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PREPARATORY ASSISTANCE TOWARDS THE ESTABLIHSMENT OF AN INSTITUTE FOR RESEARCH AND DEVELOPMENT FOR TRADITIONAL MEDICINE

UC/ZIM/85/244 ZIMBABWE

Technical Report: Conclusion and Recommendations*

Prepared for the Government of Zimbabwe by the United Nations Industrial Development Organization

Based on the work of Finn Sandberg, Consultant on plant-derived pharmaceuticals

Backstopping Officer: R.O.B. Wijesekera, Chemical Industrial Branch

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1. INTRODUCTION

This project had the following development objective:

To increase the supply of pharmaceuticals to service the national health-care programmes.

The immediate objective was to give preparatory assistance towards the formulation of a viable proposal for establishment of a Research and Development Institution for Traditional Medicine.

The expert was according to the job description-expected to make an assessment of the present research and development facilities in Zimbabwe and critically review the trained man power instrumentation, building and other facilities available.

In the light of the above, he was to propose the inputs needed and organisational frame-work for an research and development facility for the production and quality control of medicines from plants.

Traditional medicine in Zimbatwe embodies not only utilisation of medicinal plants but also psychotherapy.

There are problems facing Zimbabwe in procuring pharmaceuticals for use in the health service. The costs involved do not permit the acquisition of adequate pharmaceuticals to cater for the majority of the population. One major way in which self sufficiency in drug supply can be achieved is to make use of both the modern allopathic medicines and local traditional medicines.

The two aspects of traditional medicine-that is herbalism and psychotherapy - will have to be researched and developed for application in the various Primary Health Care programmes that the Ministry of Health has embarked upon. This will inevitably require the establishment of a research and development institute -the one included in this project proposal will deal with herbalism.

Although a project proposal is tailor made for one country, experiences in this field from other countries can also be of interest. The expert has therefore considered and made use of the experiences in Mexico (Annex. 1) and other developing nations showing that the cost of medicines in the primary health care can be considerably diminished by introducing plant-derived pharmaceuticals.

2. FINDINGS

A, General

The persons met and institutions visited once or more times during the visits in November - December 1985 and September 1986 are listed in Annexure 3.

Not only the Ministry of Health but also several departments of the University. The organisation of traditional healers ZINATHA and the Natural Products Research Association of Zimbabwe (NAPRAZ) have shown great interest in the research of traditional medicine. Some research programmes have been carried out or been started (Annex3). However, there has been no co-ordination of these researches and no new drug have come out as a result of these researches so far.

NAPRAZ organised a successful international symposium on Medicinal and aromatic Plants Research in Africa in June 1985 at the University of Zimbabwe. The Symposium was co-sponsored by the Commonwealth Research Council and the Scientific Council of Zimbabwe. This council (in the Prime Minister's Office) is very much interested in the promotion of Natural products Research in the country.

At its 1986 annual general meeting held on January 4 at the University of Zimbabwe, NAPRAZ proposed the establishment of Medicinal Natural Products Research, Development and Production Centre in the department of Pharmacy at the University of Zimbabwe. The centre should be headed by a Director, who will work under NAPRAZ and other interested parties in coordinating its activities.

B. Research capabilities

Institutions of particular relevance and importance for the present project are the following:

- a) Department of Pharmacy, University of Zimbabwe
- b) Department of Chemistry, University of Zimbabwe
- c) Department of Biochemistry, University of Zimbabwe
 - d) Department of Clinical Pharmacology, University of Zimt; bwe
 - e) Department of Chemical pathology, University of Zimbabwe
 - f) Department of Paraclinical Veterinary Studies, U.Z.
 - g) Blair Research Laboratory, Ministry of Health
 - h) Government Amalyst's Laboratory
 - i) National Botanical Garden and Herbarium
 - k) The Ewanrigg Botanic Garden

The department of Pharmacy of the Faculty of Medicine enjoys a good reputation. This department is engaged in research on pharmacokinetics of drugs, new formulations, phytochemistry and in development of new drugs from plants and traditional remedies. Some members of the staff are in close touch with the Zimbabwe National Traditional Healers Association and are quite knowledgeable about medicinal plants and traditional remedies. Given proper support, encouragement and direction a good unit for research and medicinal plants can be established in this department around the faculty members, which can serve as a nucleus for the establishment of a Zimbabwe Institute for Research and development of Traditional Medicine.

The department of 'Chemistry has some well qualified organic chemists carrying out phytochemical research on the flora of Zimbabwe. However no pharmacological testing has been carried out on the isolated substances.

In the department of biochemistry research on cytochrome P-450 and other hepatic drug-metabolising enzymes has been carried out as well as isolation of anti-neoplastic agents from marine organisms.

Clinical and Toxicological tests on medicinal plants have been performed in the departments of Clinical Pharmacology and Chemical Pathology.

The department of Paraclinical Veterinary Studies is screening plants for toxic effects on domestic animals.

The Ministry of Health has no laboratory of its own for the study of the traditional medicine. Its Blaire Research Laboratory is carrying out very good scientific work on the epidemiology of tropical parasitic diseases in Zimbabwe and s a well reputed institute. It could serve as a good biological laboratory for testing of medicinal plants of Zimbabwe against tropical diseases.

The Government Analyst's Laboratory is mainly responsible for analysis of samples in the following major categories:

a) Clinical,
b) toxicology and pesticides
e) water, f) miscelleneous. The samples are submitted by both the public and private sectors.

The botanical problems of medicinal plants are dealt with in the National Botanic Garden and the National Herbarium and Ewanrigg Botanical Garden.

The National Botanic Garden has carried out very good work on survey and identification of the flora of Zimbabwe, is maintaining a National Herbarium and has some very good publications on the flora of Zimbabwe.

The Ewanrigg Botanical Garden has one of the world's best collection of Aloes, and it is also maintaining experimental nursery of important medicinal plants. With some support this garden could be used as repository for all medicinal plants and could supply planting materials for experimental cultivation to prospective cultivators of medicinal plants.

C. Cultivation and post-harvest treatment of medicinal plants

At present there is no large scale cultivation of medicinal plants in Zimbabwe.

The department of Research and Specialist Services, Ministry of Agriculture has a long experience and excellent research record in cultivation of economically important plant and could help in standadising an agronomic practices for optimal yield of medicinal

plants and the products obtained from them. The staff members of of this department and the botanical institutions in general are well qualified and trained and these institutions have long traditions of research.

Although the agrotechnique for cultivation of all medicinal plants is principally the same, there are from medical point of view three categories of medicinal plants to be cultivated.

- I Medicinal plants used in tradional medicine
- II Medicinal plants with established usage in current allopathic medicine.
- III New medicinal plants as result of phytochemical sereening of the flora of Zimbabwe.

 These three categories are described in Annex 4.

D. Formulation of plant-derived pharmaceuticals

The pharmaceutical formulation industry in Zimbabwe is highly developed. The local production of formulation is of the value of about Z\$23 million, which is about 67% of total pharmaceutical market of Z\$35 million. The formulations produced include tablets, syrups, small and large volume parenterals creams and inhales. There are 8 major manifacturers. Over 80% of the production is accounted for by the top five companies with CAPS (Government has a 34% holding in the company) alone producing about 60%. The CAPS factory, which was visited, has very modern equipment and follows good manufacturing practice, which compares well with those in the most modern plants anywhere else. CAPS, which has a overall capacity utilisation of about 50%, is willing to produce formulations of plant-derived pharmaceuticals, provided that they obtain stardardized extracts as starting material and a detailed description of the formulation desired.

E. Conclusion and recommendation

It was found that the Ministry of Health has a strong political will to develop the traditional medicine of Zimbabwe but has no research facilities of its own for this purpose.

On the other hand, some of the departments of the University of Zimbabwe have the interest in and research facilities for such an activity.

It seems therefore logical to create a multidisciplinary Zimbabwe Institute for Research and Development of Traditional Medicine (ZIRDETRAM) as a joint venture for Ministry of Health and the University of Zimbabwe.

The primary activity of ZIRDETRAM will be decisive for this organizational framework.

The creation of ZIRDETRAM will be the content of phase I of the project proposal, whereas the establishment of the enterprise "ZIMBABWE PHYTOPHARMACEUTICALS" for medicinal plant products will be included in Phase II of the project proposal.

3. Project Proposal

PHASE I

A. Creation of R & D Institute

Based on the findings given in the previous paragraph the establishment of the multidisciplinary "Zimbabwe Institute for Research and Development of Traditional Medicine" (ZIRDETRAM) is proposed as a joint venture for the Ministry of Health and the University of Zimbabwe.

B. Method of operation

The primary activity of this institute is to provide the experimental and clinical background for introduction of items of traditional medicine in modern formulations into the market.

Therefore a strictly goal orientated "conveyor belt" method of operation is worked out and presented in annex 5 .

C. Localisation of the institute

It has unanimously been proposed that ZIRDETRAM will be located in the new research laboratory building of the department of Pharmacy, University of Zimbabwe. With some alterations and extensions (A plan is given in annex 6) this is also accepted for this project proposal.

D. Organisation and Staff

Realising the multidisciplinary nature of ZIRDETRAM, it is proposed that it is governed by an executive board with representives from the two funding bodies, Ministry of Health and University of Zimbabwe (Annexure?). Foreign Advisers, especially in the beginning stage of functioning might be very useful.

The director, responsible to the board, must be a dynamic person, a first rate active researcher, capable to conduct research programmes within a multi-disciplinary context.

The scientific personnel will consist of three categories, full time, part time and external personnel.

E. Government contribution

The Ministry of Health is expected to provide personnel, and annual budget for running costs. The Univerity is expected to provide building, some equipment and personnel.

F. UNIDO - contribution

The imput of UNIDO for phase I will be experts, training and some equipment (a pilot plant and others), evaluation/monitoring missions.

G. Output

The output for Ministry of Health - after complition of phase II-will be the provision of cheap plant-derived pharmaceuticals for the primary health care.

The output for the University will be the many possibilities in ZIRDETRAM for participating in research projects, headed by very competant scientists. This will be base for postgraduate course leading to a M.Pharm. degree, offering specialization in medicinal chemistry, pharmaceutics, phytochemistry and pharmacognosy, pharmacology and pharmaceutical technology.

The pharmaceutical technology should include training in industry, in place of the present attachment to a hospital for Clinical Pharmacy programme. The pilot plant proposed in the project will enable training in unit processes and operations, designed to produce herbal drug formulations.

H. Activities

Each main section of ZIRDETRAM will be headed by a fulltime very competant researcher. Who should also be the leader for the post-graduate students in his/her field and staff members from the departments of Pharmacy, Chemistry, Biochemistry and others may join on a part time basis. For each independent research programme a responsible staff member of ZIRDETRAM is appointed. He/she then choses suitable coworkers (M.Pharm Students, staff-members from other departments) for the completion of the programme.

All research programs will not be performed within the laboratory itself, which may the case for botanical and clinical studies, but are always guided as supervised by the institute.

The 3 C-principle will be the guide-line for ZIRDETRAM: Cooperation, Collaboration and Coordination.

PHASE II

A. Background

As mentioned in paragraph 2 C there is at present no large scale cultivation of medicinal plants in Zimbabwe.

Although the Phase I is designed for research and development of plants used, and industrial processing of the traditional medicine, there are strong reasons to include also other categories of plants (Annexure4).

In many developing countries plants continue to be an important natural resource for manufacture of a number of drugs of established therapeutic value and are also important research material for development of new drugs. Immediate attention should be given in Zimbabwe for the production of established plant derived drugs to achieve self-sufficiency in their production.

Zimbabwe, having a variety of climatic and geographical regions ranging from tropical rain forest to subtropical and temperate mountainous areas, provides a favourable environment for growth of many species of plants. It was found that a number of plants which are raw materials for the production of drugs of established therapeutic value grow wild in Zimbabwe (see annexure 5). Since no reliable data on the quantities of plants exist, a survey should be carried out on the availability of these plants and an assay of the percentage of their active ingredients to obtain data for assessing the techno-economic feasibility of starting the proposed enterprise "Zimbabwe Phyto-pharmaceuticals". For the case the wild plants are not available in adequate amounts, their cultivation will be carried out by private farmers and communal farms through the department of Research and and Specialist Services of the Ministry of Agriculture.

A number of plants and plant products are at present imported by pharmaceutical suppliers: Geddes Limited imports 96 such items - to give an example. Many of these plants can be easily cultivated in Zimbabwe. Further a number of plants of established therapeutic and/or economic value in the international market can be cultivated for export (see Annex.4). The export can be of unprocessed plants, of their standardised extracts and of pure drugs prepared from them.

Other plant products which should be considered for manufacture the raw materials of which are available in Zimbabwe include: caffeine from tea waste; nicotine from tobacco waste, papain from papaya latex; vitamin E concentrate from rice bran oil, gum from Acacia species; castor oil from the seeds of Ricinus communis.

B. Establishment of Zimbabwe PHYTO-PHARMACEUTICALS

This enterprise will deal with the cultivation, extraction and marketing of medicinal plants products. This is purposely - for economic and development reasons - designed to include the processing not only of plants from traditional medicine but also plants, the active ingrediants of which is of established therapeutic value.

C. Government input

It is foreseen that'the government through Ministry of Industry and Technology will provide housing and personnel.

D. UNIDO input

The UNIDO input will include experts, training and equipment for an annual processing of 500 tons plant material. The equipment needed and indicative cost is given in the project proposal.

ANNEX 1

HEPORT ON STUDY VISIT MADE TO THE INSTITUTE OF TRADITIONAL MEDICINE IN MEXICO CITY: MONDAY 15TH APRIL 1985 THROUGH THURSDAY 16TH APRIL 1985

BY ---- B P M VARAMEVA

INTRODUCTION

Pursuant to the Ministry of Health policy of harnessing all resources including traditional medicine, in our endeavour to accomplishing the health for all by the year 2000 goal, and given the stated need to learn, first hand, from sister countries with relevant experiences in this area, and further, following up on my earlier exposures to Chinese, Indian and Pakistani experiences, the facilitation of a study visit to the Mexican centre was deemed a most logical step. This position was further buttressed by my presence in the U.S. at the time and geographical juxtaposition and relative proximity of Mexico to the U.S. In the event, the Secretary gave his authority for the trip to be undertaken provided sponsorship of the intended trip was available. EAPNEK TRUST kindly obliged in this same regard.

Prior to the study visit and through the good offices of a Philadelphia resident, a cerebrity in this area of study, Dr Cosmiski, contact was established with the Director of the Mexican Centre, Dr Lozoya and necessary arrangements made. The visit eventuated at the end of my seven months stint at the University of Connecticut over the period as indicated above.

2. PROGRAME IN MEXICO CITY

Arrived Mexico City evening of Monday 15th April and business commenced in earnest on the morrow. Dr Lozoya took me from my hotel to the Institute where I spent the whole day. The morning session was devoted to discussions with the Director of the Institute and his staff. Part of the afternoon was shared between a conducted tour of the Institute and a courtesy call on the Minister of Health.

Vednesday morning was spent in discussion with the Mexican Permanent Secretary and her lieutenants equivalents at DMS Coplamar H/Q.

Vednesday afternoon and the Thursday morning just prior to departure for the U.S. were spect visiting some places of historical interest including their celebr ted Museum.

3. OBSERVATIONS MADE

3.1 History

The Institute started operating ten years ago with a small multidisciplinary team of experts, complete with technical support staff, drawing from the following areas:

- 1. Plant toxonomy and ecology
- 2. Parascology and Pharascy
- Phytochemistry/Pharmacognosy
- A. Allopathic medicine
- 5. Agriculture/Agronomy

The first five years of activities saw the establishment of a national inventory of Mexican Medicinal plants with corresponding taxonomic characterisations. In 1980, the certre was nominated WHO collaborating centre for the investigations, promotion and development of Traditional and Herbal Medicine.

3.2 <u>Institutes' Mission</u>

The Institute concerns itself with the scientific validation of traditional plant remedies and hence availing of these remedies to the nation at minimum cost and through commercial production of the traditional preparations.

3.3 Research Facilities

3.3.1 Laboratories, Equipment and other Tools at Institute's Disposal The research team is housed in one complex where equipment is used communally wherever possible. No one researcher has the exclusive access to any piece of machinery and work is collaborative. The laboratories are well equipped. All the busic paraphenalia for use by the initiated researcher in all of the disciplines quoted are available. Among these are monitors for muscle tissue responses. Invitro plant production gear, various physiological parameters measuring equipment, Gamma Detectors, soxhlet apparatus, chrosatography gear, Nuclear Magnetic Resonance Spectrometers and GIC. High Resolution MPR and Mass Spectoscopic analyses are undertaken at their University. The Institute stores all information in respect of the basic 4000 medicinal plants on computer tape. Thus, the popular plant name, family, genus and species, locality where collected, medicinal use, form of preparation (whether decotion or whatever) plant part used, origin (whether cultivated or not) mode of administration (oral or topical) are available at the touch of a button.

The Institute has a farm where cultivation of plants of medicinal value but in insufficient natural abundance are grown for harvesting as necessary.

3.3.2 "Conveyor-Belt" Method of operation

The conveyor-belt 'modus operandi' at this institute is 'as follows : Information gleaned from the populace facilitates identification and collection of medicinally useful plants by the taxonomist. The plants' geographical distribution is of course the problem of the plan ecologist. Before anything is done to a plant specimen, it is subjected to pharmacological screening including toxicological studies and only the potent fractions are submitted for phytochemical investigation. This is followed by further specialised pharmacological cum pharmaceutical studies. Clinicians then assist with the clinical trials, and, in conjunction with pharmacists, establish dosage forms, side effects and efficacies of any preparations that survive the screening process. Once the validations are successfully completed for a given specimen, the latter is then, per tender, swarded to a commercial pharmaceutical concern for commercial production of the preparation. The raw form (leaves, bark, root etc) of the medicament are used, and the presentation of the packaged preparation includes plant distribution, dosage and side effects. The institute therefore only does research and development work and leaves the rest to established pharmscontical concerns.

Once a plant has been confirmed as useful, this is passed on to the agronomist for cultivation if not in sufficient natural abundance. The research results of all investigations in the institute are published in either the Mexican periodical "Medicina Traditional" or foreign journals. In susmary, the general scheme of foregoing events is as dipicted in the annexure on page (7)

3.4 Support for Efforts in This Area of Endeavour

The degree of political commitment to using traditional remedies to complement allopathic preparations is total. This position was quite apparent from the enthusiasm with which the Minister of Health and his top civil servants had for activities in this sector.

This was explained in terms of the cost-effectiveness of using proven traditional remedies whose efficacies have been established as either equal to or better than western-type pharmaceuticals.

Two such preparations for coughing and diarrhea, (samples of which I brought with me to Zimbabwe) effectively cut down costs in these two areas by a factor of 100 and are universally available in the Marican context.

4. HECOMMENDATIONS

4.1 Traditional Medicine - Allopathic Practices Collaboration

It was quite clear that the scepticism that characterises much of the attitudes of Western trained doctors towards traditional medicine was, if anything, conspicuous by its abscence in Mexican context. This Mexican experience is far from fortuitors. The Mexican Westerntrained medical fratenity were deeply involved right from the centres' inception and they continue to be heavily involved in the researches at the centre. This has allayed mutual suspicion and everybody works in concert. We need to bridge the yawning chasm between allopatic Medicine and Tradition Practice in Zimbabwe.

4.2 Promotion of Herbal Traditional Remedies

Industrial production of pure active ingredients is a prohibitively costly exercise that might well millitate against much coming off

the intended institutes' research beaches. It is recommended that raw validated forms (i.e. leaves, bark, etc) be the mode of presentation.

4.5 Utilisation of Resources

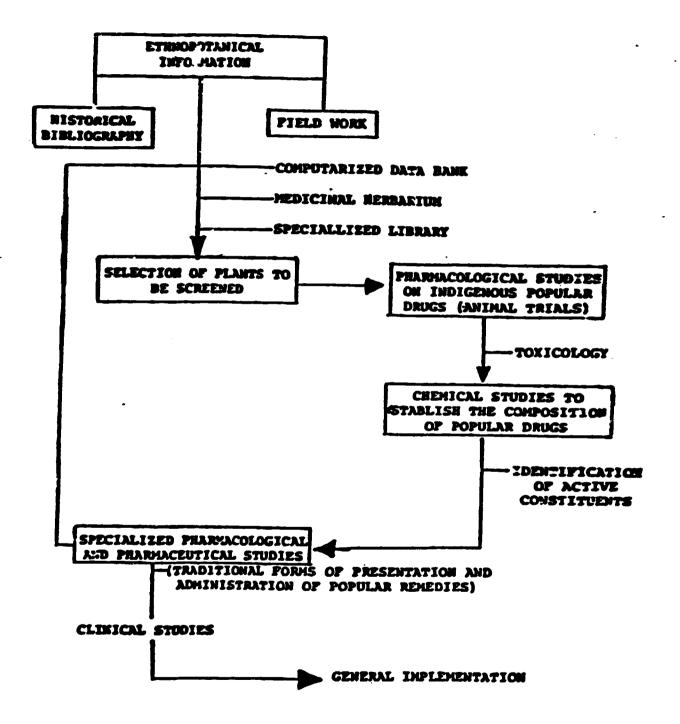
Our material and human resources are only meagre; we thus need to start from humble beginnings. A small multidisciplinary team approach for the nascent Zimbabwean Institute is mandatory. Research facilities, including equipment, should be used communally where possible. No unplanned duplications should be allowed.

4.4 Mational Inventory of Useful Species - Medicinally

The basis of any researches in this area is clearly an established compedium of viable candidates for investigation. There is thus urgent need for establishing an inventory of medicinal plants within the country and possibly within the sub-region.

5. ACKNOWLEDGERENTS

Thanks are due to the Kapnek Charitable Trust for funding the study trip and Dr. S. Cosmiski for facilitating the establishment of contact with the Mexican Centre. I am also grateful to the Secretary for Health for granting permission for the trip to be undertaken.



ANNEWIRE 2

FERSONS MET	INSTITUTIONS VISITED	
l. Dr. B.F.M. Waramba Deputy Secretary	Ministry of Health	
 Mr.A.Chidarikire Chief Pharmacist 	Ministry of Health	
 Mr. K. Stigen Development Officer 	U.N.D.P.	
 Mr. Indvar Forsberg Deputy Representitive 	U.N.D.P.	
5. Dr. E.Froese Chairman. Senior Lecturer	Department of Pharmacv U.Z	
5. Dr. M.D.Morton Lecturer	Department of Pharmacy U.Z	
7. Dr.T.E.Charwedera Lecturer	Department of Pharmacy U.Z	
3. Prof. G.L.Chavunduka President of ZINATHA	Department of Sociology U.Z	
9. Dr.J.A.Hassler Chairman	Department of Biochemistry U.2	
<pre>10. Prof.C.F.Chetsanga Dean of Faculty of Science</pre>	U.Z	
ll. Dr.Nyazema Lecturer	Dept of Clinical Pharmacology U.Z	
12. Dr. Uwaluko Lecturer	Dept. of clinical Pharmacology U.Z.	
13. Mr.E.H.Muller Director	National Botanic Garden Harare	

PERSONS MET

INSTITUTIONS VISITED

14. Mr.R.P.Drummond
 Scientific Officer

National Botanic Garden Harare

is. Mr.D.Hallan Managing Director

CAPS (PVT)LTD Harare

Mr.S.E.Machine
Manager (ethical products)

CAPS (PVT)LTD Harare

17. Mr.M.A.Mundawaran Liason Officer. Pharmaceutical Institute CAPS (PVT)LTD Harare

19. Dr. Muchena Secretary Ministry of Agriculture

19. Mr. P.L.Chisvo Curator

Ewanrigg Botanical Garden.

10. Dr. M.G.Cundidza Lecturer

Dept. of Pharmacv U.Z.

MINERUPE 3

Research Programmes on Medicinal Plants of Dimbabwe carried out or started

- 1. Quantification of Alcin in Zimbabwean Aloe Species.
- Quantification of Active constituents of Timbapwean Medicinal plants.
- Toxicological Studies on the Thymelaceae family of plants.
- 4. Insecticidal properties of the Euphorbiaceae family of plants.
- 5. Isolation and chemical characterisation of the antimicrobial agents from Myrsineaceae family of plants.
- Isolation and chemical characterisation of the antimicrobial agents from Rhamnaceae family of plants.
- 7. Extraction, characterisation and quantification studies on essential and fixed oils of Zimbabwean plants.
- 5. Soap making from plant oils.
- 9. Tumor-promoting properties of Zimbabwean Euphorbiaceae family of plants.
- 10. Molluscicidal activity of Phytolacca dodecandra.
- 11. Taxonomic studies. collection and cultivation of Zimbabwean Medicinal plants (Botanic Gardens).
- 12. Antifungal properties of Xylopia aethiopica.
- 13. Effects of Boophane disticha extracts on the CNS of the rat, mice and guinea pig: Behavioural and autonomic profiles.
- 14. Aspects of toxicology as related to domestic animals of the following plants:

Bohemia variegata. Lagertroemia indica and Cinnamomum camphora.

- 15. Computerization of available information on Zimbabwean medici.al plants.
- 16. Essential oils from Warburgia salutaris.
- 17. Antineoplastic agents from plants.
- 18. Isolation and chemical characterisation of Peltopthorum africanum.
- 19. Isolation and chemical characterization of Aloe excelsa.

- 17. Antineoplastic agents from plants.
- 19. Isolation and chemical characterisation of Feltopthorum africanum.
- 19. Isolation and chemical characterisation of Aloe excelsa.
- Isolation and chemical characterisation of phytoconstituents from Trichoderma longibrachitum.
- 21. Snake bite antidote and repellents from Simbabwean medicinal plants.
- 22. Antimalarial activities of Zimbabwean medicinal plants.
- 23. Anti-hypertensive properties of Zimbabwean medicinal plants.

ANNEXTURE 4

Medicinal Flants to be cultivated in Zimbabwe

I. Plants that probably will pass the "convevor-belt" process of testing medicinal plants used in Traditional Medicine:

Aloe species
Boophane disticha
Dioscorea species
Zingiber officinale
Chenopodium ambiosioidis
Capparis tomentosa
Cassia species
Securidaca longipedunculata
Euphobia ingens
Cissus guadrangularis
Warburgia salutaris
Gnidia kraussiana
Rauvolfia saffra
Comphocarpus frueticosus
Datura stramonium

It is proposed to make a selective approach in the choice of plants for those plants which are used for disease conditions of special importance to Simbatwe and for which experimental models can be established. These plants should include remedies for parasitic, protozoal and helminth injections—diabetes and liver disorders. In the choice of medicinal plant—their repute—in neighbouring countries should also be taken into consideration. In this way the number of plants could be brought down to a manageable size, which could be investigated in a time-bound manner.

It is understood that the experimental models are included in step 5E of the "Conveyor-belt" procedure given in annexure 6.

A few traditional remedies which are very popular could be assumed to be efficacious. But since their safety is not proven, particular in case of long term administration, their chronic toxicity (step 10 is the procedure in annex.6) should be carried out to establish their safety. The availability of reliable safety data would promote the acceptance of such remedies by modern (allopathic) practitioners.

Annex 4 Contd.

II. PLANT PROGUCTS OF POTENTIAL INTEREST FOR PHYTOCHEMICAL INDUSTRY IN CIMBABNE

	Flant Species		Product of poten- tial economic value	Therapeutic or other use
ı.	Acacia sp.	dam exadate	ợu∎	Pharmaceutical S other industrial uses.
2.	Aloe sp. A.barbadenisi: A.vera		fuice. dried or total extract. aloin. alloinosides.	purgative. anti- dermatitis general tonic.
3.	Atropa Belladona	leaves & roots	Tropane alkaloids total extract	anticholinergics, plasters
4.		leaves, fruits, bark.gum	oil, nimbidin. nimbinin, seed cake	antiinfective. cosmetics. insect- icide. fertiliser
5.	Capsicum annum	truits	capsaicin olec- resin.	antirheumatic, counter-irritant
6.	Carica papaya	latex	papain. chymopapain	meat tender- iser, herniated dis:
?.	Costus speciosus	tubers	diosgenin	steroid manufacture
3.	Curcuma sp.	rhizome	oleoresin. curcumin	antiphlogistic. antiseptic food colour
9.	Datura sp. D.metel D.innoxia D.strammonium	leaves	atropine./hyocya- mine. hyoscine	anticholinergic, opthalmic use
10	.Dioscorea sp.	tubers	diosgenin	steroid manufacture
11.	Eucalyptus	leaves	essential oil	symptomatic treatment of bronchitis and sinusitis.
12	.Cloriosa superba	seeds	colchicine .	acute gout

13. Mentha sp. whole plant essential oil. carminative, menthol symptomatic treatment of bronchitis

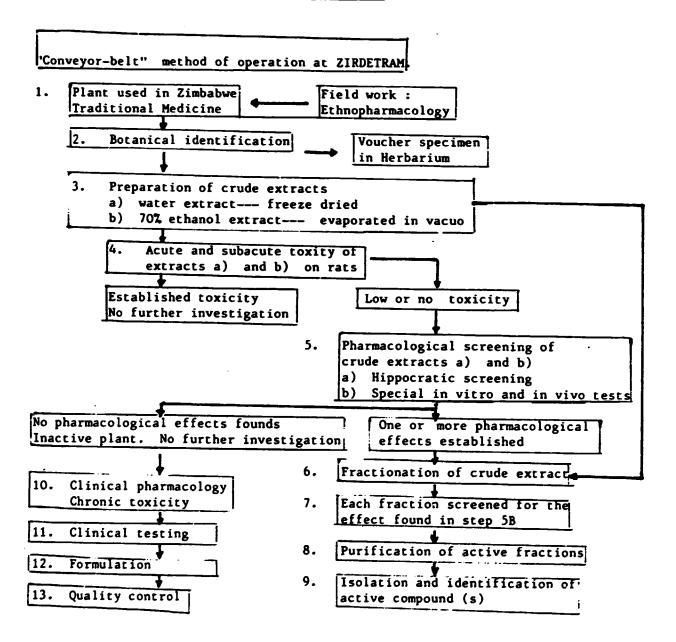
. Annex 4 Contd.

l4.Mucuna pruriens	beans	i-dopa	antiparkinscnian
if.Prunus africana	stem Dark	total extract	laxative. antineoplastic
16.Rauwoifia sp.	roots	total extract. reserpine. aimaline & other alkaloids	hypnotic. sedative. hypotensive
17.Sophora flowers	rlowers .	rutin	capillary fragility
ls.Tamarindus indica	fruit pulp	as such and total extract	laxative, astringent
19.Tea	leaves	caffeine	stimulant. diuretic
20.Tobacco	leaves	nicstine	ectopasiticide
21.Valerian sp.	rhizome	total extract.	tranquilliser. sedative
22.Vocanda sp.	seed	tabersonine	for manufacture of vincamine
23.Vinca sp.	leaves	vincamine	cerebral vasodilator

III. EYSTEMATIC SCREENING OF FLORA OF ZIMBABWE

Flants from the flora of Zimbabwe comprise about 30.000 species, of which about 6.000 are present in abundance. It would be useful to collect and systematically evaluate the biological activity of plants which have so far not been tested. It is well known that systematic screening of plants has led to isolation of compounds with new structures, a few of these compounds have been developed as new drugs, while the biological activity of some unique structures has provided new leads for synthesis of biodynamic compounds. In this programme, the systematic collection of plants from different regions of Zimbabwe should be carried out followed by preparation of their crude extracts, spot testing to determine the type of chemical constituents present in the plant and screening for biological activity. If activity is found, detailed chemical and biological evaluation of the plants should be carried out. In this way, over the years, it would be possible to screen most of the plants available in large quantity.

ANNEXURE 5



ANNEYURE 5 --------

COMMENTS

- The fieldwork can be carried out according to the WHO Step 1. protocol or similar procedure. It must include plant part uses, medical usage, vernacular name. A good voucher specimen is essential.
- Step 1. It cannot be stressed enough that a good specimen is necessary for the botanical determination of the plant species used. A plant can very seldom be identified by only a root, bark or leaf.
- Preparation of crude extract is carried cut in pilot-Step 3. plant scale with the proposed multipurpose extraction and distillation unit.
- Step 4. The acute and subacute toxicity will be carried out on
- ----- rats or mice. Step 5. The pharmacological screening will start with a ------ hippocratic screening on rats. If this gives positive results. special in vitro or in vivo tests will be anti-malarial. carried out: antiinflammatorv. anthelmintic, antidiabetic effect etc. depending on the effects anticipated owing to use in traditional medicine.
- Fractionation of the crude extract is generally performed with chromatographical method: treatment with various solvents is also used.
- The various fractions obtained in step 6 are tested Step !. for the main effect that was found in step 5. will have a much higher active fraction(2) pharmacological effect than the crude extract in step
- The purification of active fraction(s) will involve Step 8. various chemical steps, but is always motivated by a bioassay (a definite pharmacologic effect), that should show higher effect for each step of purification.
- For the isolation of the pure active compounds, methods like HPLC. GC, DDC will be used. For the identification conventional physical methods are used: NMR. GC-MS etc.
- Step 10. It is foreseen that either a crude extract (step 3) or fractionated extract (step 6) will be used ----clinically. Therefore clinical pharmacology and chronic toxicity test on two animal species (one rodent and one non-rodent) will be carried out on these extracts and not on the pure active compound(s) in step 9.
- Clinical test should if possible-be performed as Step 11. ----- multi-centre investigations.
- Step 12. If the result of step 11 and 12 are positive, the
- ----- manufacturing could be done at CAPS.

 Step 13. Methods for standardisation of extract and method of analysis of the final product will be worked out.

ANNEXURE 6

Localities for ZIRDETRAM

The localities will be at the present research laboratory. Department of Pharmacy.

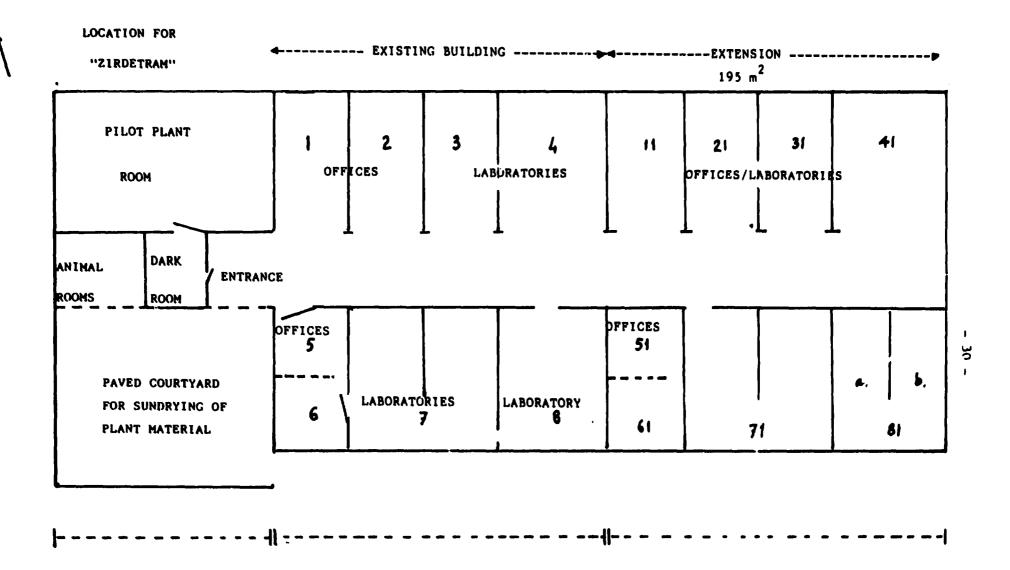
proposed that the extension (rooms 11-81) towards east. should be the same unit as the exiting building (rooms 1-8) with the same dimensions and outer appearance. so it will look as one homogenous building. This will also cut the cost to a minimum.

The space for the multipurpose pilot plant requires principally only two walls and a roof.

The usage of the various rooms/laboratories is given as follows:

Room/Usage

- Formulation pharmacist/pilot plant manager
- 2. Research workers office
- 3. Herbarium
- 4. Phytochemist. office
- 5. Instrumention room
- Formulation office 6.
- Formulation, laboratory ?.
- Phytochemistry, laboratory 8.
- 11. Director of ZIRDETRAM
- 12. Secretaries
- Pharmacologist/toxicologist, office 31.
- 41. Storage of plant material, solvents
- 51. Databank for natural products
- 61. Pharmacology lab = screening
 71. Pharmacology laboratory, general, isolated organ
 81a. Chronic toxicity
- - b. Clinic pharmacology



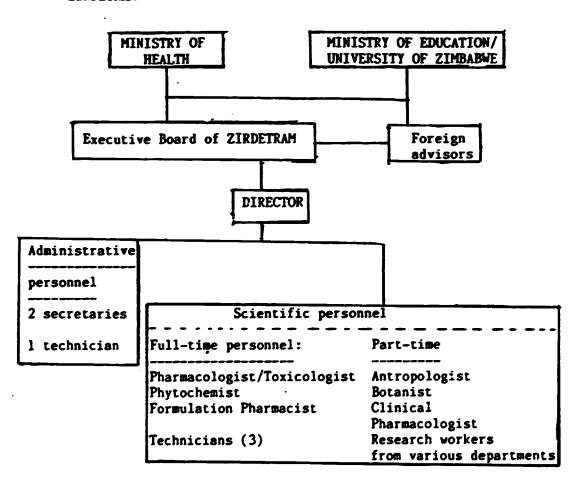
Annexure 6. SKETCH OF BUILDING FOR LOCATION OF "ZIRDETRAM"

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ANNEXURE 7

Organisation and personnel of the joint government venture ${\tt ZIRDETRAM}$



QUALIFICATIONS DESIRED IN LOCAL PERSONNEL

Comments

It is foreseen that the full-time personnel of the project will be on the payroll of the Ministry of Health i.e. the administrative personnel and three heads with one technician each.

Director

The candidate for this post must be an active top scientist, who should have a Ph.D and several years, research experience including working in recognised overseas institutions. The director would be expected to use at least half of his time for active research work, and or actively directing research and development projects.

Pharmacologist/Toxicologist

The candidate for this post should have a Doctorate on pharmacology and good experience in experimental pharmacology and toxicology methods.

Phytochemist

The candidate for this post should have a doctorate in organic chemistry and good experience in natural products chemistry, together with an appreciation of the nature and value of bioassays and biological methods.

Pharmacist (Formulation)

The candidate for this post should have a doctorate in pharmacy or equivalent experience with specialisation in galenical pharmacy and formulation. He should have basic training in pharmaceutical technology to enable him to supervise the running of the multipurpose pilot-plant unit, after suitable exposure to such technology.

The category of part-time personnel belongs to other departments of the University, where they have their teaching obligations. Their research activities will be carried out in ZIRDETRAM, where they are members of different project groups.

It is also important that Master of Pharmacy students are members of the project groups. Being a member of such a research group is an efficient way of scientific training for a young students, and the full value of the project will only be realized when such practical manpower training methods are realised.

SUMMARY

IO/R.13

27 November 1986

V.86-62577

TITLE:

Preparatory Assistance towards the Establishment of an Institute for Research and Development for Traditional

Medicine.

PROJECT NO.:

UC/21M/85/244

COUNTRY:

ZIMBABWE

AUTHOR:

Finn Sandberg

TYPE:

Technical Report

SCOPE:

To increase the supply of pharmaceuticals to service the

national health-care programmes.

CONTENTS:

Introduction, Findings, Project proposal Phase I and Phase II.

CONCLUSION:

The Ministry of Health has a strong political will to develop

the traditional medicine of Zimbabwe but has no research

facilities of its own for this purpose.