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**ASSISTANCE IN THE PRODUCTION OF PHARMACEUTICALS  
FROM THE THAI TRADITIONAL PHARMACOPOEIA**

DP/THA/87/010

THAILAND

Technical report: Evaluation and recommendations\*

Prepared for the Government of Thailand  
by the United Nations Industrial Development Organization  
acting as executing agency for the United Nations Development Programme

Based on the work of Mr. Nithya Anand,  
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\* This document has not been edited.

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Midterm Technical Report

December 9 - December 19, 1988

Nitya Anand

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A suitable strategy for the utilisation of medicinal and aromatic plants, which has a special relevance and importance for Thailand, was outlined in the report submitted in 1982. A technical review of the research and development work carried out in the first phase of the project, and recommendations arising therefrom for the continuation of the project into the second phase, was presented in the 1985 report. The main objective of the present mission was to review the movement of the project from the first phase into the second phase in the light of the project proposal DP/THA/87/010/A/01/37 submitted by TISTR/PNPD and the suggestions made in the Technical Review of 1985 for the second phase of the project. A plan of work/action has been drawn for the ongoing and new projects in consultation with Mrs. Sasithorn Wasuwat, Director PNPD and Dr. P. Somani UNIDO Expert in Pharmacology, who was also in PNPD during this period.

A significant recent development has been the signing of a Science Collaboration Agreement between TISTR (Thailand) and CSIR (India), under which PNPD (TISTR) and Central Drug Research Institute, Lucknow, India (CDRI) will have exchange of scientists and also carry out some joint research programmes. This agreement will supplement the contribution of UNIDO strengthening, and has been taken note of in drawing up the research plans, as some work can be jointly carried out between PNPD and CDRI.

A. Ongoing Projects

1. Garlic Products : The technology for the production of spray-dried garlic has already been transferred

to the industry, and a preparation "Garlic Natura" (GN) based on this technology is marketed by a company. This preparation has been shown to cause lipid lowering in experimental animals and lowering of triglycerides and increase of HDL in humans. While it is proposed to carry out some more biological studies with this preparation, it is also proposed to develop technology for the production of odourless garlic (GOD), and compare the biological properties of the two garlic preparations; GOD would have better acceptance provided the two have similar biological activities.

Work plan :

(i) Develop technology for production of odourless garlic (GOD).

(ii) Develop quality control standards for GN & GOD.

(iii) Study hypotensive (at PNPB) and in vitro platelet aggregation inhibition (at CDRI) activities of GN & GOD.

(iv) Study lipid lowering activity of GOD in experimental animals (at CDRI).

(v) If found promising in hypotensive testing at PNPB antihypertensive testing in SH rats by Dr. P. Somani in U.S.A.

2. Plygesal, an antiinflammatory cream from Z. cassumunar (Phlai oil). A cream made from Phlai Oil has been shown to possess promising antiinflammatory activity in experimental animals and in exploratory clinical studies. Further work planned for this cream includes the following.

(i) Develop quality control standards for assay of the oil and the cream; one set of standards could be the relative concentration of the three major constituents of the oil observed in the GLC.

(ii) Conclude the ongoing sub-chronic toxicity studies.

(iii) Prepare a Clinical Trial Protocol for the cream for a controlled, randomized clinical with plygesal cream or its placebo base compared trial with positive controls (methylsalicylate and phenylbutazone) creams which are largely used in Thailand.

(iv) If found safe in (ii) the cream should undergo clinical trial according to protocol drawn in (iii).

3. Ipomea pes-caprae cream for jelly fish poisoning. In laboratory studies and exploratory clinical studies the steam volatile oil obtained from the creeper Ipomea pescaprae and the cream made therefrom have shown anti-histaminic and anti-jelly fish poisoning activity by topical application. In view of the non-availability of any suitable treatment for jelly fish poisoning it seems important to develop this product. The availability of this plant is however limited. It is therefrom planned to do the following :

(i) Cultivate Ipomea pes-caprae inland in some private or government gardens (already done) make an oil from it, and compare its chemical and biological properties with the oil obtained from the naturally growing plant.

(ii) Develop quality control standards for the oil; content of damascenone, which appears to be one of the important constituent may be useful this purpose.

(iii) Carry out detailed pharmacological studies to study the nature of anti-venom protection.

(iv) Carry out a preclinical toxicity study.

(v) If found safe in (iv) carry out a clinical trial.

4. Aloe Vera cream for burns. Aloe is a highly reputed plant in Thai traditional Medicine, particularly used for inflammatory conditions and for wound healing. G.P.O. is also interested in developing and marketing a product for this purpose and would like to collaborate

with PNPD for this product. In some exploratory laboratory and clinical studies carried out with a cream made from the jelly obtained from the leaves, promising wound healing activity has been noted; in a report of a small study from Raj Hospital on about 10 patients the Aloe cream appeared to compare favourably with povidone-iodine treatment. The method of preparation of the cream, however, needs to be standardised. The following work plan is suggested.:

(i) Standardise the method for the production of the cream; extraction vs jelly preparation and freeze drying vs concentration; develop assay standards for the preparation, control of peptido-glycan or protein to polysaccharide ratio could possibly serve as a standard for the assay.

(ii) Laboratory studies for experimental burns and wounds in animals for comparative study between the cream base, Aloe cream and one or two standard wound healing or anti-burn creams such as with silver sulphadiazine and povidone-iodine.

(iii) A sub-chronic toxicity study.

(iv) An open clinical trial and comparing with a standard cream used in Thailand for this purpose.

5. Alpinia sp. essential oils for antifungal use. Alpinia rhizome essential oils are commonly used in Thailand for skin affections. A. galanga and A. conchigera are the common species growing in Thailand. In antimicrobial screening carried out with the oils of these two species it has been found that the oils though exhibiting rather weak antibacterial activity, had quite significant antifungal activity and the oil of A. conchigera was more potent of the two oils. These oils seem to offer promise for antifungal preparations. The following plan of action is suggested :



(i) Carry out a more detailed in vitro and in vivo anti-fungal screening of the two oils using as reference compounds some of the more common topical and systemic antifungal agents such as miconazol, amphotericine, griseofulvin and tolnaftate; if necessary this work could be carried out partly at CDRI.

(ii) Chemical investigation and comparison of the two oils.

(iii) Sub-chronic toxicity of the oil or its fraction decided on the basis of the foregoing studies.

6. Brucea amarissima preparations. In exploratory study aqueous extract of the fruits, which is devoid of bruceantin, a known quassinoid constituent, was found to exhibit some antiamoebic and anti-cancer activities.

In a follow-up of antiamoebic screening it has been found that the anti-amoebic activity is rather low at non-toxic level of the extract, and it has been decided to drop this study.

For anti-cancer screening the aqueous extract was separated into a number of fractions which are being tested against P 388 tumour infection in mice. The fractions tested so far have not exhibited any noteworthy increase in survival time of the infected mice. Testing should be completed with a few fractions that are left and then decide whether it is worth pursuing this study.

B. <sup>c</sup> 7. Pharmacological screening of Thai plants/products. Broad pharmacological screening of plant extracts and products prepared from traditional remedies form an important components of an integrated strategy for development of new drugs in this field. However, in view of the limited resources of PNPD it was recommended in the Technical Report of Phase I to restrict this screening for the

present to the field of cardiovascular drugs and to some studies for immunomodulation. With the arrival of Dr. P. Somani, the UNIDO expert for CVS the expertise of PNPd in this area has been considerably enhanced and up-graded by his expert advise, technology transfer and supervision; a number of new techniques have been learnt by the staff of PNPd, and this area of screening will be now be pursued regularly.

The following strategy is now suggested :

(i) Plants and remedies specifically mentioned for cardiovascular activity in the Thai Traditional Medicine texts should be collected and screened for CVS activity at PNPd.

(ii) Plants considered particularly important in Thai Traditional Pharmacopea to provide general well-being and may have immunomodulatory activity should also be collected, and their extracts prepared. While their cardiovascular activity should be screened at PNPd, their immunomodulatory and antistress activity should be screened at CDRI. A few such plants were identified in the proposed plan of work for the 2nd phase in the 1985 Technical Report.

(iii) A few selected plants which show promising hypotensive activity in PNPd screens should be tested for their antihypertensive activity in SH rats with the help of Dr. P. Somani, Unido Expert, in his laboratory, in U.S.A.

In this context the following plants are provisionally recommended for screening for CVS/immunomodulator activity; literature survey for these plants is under way and final decisions can be taken after the literature search is completed. This list has been made in consultation with the Ayurved Vidhayalai, Bangkok.

1. ACANTHUS ILICIFOLIUS
2. ALPINIA CHONCHIGERA

3. A. GALANGA
4. ANDROGRAPHIS PANICULATA
5. CEREBERA MANGHAS
6. C. OLOLLAM
7. DRYOBALENOPS AROMATICA
8. ERIBOTRYA BENGALENSIS
9. HYOROPHYTUM FARNICARIUM
10. MANSONIA GAGEI
11. MUSA SAPIENTUM
12. NELUMBO NUCIFERA
13. OCHROCAPUS SIAMENSIS
14. PANDANUS ODORUS
15. RHEMANIA GLUTINOSA
16. SALIX TETRASPERMA
17. STERCULIA LYCHNOFORA
18. TINOSPORA CRISPA (L.)
19. UNCARIA FERREA

C. 8. Production Technology. The products from the following plants, which are readily available in Thailand, are of considerable economic importance and their production in Thailand will provide value-added products. It is suggested that pilot scale technology for the production of these products be developed and entrepreneurs identified to undertake industrial production :

(i) Cananga odorata : essential oils of Extra grade and qualities i, ii and iii.

(ii) Ocimum basillicum : essential oil

(iii) Curcuma longa oleoresin, colour curcumin, and oil

(iv) Rosa damascena : rose oil

(v) Rice Bran : to prepare Vit E and B concentrates, and oryzanol

(vi) Azadirachta indica : to produce different industrial products from Neem such as insecticide preparation, antiseptic preparations, fatty oil for soaps, fertiliser etc.

D. 9. Standardisation of Plant Materials for Export.  
Increasing the export of plants is another important aspect of the utilisation of plants. However, the quality or the state in which the plant is exported has to meet high standards to withstand the international competition. And for this purpose the plant materials have to be collected in the right season, dried under standard conditions, stored carefully and packed properly. It is proposed to provide suitable inputs to improve the quality of the following plants which are required for export.

1. Ammonum Xanthioides : fruits.
2. Centella asiatica : whole plant.
3. Curcuma longa : rhizomes.
4. Hibiscus sabdariffa : flowers.
5. Psyllium : seed and husk
6. Sterculia lychnophora : fruits.
7. Zingiber officinale : rhizomes.

Projects completed/dropped

1. Papain from latex of C. papaya. The technology, for the production of good quality of papain (colourless powder, quite stable with activity of 1700 U/Gm)\* has been developed. It has not been possible to identify a client to set up an industry/unit based on this process. The main problem faced is that the lanced fruit after latex is collected is not accepted for marketing and should be processed to produce some papaya products. It is suggested that a non-technical note giving broad outlines of the project be prepared and widely circulated to bring the work to the notice of the prospective clients. A Technical Feasibility Report should also be prepared giving details

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\* Assayed by Tropical Products Institute 56-62 Gray's Inn Road London WC1 x 8 LU; the normal commercial high grade market samples of papain have about 1400 units/g.

of the project cost, investment etc., which should be supplied only on payment of a fee.

2. Cassia angustifolia preparations. Methods have been developed for the production of standardised senna leaf and pod tablets based on sennocide content, of extracts of about 20% calcium sennocide content and of senna leaf tea. These methods have been made known to G.P.O.; so far G.P.O. has started marketing only the Senna Tea. It is suggested as in the case of Papain both a Nontechnical Note and a Technical Feasibility Report should be prepared to interest new entrepreneurs in this project. There is a growing demand of senna products in the West and export possibilities should be explored.

3. Terpine-4-ol spermicide cream. The spermicidal activity of this cream, though comparable with that of nonoxynol, was not high enough to warrant continuation of this study.

4. Wax and steroids from Sugar-cane press mud. Although some exploratory laboratory work has been carried out, and a wax sample has been isolated, but due to the difficulty of recruiting a suitably qualified chemical technologist, it had not been possible to make much progress with this project. For the present this work may be kept in abeyance.

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