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OF PLANT BASED FORMULATIONS IN VIET NAM

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VIET NAM

Technical report*

Prepared for the Government of Viet Nam
by the United Nations Industrial Development Organization

Based on the work of M. K. Raina, consultant for
the production of Galenic formulations

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Chemical Industries Branch

* This document has not been edited.

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ABSTRACT

Nature has blessed Vietnam with a large number of medicinal herbs growing in abundance in almost all parts of the country. An age old Traditional System of medicine based on various combination of these medicinal herbs is practiced in the whole country which is not only very popular but quite inexpensive, which the poor population in particular are able to afford. Most of these formulations are used in the form of teas which are boiled in water and decoction used. Even ailments like hypertension, diabetes etc., such decoctions are used wherein there is no control on dosage. The medicinal herbs are collected from different provinces and are made available to the people through traders. There is no control on the quality and thus adulteration/substitution cannot be ruled out. The identification is done by visual inspection and there are no laboratories fully equipped to standardize and lay down specifications on these plants or their formulations. The Quality Control Laboratory at HCMC is trying to develop some methods but is restricted to only the products available in the market.

During my working schedule of two weeks in Hanoi at the Institute of Medicinal Plants and at the Food Technology laboratory of the Hanoi University of Technology I demonstrated to the faculty and students preparation of herbal extracts of popular products suitable for incorporation in tea leaves and also in capsule form. At the food technology laboratory, extracts of Adenosma, Sophora, Ginger and mixture of popular preparation containing Glycyrrhiza, Adenosma and Cassia were prepared and incorporated into tea leaves. At the Institute of Medicinal Plants, Centella asiatica extract was prepared and the dry extract filled in hard gelatin capsules for use as tonic. The laboratory facilities at both these centres were totally inadequate.

I worked for six weeks at the HCMC Laboratories of the Traditional Medicine Research & Training Centre; Food Technology Dept. of Polytechnic University and the Pharmaceutical Factory No. 26 producing a large number of traditional herbal formulations. At all these laboratories I demonstrated the methods of extraction of medicinal herbs of the popular herbal formulations using modern methods and evolved their specifications for quality control tests. The experiments were demonstrated and various factors responsible for processing explained to the faculty members and the students. Several pharmacopoeial Standards were introduced for the extracts and finger printing techniques employing thin layer chromatography were demonstrated. However, at all these laboratories, the facilities were completely lacking. Somehow these experiments were conducted by procuring additional glassware/equipment from other departments. And organized R&D set-up is totally lacking.

Besides holding technical discussions on a regular basis,

four Seminars were delivered as follows:-

Institute of Medicinal Plants, Hanoi

- Production and Quality Control of Herbal Medicines.

Food Technology Department, Hanoi University

- Extraction of Herbal materials for use as Tea

Traditional Medicine Research & Training Centre, HCMC

- Role of Standardization in Traditional Medicines.

Department of Food Technology, Polytechnic University, HCMC

- Use of Medicinal Plants as Food Supplements.

I also visited the KIM ANH Tea production factory at Hanoi which lacks adequate production and quality control methods though 60% of the produce is exported to some east European Countries. The production facilities are too primitive though packing is quite good being done on modern automatic machine.

I visited the farms of Institute of Medicinal Plants at Hanoi, where large cultivation programme of Artemisia is undertaken. Also some Dioscorea species are cultivated.

At HCMC I visited the Quality Control Laboratory of Ministry of Health and held discussions with the Director and other Scientific Staff on the latest techniques being adopted for Quality Control of medicines both modern and traditional, especially for spurious medicines which are quite common in Vietnam.

I also visited the Pharmaceutical Enterprises No. 24 where some traditional medicines based on powdered herbal materials are manufactured. The quality control methods adopted by the factory were discussed. This factory maintains the records of both production and quality control tests adequately.

At the Pharmaceutical Factory No.26, I demonstrated the preparation of hydro glycolic extract of Centella asiatica suitable for incorporation into skin cream base. We also prepared dry aqueous extract of Artichoke for use as tea.

Dry extracts of Sophora, Lotus, Achyranthes, Alisma, Plantago, Zizyphi, Rehmania & Morinda were prepared at the Traditional Medicine Research & Training Centre and were standardized at the laboratories of the Polytechnic University Food Technology department both for TLC finger printing and other pharmacopoeal tests like Ash value, extractive value etc.

On the basis of my mission, the following conclusions can be drawn :

* There is a need to set up an organized Research Centre for development of herbal formulations based on Traditional system of medicine. This centre should have all departments fully equipped to undertake scientific studies at par with such products in other developed countries.

* A pilot plant for preparation of herbal extracts should be installed at Pharmaceutical Factory No. 26, the largest production centre for Traditional Medicines in Vietnam.

* Suitable laboratory facilities to be augmented at Traditional Medicine Research & Training Centre, HCMC; Food Technology Departments at HCMC & Hanoi.

INTRODUCTION

Vietnam being a tropical country with different climatic and geographical features, Nature has provided a variety of medicinal plants growing wild in various regions. It is reported that over 1800 plant species grow in Vietnam, most of which have remarkable pharmacological activity and are used extensively in traditional system of medicine. Almost 80% of the population live in rural areas where people use these medicinal herbs due to their limited access to modern medicines.

These people wholly depend on the use of traditional medicines based on a combination of several plant ingredients. Thus the medicinal plants have played an important role in contribution to national health and development programme. A number of these medicinal plants have high nutritive value and are taken regularly by the people as food supplements. Over the years, these medicinal plants have played an effective role in curing common diseases and ailments.

In view of the availability of large number of medicinal plants in the country, the Government of Vietnam proposes to formulate standardized products from these medicinal herbs which could be conveniently used by the population in the form of teas and beverages. Some of these formulations could be made in modern dosage forms, fully standardized so that these medicines could be prescribed by the doctors in hospitals and primary health centres throughout the country.

It is essential that these formulations are fully stable at all climatic conditions as many parts of Vietnam have tropical climate. An effective packaging has to be selected which would ensure stability as well as will have low cost so that the finished product becomes economical to the end user.

In order to formulate these products with international standards of quality and in modern dosage forms, certain basic requirements are needed. The infra-structure for both standardization and product development activities need to be augmented suitably with adequate training to be given to the scientific personnel in organizing the studies. An effective Research and Development Centre with the requisite facilities for conducting studies on various aspects of formulation development including stability studies, standardization and toxicity studies need to be setup. Once such a Centre is established and the products developed as per international standards, the export markets of such products could be tapped. This in turn would help the local people to collect the herbs from wild sources or even organize cultivation of medicinal plants in wastelands and can generate resources for a large rural population and thus improve economic status of the people. By adopting these measures, the country will not only exploit their natural resources fully but also provide to poor people of the country,

quality medicines for common ailments in modern dosage form, with clinically proven efficacy. Besides this the export of such formulations with complete documentation and quality control data including clinical trial reports, will help the country to earn valuable foreign exchange.

At present the common form of taking these medicines are in the form of Teas. Two forms of Teas are consumed by people viz. crude herbs mixed with Green Tea/Black Tea and used as such either as Tea bags or to be added to boiling water before taking. The other common form is a combination of various crude herbs put together in plastic bags to be added to boiling water before consuming. The process of incorporating herbal extracts in green tea/black tea for use as Tea has been attempted but no definite standards are followed. The crude herbs are added in the form of small pieces of varying sizes with variable moisture content. Some of these poly bags contained herbs which were semi dried. This can lead to growth of microorganisms and fungus. Some of these medicated teas are meant as tonics or for refreshing purpose. But many of these are meant for ailments like Hypertension, Hyperglycemia, Asthma where it is necessary to control the dose. Therefore, such formulations need to be standardized and more appropriately put as extract in a convenient dosage form.

The scientific personnel need to be given adequate training in all these aspects and organize practicals in such a way that the studies leading to standardization of herbal materials, extraction process and their analytical standards are fully covered. Besides this various dosage forms which can be formulated with these extracts need to be demonstrated including their stability studies at elevated temperatures maintained in the laboratory ovens. The toxicity profile of both individual extracts and also the finished formulation is desirable to ascertain the LD₅₀ so that the dosage recommended is completely safe to the patient. Therefore, systematic approach is needed for making a herbal drug formulation based on traditional medicines which can be accepted in advanced countries and would include complete clinical data to substantiate the claim of the drug.

In order to achieve these objectives, I was assigned the task of assisting the Food Quality and Technology Centre in improving the process of herbal formulations. Originally the assignment was to be taken at only Ho Chi Minh City but subsequently I was asked to assist the Food Technology Centre at Hanoi also for two weeks. The main task was to evaluate the activities and suggest improvements in methods which could lead to quality products and to perform laboratory trials for selected formulations. Also to prepare extracts of medicinal herbs which could be added to the green tea/black tea as effective medicinal teas. Another task is to evaluate the facilities available in the laboratory as well as the factory and recommend necessary equipments to modernize the facilities (Annex 1).

ACTIVITIES

I reached Hanoi on 3rd September 1993 and worked there for two weeks. One week I worked at the Institute of Medicinal Plants and one week at the Food Technology Department of Hanoi University of Technology. At both the places I addressed the Faculty and appraised them of the system being followed for development of formulations based on indigenous herbal materials both in India and other developed countries. I also gave Seminars on different subjects of herbal formulation and their quality control at both the places wherein besides the Director and faculty members, the students also participated. A lot of questions put forward by the students and faculty were answered. An English translator was provided by the Institute for easy conversation and discussion during the Seminars. A visit to the Farms of Institute of Medicinal Plants at Hanoi and a visit to the Tea Production Factory were helpful in assessing the activities and infrastructure available with the Scientific personnel of both the laboratories and exchange of views and experiences of working on different aspect of medicinal plants.

On 18th September, 1993 I went to the Ho-Chi-Minh City and worked there till 27th October, 1993. In the first week I visited the Dept. of Food Technology, Polytechnic University (HCMC) and held discussions with the faculty. I also visited the Traditional Medicine Research and Training Centre (Ministry of Health) and held discussions with the Director and other faculty members. I also visited Central Pharmaceutical Factory 26 (OPC) where a large number of herbal formulations are manufactured in modern dosage form. I had discussions with the Director and the Departmental Heads of various production departments including Quality Control & Marketing.

I also visited the Post Harvest Technology Institute and the Food & Commodities Control Centre (HCMC) and held discussions with the Director regarding Quality Control aspects of various food commodities which are exported to several countries. Also visited their laboratory and studied the technical documents maintained for quality control. I visited the UNIPHA laboratories where a pilot plant has been set up for extraction of animal by-products like trypsin, Chemotrypsin, Pancreatin and Dry bile under UNIDO project. I had detailed discussion with the project leader and visited the Pilot Plant to ascertain if any herbal extraction could be undertaken in the plant in case of spare capacity available.

I visited the Quality Control Laboratories of Department of Pharmacy, Ministry of Health and held detailed discussions with Dr. Nguyen Van Thi, Vice-Director and his colleagues regarding quality Control testing of various products both for modern medicines and traditional medicines. The laboratories are well set up and the facilities are fairly good with many modern instruments available and older models being replaced with new models especially HPLC, UV, I.R., GC etc. A systematic approach

is followed in analyzing the samples drawn from the factories or the market and checked for any spurious products. Modern methods of analysis are followed and microbiological testing is performed. A keen interest was shown by the scientific personnel in understanding the methodology being adopted for traditional medicines in India and other parts of the world. The experiences were shared and discussed in detail.

I visited the Medical Products Import-Export Co. (VIMEDIMEX-II) and discussed about the traditional products being exported to various countries with Ph. Duong Thi Hue and Ms. Nguyen Thu True. A large number of traditional medical products manufactured in Vietnam are exported to USSR and other east European countries. However, many Chinese herbal medicines are available in Vietnam. There is limited scope of import of traditional medicines from other countries but export of these medicines made from Vietnamese medicinal plants have great potential. The details of working at different Institutes are summarised as follows :

HANOI

Institute of Medicinal Plants (One week)

This Institute has been set up in 1961 and has several laboratories, fairly well designed for conducting studies on different aspects of medicinal plant research. Separate laboratories conducting research and development activities relating to Pharmacognosy, Phytochemistry, Pharmacology including toxicity studies, Analytical chemistry, Tissue culture have been set up. A small pilot plant for production of formulations like capsules and tablets is also utilised for development work. The Institute also has a small library and museum cum herbarium where authentic medicinal plants of Vietnam are preserved for reference. A well designed and organized pilot plant set up for extraction of herbal materials with different solvents and isolation of main active constituents is laid out recently with UNIDO assistance. All necessary equipments required for selective concentration of extracts and isolation of active compounds have been added.

However, the laboratory facilities in most of the disciplines of research activities need to be augmented. The old rusted equipments and instruments need to be replaced with new ones so that the scientific personnel are able to undertake experimental work smoothly. Much of the basic infrastructure for laboratory scale activities are lacking. Most of the scientific personnel are keen to undertake systematic scientific work as per the modern methodology but their enthusiasm is slowed down due to inadequate facilities.

The laboratory has established the methods of propagation of *Stevia rebaudiana* by tissue culture and successfully

transferred the samplings to the field. The methods of isolation of the active fraction of sugar substitute has been developed. The isolation technique of Artemisinin 98% from *Artemisia annua* has been commercially taken up and pure artemisinin formulated in modern dosage form of tablets and capsules with convenient packing of Blister packs. The cultivation practices of growing the plant on commercial scale has been established in the farms of the Institute and also technology transferred successfully to various farmers who have taken up cultivation on commercial scale. I visited the Vandien farms at Hanoi (13 kms away from city) where about 10 hectares of land is under cultivation, mostly of *Artemisia annua*. Also *Dioscorea composita* and *Dioscorea floribunda*, *Cymbopogon flexuosus* have been cultivated in the farm.

Centella asiatica grows wild in Vietnam. In the Essential oil laboratory of the Institute, its volatile principles are being formulated into a soft drink. This plant is also used in India in Ayurvedic System of Medicine as brain tonic. The Scientist in-charge Prof. Dr.(Mrs) Tho desired to develop a product based on the extract of this plant and also wanted to extract volatile principle. The experiment was set up to take out the volatile principle from fresh leaves of *Centella* in Cleavanger apparatus. The fraction so collected was separated and dried under dessicator. The characterisation of the oil fraction is being attempted. Since the concentration was very low the product development work leading to its incorporation in soft drink could not be done but the method of incorporation has been demonstrated to the scientific personnel for further work.

The extraction of *Centella* was undertaken by boiling with water and concentrated leading to a thick paste form which was dried in a tray drier (yield 4.30%). This extract was then formulated in hard gelatin capsules (Black-Orange) in the Institute itself on hand filled capsule filling equipment in size 1 (125 mg of extract in each capsule of 330mg of total fill weight). Standardization of the extract could not be taken up due to non-availability of necessary equipments. Hence the TLC of volatile fraction was done and there was good separation. The methodology of standardization was explained to the scientific personnel through notes given to them. The sample of capsules (300) filled with *Centella* extract would be tried as tonic in children.

Discussions were held with Dr. Vu Kui Thu of Phytochemistry department regarding extraction of active sweet principles of *Stevia*.

A seminar was given on the Production and Quality Control of Herbal Medicines which was attended by the Director and the Scientific staff members of the Institute. The lecture was given with the help of several 35 mm slides and transparencies and was followed by a question-answer session on various aspects of development and commercial utilization of medicinal plants as is practiced in India and many other countries of the world.

Food Technology Department, Hanoi (One week)

For one week I worked in this Institute and demonstrated the process of extraction of some herbal materials for incorporation in tea bags. Two batches of 500 gms each of Adenosma (popular for use in liver disorders) were extracted by water separately and dry extract incorporated into green tea leaves and prepared sachets of 2 gms each. Similarly the dry extracts of Sophora japonica (popular for reducing blood pressure) and ginger (for sore throat) were prepared and these extract incorporated in Tea leaves and further into tea bags. The process of extraction was explained to the scientific personnel who were not having any past experience in this field. Due to limited availability of equipments, the other details could not be demonstrated but various other process and procedures were explained. Use of excipients like talc or lactose for prevention of adhering of extracts during drying process were demonstrated. Various steps involved in extraction and standardization of these extracts were given in writing to the scientist in charge Mrs. Chan and her colleagues.

I visited the crude drug market of Hanoi where I found well organized 50-60 shops selling various medicinal plants, some of which were blended combination of popular recipes used as per traditional system in Vietnam. A large number of people were buying these indicating their popularity. The shops selling modern medicines have rarely any preparation from traditional medicines. The small packs of 20-25 gms of crude herbs in polybags are to be boiled in water and extracts taken as such. One such popular product for liver disease comprising of a mixture of Adenosma, Glycyrrhiza and Cassia tora was purchased (20 pkts. of 25 gms each) and its dry extract prepared and incorporated in black tea leaves for packaging into tea bags of 2 gms each.

Another popular mixture of herbs consisting of Chrysanthemum indicum, Stemona tuberosa and Aglaia duperreana was extracted and the dry extract incorporated in the tea leaves. This is commonly taken as refreshing tea. By the end of the week we prepared five different kinds of tea bags containing dry extracts of various popular traditional herbs. Thus the scientific personnel were trained in this field. But the department needs some commonly used equipments to enable them to undertake systematic work with more precision. The various parameters needed for standardization of these extracts were explained to the scientific personnel since no instrument/equipment for undertaking these studies were available in the Department.

A seminar was delivered on "Extraction of Herbal material for use as Tea" with emphasis on techniques of preparation of different extracts and their incorporation/standardization in traditional herbal tea formulation. The Director, faculty members and the students participated in the seminar.

I visited the KIM ANH Tea factory for export which is about 40 kms from Hanoi and held discussion with the Director Mr. Le Lenh Nghi and Head of Marketing Mr. Nguyen Duy Hung. They process 3000 tonnes of tea leaves per year in this factory. The tea leaves are supplied by the state owned farms and also by local private farmers. Another production centre about 100 kms away has larger capacity to produce formulated tea. During 1994 another tea factory is scheduled to be set up with similar capacity about 120 kms away. From this factory 60% of the tea leaves is exported to Russia, Poland, England, Iraq and Libya. The balance production is for domestic consumption. Fragrances popular in Vietnam like Jasmine, Rose, Lotus are incorporated in some brands.

Some of these popular brands are -

- i) Jasmine scented tea
- ii) Lemon tea
- iii) Lotus scented tea
- iv) Mulberry tea
- v) Sweet tea with local herbs
- vi) Apple tea
- vii) Orange tea

The packing is good except that the outer pouch designing could be improved for elegance. Sachets are made in automatic Italian machine conforming to international standards. The processing of drying in pans, the sifting of tea leaves need improvement and automation. The production centre does not follow any GMP's. The storage of tea leaves and finished products are not properly maintained. There are no pallets used and the tea leaves received from tea gardens is stored on floor and even opened and mixed on ordinary floor. Lot of dust was formed around the area which is not at all desirable. The drying in the pans of 10 Kg capacity could be automated. They are using coal as the source of heating the pans and this can be modified. There is practically no quality control. Blending with herbal materials is not standardized. The factory needs to be totally renovated to make it on international standards with adequate quality control measures and proper GMP norms to be followed. The production facilities need to be automated.

Ho Chi Minh City (six weeks)

I reached HCM city on 18th September afternoon and had a detailed meeting with the local Project Leader, Prof. Dr. Luu Dzuang about the work schedule for the period of my stay here. During the first week I visited the various laboratories of Polytechnic University to assess the facilities available. I also held technical discussions with the faculty of Food Engineering Dept., of the University. The use of TLC equipments received from Desaga, Germany from UNIDO funds were demonstrated to the faculty and the students. They were not having any knowledge of the role TLC plays in standardizing the materials and all this was

explained to them. There were no solvents or books available and some of the commonly used solvents were purchased from the local market for demonstration and experimental work. There were no facilities for extraction of the herbal materials in these laboratories. Therefore, such experiments were to be conducted in another laboratory.

Therefore, I visited the other related laboratories where we could undertake the work of preparing dry extracts of common medicinal plants for both standardization as well as formulation into a suitable dosage form as tea or capsule/tablet. I along with Dr. Luu Dzuan visited the Traditional Medicine Research and Training Centre of Ministry of Health and discussed with the Director Prof. Dr. Bui Chi Hieu. This Institute is imparting training in traditional medicine to the doctors who have completed their course in modern medicine. They have a good laboratory with limited facilities for extraction of herbs and their drying. He permitted us to use his laboratory for preparing the dry extracts of medicinal plants and related work in this field. During the discussion with the Director and the faculty there, I found that a large number of traditional products are being prescribed for various diseases like diabetes, rheumatism, asthma, hypertension, sedative, liver disorders, menstrual disorders, laxative, tonics etc. All these formulations were based on a mixture of several popular herbs in their traditional system in crude form. The packs of 20 - 25 gm of these crude herbs are to be boiled in water and the decoction taken by the patient. The drugs are mixed in small pieces and some of these are powdered, but no uniformity of the coarseness of the herbs is maintained. There was no control on the moisture content thus liable for fungal growth. They do not undertake any standardization of the herbal materials being used in the formulation. Since many of these products are meant for use in patients like hypertension, where it is desirable to have a regulated dose, it is of utmost importance that such products are formulated in a convenient dosage form which could be properly standardized and dosage regulated. The Director was keen to introduce such systems but due to lack of facilities and expertise they were unable to do so.

Therefore we decided to prepare the extracts of traditional formulation which could be standardized and formulated in a convenient dosage form. A time frame was planned and one formula selected which is popular for hypertensive patients comprising of seven herbal materials. All these seven herbs were extracted individually during 15 days of my working at the Research Centre.

I also visited the Post Harvest Technology Institute for Food Product Quality Control and held discussions with Prof. Dr. Le Van To and his other colleagues. This laboratory has reasonably good facilities to undertake quality control work for food grains in particular. The Food and Commodities Control Centre has a Vice Director Eng. Truong Duang Minh who is responsible for drawing standards for the food commodities and their implementation. The laboratory has developed some in-house

technology to extract natural colours like Bixin, Chlorophyll and curcumin and their standards drawn.

They have also developed inhouse technology for processing wheat germ based cereals and some fermented products. Also some extruded products of fruits and vegetable have been developed. A pilot plant for processing 250 Kg/hour has been installed.

I visited the Central Pharmaceutical Factory No. 26 - OPC who are the largest producers of products based on traditional herbal materials. During 1992, products worth US\$ 2 million were exported to Russia and other east European countries. They produce 60 different types of formulation and this factory is one of the largest production factory of Vietnam. I had a meeting with the Director Ph. Le Minh Diem and other pharmacists in-charge of various production departments and quality control. The formulations are ranging from tonics to balms and tablets, capsules etc.

They also manufacture a number of modern medicines and in several dosage forms like tablets, sugar coated and uncoated, capsules, ointments etc. They have fairly large area with different departments. Most of the production and packing is labour oriented. There is no automation and GMP norms need a lot of improvement. Herbal extracts are prepared in several open pans and concentration done in open pans only. The methods of extraction concentration and drying can be modernised so that the active principles of the plants are retained during processing. The herbs are not pulverized to coarse powder, thus extraction would not be complete. There is no standardization of any of the extracts. The quality control laboratory is fairly good but needs improvement.

It was decided that I would spend a week in the R&D department of the factory to help the scientific personnel in preparation of *Centella asiatica* extract suitable for use in creams and Artichoke dry extract for use in tea.

I visited the Quality Control Laboratory for Drugs and Pharmaceuticals, Ministry of Health and discussed about the Quality Control measures and methods of testing of both modern medicines and traditional medicines with the Director Dr. Ngyuyen Van Thi and other pharmacists heading various laboratories. The laboratories are well set up and various modern methods of analysis including instrumental, microbiological and pharmacological/toxicological are routinely carried out. The Ministry has over 3000 formulations registered for most of which methods of analysis have been developed. But a large number of spurious medicines especially in modern system are in the market which are analyzed and detected in this laboratory. In the field of traditional products, TLC finger printing is done extensively and efforts are being made to introduce quantitative methods of estimation wherever possible especially preparations containing Ginseng. A large number of Chinese traditional medicines are also in the market for which the standards are being laid and Quality Control methods developed, to check for any spurious

medicines, especially for steroids being added. The laboratories have added new modern instruments like UV, IR, HPLC and thus are up to date in this field.

I visited the Unipha Project for production of enzymes from animal by products and held discussions with the Head of the Project Unit under UNIDO Mr. Nguyen Quang Thieu. The Pilot plant set up with the assistance of UNIDO is nearly complete and the trial production will commence as soon as the Honeywell Valves are received. The extraction is undertaken in modern and upto date set-up suitable for enzyme technology. Production of alpha-Chemotrypsin, Trypsin, Pancreatin and dry Bile are planned in this pilot plant. This set up will not be suitable for medicinal plant extraction since the conditions of extraction are totally different and divergent. The Quality Control laboratory attached to this pilot plant is also well laid with modern instruments/equipments needed for conducting quality control tests for the enzymes.

I visited the Central Pharmaceutical Enterprise No. 24 and held meeting with the Director Mr. Pham Thien Long and senior factory managers including Quality Control and Production. This factory produces a number of traditional medicines based on only powdered herbal ingredients. The factory follows certain good manufacturing practices and the overall hygienic conditions are better maintained. The workers in the production and packing areas wear face masks and hand gloves during handling of products which is not done at other factories. The Raw Material stores and the finished good stores are better maintained. Use of wooden pellets is enforced to help the proper storage unlike at other factories. The production facilities are fairly good and the Quality Control measures adequate. The records of each batch of the product is well maintained in the Q C laboratory.

The details of working at different laboratories follows :

Traditional Medicine Research and Training Centre, HCMC.

Preparation of dried aqueous extracts of the following medicinal herbs was undertaken and demonstrated to the students and other faculty. 500 gm of each herb on dry basis was extracted twice with about 4 liters of water and the combined extracts filtered and concentrated. The extracts were then dried on tray drier at 105°C, since vacuum drier was not available. The extracts prepared and their yields obtained are :-

(1) Sophora	(116g)	(5) Plantago	(78g)
(2) Lotus	(143g)	(6) Zizyphi	(51g)
(3) Achyranthes	(54g)	(7) Rehmania	(97g)
(4) Alisma	(108g)	(8) Morinda	(42g)

Seven of the above herbs (except Lotus) are taken from a popular product in traditional medicine "HA HUYET AP" for lowering blood pressure. The yields of dried extracts obtained are given in parenthesis. These extracts were then standardised at Polytechnic University by using TLC equipments. The different

methods of extraction and their merits were explained to the faculty and the students. These could not be demonstrated since no facilities of equipments and glassware were available.

A seminar was delivered by me on "Role of Standardization in Traditional Medicines" which was attended by faculty and the students of the Institute. Also the Director and some staff of Quality Control Laboratory and the Director of Ginseng Research Centre were present and gave their views on the standardization technique presented by me. All these people appreciated my views on the methodology being adopted which is at par with the methods being followed by several developed countries.

Department of Food Technology, Polytechnic University, HCMC

The dry extracts of eight medicinal plants prepared at the Traditional Medicine Research & Training Centre were taken up for standardization work at this laboratory. The necessary solvents required for TLC work were purchased. The other facilities like Drying Oven maintained at 105°C, water baths, glassware, Muffle furnace etc were organized.

Preparation of TLC plates with the Desaga equipments were demonstrated, the various precautions to be taken for handling the plates and other requirements were explained to the students. Preparation of methanolic extract of the dry extracts suitable for TLC were also demonstrated. The sample application, various solvent systems and the calculation of R_f values were explained and adequate training was given to the students by repeating the procedures several times. The ash value of the extracts; the water soluble extractives and alcohol soluble extractives as per pharmacopoeal procedures were explained and demonstrated. The various formats for preparing specifications of the extracts were given to them.

Several experiments were conducted especially for TLC with different solvent systems for all the above extract to achieve good separation. The details of the selection of effective solvent system for each of these extracts were explained so that the future experiments could be carried out accordingly. For four of these extracts, total ash and acid insoluble ash were prepared and calculated. For another four extracts, the water soluble and alcohol soluble extractives were determined and the objectives for including these in the specifications explained. They would undertake these studies for the balance samples to complete the specifications of all the extracts.

A lecture was delivered at the Polytechnic University on "Use of Medicinal Plants as Food Supplements" which was attended by the Chief Project Coordinator Dr. Dzuan, Faculty members and the Students of the Food Technology Department. Besides this Research and Development personnel from Central Pharmaceutical Factory No. 26 also attended. The processing and Standardization

of herbal extracts suitable for food products were explained with the help of slides and transparencies.

Central Pharmaceutical Factory No. 26, HCMC.

I spent one week at the R & D Laboratory of this factory which is the largest factory producing traditional medicines in Vietnam. Extraction of *Centella asiatica* leaves with propylene glycol was done and the extract incorporated into cream base suitable for dermatological disorders. The need for using different solvents for extraction for specific products were explained to the technical staff.

An aqueous extract of Artichoke, a popular refreshing tea was prepared in dry form and its standardisation techniques undertaken on similar lines as other extracts.

CONCLUSIONS

- Vietnam has a vast resource of medicinal plants growing wild all over the country.
- The Traditional System of medicine is practised extensively in the country.
- The most popular way of consuming these medicines is in the form of tea or decoction of mixed crude herbs.
- Even for major ailments like hypertension, diabetes, asthma, liver disorders etc., such preparations are used wherein there is no control on the dose given to the patient.
- The Institutes have limited knowledge and facilities to undertake standardization of medicinal plants for use in Traditional medicines or in Food products or beverages like tea, which is very popular.
- Both faculty members and students are keen to learn the new techniques and modern methods, of manufacture and Quality Control but the infrastructure for conducting these studies is lacking.
- Even the glassware, solvents required for such studies are not available and the scientific work is therefore not as per the international standards. In some Institute the instruments and equipments are very old and not usable and

thus even though the faculty members want to undertake the studies, they are unable to do so. They teach the students theoretical aspects about the methodology.

- I have demonstrated several experiments in these Institutes for extraction of medicinal plants; their concentration techniques and drying procedures with whatever limited availability of equipments/glassware.
- The standardization techniques and chemical analysis methods were demonstrated to the faculty and students.
- In view of the limitations of availability of adequate laboratory glassware/equipments etc., the good laboratory practices are non-existent. A great deal of training is required to create awareness of GLP's.
- Similarly in the factory manufacturing tea leaves for export with some medicinal plants/fragrances, the Good Manufacturing Practices are totally lacking. The Quality Control methods are primitive. The manufacturing plant is an old one which needs to be upgraded with automatic equipments. The storage facilities are very poor and inadequate. The hygienic conditions have to be improved considerably. Regular Training Programmes are required for upgrading and creating awareness of these methods.
- The factory producing traditional medicines also requires a great deal of training in regulating Good Manufacturing Practices. The extraction procedure are very old and need to be upgraded to ensure preservation of active constituents. The Quality Control system need to be improved and methods of instrumental techniques introduced to ensure no batch to batch variation in the products being manufactured. The stores for both raw material and finished products need considerable improvement.

RECOMMENDATIONS

1. Establishment of an organized Research and Development Centre for herbal based formulations including Traditional medicines and Food/Nutritional Supplements at HCM city attached to the Vietnam Institute of Science. The organized set-up and equipment proposed are given in Annexure 2 & 3. The Centre would be a model for Standardization of medicinal herbs being used in various Traditional Medicines and food Products, currently being used in the form of teas. This Centre will also have facilities for development of modern dosage form suitable for use in patients with all analytical methodology for Quality Control testing to be followed at various production factories. All the medicinal herbal materials

to be used should have complete data on their standards including acute toxicity profile and pharmacological evaluations report in experimental animals. The centre should be equipped with all the necessary equipments and instruments for conducting systematic studies on the medicinal herbs which are so abundant in Vietnam. A great deal of Training and development of Scientific personnel would be required. By establishment of such a Centre and subsequent adoption of these methods in the pharmaceutical factories, the country can produce quality herbal drugs from Traditional System of Medicines which would be fully standardised with proper documentation. Such products will have greater export potential enabling the country to earn valuable foreign exchange. Through this Centre, the awareness of the potential use of medicinal herbs would be greater enabling the country to utilise the natural wealth of medicinal plants growing wild in several parts of the country. The economic situation of the rural population will improve by collection and growing of selected medicinal plants for which agrotechniques would be developed and requisite training imparted to the farmers for mass cultivation programme.

The funds required can be estimated after the proposal is accepted in principle, which will depend upon the local Government facilities to be extended especially on land and building, manpower recruitment etc. A minimum area of about 10,000 sq. ft would be required for this Centre and a period of 2 - 3 years will be required to set up the Centre with complete infrastructure including identification, procurement and installation of equipments/instruments. The recruitment of scientific personnel and their training should be so planned that by the time the Centre is set-up, the staff should be sufficiently trained to undertake the work in the use of these equipments/instruments.

2. A Pilot plant for extraction of herbs in Pharmaceutical Factory No. 26 is recommended. This factory is the largest producer of Traditional Medicines in the country and exports some of these formulations to East European countries. The processing of herbs for extracts is very primitive at present and a modern set-up with extraction, concentration/drying using low temperature and vacuum is necessary to retain the medicinal value of the plants. The flow chart of this unit is given in Annexure III. An ideal pilot plant would be, to process about 75 - 100 Kgs of crude herbal material depending upon the nature of the herb.
3. The Research and Development and Quality Control laboratories of the Pharmaceutical Factory No. 26 needs to be upgraded with necessary equipments and instruments for testing which lacking at present. There are practically no Quality Control test procedures at present. Similarly the Research and Development laboratories of Food Technology

Department of Polytechnic University at HCMC and the Hanoi University Department of Food Technology need to be built up with appropriate equipments/instruments to process and develop herbal based formulations in a systematic manner and their testing facilities with modern instruments.

4. The research laboratory of Traditional Medicine Research and Training Centre at HCMC has few instruments/equipment for processing and testing of various extracts of medicinal plants. But these are not sufficient to undertake all the studies required. Therefore, I recommend grants to be provided for procurement of selected laboratory equipments/instruments so that the centre is able to impart more training facilities to the doctors of Traditional Medicine getting training at the Centre. The research personnel will be able to develop traditional products in better dosage forms and tested on the patients admitted in the centre itself. In my opinion this Centre plays an important role in the health needs of the country especially the areas around HCMC who regularly visit the Centre for diagnosis and treatment.



UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

JOB DESCRIPTION
SI/VIE/92/801/11-51

Post title Consultant for the production of Galenic formulations

Duration 2 months

Date required as soon as possible

Duty station Ho Chi Minh City

Purpose of mission The expert will assist Food Quality and Technology Centre personnel on the improvement of the processing of the production of plant based formulations.

Duties The following activities must be performed:

1. To evaluate the activities performed by the centre and to advise on the improvement.
2. To perform laboratory trials for selected formulations.
3. To assist on the extraction of the active principles and their introduction in the formulations.
4. To evaluate the equipment availability and to recommend the type of equipment necessary for the modernization and completion of the installation and packaging.
5. To coordinate working programme with the quality control expert.
6. To present the typed final report including conclusions and recommendations.

Applications and communications regarding this Job Description should be sent to:

Project Personnel Recruitment Section, Industrial Operations Division
UNIDO, VIENNA INTERNATIONAL CENTRE, P.O. Box 300, Vienna, Austria

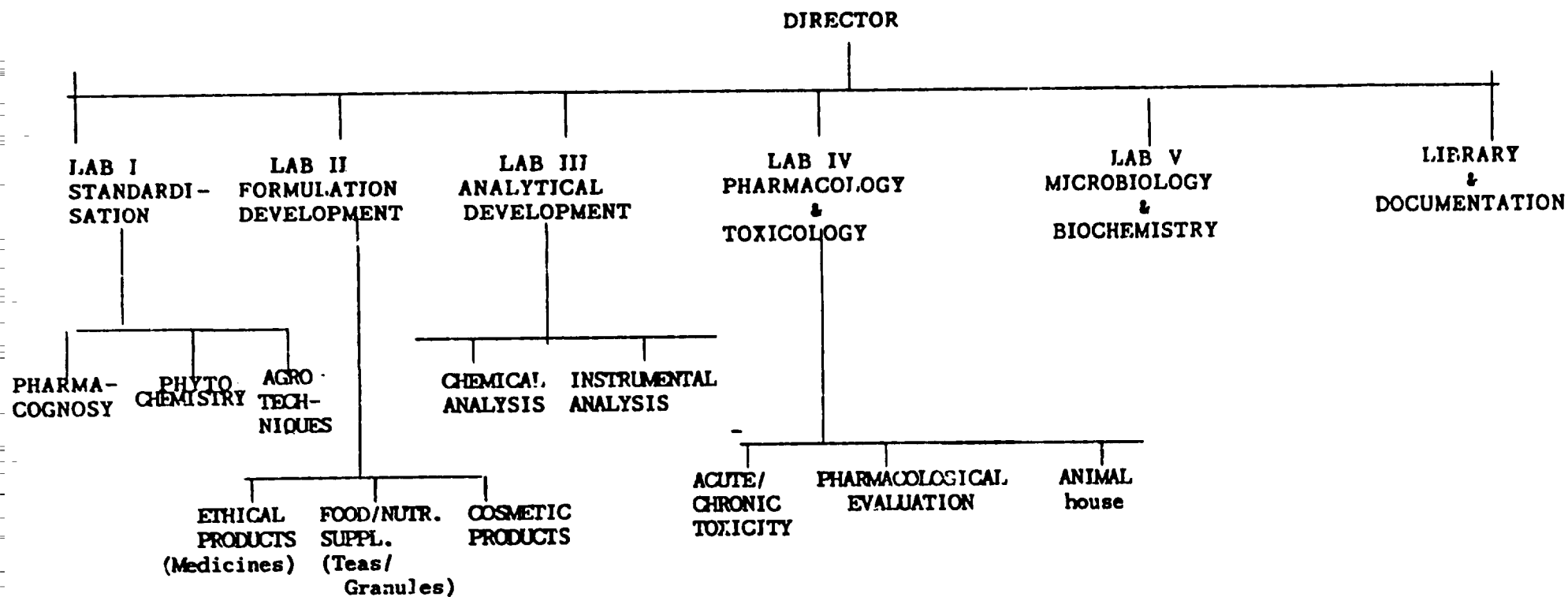
Qualifications Chemical engineer or pharmacist with wide experience in the production of plant based pharmaceutical formulations

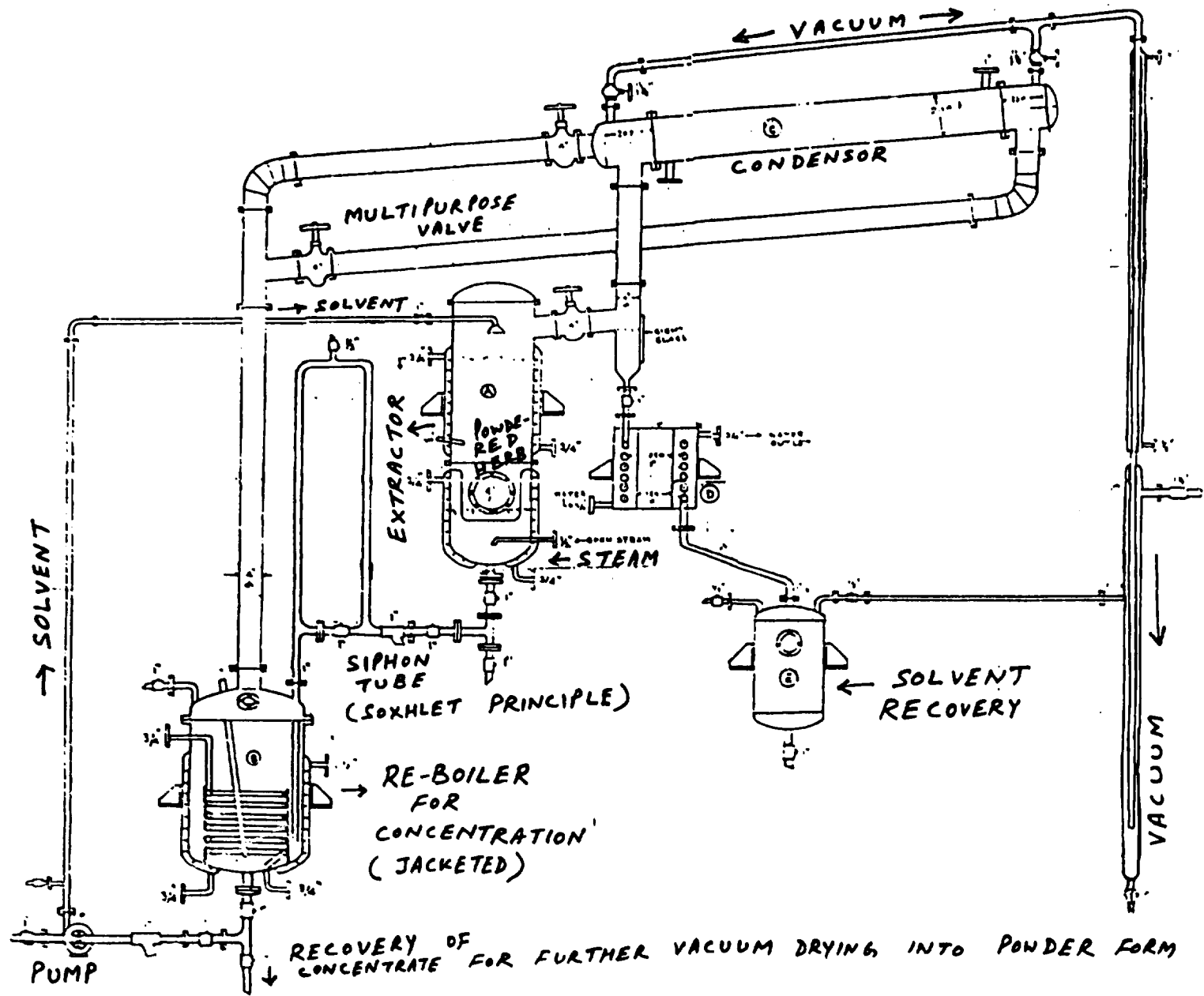
Language English

Background information

The production of pharmaceutical formulations, beverages, medicinal teas, granulates, powders, etc. that could include in their composition nutrients, vitamins or natural provitamin, anti-hypertensive, anti-insomnia, anti-cholesterol, anti-stress and other substances mainly from natural origin or by preparing combinations of natural substances with extracted and/or synthetic active components, will permit the satisfaction of national requirements for the treatment of several common pathologies which affect the population.

CENTRE FOR RESEARCH & DEVELOPMENT OF MEDICINAL PLANTS





FLOW CHART FOR A PILOT PLANT EXTRACTION UNIT

LIST OF EQUIPMENTS/INSTRUMENTS.

1. Centre for research and development of medicinal plants -
HCM City (Annexure II of report)

Lab I - Standardization

	<u>Qty.</u>
1. Light Microscope with Camera attachment for Photomicrography and projection screen with monitor	1 No.
2. Microtomes - Rotary & Sledge	1 each
3. Hot plates	2 Nos
4. Water baths	2 Nos.
5. UV Cabinet	1 No.
6. Electronic weighing balances -	
20 Kgs	1 No.
6 Kgs	1 No.
500 gms	1 No.
7. Soxhlet Extraction Units -	
500 ml	2 Nos.
1 L.	2 Nos.
5 L.	2 Nos.
10 L.	2 Nos.
8. TLC Chambers	3 Nos.
9. Tissue culture laboratory set up -	
i) Incubator	1 No.
ii) Autoclave	1 No.
iii) Laminar flow	1 No.
iv) Refrigerator	1 No.
v) Glass house	1 No.
10. Glassware, chemicals, TLC plates and other consumables	As per requirements
11. Rota vapour	1 No.
12. Heating mantles -	
500 ml	2 Nos.
1 L.	2 Nos.
5 L.	2 Nos.
10 l.	2 Nos.

Lab - II Formulation Development

	<u>Qty.</u>
1. Capsule filling machine (Hand filling)	1 Set
2. Multipurpose unit Erweka type with all attachments for Tablet, Granulation, mixing, coating, blending, ointment/creams mixing and filling etc.	1 set
3. Tablet punching machine (8 stns.)	1 No.
4. Fluid bed drier, Lab. model	1 No.
5. Vacuum pump	1 No.
6. Dehumidifier portable	1 No.
7. Stability ovens	3 Nos.
8. Tray drier (12 trays)	1 No.
9. Vacuum Oven	1 No.
10. Filtration unit	1 No.
11. Extraction unit for crude herbs	1 No.
12. Magnetic stirrers	2 Nos.
13. Hot plates	2 Nos.
14. Water baths	2 Nos.
15. Disintegration test apparatus	1 No.
16. Dissolution test apparatus	1 No.
17. Friability test apparatus	1 No.
18. Tablet Hardness tester	1 No.
19. Electronic balances - 500 gm	1 No.
6 kgs.	1 No.
20. pH meter	1 No.
21. Bottle sealing machine	1 No.
22. Tube crimping machine	1 No.
23. Impulse heat sealer	1 No.
24. Pulveriser for herbs	1 No.
25. Bulk density apparatus	1 No.
26. Humidity oven	1 No.

Lab III - Analytical development

	<u>Qty.</u>
1. High pressure Liquid Chromatograph	1 No.
2. Gas Chromatograph	1 No.
3. High performance thin layer Chromatograph	1 No.
4. I R Spectrophotometer	1 No.
5. U V Spectrophotometer	1 No.
6. Automatic absorption Sepctrophotometer	1 No.
7. pH Meter	1 No.
8. Precision Balance (Analytical)	1 No.
9. Electronic Balance - 500 gm.	1 No.
10. Centrifuge	1 No.
11. Refractometer	1 No.
12. Polarimeter	1 No.
13. Dessicators	3 Nos.
14. Hot plate	1 No.
15. Water bath	1 No.
16. Refrigerator	1 No.
Library & Documentation	
1. P.C.	1 No.
2. Books/Journals	As per requirement
3. Book racks	12 Nos.
4. Display racks for 50 journals	1 No.
5. Over-head projector	1 No.
6. Slide projector - 35 mm.	1 No.
7. Study tables/chairs	As per requirement

Lab IV - Pharmacology/Toxicology

	<u>Qty.</u>
1. Animal cages	40 Nos.
2. Transducers, Pressure, Force & Volume	1 each
3. Recorder	1 No.
4. Operation Table	1 No.
5. Organ Bath	1 No.
6. Heart perfusion assembly	1 No.
7. Activity cage	1 No.
8. Rota rod	1 No.
9. Passive avoidance reflex cage	1 No.
10. Plus maze	1 No.
11. Balance	1 No.
12. Dissection Instruments	1 set

Lab V - Microbiological Laboratory

1. Laminar flow	1 No.
2. Incubator - BOD	1 No.
3. Autoclave	1 No.
4. Oven	1 No.

Lab VI - Packaging development laboratory

1. Corrugated board Tester	1 No.
2. Micrometer	1 No.
3. Tensile Strength Measuring Apparatus	1 No.

II. Pilot plant for Pharmaceutical Factory No. 26

The equipment required have been given in Annexure No. III

III. R&D and Q.C. laboratories of Factory No. 26

Some basic equipment for development of formulations and Instruments required for Q.C. testing needs to be provided. Some of these are already available and requirement will be listed on need base.

IV. The research laboratories of Traditional Medicine Research & Training Centre at HCM City needs the basic equipment for preparations of various extracts and their standardization by TLC. These can also be identified on actual requirement.

The requirements for both the recommendations marked III & IV could be provided by the local Government on similar pattern as that of recommendation No. I and II, which are the major areas to be dealt with. The Q.C. testing would depend upon the specifications which would be drawn in the R&D Centre as suggested as per item No. I.

**Backstopping Officer's Technical Comments
based on the work of Mr. M.K. RAINA, SI/VIE/92/801**

The work carried out by the expert during his two months mission is described in detail in the report. The specialized know how of the expert has been maximally used in training scientific personnel and transferring technology to a number of institutions. Though the expert was to have served in Ho Chi Minh City, he has spent two weeks in Hanoi transferring technology and know how on production of herbal teas with added extracts and on formulation of traditional preparations. The report contains a comprehensive account of the know how transferred. Several seminars have been held to update the knowledge of counterparts. He has assessed the state of activities in the institutions visited and made specific recommendations for improvement. His recommendation for the establishment of a R & D Centre for herbal preparations in Ho Chi Minh City needs favourable consideration of the Government. It is hoped that the technology transferred will be incorporated into industrial production with adequate introduction of Good Laboratory and Manufacturing Practices. The equipment recommended should be procured if a quality standardised preparation is to be produced. The consultant has successfully and effectively carried out much more duties than envisaged in the job description.