

PD-ABB-917

ETHNOPHARMACOLOGIC RESEARCH: DISCOVERING NEW PROTOTYPE DRUGS  
THAT WILL BE USEFUL IN THE CLINIC

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A PROPOSAL SUBMITTED UNDER THE A.I.D. SMALL RESEARCH PROGRAM  
FOR HISTORICALLY BLACK COLLEGES AND UNIVERSITIES.

MARCH 21st, 1984

CONTENT PAGE

	<u>Page</u>
A. Title Page	1
B. Relevance of the Proposed Work to A.I.D.	2
1. Statement of the problem and pertinence of the proposed research to A.I.D.'s mission	2
2. Developing country participating in proposed research	3
3. Preliminary assessment of the environmental effects of the proposed experiments	3
C. Scientific Aspects of Proposed Work	4
1. Clear statement of problem to be addressed by the research.	4
2. Selected literature citations	5
3. Detailed experimental or analytical design	8
D. Qualifications of Principal Investigator	11
E. Budget Information and Estimates including budget justification	12
Bibliography	14
Appendix	16

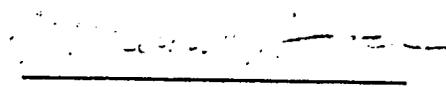
TITLE PAGE

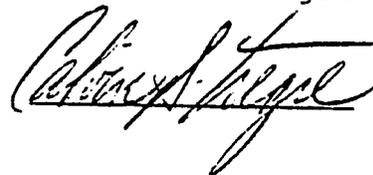
- A. 1. LABORATORIES OF PHARMACOLOGY AND TOXICOLOGY  
DIVISION OF BASIC PHARMACEUTICAL SCIENCES  
COLLEGE OF PHARMACY  
XAVIER UNIVERSITY OF LOUISIANA  
NEW ORLEANS, LA 70125 U.S.A.
2. ETHNOPHARMACOLOGIC RESEARCH: DISCOVERING NEW PROTOTYPE  
DRUGS THAT WILL BE USEFUL IN THE CLINIC.
3. Richard F. Ochillo, Ph.D., Principal Investigator.  
CHAIRMAN DIVISION OF BASIC PHARMACEUTICAL SCIENCES  
AND ASSOCIATE PROFESSOR OF PHARMACOLOGY & TOXICOLOGY
4. DATE OF SUBMISSION March 21st, 1984

5. SIGNATURES: PRINCIPAL INVESTIGATOR, Richard F. Ochillo



DEAN, COLLEGE OF PHARMACY, Dr. Marcellus Grace

  
DIRECTOR OF FISCAL SERVICES, Calvin S. Tregre



6. THIS PROPOSAL HAS NOT BEEN SUBMITTED TO OTHER SPONSORS,  
IN WHOLE OR PART, FOR FUNDING.

B. Relevance of the Proposed Work to A.I.D.

1. The immediate goal of this investigation is to isolate and pharmacologically/toxicologically characterize the components (particularly the muscle relaxant components) of an African arrow poison of plant origin as the initial phase of the establishment of a laboratory devoted to the study of African folk medicine.

Part of the mission of A.I.D. is to improve the living conditions of people in the Third World by participating with these countries in selected development programs. Proper development of any country must take into consideration the health of the people. Traditional medicine has been an important part in the health of people of Africa and it is part of their heritage which has great potential for development such that the limitedly explored treasure-house of human knowledge can be availed for the solution of problems afflicting mankind. The successful accomplishment of what is proposed in this investigation would constitute a scientific backbone in the development of an active laboratory committed to the study of traditional medicine of various ethnic groups in Africa.

Dr. Lydia Makhubu, who is professor of Chemistry and vice-rector of the University of Swaziland branch of the University of Botswana and Swaziland, has identified the need for studying traditional medicine of Swaziland. She, on behalf of her country, is collaborating with the United Nations World Health Organization in its worldwide study of the uses and potential of traditional medicine.

We have established a collaboration with Dr. Makhubu and this has been documented (see pg. 141 of Science in Africa Interviews with African Scientists by Lee Nicols of Voice of America, 1982). We believe that the proposed research would be pertinent to A.I.D.'s mission of development in the Third World in generally and Swaziland in particular, and would also foster international cooperation in technical area. Our intention is to develop our cooperation such that the field work (included identification of plants, remedies, formulation of the decoction, etc.) and preliminary extractions would be done in Africa while the separation, pharmacological/toxicological characterization and the chemical identification of the active components would be done in our laboratory in the U.S.A.

On the basis of the information available to us, we believe that the proposed work is relevant to the mission of the A.I.D. and would be considered favorably.

2. Relevance of the Proposed Work to Developing Country in Proposed Research:

Traditional African medicine is an extremely rich summarization of the experience acquired by the African people in thousands of years of struggle against disease. It is an important part of the nations brilliant ancient culture and has played a tremendous role in safeguarding the health of the African people and their vitality as they build their nations.

The ultimate aim of the proposed series of ethno-pharmacologic investigations (of which this investigation is the preliminary phase) is the validation (or invalidation) of the traditional medications, either through the isolation of active substances or through pharmacological findings. The information gathered about the different indigenous drugs/preparations will permit a feed-back for the traditional medicinal practitioners to improved the effectiveness of the profession. Additionally, such factual information will lead to the discouragement of harmful practices such as the use of plants containing rumor-producing pyrrolizidine alkaloids. On the other hand, knowledge of the active constituents in indigenous drugs may not only lead to substantial improvements in traditional therapy but will also allow the development of such agents for the benefit of the whole humanity.

In order to get a better view of the significance of the series of investigation proposed, it is important to bring into considerations some facts about the global health problems. First of all, 80% of the total world population live in the developing countries (Lambo, 1980). At present, traditional medicine has the very important task of healing about 75-80% of the world population (Marini-Bettolo, 1980). Plants represent the principal means of therapy in traditional medicine.

Swaziland, which is one of the developing countries in Southern Africa, has recognized the significance of traditional medicine in health care of its populance and the government has committed a significant part of their limited resources into developing this part of their heritage. We believe that if this project is funded and we successfully succeed in working with Dr. Lydia Makhubu of Swaziland her country will derive tremendous benefit from the success of this series of investigations. We have already established a link and the potential benefit to Africa in general and Swaziland in particular is great.

3. Environment Effects of The Proposed Investigation:

There is no apparent environmental effects of the

27

proposed investigation and therefore a preliminary assessment is not necessary.

C. Scientific Aspects of Proposed Work

1. Statement of the problem to be addressed by the research:

Our ultimate goal of establishing a laboratory committed to ethnopharmacology, with special interest in African traditional medicine, is to find new prototype drugs and to make them available for the treatment of disease. We have selected Africa as the best source of our folk medicine and especially areas in Africa where Western civilization has had the least influence. In such areas, the natives must rely on effective plants for their drug needs. It is important to remember that no person willingly will take an inactive drug when he or she is sick. Therefore, most of the plant drugs used in these areas have some real benefit and relatively little toxicity. In essence the clinical trials for these drugs have all been run before scientists like us arrive and all we have to do is to isolate and define that useful activity in an orderly way. Therefore, the investigation proposed will focus on the isolation and characterization of the active component(s) of a specific African traditional medicine, the African arrow poison.

The African folk medicine we have selected for this investigation is an arrow poison of plant origin which kills prey through muscle paralysis/relaxation and cardiotoxicity. The objectives of this investigation are severalfold:

1. carry out toxicological/pharmacological investigations of crude arrow poison using isolated preparations and intact animals;
2. separate the active component(s) of the toxin and identify the component(s) for further elucidation of the mechanism of action;
3. develop bioassay techniques for the crude toxin and the isolated active components and;
4. chemical identification and eventual synthesis of the identified active component.

Because of the limitation of funds, personnel and the duration permitted for Small Research Program of A.I.D., the objective #4 will not be carried out during the tenure of this proposal if the grant is funded.

2. Selected Literature Citations pertinent to feasibility of proposal

A prototype drug as considered in this grant proposal is one that has a wholly different chemical structure from existing agents and wholly different medical applications. The estimation of the magnitude of the changes which the discovery of such a drug and/or drugs may cause in the practice of medicine can best be visualized when, in retrospect, consideration is given to: a) the impact of the discovery and clinical application of curare on the art of surgery; b) that of penicillin G on mortality from infectious disease and c) the impact of reserpine on the treatment of mental disease to mention only a few.

The odds for discovering a new prototype drug based on sound ethnopharmacologic principles are significantly better than the odds for the discovery of a new prototype drug in all chemical synthetic program (Malone, 1982). This observation puts the U.S.A., which has in the past enjoyed a position of world leadership in drug development, in a terribly backward position when two factors are considered. Firstly, in the United States, pharmacological natural product research is currently at an all time low (Farnsworth and Bingell, 1977). Secondly, only a fraction of the world's plants, especially those with active medicinal ingredients, have been identified and studied. Therefore, the need for such an investigation in the U.S.A. is strongly indicated if not for the benefit of mankind then for the national pride and the desire for world leadership.

It is tempting to echo the feeling that we are now "living better through the magic of synthetic chemistry", therefore we should use synthesis to develop novel pharmacologic agents. The odds of discovering prototype drug from traditional medicinal source is 1:100 odds compared to 1:2600 odds via the synthetic route. For example, a program emphasizing chemotherapeutic screening was set up by Eli Lilly and Company in 1956, and by 1976 the screening of 400 plants had yielded vinblastine and vincristine, 9-methoxyellipticine, and acronycine (Farnsworth and Bingel, 1977). In contrast, approximately 114,600 chemicals were synthesized by the pharmaceutical industry for testing (Irwin, 1962). Of these 1900 went for clinical trial (1:60 odds), but only 44 were placed on the market (1:2600 odds).

We believe that pharmacological studies of traditional medicinal agents should be initiated prior to, or in parallel with chemical research and should be directed to the isolation, identification and characterization of active principles.

Recent surveys have shown that the percentage of natural products in the modern drug armamentarium is considerable, estimates varying from 35% to 50% (Holmstedt and Bruhn, 1983). Almost every class of drug includes a model structure derived from nature, exhibiting the classical effects of that specific pharmacological category. A great number of these natural products have come to us from the scientific study of remedies traditionally employed by various cultures. Most of them are plant-derived, and pilocarpine, vincristine, emetine, physostigmine, digitoxin, quinine, atropine and reserpine are a few well-known examples (Farnsworth and Bingel, 1977). Evidently, the ethnopharmacological impulse to modern medicine can lead to many novel useful drugs, but modern and traditional uses may be entirely different. For example, the plant material studied at the National Cancer Center Institute (Bethesda, Maryland) has been collected at random, but the analysis performed by Spjut and Perdue (1976) (Summarized in Table 1) shows that if antitumor screening had been guided by the knowledge of medicinal folklore and poisonous plants, the yield of active species would have been greatly increased.

The above data support the conclusion that traditional medicine is a general, powerful source of biological activity.

TABLE 1: PLANT FOLKLORE: A TOOL FOR PREDICTING SOURCES OF ANTITUMOR ACTIVITY?

<u>Plant Types</u>	<u>% Active</u>
Plants collected at random	10.4
Plants traditionally used against cancer	19.9
Anthelmintics	29.3
Fish poisons	38.6
Plants poisonous to man	50.0
Arrow poisons	52.2

Our laboratory has already demonstrated interest and capability to carry out the types of studies proposed in this investigation (Cook, Dennis and Ochillo; 1981, Dennis and Ochillo, 1981; Tsai and Ochillo, 1984; Ochillo and Tsai, 1984). We have had success with investigations of similar natural products of ethnopharmacologic significance (Ochillo, 1980; Ochillo, Tsai and Tsai, 1981) and we have also synthesized and successfully investigated the analogs of the natural products (Ochillo, Chaudhurvedi and Sastry, 1978). Therefore, we strongly believe that the proposed investigation is feasible and if funded will be carried out successfully.

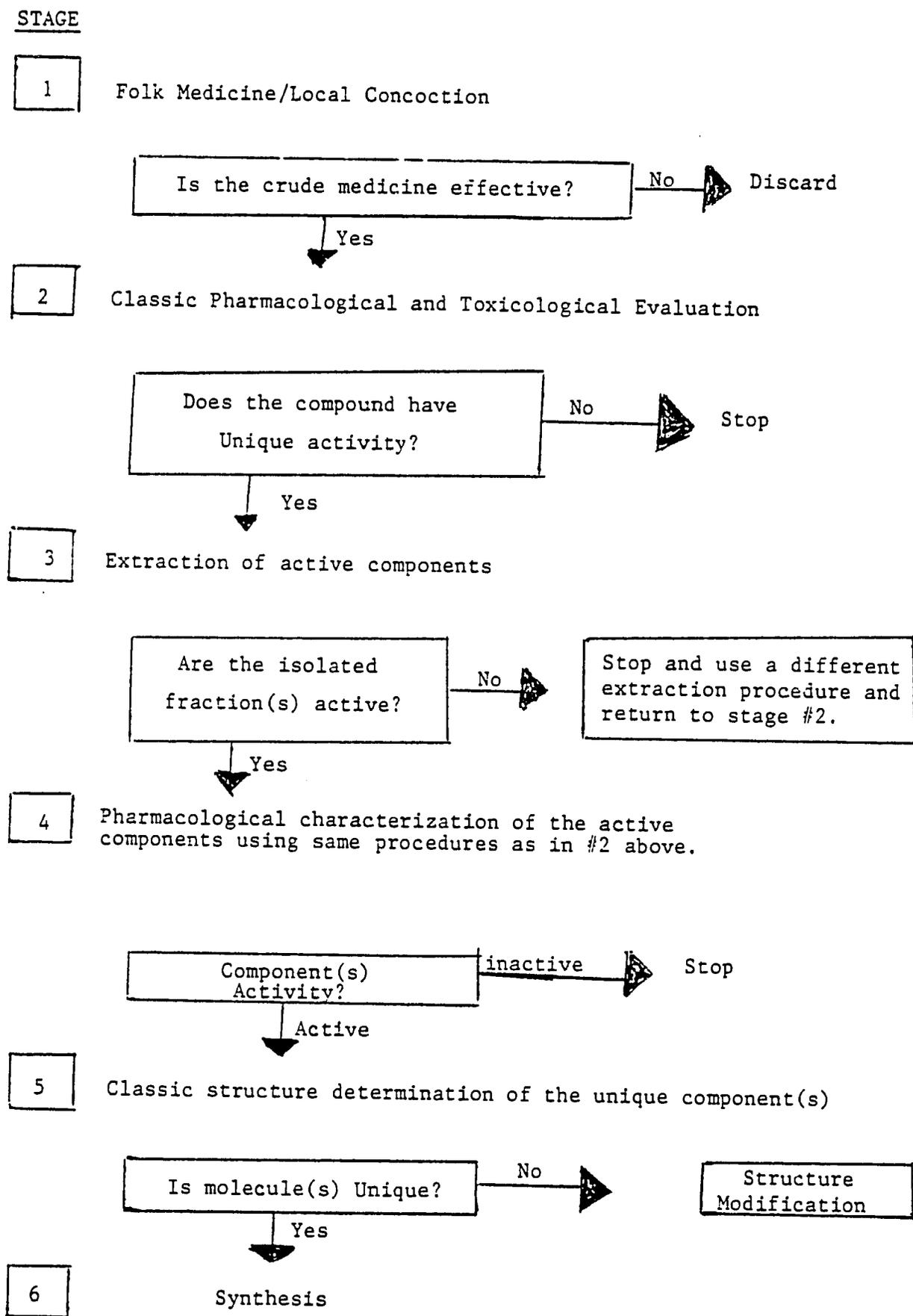


Fig. 1. Illustration of the series of experiments we propose to follow in order to answer critical questions which are central to the realization of our goal.

3. Detailed Experimental Design, Methodologies and Techniques:

The Design: The experimental design for the investigation and some of the questions which the results of this investigation will be directed to answers are presented in Fig. 1.

Availability of The Arrow Poison

At present we have sufficient amount of the arrow poison in our laboratories. These had already been sent to us from Africa and we have been using them on and off in our investigation depending on the availability of time. Therefore, if this grant is funded, we would be able to start working on the project immediately.

Separation of the Active Component(s) of Arrow Poison Using High Pressure Liquid Chromatography:

The arrow poison ( 200 mg) will be dissolved in distilled deionized water (10 ml) and the resulting solution will be filtered through a millipore filter (pore size, 0.45 um). A 20 ul aliquist of the sample will be injected into the sample port of a Beckman High Pressure Liquid Chromatograph (HPLC) equipped with a deuterium power supply, a digital programmer, an optical unit for detection of UV absorption at a selected wavelength, a stainless-steel HPLC column (25x0.26 cm) packed with Silica-A and a recorder. We have previously established this type of toxin to absorb UV hght at the wavelength of 260 mm, which will therefore be the setting for the HPLC during the separation (Dennis and Ochillo, 1981). Also, we have tried different solvent systems (Dennis and Ochillo, 1981) and found the gradient elution with sodium chloride (0.02M)/acetonitrile (45-95%) to give the best separation of the different components of the poison.

Effects of Toxin and isolated components on the Cardio-respiratory Systems

The rats will be anesthetized with sodium pentobarbital (30 mg/kg, I.p.). The respiratory rate will be measured using a pair of subcutaneous needle electrodes (Lead II). The electrodes will be connected to an impedance pneumograph coupler (Type 7212, Narco biosystems, Houston, TX). The setting of the coupler and amplifier will be: Filter, 3H2; variable scale 20ml/cm; and the polarity is +. The respiratory rate will be expressed as rate per minute.

The heart rate will be measured by coupling the impedance pneumograph coupler to an ECG high-gain coupler (Type 7171, Narco Biosystems, Houston, TX). The setting

*No travel to collect!*

of coupler and amplifier will be: Gain; 3.2 x 100 filter 3H2: variable scale, 10 ml/cm; and the polarity will be +. The heart rate will be measured as beats per minute. The femoral vein will be cannulated and the dose of the toxin and each of the isolated fractions will be infused through the cannula in a total volume of 0.2 ml. After giving the toxin and/or fraction, the cannula will be flushed with 0.4 ml of heparinized saline.

#### Effects of Toxin on the Mean Arterial Blood Pressure, Pulse, Systolic and Diastolic Blood Pressure.

A technique which allows a cannula to be placed in the descending aorta of anesthetized rat will be used (Harms and Ojeda, 1974). The cannula surfaces on the neck where it is held into position by a collar such that the rat can not destroy the cannula. The cannula is then plugged. After recovery from surgery, the plug is removed to determine cardiovascular parameters while the animal is awake and is moving freely.

The cannula will be connected to the analog cardiovascular model (Type 9030) which is an integral part of Narcotrace 80 Data Acquisition System (Narco Biosystems, Houston, TX). The module measures mean arterial blood pressure, peak dp/dt and up to four other functions applied to the frontal panel jacks. These parameters can be derived from a single direct arterial pulsatile signal. The same procedure will be repeated after the toxin has been given.

#### Effects of Toxin on Rat Phrenic Nerve Hemi-diaphragm Preparation.

The rats will be stunned and then decapitated rapidly. The diaphragm will be surgically removed with the left and right phrenic nerves intact. The diaphragm will be carefully cut in the middle such that each hemidiaphragm will be attached to the corresponding phrenic nerve. The preparation will be mounted to a special holder with platinum electrodes with one end of the preparation threaded to an F-60 Myograph transducer (Narco Biosystems, Houston, TX). Each preparation will be left to equilibrate for 20-30 minutes at 37°C in aerated (95% O<sub>2</sub>-5% CO<sub>2</sub>) Tyrode's Solution whose composition we have published previously (Ochillo et al 1981). The preparation will be then subjected to an initial tension of 1.0 gm and then left to equilibrate for an additional 30 minutes. During this period, the tyrode's solution will be changed every 10 minutes. The nerve will be stimulated with rectangular pulses at 0.2 ms duration at a frequency of 0.2 Hz using a Grass S-88 stimulator. Supramaximal stimuli will be used throughout.

The resulting isometric contractions will be displayed on a Narco-Biosystems Dmp-4A physiograph. In order to investigate the effects of the toxin on the preparation, aliquot of a concentration solution of the toxin will be added to the Tyrode's solution in the tissue chamber such that the desired concentration around the preparation is reached after dilution.

#### Effects of Toxin on the Satorius Nerve-muscle Preparation of the Frog

The frogs will be decapitated, pitched, and the Satorius nerve-muscles will be carefully dissected from both legs. The nerve-muscle preparation will be mounted to a special holder with platinum electrodes such that the nerve and muscle can be stimulated separately. Each muscle will be left to equilibrate for 20-30 minutes at 22°C in aerated (95% O<sub>2</sub>-5% CO<sub>2</sub>) Frog Ringer Solution. The preparation is then subjected to an initial tension of 0.5 gm and then left to equilibrate for additional 30 minutes. The nerve will be stimulated with rectangular pulses at 75 ms duration at a frequency of 1Hz using a Grass S-88 stimulator. The muscle will be displayed on a Narco-Biosystems. Dmp-4A physiograph. After the control contraction is established, the toxin will be added to the Frog Ringer's solution in the tissue chamber. The effects of the toxin will be observed.

#### Effects of Toxin on the Isolated Rectus Abdominis Muscle of Frog

The frogs are decapitated, pitched and the rectus abdominis muscle is carefully dissected from the pelvic girdle and the cartilage of the pectoral girdle insertion points according to the method of Burn (1952). Thin, longitudinal strips of the muscle will be cut and mounted in an organ bath containing 20 ml of aerated (95% O<sub>2</sub>-5% CO<sub>2</sub>) Frog Ringer solution. The organ bath and the preparation is maintained at room temperature. The preparation will be left to equilibrate for 30 minutes before subjecting it to a tension of 1 gm and then allowed to equilibrate a further 30-60 minutes. It is then repeatedly challenged with a fixed dose (10<sup>-5</sup>m) of acetylcholine (ACh) until the preparation gives consistent response. A dose-response curve for ACh will be constructed in the absence and presence of the toxin. The contractions will be measured by F-50 Microdisplacement Myograph Transducer and recorded on a DMP-4A physiograph (Narco-Biosystems, Houston, TX).

#### Effects of Toxin on the Isolated Longitudinal Muscle of Guinea-pig Ileum

The guinea-pigs will be killed by cervical dislocation on the day of experiment. The abdomen will be

opened and the ileum will be carefully removed, cleaned and kept in a modified Tyrode's solution. The solution was gassed with 95% O<sub>2</sub> and 5% CO<sub>2</sub>. The longitudinal muscle of the ileum will be dissected according to the method of Ochillo, Rowell & Sastry (1978).

A piece of the longitudinal muscle approximately 2.0 cm long will be tied at both ends and suspended in a 20 ml bath containing Tyrode's solution. The preparation will be left to equilibrate for 20-30 minutes at 37°C before subjecting to a tension of 0.5 gm and allowing it to equilibrate for an additional 30 minutes. Each preparation will be challenged with a dose of ACh (10<sup>-6</sup>m) until the contraction of each preparation is consistent. The tracing of the contraction of each preparation will be allowed to come back to the baseline after each wash (approximately 7 minutes) before the next challenge with ACh. A dose-response curve for ACh will be constructed in the absence and presence of the toxin.

D. Qualifications of Principal Investigator

EDUCATION

1. 1973-1977, Ph.D. Vanderbilt University, Nashville, Tennessee.
2. 1969-1971, M.Sc. Dalhousie University, Halifax, N.S. Canada.
3. 1965-1969, B.Sc. University of Victoria, B.C. Canada.

TEACHING EXPERIENCE

- 1981- Associate Professor of Pharmacology & Toxicology, Xavier University.
- 1983- Chairman, Div. Basic Pharmaceutical Sciences, Xavier University.
- 1977-1981 Assistant Professor of Pharmacology & Toxicology, Xavier University.
- 1971-1973 Lecturer in Physiology and Molecular Biology, University of Nairobi, Kenya.

RESEARCH EXPERIENCE

- 1.) Have been awarded 9 grant proposals from National Institutes of Health, National Science Foundation etc. totalling approximately \$1,000,000.
- 2.) Have developed and directed an active toxicology/pharmacology laboratory at Xavier University College of Pharmacy.

PUBLICATIONS

- |   |    |
|---|----|
| 1.) Published Papers in Referred Journals | 19 |
| 2.) Published Abstracts                   | 88 |
| 3.) Manuscripts Submitted                 | 6  |
| 4.) Manuscripts in Preparation            | 11 |

Detailed curriculum vitae is presented in the Appendix.

E. BUDGET INFORMATION AND ESTIMATES FOR THE PROJECT PERIOD:

a.) PERSONNEL

Richard F. Ochillo Principal Investigator  
100% Effort for equivalent for 1 month \$ 3,500  
Research Assistant Investigator 50% Effort  
for the 12 month period \$12,055

c.) Fringe Benefit @ 14% of salaries  
and wages \$ 2,178  
Subtotal \$17,733 \$17,733

b.) CONSULTANTS -----

e.) EQUIPMENT

Service contracts and minor equipment \$ 1,000

e.) SUPPLIES

Animals (Guinea pigs, rabbits, rats  
and mice) \$ 2,398  
Glassware including chromatographic  
columns \$1,097  
Chemicals and reagents \$ 250  
Subtotal \$3,745 \$ 3,745

d.) TRAVEL

Field trip to Africa to document sample  
collections and to coordinate with  
Dr. Lydia Makhubu (in Swaziland) to  
put together a joint proposal to be  
submitted to A.I.D. for funding \$ 3,500

f.) Other direct cost -----

g.) Indirect Cost (58% of \$15,555) \$ 9,022  
-----

GRAND TOTAL

\$35,000

*Handwritten notes:*  
This is the only proposal  
1/17

## BUDGET JUSTIFICATION

- a.) Personnel: Xavier University College of Pharmacy is primarily a teaching institution which is currently moving aggressively into research. The teaching load is heavy. Therefore, I am requesting funds in this proposal to pay a part time technician who will put at least 20 hours per week on this project if the proposal is approved and funded. In addition, I am requesting funds to pay my salary for the equivalent of 1 month for the duration of the project period. Generally, we work in my laboratory for 6 days a week and if this proposal is funded I plan to spend approximately the equivalent of one working day (8 hours) a week on the project for the duration of the grant. In our assessment the requests are modest and we hope they will be considered favorably.
- c.) Equipment: We are requesting \$1,000 for service contracts and minor equipment to be used in this investigation. At present my research laboratory is equipped with Beckman High Pressure Liquid Chromatography, Beckman DU-8B Spectrophotometer, Beckman LS-8100 Scintillation Counter, Narco-trace-80 and 4 other Narco-Biosystems recorders, fraction collector etc. All these pieces of equipment are covered with service contract. Since some of the series of experiments proposed in this investigation will require the use of these pieces of equipment, the request for funds for service contracts is justified.
- e.) Supplies: The requests for supplies is modest and is justifiable on the basis of experimental design and the understanding of the proposed experiments.
- d.) Travel: In order to realize our goal in the series of investigations we plan to carry out (of which this one is a preliminary phase) it is necessary for us to carry out a field trip to consult with Dr. Lydia Makhubu in Swaziland. The usefulness of the trip is severalfold. Firstly, the trip will enable us to discuss and formulate a common focus for the series of investigations we propose to carry out. Seocndly, the visit will, apart from providing me with the opportunity to collect additional samples, enable me to document the process of sample collection and make an on-the-spot assessment of the types of on-the-site extraction procedures which can be done in Swaziland. Thirdly, the trip will provide Dr. Makhubu and myself a chance to put together a joint proposal to be submitted to A.I.D. for funding. The request for travel is important for the secondary phase of our investigation.
- g.) Indirect Cost: This is based on 58% of the cost for personnel as per the University and government agreement.

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APPENDIXCURRICULUM VITAE

NAME Richard F. Ochillo

ADDRESS WORK Laboratories of Pharmacology & Toxicology  
College of Pharmacy  
Xavier University of Louisiana  
New Orleans, LA 70125 U.S.A.  
Phone (504) 483-7433 or (504) 486-7411

MARITAL STATUS Married to Yvonne Ochillo and has 4 children

EDUCATION 1.) 1973-1977 Ph.D. Vanderbilt University,  
Nashville, Tenn.  
Major: Pharmacology/Toxicology  
Minor: Biochemistry and Pathology

2.) 1969-1971 M.Sc. Dalhousie University,  
Halifax, N.S. Canada  
Major: Physiology  
Minor: Biophysics

3.) 1965-1969 B.Sc. University of Victoria,  
Victoria B.C. Canada  
Major: Biology  
Minor: Chemistry

TEACHING EXPERIENCE

1981- Associate Professor of Pharmacology & Toxicology, Xavier University of Louisiana, New Orleans.

1977-1981 Assistant Professor of Pharmacology & Toxicology, Xavier University of Louisiana, New Orleans.

1973-1977 Predoctoral Studies  
Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tenn.

1971-1973 Lecturer in Physiology and Molecular Biology in the Faculties (Schools of) Medicine and Science, University of Nairobi, Nairobi, Kenya.

1969-1969 (One academic year) Science Lecturer, Siriba Teacher Training College, Maseno, Kenya.

1962-1965 High School Science (physics, chemistry, biology and Mathematics) Ambira Secondary School, Ugunja, Kenya.

CAREER OBJECTIVE: Excellence in biomedical research and teaching

RESEARCH INTEREST:

1. Pharmacodynamics of autonomic and cardiovascular agents with special interest in the cholinergic system. Most of my investigative efforts have been directed to the studies of the components of the cholinergic neuro-effector junction paying particular attention to DL-muscarine and analogs as the prototype agents which act at the site. Our progress in this area has reached the level at which we have developed sufficient data to also investigate the interrelationship between the cholinergic system and the adrenergic and cardiovascular systems in vivo and in vitro.
2. Toxicology of the neuro-effector junction in isolated preparations and also in intact animals. We are particularly interested in natural toxins like muscarine and synthetic poisons like organophosphates and DDT. Also, we are interested in the general toxicology of natural toxin as a probe in elucidating vital body function which if impaired lead to death, and the effect of ionizing radiation on autonomic nervous system.
3. My other area of interest is in folk medicine, an interest directed at isolating the active principle(s) of some known folk medicine.

4. Pharmacy education is my none-test tube research interest. For the last 4 years, I have been analyzing factors contributing to the low Grade Point Average of pharmacy students during their professional training at Xavier University. The preliminary results of this investigation were presented at the National Pharmaceutical Association Meeting in Orlando in 1981. The investigation is still in progress.

Areas of Teaching Interest

1. Pharmacology
2. Toxicology.
3. Pathology.
4. Research

Membership in Professional Organizations

1. The American Society of Pharmacology and Experimental Therapeutics.
2. The Society of Toxicology.
3. The New York Academy of Science.
4. The International Society for the Study of Xenobiotics.
5. The American Association for the Advancement of Science.
6. The American Pharmaceutical Association.
7. Academy of Pharmaceutical Science.
8. The American Association of Colleges of Pharmacy.
9. South East Society of Pharmacology.
10. American Society of Gerontology.

ADMINISTRATIVE EXPERIENCE

1. I have established and direct the Laboratories of Pharmacology and Toxicology at Xavier University College of Pharmacy. The group is actively involved in biomedical research and training of students.
2. Have been co-ordinator for the pharmacology course at Xavier University involving lectures and laboratory exercises for 70-80 students from 1977 to the present time.
3. Have been co-ordinator for a course in Toxicology involving lectures to final year Pharmacy Students from 1977 to the present time.
4. Have served as a member of the University Research Committee for accreditation Self-Study.
5. Have served as chairman of the Animal Committee 1977-present.
6. Have served as an active member of the library Committee and played a key role in bringing our Library holding in the areas of Pharmacology/Toxicology to a respectable level.
7. Have served in the following committee: Graduate Education, Continuing Education, Research Committee and, African/Afro-American Advisory Committee for the President of Xavier University.
8. I am a member of the Academic Standing Committee of the College of Pharmacy.

9. I have been a member of the University Animal Committee from 1977 - present and I am currently the chairman of the Committee.
10. I have been responsible (1979 - present) for the coordination and teaching a general pharmacology course at St. Mary's Dominican College for the Nursing and Respiratory Therapy students.
11. Chairman, Division of Basic Pharmaceutical Sciences, Xavier University College of Pharmacy.
12. Member of The University Academic Council.
13. Member, Management Team, College of Pharmacy, Xavier University.
14. Member, College of Pharmacy Accreditation Self-Study Committee.

RESEARCH GRANTS HELD:

1. National Institute of Health 1978-1980.  
"Pharmacodynamics of Muscarine and Analogs and potential for their use in experimental hypertension".
2. Cancer Society of Greater New Orleans 1978.  
"Isolation and characterization of antineoplastic alkaloids of plant origin".
3. Schlieder Foundation 1978-1982.  
"Cholinergic/parasympathetic system and experimental parkinsonism".
4. National Institute of Health 1980-1983.  
"Toxicological and Pharmacological studies of Natural Toxins and some of their Analogs".
5. National Science Foundation 1980-1981.  
"Research apprenticeships for minority high school students".
6. The Department of Energy and IRDEN 1981-1984.  
The effects of low level ionizing radiation on the autonomic nervous system. Approved, but not funded.
7. NIH, Division of Research Resources.  
"Minority High School Student Research Apprentice Program". 1982-1984.
8. National Institute on Aging 1982-1983.  
"Cholinergic muscarinic Receptor and Aging"
9. National Institute of Health 1983-1987.  
"Parasympathetic system in the pathogenesis of hypertension".

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2. Ochillo, R. F. (1972). The Occurrence and Nutritional Potential of Crayfish in Kenya, Technical Paper #1 on Crayfish, The Department of Fisheries, The Ministry of Tourism, Game and Wildlife, The Republic of Kenya, Nairobi, Kenya.
3. Ochillo, R. F. (1977). Pharmacodynamics of Furan Analogs of Muscarine, A Ph.D. dissertation submitted to the School of Graduate Studies. Vanderbilt University, 1977.
4. Ochillo, R. F.; S. T. Kau and B. V. R. Sastry (1977). Nicotinic activities of 5-methylfurfuryltrimethylammonium iodide, an analog of muscarine. Pharmacol. Research Comm. 9:719 - 727, 1977.
5. Ochillo, R. F.; P. P. Rowell and B. V. R. Sastry (1977). Effects of cooling on the levels of acetylcholine, cholinesterase, choline acetyltransferase and the intramural electrical stimulation of the guinea pig ileum. Pharmacology 16:122 - 130, 1977.
6. Ochillo, R. F.; A. K. Chaturvedi and B. V. Rama Sastry (1978). Toxicological and pharmacological effects of furan analogs of muscarine. Toxicology and Applied Pharmacology 43:73 - 83. 1978.
7. Ochillo, R. F., A. K. Chaturvedi and B. V. R. Sastry (1978) Toxicology of 5-methoxyfurfuryltrimethylammonium iodide, an analogue of muscarine, with novel pharmacological action. Proceedings of the First International Congress on Toxicology. Plaa, G. L. and W. A. M. Duncan Edits. Academic Press, New York, N.Y. pg. 462 - 463.
8. Ochillo, R. F. and C. S. Tsai (1980). A possible role of parasympathetic system in alcohol withdrawal syndrome. Drug Alcohol Dependence 6:215 - 217.
9. Ochillo, R. F., C. S. Tsai and M. H. Tsai (1981). Mechanism of action of muscarine on the longitudinal muscle of the guinea-pig isolated ileum. Brit. J. Pharmacol. 72, 225 - 232.
10. Ochillo, R. F. (1980). Apparent activity of 5-methylfurmethide at muscarinic receptors. Arch. int. Pharmacodyn. 248, 69 - 75.

11. Cook E.B.; M. Dennis and R.F. Ochillo (1981). Application of thin layer, ion exchange and high performance liquid chromatography to separate pharmacologically active components of an african arrow poison of plant origin. J. Liquid Chromatography 4 (3), 549-557.
12. Dennis M. and R. F. Ochillo (1981). Selection of suitable solvent system for the isolation of toxicologically active components of an african arrow poison of plant origin. J. Liquid Chromatography 4 (10). 1847-1854.
13. Ochillo, R.F. (1981). Pharmacology of corticosteroids: Some Aspects of Current Status of Therapy and Research. In Progress In Research and Clinical Applications of Corticosteroids. H. J. Lee and T.J. Fitzgerald (Edits.) Hayden and Son, Inc. Philadelphia, Pa 19104 pp. 215-229.
14. Ochillo, R.F. and C.S. Tsai (1982). Influence of verapamil on the frequency and amplitude of cholinergic-initiated spontaneous contractions of gastric muscularis muscle Bufo marinus. Pharmacology 24, 185-192.
15. Ochillo, R.F. and C.S. Tsai (1982). The effect of indomethacin and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) on the cholinergic-initiated contractions of gastric muscularis muscle of Bufo marinus. Arch. Int. Pharmacodyn. 257, 104-113.
16. Ochillo, R.F. (1982). Parasympathetic system in the pathogenesis of hypertension: recent developments in prusuit of an idea. In Research and Clinical Correlates of Anti-hypertensive Therapy. M. Holder (Edit). Hayden and Son, Inc. Philadelphia, Pa 19104. (In Press).
17. Ochillo R.F. and D. A. Pugh (1982). Atropine and mepenzolate mydriasis in rabbits: a comparative pupillographic analysis of two antimuscarinic agents. Res. Comm. Chem. Path. Pharmacol. 36, 503-506.
18. Tsai, C.S. and R.F. Ochillo (1983).. Preliminary pharmacological characterization of the isolated circular strips of gastric muscularis muscle of Bufo marinus : a new preparation. J. Pharmacol Methods. 10:45-53
19. Ochillo R.F. (1983). Biphasic hypotensive effects of 5-Methylfurmethide on the mean arterial blood pressure of rats. Res. Comm. Chem. Path. Pharmacol. 39,511-514.

20. Ochillo, R.F. (1983). The Autonomic Nervous System and Aging: Pharmacological and Therapeutic Implications In The Pharmacodynamics and Pharmacokinetics of Drug Therapy in the Elderly. (In press):
21. Ochillo, R.F. and C.S. Tsai (1983). Characterization of The Antagonism Between Acetylcholine and Mepenzolate at Muscarinic Receptors of The Longitudinal Muscle of the Guinea-pig Isolated Ileum. Arch. int. Pharmacodyn. (Submitted).
22. Tsai, C.S. and R.F. Ochillo (1983). Comparative Studies of Cardiovascular "Effects of A New Dopamine Agonist (SK&F 38393A) and Dopamine. Arch. int. Pharmacodyn. (Submitted).

Completed Research and Manuscripts in Preparation

23. The relaxant effects of prostaglandin E<sub>2</sub> on the acetylcholine-induced contractions of isolated gastric muscularis muscle strips of Bufo marinus.
24. Analysis of grade point average of pharmacy students during their professional training at Xavier University of Louisiana.
25. DDT-induced cholinergic hypersensitivity of rat isolated ileum.
26. A method for the analysis of hypersensitivity and atypical dose-response curves.
27. Antagonism between acetylcholine and mepenzolate at muscarinic receptors of rat isolated ileum.
28. The role of socio-economic status of a hospital as a major determinant of the prescribed medication per patient.
29. Substitution Law as a basis of therapeutic discrimination and/or an index of economic status of the patient.
30. Development of a bioassay method for an African arrow poison of plant origin.
31. The influence of morphine on the mechanism of action of DL-muscarine on the isolated longitudinal muscle of the guinea-pig ileum.
32. The influence of norepinephrine of the mechanism of action of DL-muscarine on the isolated longitudinal muscle of the guinea-pig ileum.
33. Ochillo, R.F. Illustrated Pharmacology: An Introductory Text for Students in Health Professions and Biology.

Abstracts

1. Ochillo, R. F., A. K. Chaturvedi, B. V. Rama Sastry and S. T. Kau (1976). Toxicology and Pharmacology of 5-methylfurfumethide and related Compounds. Toxicol. Appl. Pharmacol. 37:184, 1976.
2. Ochillo, R. F. and Peter P. Rowell (1976). Influence of low temperature on the cholinergic system of guinea pig ileum. Fed. Proc. 35:842, 1976.
3. Chaturvedi, A. K., P. P. Rowell: R. F. Ochillo and B. V., R. Sastry (1976). Relationships between pharmacological activities and chemical structures of furfuryltrimethylammonium iodide and related compounds. Pharmacologist 18:147, 1976.
4. Ochillo, R. F.: A. K. Chaturvedi and B. V. Rama Sastry (1977). Toxicology of 5-methoxyfurfuryltrimethylammonium iodide, an analog of muscarine, with novel pharmacological action. Abstract pg. 7. The 1st International Congress of Toxicology, Toronto, Canada, 1977.
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9. Ochillo, R. F.; A. K. Chaturvedi and B. V. Rama Sastry (1981) Toxicological and Pharmacological Effects of Furan analogs of Muscarine. Pharmacy Digest (in Press).
10. Cook, E. B.; M. Dennis and R. F. Ochillo (1979). Separation of the active components of an African Arrow Poison. Toxicology Appl. Pharmacol. 49:A 41, 1979.
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  15. Cook, E. B., Dennis and R. F. Ochillo (1979). Application of chromatography in the separation of pharmacologically active components of arrow poison. The Seventh Annual Minority Biomedical Support Symposium. Division of Research Resources, National Institute of Health, Bethesda, Maryland, April, 1979, Atlanta, Georgia. -page 158.
  16. Brown, C., M. O. Smith and R. F. Ochillo (1979). Toxicological and pharmacological Studies of (2-Benzoylethyl)-trimethylammonium chloride: A new selective inhibitor of choline acetyltransferase. The Seventh Annual Minority Biomedical Support Symposium. Division of Research Resources, National Institute of Health, Bethesda, Maryland. April, 1979, Atlanta, Georgia. page 158
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25. Tsai, M. H.; Cheng S. Tsai and R. F. Ochillo (1980). Pharmacological characterization of muscularis muscle of Bufo marinus. The Eighth Annual Minority Biomedical Support Symposium. Division of Research Resources, National Institute of Health, Bethesda, Maryland. April, 1980, Atlanta, Georgia. pg. 89.
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29. Tsai, S., H. Tsai and R. F. Ochillo (1980). The role of Na<sup>+</sup> and K<sup>+</sup> ions on the spontaneous contractions of muscularis muscle of Bufo marinus. The Eighth Annual Minority Biomedical Support Symposium. Division of Research Resources, National Institute of Health, Bethesda, Maryland. April, 1980, Atlanta, Georgia. page 89.
30. Wahab, R. F. Ochillo, F. Smellie, and Nghiem Nguyen (1980). The influence of socio-economic status on the prescription pattern in selected Nursing Homes in New Orleans. The Eighth Annual Minority Biomedical Support Symposium. Division of Research Resources, National Institute of Health, Bethesda, Maryland. April, 1980, Atlanta, Georgia. pg. 191.
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32. Ochillo, R. F. (1980). Toxicological and pharmacological studies of DL-muscarine. The Eighth Annual Minority Biomedical Support Symposium. Division of Research Resources, National Institute of Health, Bethesda, Maryland, April, 1980, Atlanta, Georgia. pg. 91.
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34. Ochillo, R.F. and S. Tsai (1980). Muscularis Muscle of Bufo marinus as a pharmacological preparation. Pharmacologist 22:281.
35. Ochillo, R.F. and C.S. Tsai, (1981). Competitive antagonism of acetylcholine and mepenzolate at muscarinic receptors, Fed. Proceed. 40:320.
36. Tsai, C.S. and R.F. Ochillo (1981). A comparative cardiovascular study of dopamine and a new dopamine agonist. Fed. Proceed. 40:736.
37. Tsai, C.S., Tsai, M.H. and R.F. Ochillo (1981). Cardiovascular effects of a new piperazine dopamine agonist. Sixth Annual Clinical Pharmacy Symposium, Florida A & M University, Tallahassee, Florida (In Press).
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41. Cook, E.B., M. Dennis and R.F. Ochillo (1981). Application of thin layer, ion exchange and high performance liquid chromatography to separate pharmacologically active components of an african arrow poison of plant origin. Journ. Liquid Chromatography 4 (3), 549-557.
42. Ferdinand Vickie, Adrienne P. Mitchell, Marcellus Grace, and Richard F. Ochillo. Influence of Level of Formal Education on Compliance to Anti hypertensive Drug Therapy. The Seventh Annual Minority Biomedical Support Symposium pg. 158.
43. Julie E. Allen and Richard F. Ochillo Pharmacological Characterization of Helical Strips of Rabbit Aortae. The Seventh Annual Minority Biomedical Support Symposium pg. 157.
44. Ochillo, R. F. (1980). Toxicological and pharmacological studies of DL-muscarine. The Second International Congress on Toxicology. Brussels. Belgium. Also, Toxicology Letters S. 1 No. 1. 0.53 pg. 42.
45. Ochillo R. F. and C. S. Tsai (1981). Graphic and quantitative analysis of hypersensitivity. The Ninth Annual Minority Biomedical Support Symposium. Division of Research Resources, National Institute of Health, Bethesda, Maryland. April 3-6 Albuquerque, New Mexico. Abstract No. 99.
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60. Cheng S. Tsai and Richard F. Ochillo (1981). Pharmacodynamics of SK&F3893: a new dopamine agonist (DAA) with novel cardiovascular effects. South East Pharmacology Society 2nd Annual Meeting Abstract #21 pg. 26.
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62. Newton C. and R.F. Ochillo (1982). Hematological effects of Methylmercury (MeHg) toxicity in male Sprague-Dawley rats. Fed. Proceed. 41, 157 Abst. #7630.
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64. Vaughn G.; Sesi, S.J.; C. S. Tsai and R.F. Ochillo (1982) Characterization antagonism between acetylcholine (ACh) and mepenzolate (MPZ) at muscarinic receptors (MR) of the rat isolated ileum. Fed. Proceed. 41, 1308 Abst. #6065.
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67. Ochillo, R.F. (1982). Pharmacological studies of 5-methylfurmethide: an analog of muscarine with acetylcholine releasing properties. The 10th Annual Minority Biomedical Research Symposium, Division of Research Resources National Institute of Health, Bethesda, MD., Abstract #169.
68. Pugh, D.; Dennis, M.; E. B. Cook and R.F. Ochillo (1982). Further studies of the toxicology and Pharmacology of an african arrow poison of plant origin. The 10th Annual Minority Biomedical Research Symposium, Division of Research Resources, MD. Abstract #447.

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114

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