognosy began its specialization into a descriptive botanical science. It did not change significantly for the next 85 years. In the United States, botanical emphasis in Pharmacognosy started in the early 1900's out of a need to establish the quality of, and adulterants in,

plant and animal drugs. Initially, the pharmacognosist engaged in his pursuits with the aid of his five senses, i.e. sight, sound, odor, taste and touch; reinforced at times with the microscope and a few chemical color reactions. Almost without exception, his academic training and education was in the field of Botany. In the early 1900's this type of individual was functioning adequately to meet the demands of society and science with respect to problem-solving requiring these types of skills.

As science advanced, particularly the areas of organic chemistry, biochemistry and pharmacology, the pharmacognosist either did not, or could not, interrelate his discipline with these subjects, which eventually became entrenched solidly as the foundation of the modern Pharmacy curriculum. The botanically-oriented science of Pharmacognosy became stagnant. Up to about the year 1940, all of the useful crude drugs had been thoroughly studied botanically and histologically; new crude drugs of plant and animal origin were destined to be discovered at the rate of only one every two or three decades. The skills and talents of the pharmacognosist of that era were no longer required, and his discipline began to decline in importance. He was relegated to a 100 per cent undergraduate teaching role. A few pharmacognosists of that period attempted to become involved in pharmacological, biochemical and/or chemical research on plant and animal drugs, but their efforts were not of high enough quality to compete with the emerging and strengthening areas of pharmaceutical chemistry and pharmacology.

In 1950, at least in the United States, a typical Pharmacognosy course taught to Pharmacy students, consisted of a series of lectures in which the student was required to memorize information concerning all plant and animal drugs, whether or not they were in current use, such as (a) the Latin binomial, (b) the part used, (c) the production and commerce, (d) the characteristic cellular elements found on microscopic examination, (e) names of active principles, many of which were unknown, (f) the use for the crude drug and (g) the posology associated with crude drugs and their Galenical preparations. A typical course dragged on for 30 weeks; a total of 90 one hour lectures and 90 hours of laboratory work made up the curricular requirement. Students looked through the microscope, but

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drew pictures for the Professor, of the elements they were supposed to see, from illustrations in their textbook. I know this, for I was one of those students at the Massachusetts College of Pharmacy, in 1950 and 1951. A thought that was continuously on my mind in those days as a student was "there must be a better way to teach this course; why isn't it made more interesting and useful for us?"

Shortly after this period in history (1950), a rapid series of events took place in pharmaceutical education in the United States. Each of these events served as a catalyst to speed up the elimination of pharmacognosy from the curricular requirements. These events were as follows, in chronological order.

- a. The pharmacy curriculum changed from four to five years. The extra year was primarily for the addition of "educational" courses.
- b. Addition of Physical Pharmacy to the curriculum.
- c. Addition of Biopharmaceutics to the curriculum.
- d. Addition of Pharmacokinetics to the curriculum.
- e. Addition of Clinical Pharmacy to the curriculum.
- f. Addition of externship training to the curriculum.
- g. An impending required six-year Pharmacy curriculum.

All of these changes in the academic curriculum were designed to prepare the pharmacy student for a role in Society that was theoretically commendable, but which in fact did not exist. For example, during the decade following 1950, it was generally agreed that the curriculum should be designed around the pharmacist as the dispenser of quality drugs; from 1960 to 1970 the pharmacist was to be the "drug expert" and advise both the physician and patient, but no provision was made in the system to reimburse the pharmacist for this activity. Finally, from 1970 to present, it has been proclaimed that the pharmacist should have a "clinical orientation". In other words, he should be patient-oriented, maintain patient drug and medical records, monitor drug use and utilization and

recommend proper drug therapy for patients after diagnosis was made by the physician. Again, there was no provision in the health-care system to reimburse the pharmacist for this role.

As these new areas were added to the curriculum in order to produce the theoretical end product, others had to be reduced or eliminated. Pharmacognosy was the prime target, and perhaps justifiably so. During this period of time, many pharmacognosy departments consisted of a single faculty member, usually a botanically-trained individual, who had not been cognizant of the need to keep the Pharmacognosy course responsive to the needs of the profession, the students, or to science. As such individuals retired, they were replaced with faculty members in other disciplines, and the Pharmacognosy course was eliminated in those colleges. However, it was not only Pharmacognosy that was affected; reduction in many basic science courses, such as physics, physical chemistry, botany, zoology, inorganic and analytical chemistry, and others as well. In recent years, medicinal chemistry has been treated similarly.

Today, in the United States, there is a heavy emphasis on "Clinical" education and experience, which has been introduced into the curriculum at the expense of basic science courses.

About 15 years ago in the United States, colleges of Medicine decided that less basic science was needed in the medical curriculum. Almost universally, basic science was deemphasized, with a concurrent increase in *clinical training* for the embryonic physician. Today, medical educators are in almost universal agreement, that graduates of colleges of Medicine are *less* qualified to practice medicine than the graduate of a *decade or more ago*. Most attribute this tragedy to a deemphasis in basic science education, and the pendulum is now swinging back to correct this deficiency.

Ironically, *pharmaceutical* educators seem unwilling to take advantage of this experience by their sister profession, and they are charting a course for pharmaceutical education, through drastic curricular changes, that will most surely result in producing pharmacy graduates with a lesser proficiency than in the past.

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Based on experiences in the United States, what are the conclusions that can be drawn from these historic events, and of what value can they be for the future of Pharmacy and Pharmacognosy in France and Europe. In order to present these conclusions, I must first interject some personal opinions, many of which are unpopular, even with some of my colleagues in the United States, and may be unpopular here today. Nevertheless, these opinions are based on a great deal of experience and personal observations of the practice of Pharmacy and Pharmacognosy throughout the world.

First, it is clear to me that Society is becoming increasingly more demanding of University faculties to be *accountable* for their time and activities. Since this same Society is financing institutions of higher learning, this is not an unreasonable attitude. Society expects, and should receive *relevant* teaching and inquiry for new knowledge, consistent with established needs. We no longer live in a world where academicians can do as they please, regardless of how difficult this may be for most of us to accept.

Second, I feel that the major research mission of faculties of pharmacy should be concerned with drug development, in its broadest context. Thus, relative to pharmacognosy, I personally do not feel that research directed *only* toward the isolation and structure-elucidation of chemical compounds from natural sources, can be justified within a Faculty of Pharmacy. Similarly, I consider studies on the biosynthesis of natural products to be a marginally justifiable area of research, as would be pure chemotaxonomic studies.

Third, unique individual and collective potentials for meaningful biomedical research exist within pharmaceutical faculties, that are found in no other institution. The research activities just mentioned *do not require* these unique capabilities, and I would contend that for the most part, pure phytochemical, chemotaxonomic, and biosynthetic studies, unless *directly* involved with other biomedical aspects of research, are just as well carried out by scientists who do not have a pharmacological orientation. I would further offer an opinion that the search for new biologically active agents from natural sources would be most effectively

carried out by team efforts within faculties of pharmacy, or within university medical centers.

Natural product drug development programs *within the pharmaceutical industry* have been almost universally *unsuccessful*, exclusive of antibiotic discovery, simply because industry does not have the expertise required for implementation of effective programs, and is unwilling to invest to acquire this talent.

On the other hand, pharmacy faculties have always had a wealth, perhaps an overabundance of talent, to engage successfully in the search for new natural products with drug potential. However, there has been a lack of cooperative *organization* of these talents within pharmacy faculties in the past, and in almost all cases, pharmacy faculties are burdened with excessive teaching loads (relative to basic science units in faculties of medicine) that have precluded proper attention to such programs. Drug development teams within pharmacy faculties, however, *must* have close working arrangements with industry, since industry involvement is required to bring the laboratory discovery to the market place, where it will prove useful to mankind.

If we restrict our remarks to the search for new drugs in plants, and can agree that the arena most suitable for this enterprise is within pharmacy and/or medical faculties, the individual who by training and experience that is best suited, in my opinion, to assume a key leadership role, is the modern pharmacognosist. He is most frequently the only individual who will have been trained in botany, chemistry and pharmacology; these disciplines being essential for success in this field. It is virtually impossible for an individual to have equivalent high competency in all three of these areas, which then presents fertile ground for collaboration between pure chemically, botanically and/or pharmacologically oriented faculty in a given institution.

Reluctance of pharmacy faculty to become involved in free and unselfish interactions, both in teaching and research, has contributed to the impending threat of extinction for pharmacognosy as an academic discipline in the United States. Should this continue, Society may not reap the benefits of new and better drugs from Nature, within our lifetime.

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This then, concludes my remarks relative to the "bad news" that I intended to present, let us now look at the other side of the coin.

THE FUTURE OF PHARMACOGNOSY - My remaining remarks will be directed toward the future of Pharmacognosy, relative to prospects for meaningful and productive research opportunities. I strongly believe that Pharmacognosy must define its primary mission as being directed almost exclusively toward the discovery of new biologically active substances from natural sources, and my remarks will be centered around this mission.

Logic could only lead one to conclude that plants are a fertile hunting ground for new drugs. A few years ago we carried out an analysis of the American prescription market and found that during the period 1959-1973, 25 per cent of all new and refilled prescriptions dispensed from community pharmacies contained one or more substances still extracted from higher plants as active ingredients. This percentage never varied more than ± 1.0 per cent during that 15-year period, thus indicating that this is a very stable market. In 1973, a total of more than 1.03 billion prescriptions were dispensed, and the American public paid in excess of \$3 billion for them. Further, in 1974 the American pharmaceutical industry invested \$1 billion for research and development; less than \$200,000 of this amount being used for drug plant research. There are many reasons for this lack of interest within the pharmaceutical industry in the United States, but I do not want to belabor this point. It should be adequate to indicate that industry has made a number of costly mistakes in the past relative to such programs. In addition, there are patent problems relating to natural products that are not equally troublesome for synthetic drug development. Industry is overly concerned with "too much biological variability" when dealing with plant extracts. They also are concerned over control of raw materials, which is often a problem when such materials are plants indigenous to foreign lands (2).

Of greatest importance, however, is that beyond any doubt, plants *are* a current major source of prescription drugs in the United States, and elsewhere. I am confident that at the proper time, interest by industry must be directed toward establishing research

programs in this area, and I believe that this time is not far away.

Prior to two years ago, the Hoffman La Roche Pharmaceutical Company in the United States had no organized program designed to study higher plants for new drugs. In 1974, the vice president for Research of Hoffman La Roche was a member of the Herbal Pharmacology Delegation that visited the People's Republic of China for 26 days, as the third of nine official exchange scientific delegations arranged by former President Nixon. I was also a member of that delegation. It is my belief that this Vice President was impressed with the manner in which crude plant decoctions were being used, as a major contributing factor of the successful health care system in that country of 900 million people. During the past two years, a number of publications have appeared from the research laboratories of Hoffman La Roche, reporting on novel plant constituents. This seems to suggest that this program could have been initiated as a result of the trip to China by this Vice President.

Another pharmaceutical firm, Ortho Pharmaceuticals, has been engaged in a substantial research program during the past three years, involving the search for fertility-regulating agents in plants. Several patents have already been recently assigned to Ortho on the basis of these efforts. Several other industrial firms in the United States are now considering the implementation of programs to find new drugs in higher plants and one can look forward to a great deal of activity, within the United States, very soon.

Major interest in drug plant research, has been initiated in recent years at the international level. The World Health Organization and UNESCO recently completed a five-year study on the state of the health of the world. It was concluded that if all people of the world are to have adequate health care by the year 2000, methods other than those currently being employed in developed countries, will have to be employed.

In May of 1978, a resolution was adopted by the Thirty-first World Health Assembly, which requested the Director General of WHO to initiate programs designed to evaluate and utilize Traditional Medicine to meet world health needs by the end of this century. The

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resolution contained provisions for (a) compilation of an inventory of useful medicinal plants, (b) standardization of nomenclature for these plants, (c) review of published scientific data associated with these medicinal plants, (d) dissemination of this information to member states, (e) establishment of research and training centres throughout the world to evaluate the effectiveness of Traditional Medicine, to mention only a few points.

Several meetings have been convened by WHO during the past two years and much research activity involving the scientific evaluation of plants used in Traditional Medicine is in progress. Let me bring you up-to-date on a few of these developments.

On January 1, of this year, the World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, funded a \$600,000 Programme on Indigenous Plants for Fertility Regulation. This funding was awarded to six collaborating centers in Brazil, Sri Lanka, South Korea, Hong Kong, London and Chicago. Protocols are being followed and close research collaboration between reproductive pharmacologists, botanists and natural product chemists is in progress. Isolation of active principles, is coupled with appropriate bioassays to monitor fractionation procedures. I am not in a position to give you any details at this time, but there are a number of extremely promising plants that have been uncovered in less than one year, which have distinct possibilities of yielding useful agents to regulate fertility in humans.

This programme was organized, shortly after our research group had published a major 2-part review article on antifertility plants in 1975 (3,4), and we have been heavily involved in the planning and implementation of this WHO effort since that time. In fact, a unique feature of the WHO program is that all of the plants assigned for pharmacological and chemical work in the WHO Six Collaborating Centres, have been selected entirely through the unique application of artificial intelligence to analyze data on plants alleged useful as contraceptives, or for which experimental evidence suggests such effects. This programme has been carried out through use of

our natural product literature surveillance program, which has now been given the name NAPRALERT (Natural Product Alert). The computer selectively analyzes all data, based on appropriate coding and programming, for a given priority use-group of plants. For example, all data relating to plants as potential male contraceptives were analyzed. The plants were rank-ordered into a priority list, based on numbers of points assigned to each plant by the computer for various types and categories of information (5-7).

Although the program has been in existence for less than one year, to the best of my knowledge, almost all plants studied in each of the Six Collaborating Centres, have been shown to be active in the first of three bioassays systems.

Thus, the application of artificial intelligence to select promising plants to investigate for useful biologically active agents, represents a significant contribution by Pharmacognosy toward the *rational* selection of investigational plants. This will eliminate the need for random selection and mass screening approaches, or strict reliance on folklore, which have been *major deterrents* in the decision to support programs to investigate plants as sources of new drugs.

One year ago, WHO initiated a major research program to address the important area of tropical disease, since methods for treating most of these are at best poor. Malaria, encephalitis, filariasis and many other parasitic diseases will be studied in this world wide research program, which was funded during its first year at the \$18 million level; \$5 million being allocated for chemotherapy. It is my own feeling, that this is one of the more promising areas to explore, relative to discovering biologically active principles in plants. Available data, on which logical plant selections can be made, seem more abundant and reliable, than for other types of diseases. The Pharmacognosist has all of the qualifications to compete successfully for funds from WHO and other agencies to make significant contributions in this area of research.

Recently, I attended an unusual Consultation meeting at WHO, concerned with "The Potential Value of Plants Used in Traditional Medicine for Cancer Therapy." One of the recommendations from the consultation meeting, was for
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WHO to set up a "Task Force on Traditional Medicine and Cancer" as the first step toward establishing further research and development programs in this important area of human illness.

Up to now I have concentrated on current and future research activity at the international level, with major emphasis on programs being initiated by the World Health Organization. It should be pointed out that WHO is interested primarily in assisting member states to initiate their own research programs, rather than to plan and implement the research themselves. Thus, funding and expert assistance should become more readily available from WHO for these types of programs. Developing countries will be the primary recipient of these funds, but good solid research proposals from developed countries, in which evidence of reproducible biological activity can be presented, are always welcome and given full consideration. For example, Robert Anton, Professor of Pharmacognosy at the Louis Pasteur University in Strasbourg, was funded recently by WHO for an exploratory study of the fertility-regulating potential of two plants.

What are the prospects for future involvement by Pharmacognosy, other than at the international research level? Many medicinal scientists are reluctant, in fact some refuse, to accept certain "unorthodox" methods for treating human illness as valid. These methods vary from so-called "faith healing" to homeopathy and naturopathy. If we consider only those methods involving the use of plants as adjuncts to the healing process, it must be recognized that there is an increasingly expanding interest by many physicians and patients throughout the world, to employ less drastic means of disease treatment than is often prescribed by "orthodox" practitioners. Many physicians in Europe and in the United States are treating patients in increasing numbers, without a great deal of publicity, with herbal extracts, diet and exercise, to mention a few. Many are claiming good results, yet scientific reasons for the alleged success are lacking. When it is considered that annual hospital costs for patients who require treatment only for drug-induced illnesses in the United States, are in excess of \$3 billion, it becomes almost mandatory to take a closer look at some of the so-called "unorthodox"

treatment modalities, which rarely induce iatrogenic diseases.

There is no doubt in my mind that the pharmacognosist can play an important role in the research that will be required to establish the rationale for successful employment of crude plant extracts in disease treatment. In addition, he(she) will be necessary to impart information to pharmacists and pharmacy students which will enable them to function as advisors to the patient and physician regarding the possible effectiveness and/or adverse effects of these types of medications.

For example, who else but the pharmacist having adequate education in pharmacognosy, can bring to the attention of the medical profession and the public an awareness that a plant widely used as a tea by the lay public, Symphytum officinale (Comfrey) is known to contain pyrrolizidine alkaloids that are highly hepatotoxic? One of these alkaloids in Comfrey (lasiocarpine), has been shown to cause liver cancer in rodents, following feeding studies at a level of 50 ppm. Further, well controlled studies have shown that 0.5 per cent of Comfrey leaves incorporated into the diet of rodents, is sufficient to induce liver and bladder cancer in feeding studies. In the United States, Comfrey is the most common herbal tea sold to the American public. Since there are no FDA restrictions on its sale, who else but the properly educated pharmacists can advise the consumer of the potential dangers of long-term use of Comfrey tea?

Because of a definite trend throughout the world for people to use many obscure herbal preparations, the need for proper dissemination of information on the safety, efficacy and/or potential hazards of herbal teas represents a challenge for the pharmaceutical profession, and points out the need for pharmacologically oriented pharmacognosy as an important and integral component of the pharmacy curriculum. This emphasis on Pharmacognosy, however, will have little meaning, if there is not a proper mixture of botany, chemistry and pharmacology involved. Thus, I am again predicting, that unless Pharmacognosy in Europe awakens to the need for this type of orientation, the predictable half-life of this discipline will parallel that previously indicated for the United States.

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I would like to conclude this presentation by leaving a few thoughts for you on an area of Pharmacognosy research that could assume great importance in the years ahead. As most of you may be aware, the average life expectancy for people in most countries of the worlds, is increasing every year. In the United States there are major research programs now being initiated to study geriatric diseases. Many of the elderly have degenerative organic diseases for which little can be expected in the way of improvement. A large number, however, seem only to require assistance in coping with the stress of day-to-day living, and to build up resistance to adverse environmental conditions.

Much has been said of the possible "adaptogenic" effects of Panax ginseng. This is a difficult concept for the established scientific community to accept, since an "adaptogen" by definition is claimed to increase "non-specific resistance" in an individual. Further, an "adaptogen" has no true pharmacologic effect per se, but rather has a tendency to "normalize" abnormal conditions. What substance could be capable of such an effect? Would it have potential value for geriatric diseases? Will we not all eventually be personally concerned with this problem?

Not too long ago we became interested in attempting to show whether or not plant extracts could induce adaptogenic effects. After considerable library research we selected three plants; Panax ginseng was not one of them. A series of experiments was designed to show if the plant extract could decrease the toxicity of a known toxic substance. We did this by administering the plant extract orally to a large number of mice. One hour later, the oral LD₅₀ of methotrexate was determined in the treated mice. Previously, it was determined that methotrexate had an acute oral LD₅₀ of 78 mg/kg. However, in mice pre-treated with a single 80 mg/kg oral dose of the plant extract, the LD₅₀ of methotrexate was increased to 850 mg/kg. Thus, the plant extract, had decreased the toxicity of methotrexate by a factor of more than 10. This was an acute test and all of the methotrexate-treated animals died within three or four days after the test.

A second series of studies involved pre-treatment of groups of mice with the plant extract orally at 80 mg/kg daily for five days.

On the fifth day, methotrexate was administered orally and it was found that no animals were killed at doses up to 850 mg/kg. This indicated that the toxicity was decreased by a factor of at least 20. More important, however, was that all of the treated mice were still alive two months after the experiment.

We are now studying this phenomenon further, with regard to elucidation of the mechanism for the decreased toxicity, and have extended the studies to other toxic substances as well. Of importance, however, is that it appears that there are substances in plants that have this so-called "adaptogenic" effect, and the implications for applying this to the alleviation of many problems involved with human suffering are enormous.

During this presentation I hope that I have been able to at least point out to you that the future of Pharmacognosy is indeed promising. The types of research possibilities that have been briefly described would be difficult to approach and solve by a person trained only in botany, or chemistry or pharmacology, or pharmaceuticals. Such problems, in order to be understood, rationalized and solved, require a team approach, involving all of these disciplines. It is my thesis that such research programs would be best organized and implemented within pharmacy faculties, and that the pharmacognosist should have a leadership role in this team effort.

Many of you will undoubtedly disagree with some of my statements concerning the continued need and role of Pharmacognosy and Pharmacognosists in the Pharmacy curriculum and in Pharmacy Faculties; some of you will undoubtedly agree. It has not been my intent to convey to you that new drugs will remain undiscovered from natural sources should Pharmacognosy be eliminated as a science. This would be foolish. However, I am personally convinced that this science can contribute appreciably to the more *effective* and *rational* search for new drugs from plants and animals, and that it has a place in the curriculum of Pharmacy. If all that I have accomplished during this lecture is to stimulate some of you to objectively assess this problem, my trip to France will have been of value. If the American experience is an indicator of how pharmaceutical education will

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develop in Europe, all of the basic pharmaceutical sciences, not only Pharmacognosy, are in jeopardy. Students attend a University, not only to acquire the skills to practice Pharmacy, but to derive an education that will allow them to become productive members of Society. Deemphasis of the fundamental building blocks of science, can only be detrimental in attaining this objective.

At the beginning of this lecture I pointed out that there are methods that can be employed to extend the biological half-life of a drug, and that these methods might also be applicable to extending the half-life of disciplines in the pharmaceutical curriculum. The two fundamental approaches that can be used are (a) to block the metabolism of the material; that is the approach that pharmaceutical educators have been using for many years, but it only seems to delay the inevitable, and (b) to increase binding capacity. A final thought that I would like to leave is that longevity of the basic pharmaceutical sciences will be assured by an increased binding of mutually compatible disciplines, in a manner similar to that conveyed in this presentation.

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MEETING REPORTS

THE FIFTH DUTCH SYMPOSIUM ON PHARMACOGNOSY
REPORTER: DR. R.P. LABADIE - UNIV. OF UTRECHT

Since 1974, scientific meetings have been organized annually, in turn, by the Department of Pharmacognosy of the University of Leiden, Utrecht and Groningen. The fifth symposium in this series, held in Utrecht in November, 1978, focused on the status, role and research of "Plant Drugs in Health Care".

In his contribution entitled "The plant kingdom as a resource for drugs", Prof. R. Hegnauer (Leiden) stressed the fact that plants and biological organisms, in general, are still important and, in some countries, the major source of biologically active compounds and therapeutically valuable drugs. He developed this theme through historic facts and developments and recent advances in the scientific evaluation of plant drugs. Further he emphasized the need for an interdisciplinary approach in research, especially a collaboration between pharmacognosists and pharmacologists.

Professor E. Leistner (Münster) discussed "The production of secondary metabolites in plant cell cultures". He indicated that the great advances recently achieved in the field of cell and tissue culture, suggest promising possibilities for the production of plant drugs and pharmaceutically important compounds. By means of instructive examples he elegantly illustrated the experimental problems and possibilities of the production of anthraquinones (Galium), cardio-active glycosides (Digitalis), and alkaloids (Catharanthus).

"The pharmacological aspects of plant drugs and their constituents" was discussed by Professor H.P.T. Ammon (Tübingen). He pointed out that different levels of pharmacological knowledge about the action of plant drugs and their constituents can be distinguished. These levels range from detailed information on the molecular pharmacology of isolated and identified strongly active plant constituents, to insufficiently characterized or unidentified plant constituents or plant preparations which do not demonstrate dramatic pharmacological activity. In the latter examples especially, the insufficient information and understanding is due, partially, to the lack of interdisciplinary collaboration. Professor
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Ammon illustrated the status and different levels of pharmacological knowledge through work on Crataegus, alkaloids which influence the cholinergic system; and morphine, and the endorphines and enkephalines.

"The pharmacotherapy of single neutral compounds and complex plant drugs" was presented by Professor F.A. Nelemans (Utrecht). According to his survey upwards of a hundred of the 2500 registered drugs on the Dutch market are based on plant products. In answering the question whether the application of plant products in official medicine evolve to a definite end, he stated that there is enough experimental data available which justifies more serious attention for clinical research and application of complex plant drugs.

Presenting the aspects of traditional medicine a contribution on "Ayurvedic medicine in the health care of Sri Lanka" was presented by Professor T. deSilva (Colombo). Ayurveda represents a complete health and medical system which originated in India a few thousand years B.C. The Ayurveda health care delivery system serves about 80% of the population of Sri Lanka. The Ayurveda concept is based on two theories: (a) the Panchabutha Theory, that is the theory of the states of matter, and (b) the Tridosha Theory, the theory dealing with the three bioregulators Vatha, Pitta and Kapha. A person becomes ill when there is an imbalance in any or all of these bioregulators of the body. Treatment with drugs is only a part of the therapeutic aspects of Ayurveda. Diagnostics and diet are well-developed and are of central importance in the maintenance and promotion of health. Over 2000 herbal preparations and an equal number of metallic preparations comprise the drug treasure-house of Ayurveda.

Homoeopathy, as another medical approach in health care was treated by A. Vrijlandt (Nijmegen) in a paper entitled: "Homoeopathic application of plant drugs." The speaker, an experienced physician, dealt with the subject on the basis of the three main features of homoeopathy: (1) the term "autocracy" in practice, (2) preparation of homoeopathic drugs, (3) the rule of "similia similibus curentur". In respect to homoeopathic drugs of plant origin in high dilution the speaker invited researchers to investigate and explain the therapeutic effects; he, as a practitioner,

would not like to do without his "unexplained dilutions" in his medical practice.

The papers presented in the afternoon session of the symposium were dedicated to pharmacognostic investigations of research groups of the Departments of Pharmacognosy in the Netherlands and Belgium.

In a paper "Separation methods of pyrrolizidine alkaloids", Dr. H. Huizing (Groningen) reviewed the applicability of methods described in the literature for the separation of pyrrolizidine alkaloids, and reported results he obtained by using ion-exchangers for the isolation of larger amounts of these alkaloids.

The use of electron-exchangers for the reduction of N-oxides proved beneficial. The separation of symphitine and echimidine from Symphytum officinale has been achieved on XAD-resins by applying pH-gradient elution.

"Gas chromatographic analysis of coumarin derivatives" was the title of the paper presented by Miss C. André (Brussels). The study was done to provide a method which could serve for the systematic screening of large series of species for coumarins. Naturally occurring Angelica silvestris collected in Belgium, and twenty-five reference coumarins were studied. GC proved to have an advantage over TLC and PC for the purpose, because its separation capacity is superior, and automatic injection and quantitative data control allowed quick analysis of a large amount of samples. Using two capillary SE30 columns under isotherm oven conditions, absolute identification of coumarin compounds proved possible. In addition data concerning coumarin content in different growing stages, variations in coumarin pattern in different parts of the plant, and coumarin accumulation in relation to the habitat could be collected by this method.

Dr. J.J.C. Scheffer (Leiden) presented a paper on "Separation methods of lower terpenes". Taking the complicated composition of lower terpenes in etherial oils into account, their proper analysis is based on pre-fractionation of a silicagel column in advance to gas chromatographic separation and characterization. The pre-fractionation is carried out by elution with pentane and a gradient of pentane/ether mixtures. In the fractions obtained the hydrocarbon monoterpenes are

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separated from the oxygenated monoterpenes. Minor components are so concentrated in enriched fractions. This facilitates the purification and isolation of single compounds from these fractions by means of gas chromatography. GC separation is performed in three eight meter columns, using polyethylene-glycol 20.000, β, β' -oxydipropionitril, and silicone SF 96 respectively as stationary phases.

Miss M. Ieven (Antwerp) presented a paper on "Antimicrobial and antiviral screening of higher plants". She argued that it is scientifically and clinically justified to search for new and less toxic antibiotic plant drugs acting against Gram-negative bacteria, fungi and viruses. On the basis of literature data on the biological activity of plant constituents it can be assumed that novel chemical structures with antimicrobial activity can be found in higher plants. 130 plant species selected on the basis of literature data and traditional use in folk medicine have been tested. The complex compound mixtures present in plant extracts require a special approach and various test methods for antimicrobial activity have to be used in order to detect activity. Detection of a potential antibiotic component in a plant extract is influenced by the applied test method, by its stability during extraction, and by its solubility in the solvents used. The high percentage of antimicrobial active species found within the plants selected, on the basis of traditional medicinal use, indicate that folklore medicinal data provides important criteria for such screening investigations.

As a contribution of the department of Pharmacognosy of Utrecht, Dr. J.H. van Meer (Utrecht) read the paper "Some application possibilities of thin layers and high pressure liquid chromatography in pharmacognostic research". Investigations were carried out on the basis of two lines in pharmacognostic research. (1) With respect to analysis and characterization of bio-active components in plant drugs, novel results were reported on the HPLC separation of glycyrrhizic acid and (related) accompanying compounds in *Liquiritiae Radix* preparations. The closely related β -glycyrrhetic acid, α -glycyrrhetic acid and liquiritinic acid have been separated on adsorption and

reverse phase columns. The quantitative determination of glycyrrhizic acid is performed by means of HPLC and the SP 4000 computer system. (2) With respect to the *in vitro* study of biological activity, the use of a method on thin layer plates was reported to evaluate antibiotic and haemolytic action of polyene antibiotics, saponins and reduction products of anthraquinones. This simple method allows evaluation of the mechanistic interaction between these bio-active compounds and sterols like cholesterol and ergosterol.

The full papers presented will be published by Bohn, Scheltema and Holkema (Utrecht, Holland) as Proceedings of the fifth Dutch Symposium on Pharmacognosy, in the course of 1979.

THE 176TH AMERICAN CHEMICAL SOCIETY MEETING
REPORTER: DR. S. GOULD, UNIV. OF CONNECTICUT

The annual meeting of the ACS was held in Miami Beach in September. Two symposia were particularly noteworthy for ASP members and there was something for just about everyone.

The Medicinal Chemistry Section sponsored a symposium on "Bioactive Agents from Plants" in memory of S.M. Kupchan and the Microbial and Biochemical Technology Section held a symposium on "Antibiotic Biosynthesis."

John Duros of the NCI led off the Medicinal Chemistry symposium with some very heavy numbers: 35,000 species and 108,330 extracts have been screened to date and 11 pure compounds are now in advanced testing. Despite the use of folklore and botanical relationships, random screening is still the best methodology. NCI has 100 gm of taxal - which is in advanced testing - for which they have not yet found a good soluble formulation for humans. Koji Nakanishi gave an excellent talk on new compounds discovered through his insect-antifeedant screen and described the use of a powerful new microseparation technique: Droplet Counter Current Distribution (D.C.C.)

The first speaker at the antibiotic biosynthesis symposium, Larry Hurley, gave an excellent account of the use of $^3\text{H}/^{14}\text{C}$ labeling to work out the intricacies of the anthramycin pathway. The power of stable isotope techniques was very much in evidence during the day. Work from the group of Kenneth Rinehart on pactamycin biosynthesis made extensive use of ^{13}C NMR to show that this

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highly unusual structure is yet another one elegantly derived, by Nature, from glucose. David Cane, described the use of deuterium NMR to study mechanisms in terpenoid biosynthesis. Steve Gould, Ian Scott and Barry Bycroft discussed the use of ^{15}N - ^{13}C heteronuclear spin couplings in ^{13}C NMR to simultaneously study the secondary metabolism of nitrogen and carbon. Perhaps the most exciting report came from Ian Scott on his work using whole cells in the NMR tube and watching them metabolize added ^{13}C -enriched substrates. Over a 161 hour period the disappearance of the signal from added 3- ^{13}C -valine and the appearance of enriched signals as well as what may have been 3-methyl- α -ketobutyric acid could be observed.

FIRST NATIONAL WU-CHA SYMPOSIUM
REPORTER: DR. W.H. LEWIS (WASHINGTON UNIV.)

We are pleased to announce the successful conclusion of the First National Wu-Cha (Acanthopanax) Symposium in Harbin, China, September 21-26, 1978. The symposium, which focused on tsu-wu-cha (Acanthopanax senticosus) was hosted by the Heilungkiang Institute of Traditional Chinese Medicine and the Fmali Herb Company of Santa Cruz, California. Press coverage was provided by Mike Chinoy of NBC News, Hong Kong, who filmed and recorded the proceedings.

Concurrent sessions were held on the taxonomy, cytology, pharmacology and phytochemistry of tsu-wu-cha, ginseng and related araliaceous genera. Dr. Kao Kwei-bih, Vice President of Traditional Chinese Medicine, chaired the symposium and discussed "Clinical and Medical Evaluation of Tsu-wu-cha." Dr. Fu Keh-chi, Assistant Professor of Medical Botany and Pharmacology, provided a well-illustrated lecture "Comparative Anatomy of Acanthopanax." Dr. Meng Ching-sheng, Assistant Professor of Medical Botany, discussed "Taxonomy and Ecology of Tsu-wu-cha." Dr. Shi Giu-liong, Assistant Professor of Phytochemistry, presented "Chemistry of Twu-wu-cha in Treating and Preventing Cancer." Dr. Walter H. Lewis, Professor of Biology at Washington University, presented an invited paper "Populations of Wild and Cultivated American Ginseng (Panax)." Dr. James A. Duke, Chief, Medicinal Plant Resources Laboratory, USDA, at the invitation of the Chinese hosts, presented an illustrated lecture "The Cancer

Screening Program at USDA," Subhuti Dharmananda, Director of the Botanical Research Foundation of Santa Cruz, California, discussed his "Studies of Chinese Herbs." Ben Zaricor, Director of the Fmali Herb Company, summarized "Import-Export Problems of the American market and the work of the Herb Trade Association." Excellent translation of the formal presentations and question-answers that followed were provided by Ms. Hsiung Li-li of the China National Native Produce and Animal By-products Import and Export Corporation.

The key field trip of the symposium was an overnight visit to Nan Cha for the study of wild Acanthopanax and cultivated Panax. Other scheduled trips included visits to the Heilungkiang Forestry Institute, the Provincial Museum of Natural History, the Agricultural Academy of Science of Heilungkiang Province, and a boat tour of the Sungari River at Harbin.

After an amicable and productive exchange of specimens, literature, and most importantly questions and answers, the symposium was successfully concluded. Although plans for the Second International Wu-cha Symposium have not yet been formulated, scientists interested in participating should send an abstract of research papers dealing with Acanthopanax to one of the following: James A. Duke, Chief, Medicinal Plant Resource Laboratory, USDA, Beltsville, Maryland 20705; Walter H. Lewis, Professor of Biology, Washington University, St. Louis, Missouri 63130.

REVIEW ALERT

ANNUAL REVIEWS OF MICROBIOLOGY, VOL. 32, 1978
REVIEWER: DR. MARILYN K. SPEEDIE (MARYLAND)

The current volume of Annual Reviews of Microbiology contains two excellent articles of great interest to persons interested in antibiotic biosynthesis. The first is "Ex-trachromosomally Determined Antibiotic Production" by D.A. Hopwood. Dr. Hopwood discusses the role of plasmids in the biosynthesis of antibiotics.

The review begins with a discussion of acceptable evidence for plasmid determination of biosynthesis including failure to segregate, infectious transfer of the plasmid-determined character, correlation of antibiotic synthesis with the presence of plasmid DNA, and instability and curing of the

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function carried on the plasmid.

The article then discusses in some detail the evidence accumulated for plasmid-linked antibiotic synthesis in eubacteria and in streptomycetes (the four fungal-produced antibiotics which have been studied have all been found to be chromosomal). In streptomycetes, a significant proportion of antibiotic-producing organisms show evidence that antibiotic production is at least partially determined by plasmids. These antibiotics include methylenomycin, chloramphenicol, kasugamycin, aureothricin, holomycin, turimycin, and oxytetracycline. However, the question remains whether the plasmid-linked genes are structural or regulatory genes. Only three systems have been studied to the point that extensive series of point mutations apparently blocking steps of biosynthetic pathways have been mapped. Of these, for two antibiotics (antimorphin in *S. coelicolor* and oxytetracycline in *S. rimosus*) all such mutations are chromosomal. On the other hand, all the mutations in the production of methylenomycin in *S. coelicolor* were plasmid linked. Evidence accumulating for numerous other systems; e.g. holomycin, turimycin, chloramphenicol, also points to an indirect or regulatory role for the plasmid, with structural genes linked to the chromosome.

In a final section, Hopwood discusses the possibilities for plasmid manipulations resulting in improved antibiotic production. These include transfer of production to new strains more suitable for industrial production, yield enhancement by increased gene dosage, and qualitative changes in the antibiotics. His discussions support strongly the value of continued and expanded research effort on the plasmids involved in antibiotic synthesis.

A second article of interest is "Mutants Blocked in Antibiotic Synthesis" by S.W. Queener, O.K. Sebek, and C. Vezina. The authors begin with a general discussion of the use of blocked mutants for the study of biosynthetic pathways through accumulation of biosynthetic intermediates. They present an especially valuable discussion of the limitations of the method in antibiotic-producing pathways in which broad enzyme specificity often results in conversion of the intermediate to other products. Despite the limitations, the utility of the method becomes obvious as the authors review a large number of specific examples of

biosynthetic pathways elucidated in this manner. Examples can be found in the biosynthesis of cephalosporins and penicillins, the aminocyclitol antibiotics, and the tetracyclines, as well as numerous others.

The authors also present a brief discussion of the use of blocked mutants for the creation of new antibiotic substances through the process of "mutasynthesis". This technique, which involves incorporation of precursor analogues by blocked mutants, has been most extensively applied to the production of new aminocyclitol antibiotics.

In their concluding analysis of the future use of antibiotic-blocked mutants, the authors call for increased collaboration between industrial and university scientists so that genetic lesions can be precisely identified and the corresponding biochemical lesions elucidated in detail. They cite the need for isolation and study of antibiotic-committed enzymes and predict that the advances in techniques using protoplasts and their lysates will greatly facilitate further study in this field.

FUTURE MEETINGS

TWENTIETH ANNUAL MEETING OF THE AMERICAN SOCIETY OF PHARMACOGNOSY

The 20th annual meeting of the ASP will be held at Purdue University, West Lafayette, Indiana from July 29 through August 3, 1979. The meeting will feature an International Symposium on "Recent Advances in Antibiotics and Alkaloids" as well as contributed papers in the area of natural products chemistry and biochemistry.

VI INTERNATIONAL FERMENTATION SYMPOSIUM

The VIth International Fermentation Symposium in conjunction with the Vth International Symposium on Yeasts will be held in London, Canada from July 20-25, 1980. In addition to the symposia, there will be poster sessions, round table discussions, equipment displays, optional field trips, a banquet and other social events of interest to registrants and their families. If you wish further information or to receive mailings, please contact: K. Charbonneau, Executive Secretary, VIth International Fermentation Symposium, Vth International Symposium on Yeasts, National Research Council of Canada, Ottawa, Ontario KIAUR6, Canada.

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FUTURE MEETINGS *(Continued from previous page)*

SYMPOSIUM ON CANCER CHEMOTHERAPY

The American Chemical Society, Southeastern Regional Meeting in Roanoke, Virginia, on October 24-26, 1979, will include a Symposium on Cancer Chemotherapy. Speakers of the symposium will include Dr. Richard Adamson (NCI), Dr. John A. Montgomery (SRI), Dr. Monroe Wall (RTI), Dr. A.I. Meyers (Colorado State University), Dr. John D. Duros (NCI) and Dr. Sidney M. Hecht (University of Virginia). Contributions in the area of naturally occurring or synthetic anticancer agents are invited from members of the ASP and will be included as part of the Symposium. Further information and abstract forms may be obtained from Dr. David Kingston, Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061.

ANNUAL MEETING OF THE GESELLSCHAFT FÜR ARZNEIPFLANZENFORSCHUNG

The Gesellschaft für Arzneipflanzenforschung will hold a meeting from July 16-22, 1979 in Budapest, Hungary. The following subjects will comprise the scientific program: Theoretical and practical aspects of internal factors determining the metabolism and productivity of medicinal plants; The effect of external conditions on the increase of medicinal plant metabolism and productivity; Phytochemical, technological and phytotherapeutic aspects of medicinal plant research and processing. A three day trip will be arranged to spice and medicinal plant growing and processing farms and research areas in central and southern Hungary. For further information contact 2nd ISHS-Symposium "Spices and Medicinal Plants", GA 27th Scientific Meeting, Research Institute for Medicinal Plants H-2011, Budakala 52, Pf. 11, Hungary.

THIRD CONFERENCE ON AFRICAN MEDICINAL PLANTS

The Organization of African Unity's Scientific Technical and Research Commission has planned its Third Conference on African Medicinal Plants for September 25-29, 1979 in Abidjan, Ivory Coast. Further details about the conference may be obtained from the Executive Secretary, OAU/STRC Secretariat, P.M.B. 2359, Lagos, Nigeria.

NEWS AND NOTES

RESEARCH INTO AFRICAN MEDICINAL PLANTS NEWSLETTER

A Newsletter on Research into African Medicinal Plants has been inaugurated. It is published for the Organization of African Unity's Scientific Technical and Research Commission by the Drug Research Unit of the Faculty of Pharmacy, University of Ife. All scientists interested in receiving copies of this six-monthly Newsletter should contact: Dr. E.A. Sofowora, Editor, Newsletter on African Medicinal Plants, Faculty of Pharmacy, University of Ife, Ile-Ife, Nigeria. He would also welcome any information of particular interest to Africans in this field of research.

INTERDISCIPLINARY RESEARCH GROUP FORMED

Under the auspices of the Deutsche Forschungsgemeinschaft an interdisciplinary research group involving scientists from pharmaceutical biology (i.e. pharmacognosy), botany, microbiology and plant biochemistry has been established at the University of Münster/W. Germany. Speaker of this group is Dr. W. Bary and other members are Drs. W. Hösel, W. Hüseemann, E. Leistner, E. Meyer, H. Pape, R. Wiermann and their coworkers. It is intended to closely collaborate on various aspects of the biochemistry and physiology of secondary products and plant cell culture research.

PROMOTIONS, APPOINTMENTS AND AWARDS

Dr. William L. Lasswell has been appointed Assistant Professor of Pharmacognosy at the University of Rhode Island. Prior to his appointment he held a post-doctoral position at the University of Kentucky and received his Ph.D. in Pharmacognosy from the University of Mississippi.

Dr. Milton J. Zmijewski, Jr. has been appointed to an Assistant Professorship at the College of Pharmacy, University of Utah. He received his Ph.D. in Pharmacognosy from the University of Kentucky.

Dr. Siri von Reis Altschul, Honorary Curator of Ethnobotany at the New York Botanical Garden will spend the summer as a scholar-in-residence at the Rockefeller Foundation's Bellagio Study and Conference Center on Lake Como, Italy. She will be working at the Foundation's Villa Serbelloni, on a book that

(Continued on next page)

NEWS AND NOTES (Continued from previous page)

will serve as source material for chemical or biological investigations of unusual plant materials relating to drugs and foods.

Dr. Heber W. Youngken was recently reappointed by the Governor of Rhode Island to the State-wide Health Coordinating Council. He was also honored by having the popular Annual URI Pharmacy Clinic named the Heber W. Youngken, Jr. Pharmacy Clinic. Dr. Youngken will retire from the college Deanship June 30, 1979.

Dr. Julia F. Morton, Director, Morton Collectanea, University of Miami was honored by being named as the first Distinguished Economic Botanist by the Society for Economic Botany.

Dr. David Pearlman, University of Wisconsin was honored by the presentation of the James M. VanLanen Award from the Division of Microbial and Biochemical Technology of the American Chemical Society.

GENERAL

Dr. Monroe E. Wall, Research Triangle Institute, has presented talks on "Determination of Paraquat in Marijuana Pyrolysis Products at the Third International Conference on Stable Isotopes"; "Marijuana Chemistry and Metabolism" at the International Pharmacology Meeting (Paris); "Applications of Mass Spectrometry in Cannabinoid Research" at the Symposium on Marijuana, (Reims); "Chemistry and Biological Activity of Taxol" at the International Cancer Symposium (Buenos Aires) and "Structure-Function Relationships with Certain Plant Antineoplastic Agents" at the Walter Hartung Memorial Lecture (N. Carolina).

Dr. Julia F. Morton, University of Miami, has been elected President of the Florida State Horticultural Society.

Dr. Yuzuru Shimizu attended the second IUPAC Symposium on Marine Natural Products (Sorrento) and chaired the workshop on marine toxins. He was also an invited speaker and chaired a workshop at the Second International Conference on Dinoflagellate Blooms, (Key Biscayne). He also served as a WHO expert consultant on Paralytic Shellfish Poisoning.

CORRESPONDENTS

The following members have agreed to serve as regional correspondents. The Editorial Board would appreciate, greatly, any help that you can give them, if they need, by doing meeting reports, reviews of reviews, describing new equipment or techniques.

Dr. E. Leistner, Westfälische Wilhelms-Universität, Institut für Pharmazeutische Biologie und Phytochemie, D-44 Münster (Westf.) Hittorfstraße 56, Germany.

Dr. Mikhail D. Antoun, Faculty of Pharmacy, University of Khartoum, P.O. Box 115, Khartoum, Sudan.

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Dr. Gary W. Elmer, Department of Pharmaceutical Sciences, School of Pharmacy, University of Washington, Seattle, Washington 98195.

Dr. David G.I. Kingston, Department of Chemistry, College of Arts and Sciences, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061.

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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 pharmacognosists of all nations and to other interested persons. Annual dues are \$25.00 and include a subscription to LLOYDIA, the official journal of the Society. Graduate students in pharmacognosy may become associate members upon payment of \$2.00 per annum. 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 \$1000 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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