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AN INTEGRATED APPROACH TO RESEARCH ON MEDICINAL PLANTS *

by

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1. Introduction

The importance of plants as a source of medicaments cannot be overemphasised. Plant drugs form the mainstay of medicare programmes in many of the developing countries. Even in a highly sophisticated society like U.S.A., a survey has shown that 25% of all the prescriptions dispensed between 1959 and 1974 contained (i) crude plant material, (ii) extract of a plant or (iii) a pure active constituent. Over ninety crude drugs or extracts of plants and some seventy six pure constituents were encountered in this prescription survey. In 1974 the sale in America of drugs derived solely from higher plants was to the tune of $ 3 billion (1, 2). A similar survey conducted between 1959 and 1967 indicates that the relative importance of plant drugs has remained practically unchanged. In fact, from that figures of export of crude drugs from India, it would appear that the use of some of these drugs has risen sharply in recent years, particularly of senna glycosides, psyllium seeds and husk and Catharanthus roseus alkaloids.

2. Role of Traditional Remedies

The relevance and role of traditional systems of medicine in a country's health care programme, however, remains a controversial subject. On the one hand we have the supporters of traditional medicine who claim that for almost every disease condition a remedy is available in these systems; on the other, the protagonists of modern medicine firmly believe that the usefulness of such remedies is grossly exaggerated. Both these views are extremes,

and the truth lies somewhere in between. However, it cannot be overlooked that in most of the developing countries a majority of the population depends upon traditional systems of medicine. In India it is estimated that over 75% of the population mainly consult the traditional physician; this is confirmed by the sales turnover of indigenous medicines which is 1.1/2 times that of modern drugs.

Important factors for the continued popularity of traditional remedies in any country are their cheapness compared to modern drugs, which brings them within the reach of the poorer sections, and the faith of the people in the traditional doctor, as he is a part of the community. Thus traditional remedies just cannot be ignored and efforts will have to be made to integrate them into medicare programmes. What is important is the cure of the disease or alleviation of suffering, not the source of a drug or the system of treatment which prescribes it.'

A clear perspective of the possible role of traditional systems of medicine in medicare programmes of developing countries has been given by Dr. Halfdan Mahler in a recent issue of World Health devoted to Traditional Medicine [3]:

"For far too long, traditional systems of medicine and 'modern' medicine have gone their separate ways in mutual antipathy. Yet, are not their goals identical - to improve the health of mankind and thereby the quality of life? Only the blinkered mind would assume that each has nothing

to learn from the other. Unfortunately that divergence between the two systems of medicine has almost exactly paralleled the division of the world between the rich and the poor. In some parts of the world, even when modern medical care is available, the majority actually prefer the traditional healer, whom they know and trust.

This is why WHO has proposed that the great numbers of traditional healers who practise today in virtually every country of the world should not be overlooked. For the most part they are already living in those remote communities, intimately involved with the life there, conscious of their neighbours' needs and trusted by them.

Let us not be in any doubt : modern medicine has a great deal still to learn from the collector of herbs. Whatever the outcome of such scientific testing, there is no doubt that the judicious use of such herbs, flowers and other plants for palliative purposes in primary health care can make a major contribution towards reducing a developing country's drug bill."

Active principles obtained from a number of plants used in traditional medicine are now well accepted in modern medicine, outstanding examples being reserpine from Rauwolfia serpentina, psoralen from Psoralea corylifolia, xanthotoxin from Ammi majus, emetine from Ipecac, morphine from opium, ephedrine from Ephedra spp., vincamine from Vinca spp., quinine from Cinchona bark. Further, the fact that much of the progress in modern drugs research has been based upon leads provided by the products obtained from

plants used in traditional systems of medicine supports the view that there is need to investigate traditional remedies and integrate them into modern therapeutics.

3. Research on Medicinal Plants

We have now to consider the strategy to be adopted for the scientific evaluation of traditional remedies to make them acceptable to modern physicians, to sift out drugs that are therapeutically effective from the ineffective ones, and to compare the effective ones with other drugs having similar action available today. In this context it would be pertinent to point out that a differentiation has to be made between indigenous medicaments and medicinal plants. In common parlance both the terms are used loosely and have become almost synonymous. This has to be kept in mind in any programme of scientific evaluation of traditional remedies. Most traditional remedies are compounded of more than one plant drug. The commonly followed method of investigating each component plant separately may not be satisfactory in every case. It is not inconceivable that different chemical constituents of a compounded medicament may synergise the action of each other, or the toxicity of a constituent may be moderated or neutralised by another constituent. Therefore, for initial screening for biological activity it would be advisable to evaluate the compounded drugs as they are used in clinical practice. If activity is confirmed, then testing of each individual plant can follow.

3.1 Household remedies : In case of remedies for non-acute conditions, such as cough, cold and minor diarrhoea, which account for a large proportion of the disease conditions prevalent in any country, even drugs that are somewhat less effective than modern drugs could be profitably employed if these are sufficiently cheap. These could be accepted outright without any clinical/ pharmacological testing. It would only be necessary to standardise these drugs both in regard to method of preparation and final composition. Centralised production of such drugs would ensure that properly identified plant ingredients are used in the proper proportion, and hence the final product would be of the specified standard. As regards quality control of compounded remedies, it may be difficult to evolve a method of chemical assay - bio-assay would be necessary.

3.2 Direct clinical evaluation of drugs : For a number of non-infectious diseases such as diabetes, hypertension, gout, arthritis, etc., it is relatively easy to assess the clinical efficacy of a drug. Reputed traditional remedies could be selected for clinical trials, under controlled conditions, at two or three hospitals in the country. These trials would provide direct answers to the therapeutic effectiveness or otherwise of such drugs. Since these disease conditions are not acute, if a patient is put on an experimental drug for some time and the trial is a failure, no harm is done to the patient.

3.3 Safety studies : Another important aspect to be considered is the safety of traditional remedies. It is true that most of them have been used for centuries, and the chances of their having toxic effects are remote. But still, if data could be provided regarding their safety, their acceptability by modern physicians would be greater. Some laboratories which are adequately equipped for chronic toxicity and Phase I clinical pharmacology studies could undertake these studies on more commonly used traditional remedies, particularly those which have to be used over long periods, contain metals or plants which are now known to be toxic.

3.4 Broad biological screening : Another approach is to carry out preliminary biological evaluation of the medicament in a large number of test systems, in vitro and in vivo, prior to clinical trials. This approach is particularly appropriate for those medicaments that are not very commonly used. Once biological activity is detected in the drug, individual component plants can be put through the same screen to pinpoint the plant responsible for the activity. Even plants for which no definite clinical or biological data is available should be put through the same screen. Such a programme of biological testing involves collection of fresh plants, their correct identification, preparation of total extract, screening of the extract in a broad spectrum of test systems, particularly for those conditions for which the drug may be mentioned in literature.

Those plants which show activity are then subjected to more detailed evaluation, which includes chemical fractionation monitored by biological evaluation, followed by toxicity study of active principles and their clinical trials.

Such investigations are likely to lead not only to the discovery of new drugs but, what is more important, the uncovering of new types of chemical structures having some biological activity, which in turn could provide useful leads for modification of the structure to enhance the activity/reduce side-effects or for synthesis of analogs having better activity. It would not be an exaggeration to say that modern drug research is drawn heavily on such leads obtained from traditional remedies. Many examples are known where the starting point for synthesis of a new drug was a preparation used in traditional medicine. Salicylates owe their origin to the reported analgesic/antipyretic activity of salicylic acid, the active principle of the essential oil of Spiraea ulmaria. The discovery of local anaesthetics started from cocaine, development of analgesics can be traced to morphine and atropine, and of antimalarials to quinine. More recently, detection of the anti-asthmatic activity of khellin has led to the development of cromoglycic acid which represents an entirely new class of anti-asthmatics. World-wide investigation of natural products has uncovered anti-cancer activity in a wide variety of structures which, apart from the possibility of providing anti-cancer drugs, may provide many new leads

for synthesis of new anti-cancer agents. Thus, this generation of leads for synthesis of new biologically active molecules, is one of the most important aspects of research on indigenous drugs in particular and natural products in general.

3.5 Another aspect of the work on indigenous drugs, which is not given due significance, is the possibility of modifying active chemical constituents isolated from them to obtain new biological activities. For example, Glycyrrhiza glabra has been used in India for a long time for various purposes, particularly as an antitussive agent. It has now been found to be very rich in triterpenic acids which are quite effective in controlling/curing gastric ulcers. Modification of the constituent glycyrrhetic acid has led to the development of perhaps one of the most effective agents known today for the treatment of gastric and duodenal ulcers.

3.6 Experience of Work on Indigenous Drugs at Central Drug Research Institute : One of the objectives of the Central Drug Research Institute, Lucknow, is the integrated multi-disciplinary investigation of indigenous drugs, and broad spectrum screening of such drugs is an important programme of the Institute. In this programme about 200 plant extracts are made annually and passed through a battery of about 100 tests for antifertility, anti-microbial, anti-protozoal, anti-helminth and antiviral activities; their effects on central nervous and cardiovascular systems and on lipid and carbohydrate metabolism are also evaluated.

Extracts which show activity in the preliminary screening are followed up by chemical fractionation in order to ultimately isolate the pure active principles, the fractionation being monitored by the biological activity. Only those fractions/compounds which show promising activity are then investigated in detail, both chemically and biologically. I may add here that we have not gone into the study of ecological factors yet.

We have so far examined about 2000 plants from almost all over India; screening data on 1800 plants has been published [4 - 9] [Appendix 1-6]. The overall picture of the distribution of these plants within the higher taxa is as follows : Mycophyta 2; Lycophyta 1; Pteridophyta 41; Gymnosperms 21 and Angiosperms 1704. These plants cover about 1000 genera and the higher plants (angiosperms and gymnosperms) belong to about 176 families in terms of Engler and Prantle classification. Although the collection was not limited to plants mentioned in Materia Medica but was based on the availability of plants in a particular region, 393 of these plants have been included by Chopra in 'Indigenous Drugs of India' . Activity-wise these plants can be classified in nine broad groups:

	Active	Weakly Active
Anticancer	81	-
CNS (Depressant, antiamphetamine, antistrychine)	20	40
CVS	22	29
Cardiotonic	2	1
Diuretic	9	13
Anti-inflammatory	12	9
Spasmolytic	14	19
Hypoglycemic	-	6
Anti-bacterial/fungal	11	-
Antiviral	6	1
	177	118

No plant showed anthelminthic activity. Plants showing anti-fertility activity have been grouped under three subheads : spermicidal 24, semen-coagulant 20, and abortifacient 6. The spermicidal activity of a plant has found useful practical application.

Thus, activity has been confirmed in 285 plants, i.e. 15% of the plants collected by us. 12.5% of these active plants are included by Chopra in "Indigenous Drugs of India" and 17% do not find any mention in medical literature. In other words, the percentage incidence of activity is almost the same in both groups of plants. This, I may add, justifies our method of collection that of not restricting ourselves to the plants mentioned in old texts only.

In the follow-up chemical and pharmacological studies 117 plants have been investigated and active substances from 36 plants have been isolated and identified.

An analysis of the follow-up studies is given below :

Type of Activity	Total plants being investigated	A Active constituents isolated	B Fn. active, inactive constituents	C Fn. active, inactive constituents	D Constituents known
Anticancer	47	13	4	20	8
CNS	22	3	2	3	-
CVS	16	6	2	2	2
Diuretic	7	3	-	1	-
Anti-inflammatory	6	1	1	2	-
Spasmolytic	15	6	1	2	-
Antibact./fungal	4	3	-	-	1
Cardiotonic	1	1	-	-	-
	117	36	10	30	11

We have come across solubility problems; for example, an active substance, though soluble in the total extract, was found to be highly insoluble in the pure state so much so that its proper evaluation was not possible.

We have also encountered plants whose fractions were active but pure active constituents could not be isolated from these fractions. This has led us to consider whether it is absolutely necessary to isolate active compounds in cases of very active plants where such isolation has been found difficult or efforts have failed. We feel that where potency of the plant warrants, purified active fractions could be standardised and taken up as such for drug development.

We feel that the introduction into modern medicine of new drugs from plant sources would indeed be a formidable task. However, if one considers the results in terms of (a) discovery of new biologically active compounds; (b) finding alternative sources of already known drugs or their penultimate intermediates; (c) providing new structures knowing activity and thus giving new leads for synthetic drugs; and (d) providing complex molecules [active or otherwise but of chemical interest] which could be easily modified synthetically, the net gains are substantial.

I may mention another approach which we have decided to introduce in our programme. In order to make use of the experiences of the physicians of traditional systems (Kavirajes and Hakims), we intend to take up for investigation medicaments as they are used in the traditional systems. The methodology of such investigations have to be worked out. Suitable assay methods (preferably biological) and test models would have to be developed for this purpose.

This outlines our philosophy and methodology of research on indigenous plants. We are following a three-pronged approach. While we are fully involved with the first one, the other two approaches are in the initial stages.

Following these approaches, interesting and useful results have been obtained at the Central Drug Research Institute, which include : characterisation of a lipid-lowering principle from the resin of Guggul (Commiphora mukul) [10, 11], spasmolytic sesquiterpene alcohol, himachalol and isohimachalol from Cedrus deodara, [12 - 14], a spasmolytic coumarin, clausmarin, from Clausena pentaphylla [15, 16], anticancer saponins, celsiosides A & B from Celsia coromandeliana (17), sesquiterpene lactones, tagitinines from Tithonia tagitiflora [18, 19], a naphthoquinone, arnebin-1, having antimicrobial, antiviral and reverse-transcriptase inhibiting activities from Arnebia nobilis [20 - 22], a cardiotonic glycoside asclepin from Asclepias curassavica [23 - 24], a hypotensive diterpene alcohol coleonol, from Coleus barbatus [250, a hypotensive alkaloid N-methylcrotsparine from Croton sparsiflorus [26].

4. Plants reported for their activity against communicable diseases

Though a number of plants and medicaments prepared from those plants are used by practitioners of traditional systems of medicine against a variety of communicable and infectious diseases, only a few of them have gained acceptance in modern therapeutics. Given below is a list of plants that are mentioned in the texts of traditional systems of medicine in the Indian sub-continent [27, 28] and Cuba & Mexico [29, 30] which is followed by a description of some of those plants which are commonly used and are of economic importance.

4.1 Plants for helminth infections

TABLE-I

Antihelminths

Indian sub-continent

Adina cordifolia (Roxb.)
Albizzia odoratissima
Ananas sativus
Artemisia siversiana
Artemisia vulgris
Averrhoa carambola
Argemone mexicana
Achyranthes aspera
Acorus calamus
Ailanthus excelsa Roxb.
Alstonia scholaris
Areca catechu (roundworms)
Adhatoda vasica (tapeworms)
Barleria prionitis,
B. cristata.,
B. strigosa

Butea frondosa (ascaris)
Caesalpinia crista
Caesalpinia sappan
Chenopodium album
Cinchona officinalis
Croton tiglium
Curcuma longa
Convolvulus scammohia
Citrullus colocynthis
Calotropis procera
Centipeda minima
Carum copticum
Cocos nucifera (tapeworms)
Erythraea roxburghii
Embelia ribes (tapeworms
roundworms
hookworms)

Eclipta alba Hassk
Emblica officinalis
Erythrina indica
Ficus carica
Foeniculum capillaecam
Hibiscus cannabinus
Holarrhena anti-dysenterica
Hyoscyamus niger (tapeworms)
Ipomoea turpethum
Linum usitatissimum
Luffa acutangula Roxb.
Langenaria sinceraria (tapeworms)

Cuba/Mexico

Allium sativa
Annona glabra
Asclepias curassavica
Chenopodium ambrosioides
Coffea arabica
Cocos nucifera
Coluxbrina reclinata
Caesalpinia crista
Exostema caribaeom
Ecbalium elaterium
Luffa cylindrica
Mammea americana
Mangifera indica
Pourteria mammosa
Spilanthes oleracea
Simaruba glauca
Vanilla eggersi

Indian Sub-continent

Melia azadirachta
Moringa pterygosperma
Musaka parni
Mentha sapicata
Mimusops elengi
Melia azedarach (roundworms & tapeworms)
Melia azadrachta (roundworms)
Mallotus philippinensis
Morus alba (tapeworms)
Nyctanthes arbortristis
Nigella sativa
Ocimum sanctum
Operculina turpenthum
Oxyxylum indicum
Piper chaba Hunter
Plumbago zeylanica
Prongamia glabra
Piper nigrum
Peganum harmala
Prunus armeniaca
Prunus persica (threadworms)
Psoralea corylifolia
Pyrethrum indicum
Punica granatum (tapeworms)
Rheum emodi
Ricinus communis (roundworms)
Swertia chirata Buch.-Ham.
Semecarpus anacardium
Solanum xanthocarpum
Terminalia chabula
Terminalia belerica
Triachyspermum capillaecam
Tinospora cordifolia
Vitex negundo
Zingiber officinale

Butea frondosa Koen, ex Roxb. family Papillionaceae, (Hindi name: Palasha) is one of the commonly used drugs in Ayurvedic system in helminth infections. This is a moderate sized deciduous tree found throughout India extending to the north-west Himalayas. Fresh ground seeds have been recommended for ascaris infections; palasonin isolated from the seeds appears to be the active constituent (32).

4.2 Drugs for Dysentery and Diarrhoea

TABLE II

Antidysenteric Drugs

Indian sub-continent

Acacia Arabica (gum)
Acacia catechu
Aegle marmelos
Alstonia scholaris
Asteracantha longifolia
Bauhinia racemosa
Boswellia glabra
Calotropis procera
Camphora officinarum
Cannabis sativa
Cassia fistula
Cinnamomum zeylanicum
Cochlospermum gossypium
Cordia latifolia
Cydonia oblonga
Emblica officinalis
Eugenia jambolana
Ficus bengalensis
Ficus carica
Ficus glomerata
Helicteres isora
Holarrhena antidysenterica
Hyoscyamus niger
KHASTE AMBA
Malva rotundifolia
Malva sylvestris
Mentha arvensis
Mesua ferrea
Mimosa pudica
Mimusops elengi
Mussaendra frondosa
Myrtus communis
Ocimum pilosum
Phyllanthus maderaspatensis
Papaver somniferum
Plantago major
Plantago ovata
Polygonum viviparum
Punica granatum
PATHOON
Quercus infectoria
Rosa damascena & sugar
Rubia cordifolia
Rumex vasicarius
Veteria indica
Vitex trifolia

Cuba/Mexico

Annona squamosa Lin.
Adansonia digitata L.
Ageratum conyzoides L.
Adenanthera pavonia L.
Adantum tenerum Sw.
Acacia species
Achras sapota
Althaea officinalis
Anacardium occidentale
Annona species
Arachis hypogaea
Arctostaphylos pungens
Argemone species
Aristolochia species
Avicennia nitida
Bursera gimaruba Sarg.
Bursera microphylla
Cuscuta americana L.
Cedrela maxicana M Roem.
Cocos nucifera L.
Coriandrum sativum L.
Chrysobalanus icaco L.
Crescentia cujete L.
Cacalia species
Caesalpinia vesicaria
Calea zacatechichi
Calliandra anomala
Canavalia villosa
Cannabis sativa
Capriola dactylon
Capsicum annuum
Castela species
Castilloa elastica
Celosia virgatu
Cenchrus echinatus
Cephalanthus occidentalis
Cercis canadensis
Citrus aurantifolia
Coccoloba unifera

Coutarea latiflora
Crescentia alata
Cupressus sempervinens
Cydonia oblonga
Cyrtocarpa procera
Deanea tuberosa

Cuba/Mexico

Desmodium amplifolium
Didymaea mexicana
Diospyros erenaster
Dipteryx odorata
Emilia sonchifolia (L.)DC
Elaphrium fagaroides
Eryobotria japonica
Eupatorium collinum
Euphorbia species
Foeniculum vulgare Miller
Gossypium barbadensa L.
Galinsoga parviflora
Galphimia glauca
Garrya laurifolia
Gonolobus nummularius
Grindelia species
Helianthus annus L.
Harnandia sonora L.
Haematoxylon campechianum
Halimium glomeratum
Hedeoma piperita
Hibiscus pentacarpos
Jacobinia spicigera
Jateorrhiza columba
Juncus Loureiranus
Kohleria deppeana
Krameria species
Leonotis nepetaefolia (L.)
R.Br.
Lantana camara
Mikania cordifolia (L.f)
Willd.
Malus communis
Malva scoparia
Malvaviscus species
Mangifera indica
Mirabilis jalapa
Myrica species
Nymphaea alba
Ocimum basilicum L.
Oryza sativa L.
Opuntia Karwinskiana
Oryza sativa

Pachyrhizus palmatilorus
Palicourea densiflalora
Pellaea ternifolia
Peperomia galioides

Cuba/Mexico

Perezia hebeclada
Persea gratissima
Physalis coztomatl
Pimpinella anisum
Piraropappus roseus
Piper sanctum
Pithecellobium albicans
Protentilla species
Priva tuberosa
Prosopis dulcis
Prunus species
Psidium guajava
Pterocarpus draco
Quercus castanea
Randia echinocarpa
Riddellia tagetina
Rosa gallica
Ruellia albicaulis
Rumex species
Ruta graveolens
Scoparia dulcis L.
Simaruba glauca DC
Sambucus mexicana
Sanvitalia procumbens
Selenicereus grandiflorus
Selloa glutinosum
Simaruba amara
Spondias purpurea
Stachytarpheta jamaicensis
Terminalia catappa L.
Triumfetla Usemitriloba Jacq
Talauma mexicana
Taraxacum officinale
Taxodium mucronatum
Terebinthus longipes
Thalictrum species
Vitex species
Vitis vinifera
Waltheria americana
Zanthoxylum martinicense
(Lam.) DC.

4.3 Antimalarials

TABLE III

Indian sub-continent	Cuba/Mexico
Acidum arseniosum	Achras sapota
Aconitum heterophyllum	Allium sativum

Allium sativum
Aristolochia indica
Azadirachia indica
Berberis aristata
Caesalpinia aristata
Cinochona officinalis
Ocimum basilicum
Swertica chirata
Tinospora cordifolia

Andira species
Andropogon citratus
Artemisia mexicina
Asclepias species
Baccharis glutinosa
Bixa orellana
Bouvardia erecta
Brickellia cavanillesxii

Caesalpinia crista
Calea species
Calendula officianalis
Calliandra species
Carya illinoensis
Cassia occidentalis
Cephalanthus occidentalis
Cinchona species
Cissus trifoliata
Citrullus vulgaris
Citrus limonium
Colubrina guatemalensis
Coutarea latiflora
Croton species
Didymaea mexicana
Diospyros erenaster
Dorstenia contrajerba
Ephedra species
Eucalyptus globulus
Euphorbia calyculata
Exostemma caribaeum
Galphimia glauca
Gelsemium sempervirens
Gliricidia sepium
Gonolobus nummulartus
Guazuma tomentosa
Guilandia bonducella
Helianthus annuus
Heliotropium peruvianum
Heterotheca inuloides
Iostephane heterophylla
Iresine calea
Juliania adsthringens
Lemna minor
Lonicera pilosa
Mentha rotunditolia
Mikania guaco
Mimosa sensitiva
Myriocarpa tetraphyllus

Cuba/Mexico

Nicotiana rustica
Persea americana
Pectis capillaris
Peperomia umbilicata
Perezia hebeclada
Perzia gratissima
Persea angulata
Physalis angulata
Piper sactum
Piqueria trinervia
Plantago mexicana
Pluchea odorata
Plumbago species
Porophyllum species
Prosopis dulcis
Prunus species
Psittacanthus americanus
Psoralea pentaphylla
Randia echinocarpa
Salvia species
Selloa glutinosum
Senecio species
Silybum marianum
Simaba cedron
Stevia species
Swietenia mahogani
Tagetes species
Talauma mexicana
Verbena officinalis
Zornia diphylla

Drugs for Leprosy

Indian sub-continent	Cuba/Mexico

TABLE IV

Achyranthes aspera	Albizzia lebbeck
Acacia catechu	Cassia Alata
Calophyllum apetalum	Cucurbita maxima
Cyclea burmanii	Erythroxylom minutifolium
Dioscorea alata	Renealmia aromatica
Tinospora cordifolia	Zanthcxylum martinicense

Achyranthes aspera Linn, family Amaranthaceae (Hindi name: Latjira) is one of the importan drugs recommended for leprosy. It is a small herb, which is found all over India. The seeds, leaves and twigs of the plant are reported for the treatment of renal dropsy, bronchial affections and leprosy. It has been reported that leprosy patients when given a decoction of the whole plant showed distinct improvement in their clinical condition, bacterial status and general health, but the clinical improvement was not as good as with DDS. However, the improvement with a combination of the decoction of the plant and DDS was better than with either alone (31).

4.5 Kalazar

Indian Sub-Continent

Berberis asiatica

5. Cultivation and production technology

Many of the developing countries with their varied climatic conditions and topography provide a very appropriate environment for cultivation of a large variety of medicinal plants, and in fact some of these countries are the leading suppliers of vegetable drugs. India alone exports over Rs 25 million worth of drugs of plant origin. In spite of the considerable advances that have taken place in the pharmaceutical field, especially in the introduction of synthetic drugs and antibiotics, plants and products derived from them have been able to maintain their position; in fact, there appears to be a tendency in the advanced countries, namely West European countries and USA, to go in more and more for natural drugs in preference to synthetic ones. In this context, it is most appropriate and timely that UNIDO has decided to hold this symposium - thus underscoring the continued and growing importance of this field. And what is more important is the fact that many of these plants are now not used as such in the countries of their origin, but are exported to more developed countries which process them for their active ingredients and then export back the latter. Naturally, the price of the active ingredients is much higher than that of the crude drug. From various points of view such as eliminating the cost of transport, development of indigenous industry, it would be useful for the crude drug exporting countries to process these plants to meet their own requirements and also for export. For example, the total imports by the

OECD countries of crude drugs during 1971 was about Rs 710 million, while the total trade in active ingredients by the six leading producing countries amounted to Rs 5570 million. (Rs 2970 million imports and Rs 2600 million exports).

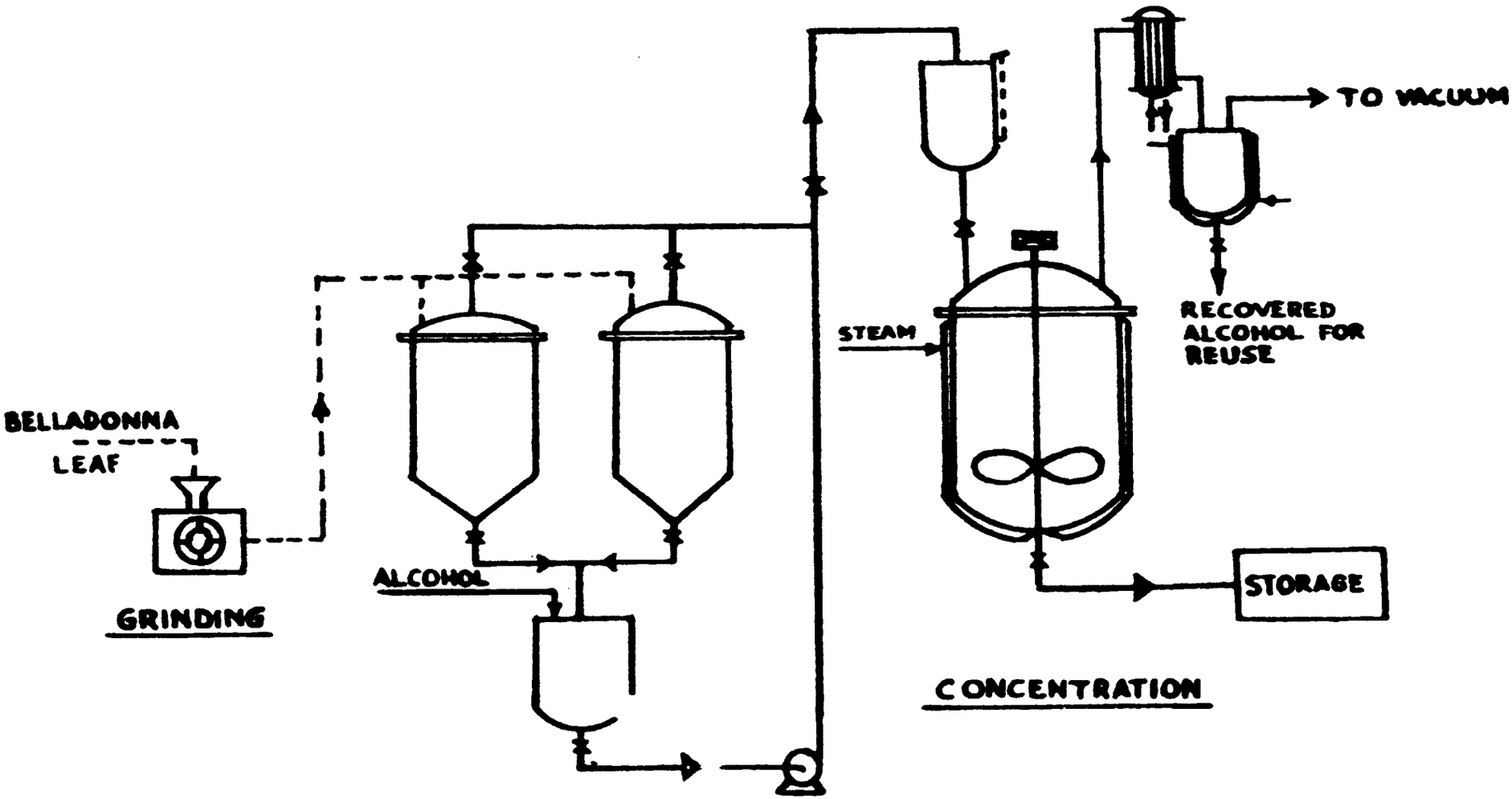
While a large number of medicinal plants are mentioned in the pharmacopoeas of different countries, the principal botanical drug and/or their active ingredients which have a sizeable market are not too many and include : Aconite, Aloes, Ammi majus, Belladonna, Gum Benzoin, Buchu, Catharanthus, Cinchona, Dioscorea, Digitalis, Ephedra, Ergot, Ginseng, Hyoscyamus, Hydrastis, Ipecac, Psyllium, Liquorice, Opium, Papain, Podophyllum, Rauwolfia, Rhubarb, Senna, Stramonium, Valerian. It is, therefore, necessary to first concentrate our attention on these plants. Efforts should, therefore, be made to promote the cultivation/collection of these plants, mainly of production of their active constituents.

5.1 BELLADONNA (A. belladonna and A. acuminata fam. Solanaceae)

5.1.1 The drug Belladonna is obtained from dried leaves and roots of A. belladonna and the related species A. acuminata. The plant is a perennial herb indigenous to central and southern Europe, where it still grows wild in Balkans. The related species A. acuminata has been growing wild in the mountains of Jammu & Kashmir and Himachal Pradesh. However, the wild drug has almost become extinct because of indiscriminate collection.

Although a part of Belladonna is still obtained from wild growth in Europe, most of the supply of this drug is met by commercial cultivation, which is mainly confined to England, Germany, Hungary, Czechoslovakia, USSR, United States and India. In India all the cultivation is confined to farms of Central Indian Medicinal Plants Organization in Kashmir Valley where approximately 25 tonnes of dried leaves are produced annually.

Belladonna is cultivated as a perennial crop and it is mainly propagated by seeds. The seeds are planted on raised beds either in early autumn or spring. Seedlings are ready for transplanting within 3-4 months, after which they are transplanted in the field at a distance of 60 cms in rows which are 90-100 cms apart. Liberal amount of fertilizers is needed for optimum growth and at least 4-6 irrigations are required during this period when there are no rains. The crop is kept free from weeds by regular interculture. The first crop of leaves is obtained after about 8 months of growth after which regular cuttings can be obtained every 2-3 months. In Kashmir 5-6 harvests are obtained annually in the 2nd, 3rd and 4th year. The leaves alongwith twigs are harvested when the plants are in flowers. The leaves are dried in shade or electrically operated drier. Normally once planted Belladonna gives good harvests upto 3-4 years, after which the roots are also harvested and used as a source of alkaloids. On an average 600-800 kg dried leaves are obtained per hectare. However, under proper management an yield as high as 1200 kg per hectare can be obtained, having total alkaloid content of 0.4 - 0.5%.



FLOW-SHEET FOR THE MANUFACTURE OF CONCENTRATED BELLADONNA EXTRACT FROM BELLADONNA LEAF.

5.1.2 PROCESS DESCRIPTION : A brief description of the process to be employed for the manufacture of Concentrated Extract of Belladonna from BELLADONNA LEAF is presented below. The flowsheet appended to this report indicates only the major equipment required for the manufacture of the particular product.

Extraction : The powdered BELLADONNA LEAF (16 mesh) is charged into a percolator wherein the material is washed with alcohol for complete extraction of alkaloids.

Concentration : The extract is concentrated initially at atmospheric pressure and then under vacuum to recover the solvent. The liquid residue is assayed for alkaloids and packed.

Raw material consumption per ton of product :

	Material	Kg/1000 Kg of product
1	Belladonna leaf	10,000
2	Alcohol	20,000

Major Process Equipment

1 Grinding machine with sieving arrangement

2 M.S. percolator

3 M.S. jacketed distillation unit with agitator, condenser, receiver and losing tank

4 M.S. Storage tank

Service Equipment

1 Vacuum Pump
2 Steam generating plant
3 Refrigeration plant for chilled water
4 Circulation pump

5.2 Cinchona (family Rubiaceae) : Stem bark of Cinchona species contains a number of alkaloids, the most important of which are mainly Quinine and Quinidine. Although more than a dozen species are known, the most common species exploited throughout the world are C. ledgeriana, C. succirubra, C. calisaya and a number of related species and hybrids.

The plant is a tree indigenous to mountains of Equador and Peru at an altitude of 3000-9000 ft. and also cultivated in Indonesia and India. There are at least 30 known species and hybrids. In India its cultivation is confined to Darjeeling district in North Bengal, and Nilgiris in Tamilnadu. Hills in humid tropical areas are ideal for cultivation of this tree.

The plants are propagated by seeds. Selected seeds are planted in beds and the seedlings are ready for transplanting after two years. The maximum alkaloid is obtained from the trees which are 6-9 years old. In India the first harvest is taken after 7-8 years when the stems are cut near the ground level. This gives rise to growth of several shoots near the cut ends and another harvest is obtained after which trees are uprooted and replanted. The average alkaloid content ranges between 6 to 7%. However, trees are known to have as much as 12-20% of alkaloids. There are 20 different alkaloids which are known to occur in Cinchona. However, only Quinine and Quinidine constitute the major portion which are being exploited commercially.

5.3 ARTEMISIA

Certain species of Artemisia, [illegible] A. maritima and A. cinna contain 1-2% of Santonin. A. [illegible] and the related species are mostly found growing wild in the Central Asian regions of Soviet Union and [illegible] Asia. Another species A. maritima is found growing in the mountains of India, Pakistan and Afghanistan. This is the plant grown from Kumaon to Kashmir as well as in Himalayan mountains of Pakistan. Only the plants growing in arid and semi-arid areas of Kashmir, Pakistan Punjab, Afghanistan and Baluchistan contain the most amount of santonin. Although a number of attempts have been made for cultivation of this plant in Russia as well as India, the yield of santonin from the cultivated Artemisia is generally poor and most of the supply of santonin is obtained from the plants found growing wild in the arid and semi-arid areas of India, Pakistan and USSR. The plant is generally collected when the flowers are just [illegible], as the unopened flowers contain the maximum amount of the drug.

5.4 AMMI MAJUS

5.4.1 The plant is indigenous to Middle-East, specially Egypt and adjoining areas where it is found growing wild in the semi-arid deserts. Seeds of this plant contain several Coumarins, the most important of which is Xanthotoxin. The plant is at present cultivated in USSR, India and to some extent in Egypt. It is also exploited from wild growth in Egypt and surrounding areas.

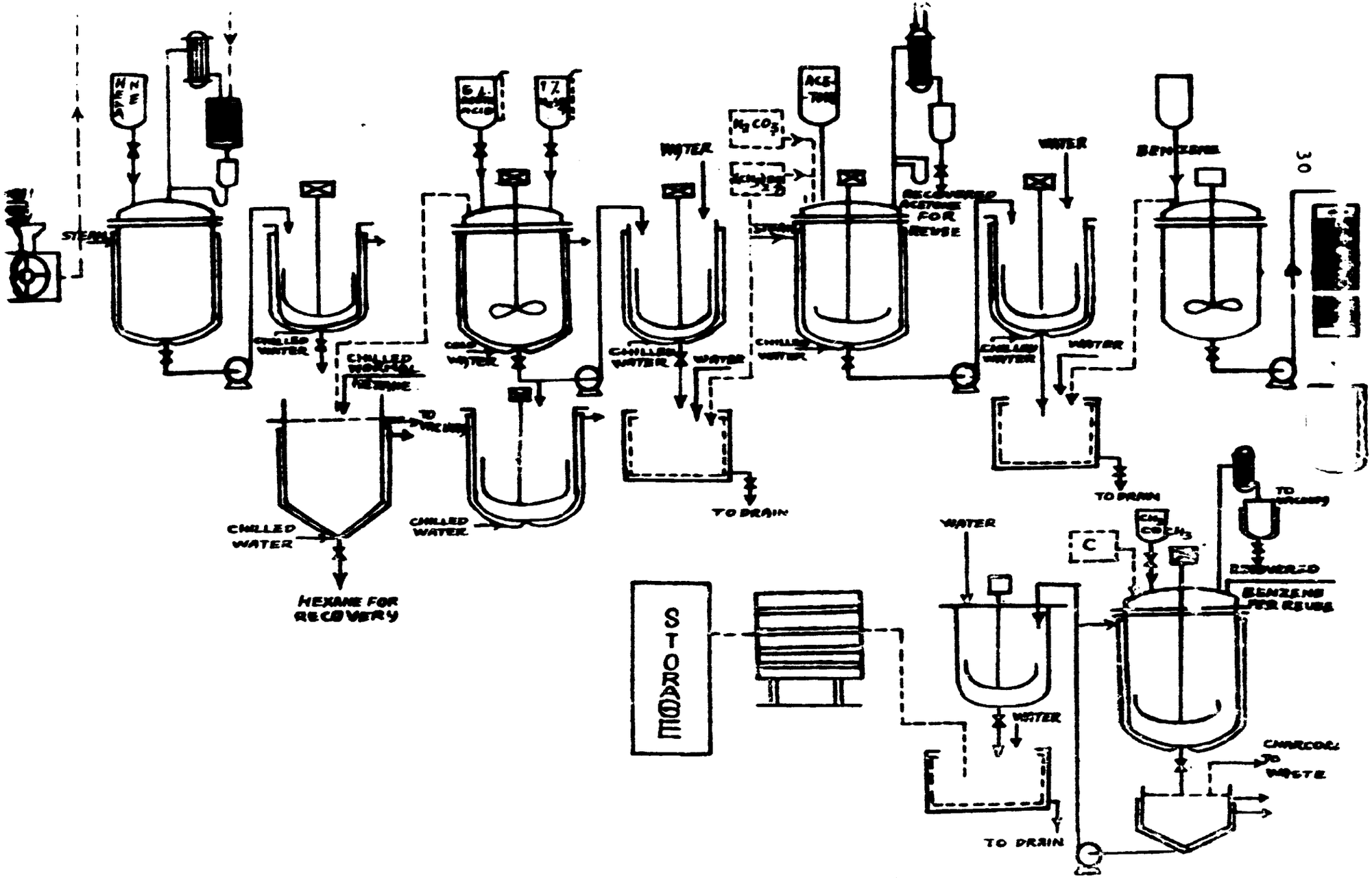
The plant which is an annual herb, is cultivated as a summer crop in temperate areas like USSR whereas it is cultivated as a winter crop in semi-tropical areas of Egypt and India. In India the seeds are broadcasted in the months of October and November. The plant requires at least two irrigations and a moderate dose of nitrogenous fertilizers (60 kg per hectare). The umbels are ready for harvesting during the months of May-June. The seeds are thrashed and cleaned before processing. On an average, about 400-500 kg seeds are obtained per hectare. However, under good management and in fertile soils as much as 1000 kg seeds per hectare can be obtained.

5.4.2 XANTHOTOXIN

PROCESS DESCRIPTION : A brief description of the process to be employed for the manufacture of Xanthotoxin from Ammi Majus seed is presented below. The flowsheet appended to this report indicates only the major equipment required for the manufacture of the particular product.

Extraction : The powdered 'AMMI MAJUS SEED' is extracted with normal hexane in a Soxhlet type extraction unit. The extract on cooling gives a mixture of coumorines which is filtered under vacuum washed with hexane and subjected to dealkylation.

Dealkylation : The coumorine mixture is dissolved in glacial acetic acid and Sulphuric acid is added to this solution under stirring. The reaction mixture is kept for some time and then treated with cold water where the precipitation takes place. The precipitate is filtered, washed and dried under vacuum.

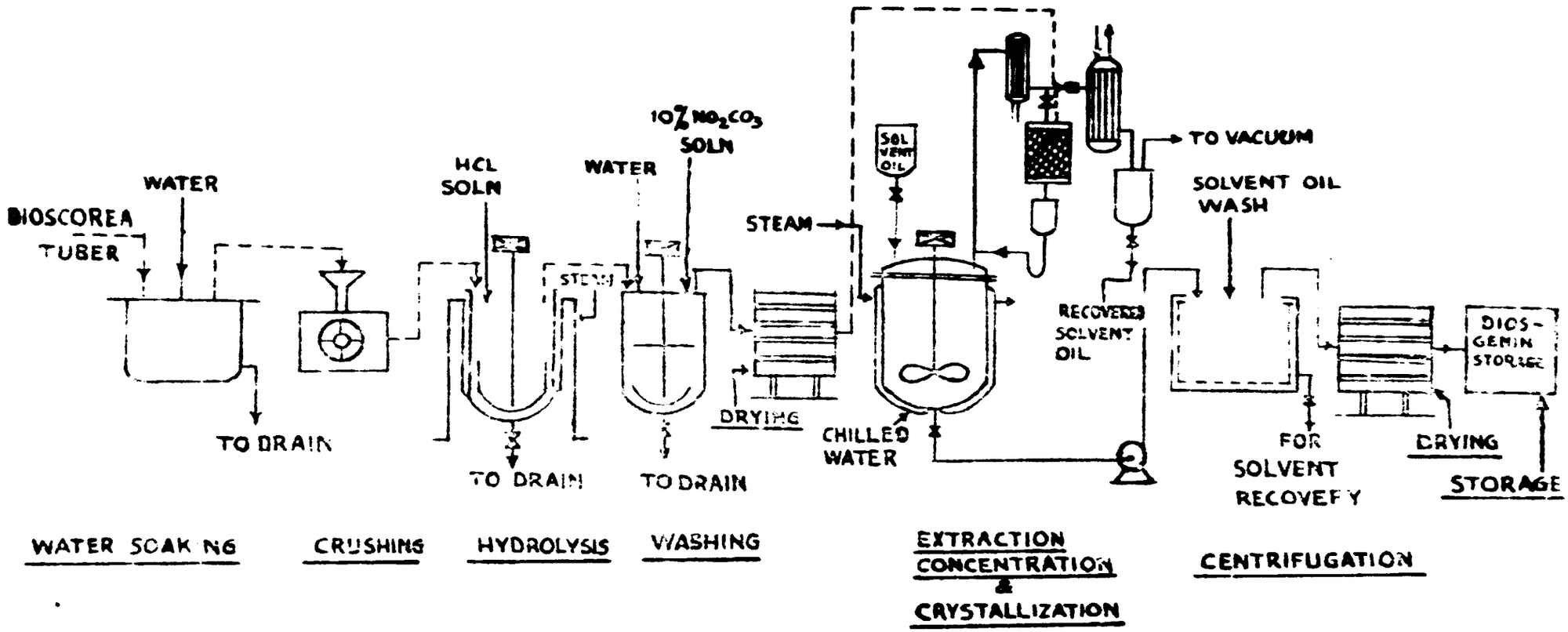


PROCESS FOR THE MANUFACTURE OF XANTHOTOXIN

Methylation : The brine soaked fruits is treated with benzene and the mixture on filtration gives X-oil. The separated X-oil is refluxed with distilled acetone. Potassium carbonate and Dimethyl sulphate are added to the refluxed mixture and heated for two to three hours until the conversion of X-oil to Xanthotoxin is complete. The reaction mixture is concentrated, cooled and poured in cold water. The separated Xanthotoxin, obtained after the filtration of the slurry, is dissolved in benzene and the solution is passed through a column of aluminium oxide. The light yellow coloured material, on complete removal of benzene, is dried and dissolved in acetone. The acetone solution is treated with charcoal and filtered. The filtrate is poured in water and the prepitate is filtered off. The white crystalline Xanthotoxin cake is dried under vacuum and packed.

5.5 DIOSCOREA SPECIES

5.5.1 A group of species of Dioscorea has been recently used as source of steroidal sapogenin, Diosgenin. These include D. floribunda, D. composita and the related species D. spiculiflora and D. friedrichsthalli. They are found growing wild in Mexico and other central American countries like Guatemala and Honduras. Most of the drug of commerce comes from the forests of Mexico and the central American countries. However, cultivation methods have been developed for Dioscorea floribunda, D. composita and D. spiculiflora in Mexico, United States and India and small plantations have been established.



FLOW-SHEET FOR THE EXTRACTION OF DIOSGENIN FROM DIOSCOREA TUBER

Sapogenin bearing Yams can be propagated from seeds, tuber pieces as well as single node stem cuttings. According to American authorities seed propagation is very economical in case of commercial plantations, whereas tuber propagation or stem cuttings can be used for multiplying high yielding clones. In India it has been found that planting tuber pieces is more successful than seedlings. In case of seedling multiplication, seeds are planted in trays or pans either in June-July or August-September. These germinate within 3-4 weeks. Seedlings are allowed to grow in nursery for about 3-4 months after which they are planted in the field. Rainy season August-September or spring months of February-March are ideal for planting. The seedlings are planted at a distance of 60 cms from plant to plant in rows which are 70-90 cms apart. In case of tuber pieces, 50-70 gm tuber pieces are sprouted in sand and the sprouted tubers are planted in the field. As soon as the vines start growing, these have to be provided in the form of bamboo sticks where they are available. The ideal plantation should be provided with wire trellis supported on 6-8 ft. tall stone, iron or wooden pillars. The plant requires liberal supply of farmyard manure and mixture of Potash, Nitrogen and Phosphate for getting optimum yield. 6-8 irrigations should be given during the period when there are no rains. The tubers are harvested after a period of 2-3 years. On an average 8-10 tonnes of dried tubers containing 2-5 per cent Diosgenin, are obtained from one hectare plantation after two years.

5.5.2 PROCESS DESCRIPTION : A brief description of the process to be employed for the manufacture of 'Diosgenin' from DIOSCOREA TUBER is presented below. The flow-sheet appended to this report indicates only the major equipment required for the manufacture of the particular product.

Hydrolysis : The water soaked and powdered DIOSCOREA TUBER is hydrolysed for 6-7 hrs with 5-6% solution of hydrochloric acid.

Washing and Drying : The hydrolysed material is washed initially with water and then with 10% soda ash solution for the complete removal of excess acid. The acid-free material is dried and then taken for extraction.

Extraction and Concentration : The dried material is charged in the extractor and washed several times with solvent oil (boiling range 55-110°C). The solid residue is discarded and the liquid extract is concentrated for solvent recovery.

Centrifugation : The concentrated liquid extract containing diosgenin is cooled and then centrifuged. The centrifuged material is dried and packed after assay.

5.6 Ipecac

Cephael's ipecacuanha consists of dried rhizomes of Ipecac (Brazilian Ipecac) or C. acuminata (Cartogena, Nicaragua or Panama ipecac). The plant is a low perennial herb with much branched annulated root. C. ipecacuanha is indigenous to Brazil and cultivated in India and Malayasia, while C. acuminata is found growing wild in Columbia, Nicaragua and Panama. The roots of both the species contain 2-2.5% total alkaloids consisting mostly amentine and cephaeline.

In India the plant is cultivated in Rungo and Mungpoo hills of Darjeeling district (North Bengal).

The plant can be propagated both by seed as well as by vegetative propagation of root or leaf cuttings. Rich loam soil having plenty of humus is considered ideal for cultivation of this plant. Hills in the humid tropics with 100-200" rains and with minor difference between day and night temperature provide the optimum climate for the growth of this plant. In case of propagation by seeds, the seeds are planted in specially prepared raised beds containing soil and leaf mould. The nursery bed is protected from sun by artificial shade provided by thatched roof or bamboo-splits. After the plants have grown, they are transferred to the permanent beds. The ideal way to cultivate Ipecac is from root or leaf cuttings. These cuttings are raised in special pans containing sand. After the cuttings are rooted, they are transferred to nursery bed containing leaf mould, soil and sand. Well established cuttings are then planted in permanent beds, which are specially prepared and fertilized well with leaf mould. These beds are also protected by creation of artificial shade. The plant is ready for harvesting generally after 3 years, when the roots are dug, thoroughly washed and dried in sun.

5.7 Mucuna prurita Hook is an annual twining herb belonging to the family Leguminosae.

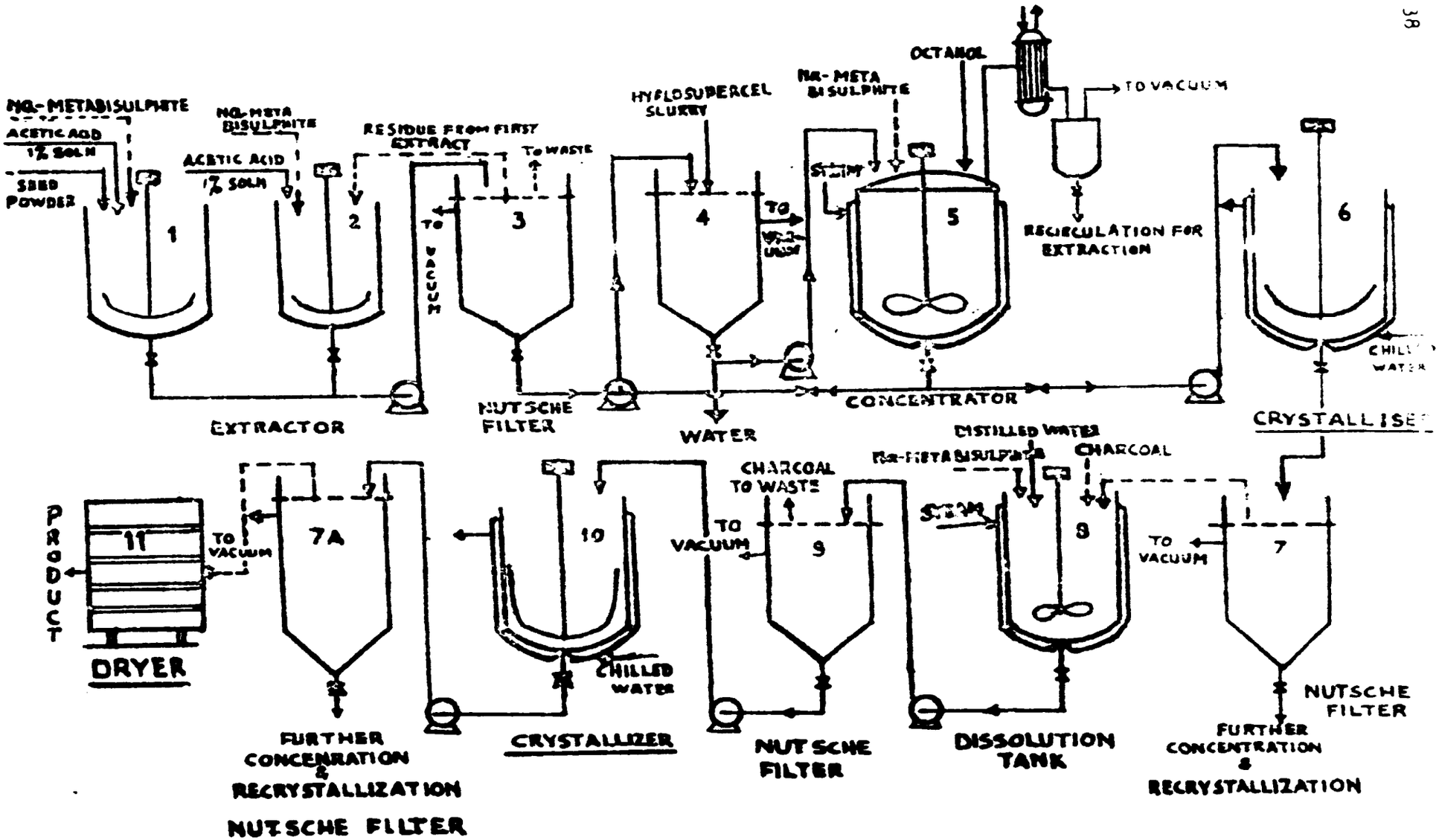
5.7.1 Mucuna prurita commonly known as Velvet Beans is a climbing herb found growing wild throughout Northern India, mostly in the foot-hills of Uttar Pradesh and Bihar. The plants

have a thick stem which bifurcates into branches after attaining a height of about 50-60 cms. Under wild conditions, the branches twine and climb as high as 10 to 15 meters. The plant has been used in indigenous system of medicine for a considerable period of time. However, recently it has been found a good source of L-Dopa. Most of the demand of this drug is obtained from wild growth. However, the plant can be cultivated easily both in North as well as South India. The plant has been found to grow in different types of soil. The plant thrives best in sandy loam well drained soils. The land should be ploughed twice in the month of April. When the soil becomes well pulverised, the field should be well levelled. The seeds should be sown in rows at a distance of 3 metres. At each row pits of 30 cms x 30 cms should be dug and two baskets of well rotten farmyard manure should be mixed. Seeds should be sown in the month of May and June. However, it can also be sown in September after the rains but the growth will be poor. Seeds should be sown at a depth of about 3.0 to 4.0 cms in the soil. The seeds start germinating after 4-5 days, the shoots appear above the ground in about 10-15 days. About 2000 seeds are required for planting per hectare. When the seeds are stored for too long they loose their viability very soon. Therefore, every year fresh seeds should be used for planting. As soon as the vines start growing, they should be provided with support of at least 4 ft. tall in order to allow the vines to grow with flowers and fruits. Flowering starts

from middle of December and continues upto May. September-October planted crop flowers 1 to in January. Pod formation starts after about 15 to 20 days of flowering and they get matured in the months of April and May. In Southern India two crops a year can be obtained. The pods are harvested as they mature. The leaves are generally affected heavily by yellow mosaic virus. Aphids also attack the plants decreasing the crop yield considerably. Depending upon the nature and fertility of the soil on average yield of 8-10 quintals seeds per hectare may be procured. The crop requires 5 to 6 irrigations. However, depending upon the weather conditions, 2-3 times from April to June and 2-3 times from October to March.

5.7.2 Process Description : A brief description of the process to be employed for the extraction of L-Dopa from Mucuna prurita seeds is given below. The flow chart appended to this report indicates the major equipment required for the particular product.

Pulverised (20-60 mesh) MUCUNA PRURITA Seeds (black variety) are extracted with 1% acetic acid solution containing sodium metabisulphite. The clear extract is concentrated under vacuum of 60 mm to a desired concentration. The concentrated liquor is cooled to 3°C for crystallization. The slurry containing L-Dopa is filtered. The mother liquor goes for further concentration and crystallization. The impure L-Dopa is further purified by recrystallisation from distilled water.



FLOW-SHEET FOR THE EXTRACTION OF L-DOPA FROM MUCUNA PRURITA

SEED POWDER

5.8 DATURA METEL

Datura metel is indigenous to Middle-East Africa and found growing wild in different parts of Egypt, Sudan, Iraq, Syriya, India and Pakistan. It is found growing mostly on waste lands in tropical and sub-tropical areas. The plant is also cultivated in certain European countries. The cultivation methods have been developed in India. However, no commercial plantations have been established. In case of cultivation, the plant can be propagated through seeds. Seedlings are raised on raised beds during the months of May and June and planted in the field during rainy season in July-August when they are 4-6 weeks old. Seedlings are planted at a distance of 60 cms in rows which are 70-80 cms apart. No irrigation is required during the rains. However, 2-3 irrigations are needed after the rainy season is over during the months from October to March. The crop is ready for harvesting sometime during the month of October when it is in flowers. Leaves alongwith terminal twigs are picked up by sickle or knife. Three such crops can be obtained during the growing period of nine months. The leaves are dried in shade. A hectare of crop gives 1000-1200 kg dried leaves having 0.4 - 0.6% total alkaloids, 70% of which is Hyoscine.

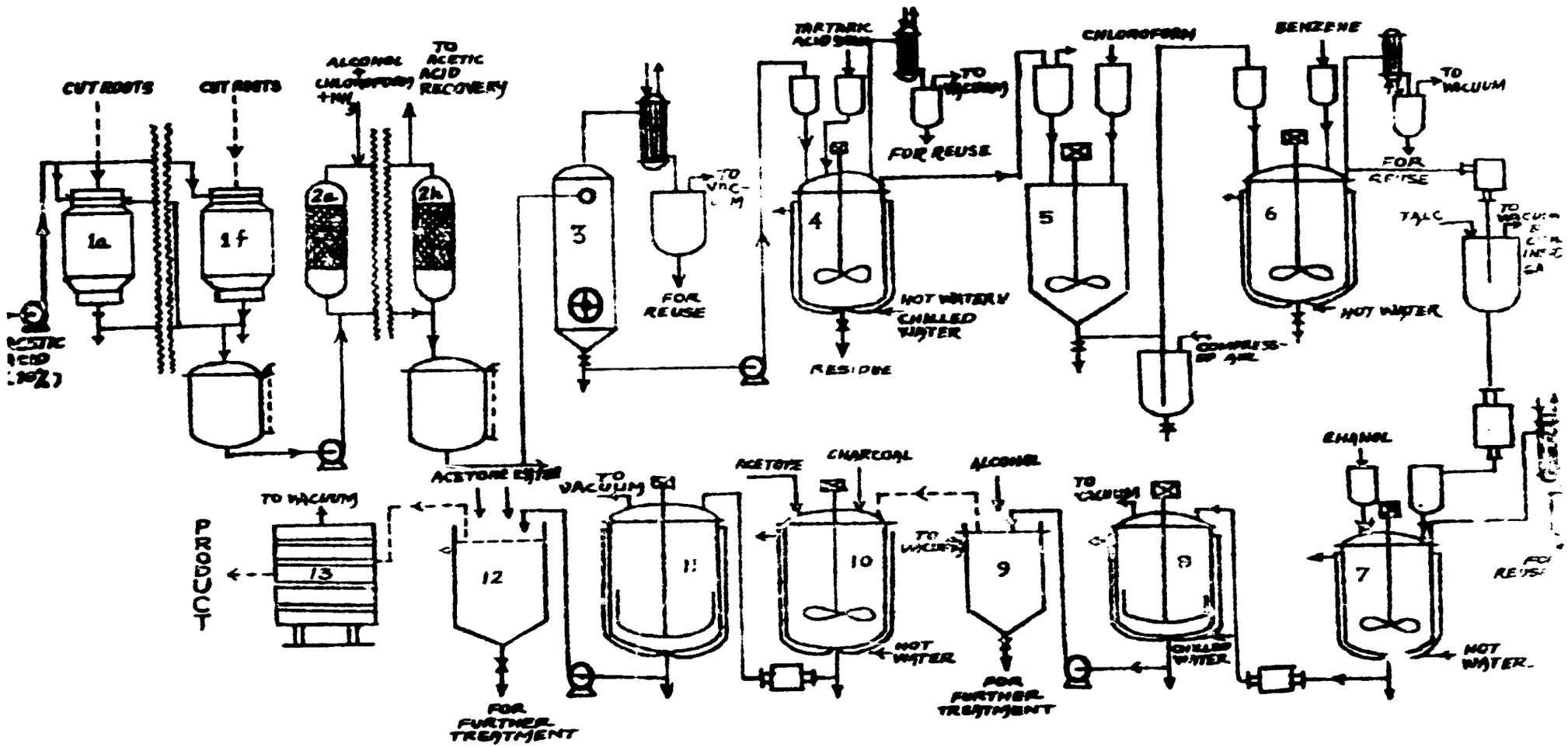
5.9 RAUWOLFIA SERPENTINA : The plant is erect shrub indigenous to India and Bangladesh. It is found growing wild in the forests of Uttar Pradesh, parts of Bihar, Bengal, Assam, Andhra Pradesh and Kerala. Most of the present requirement is obtained from wild growth. Very few commercial plantations have been established. However, it has been shown that the plant can be grown commercially.

5.9.1 R. serpentina is a tropical plant and thrives well in hot humid climate. Plains of Bengal, Assam and the coastal areas in Kerala, Tamilnadu and Andhra Pradesh are ideal for cultivation of this plant in India. The seeds are planted in flats or raised beds during the months of May-June. These germinate within a period of 15-30 days. 2-3 months old seedlings are transplanted in July-August at a distance of 45-60 cms in rows which are 60-70 cms apart. The field is kept free from weeds by regular interculture and the crop is harvested after 2 years. Roots are dug, washed free of soil and dried in sun. A hectare of good crop gives 800-1000 kg dried roots containing 0.6 - 1% total alkaloids.

5.9.2 Process Description for Reserpine : A brief description of the process to be employed for the extraction of Reserpine from the roots of RAUWOLFIA SERPENTINA is presented below. The flowsheet appended to this report indicatesø only the major equipment required for the particular product.

Extraction and absorption : Cut Rauwolfia roots are extracted with 10% acetic acid solution in a battery of extractors. The extract is then passed through a battery of absorbers containing ion-exchange resin. Alkaloids present in acetic acid extract are absorbed in the resin and the residual extract goes for recovery of acetic acid.

Elution and concentration : Absorbed alkaloids are eluted from the resin by alcohol-chloroform mixed solution containing dissolved ammonia. The eluate is concentrated at 40°C and 60 mm. Hg pressure. The resin goes for recovery and the alcohol-chloroform mixed solution is recycled.



FLOW-SHEET FOR THE EXTRACTION OF RESERPINE FROM THE ROOTS OF RAUWOLFIA SERPENTINA

Extraction by tartaric acid solution and chloroform : The concentrated sludge is repeatedly treated at 40-50°C with 3% tartaric acid solution. The tartaric extract is subsequently cooled and extracted with chloroform. The chloroform extract is dried and concentrated at 40°C under 150 mm. Hg pressure. The recovered chloroform goes for reuse.

Extraction by benzene and crystallization of crude reserpine: The concentrated chloroform residue is repeatedly extracted with benzene at 40°C. The benzene extract is concentrated and the recovered benzene goes for reuse. The residue is dissolved in ethyl alcohol and the solution, after filtration, is allowed to crystallize. The slurry is filtered for crude (technical) reserpine and the alcohol-mother liquor is delivered for further treatment.

Purification of reserpine : Technical reserpine is dissolved in acetone. The solution, after activated charcoal treatment and filtration, goes for crystallization. The slurry is filtered for reserpine and the mother liquor is delivered for further treatment. Filtered reserpine is washed and dried at 40-45°C under vacuum.

5.10 LIQUORICE (GLYCYRRHIZA)

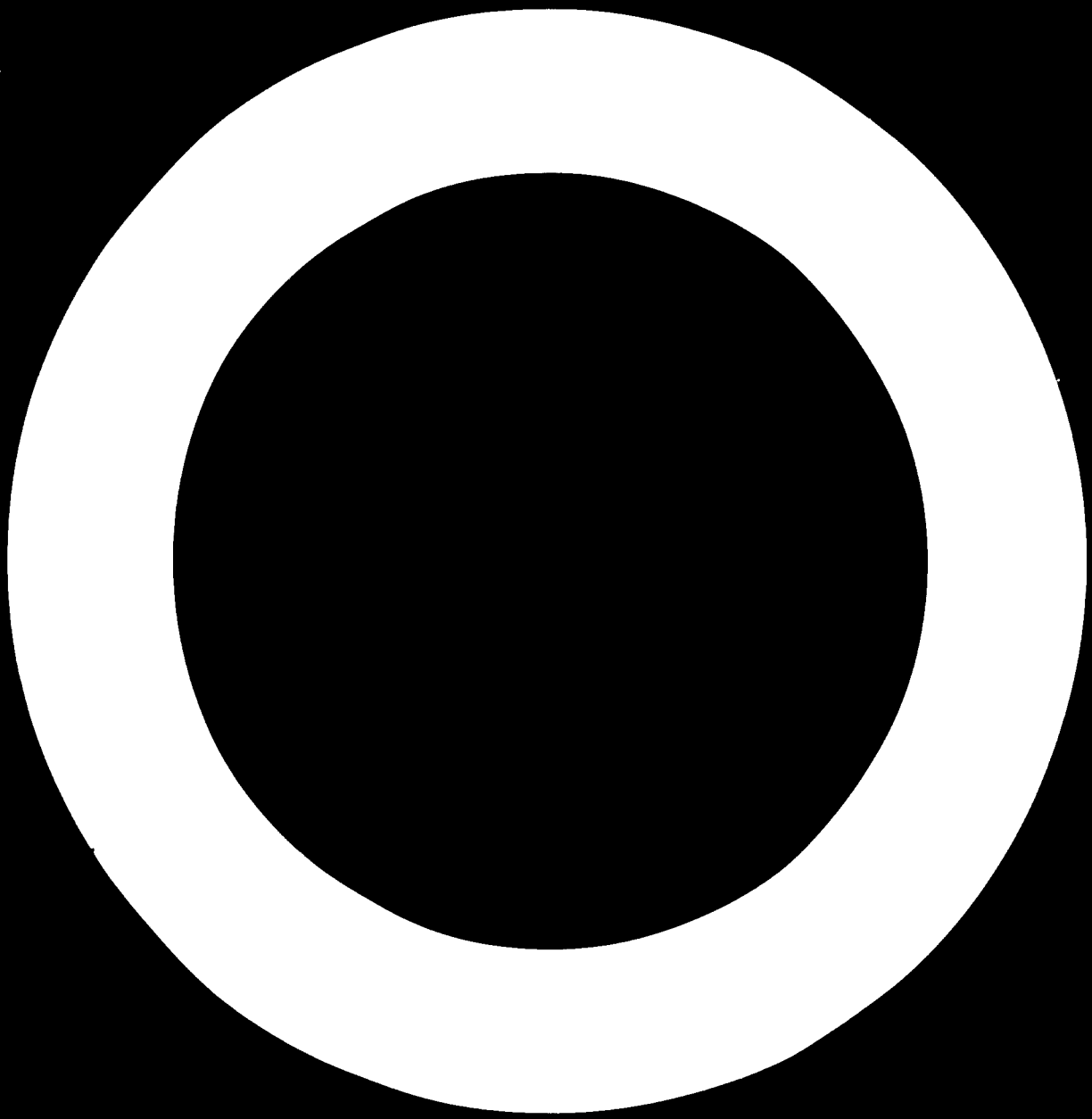
5.10.1 Licorice is obtained from dried roots and rhizomes of Glycyrrhiza glabra (Spanish Licorice) or G. glabra var. glandulefera (Russian Licorice). The plant is a perennial herb indigenous to Turkey, Greek, Asia, Libor and USSR. Most of the Liquorice of commerce is obtained from Turkey, Iraq, Syria, Afghanistan, USSR and Spain, where it is found growing wild in semi-arid and arid areas.

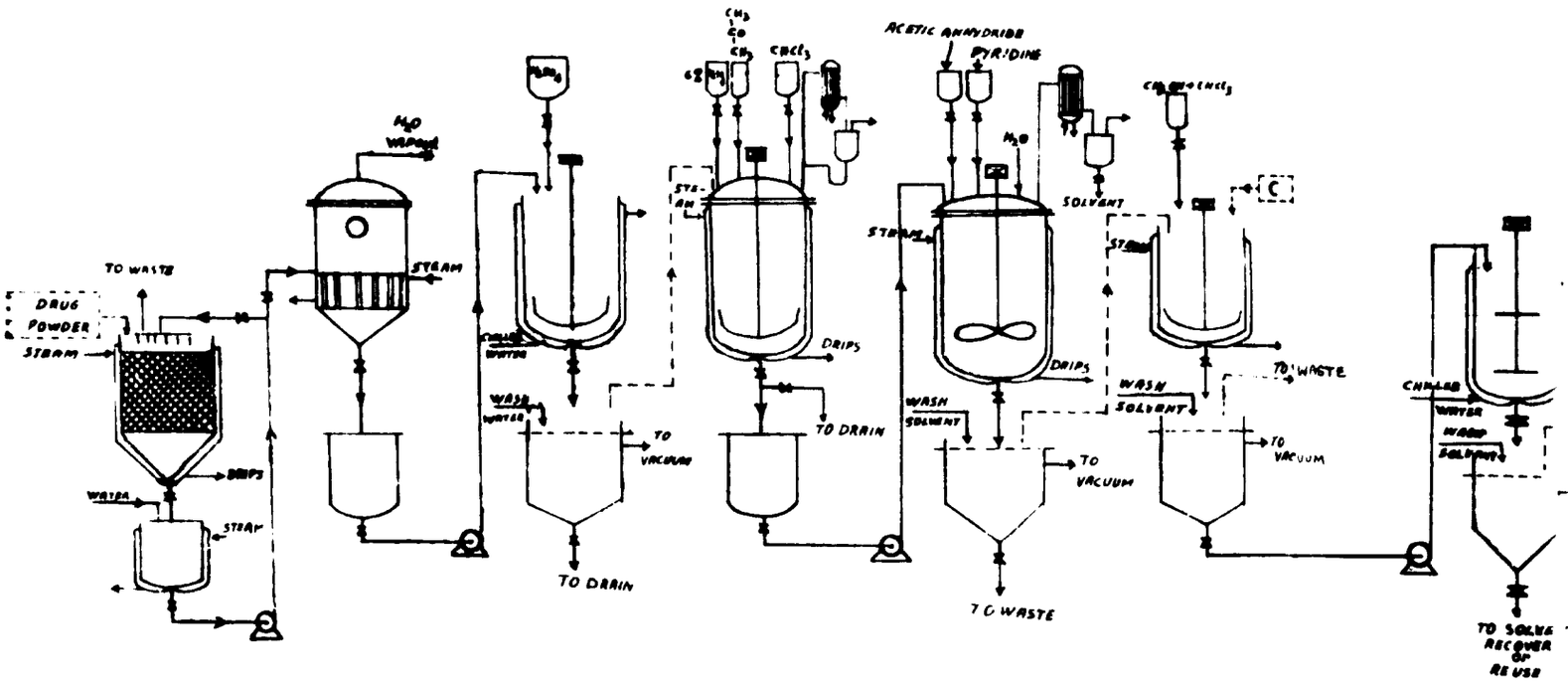
As sufficient amount of the drug is available from the wild growth, very few commercial plantations have been established. However, experimental methods have been developed for cultivation of the crop in countries like India where the plant is not indigenous to the region.

Rhizome cuttings are planted in autumn or the rainy season at a distance of 70-90 cm in rows which are 90-100 cms apart. The crop does not need any special care, except that it should be kept free from weeds in early stages. The crop is ready for harvesting after 2-3 years when the roots and rhizomes are dug, washed free of the soil and dried in the sun. The plant grows better in semi-arid and arid areas having light soil.

5.10.2 Process Description : A brief description of the process to be employed for the production of Glycyrrhitic acid from Glycyrrhiza glabra root (liquorice) is presented below. The flowsheet attached to the report indicates only the major equipment required for the particular product.

The preparation of glycyrrhitic acid involves numerous processes. The powdered 'Glycyrrhiza glabra' root is extracted with hot water, the aqueous extract concentrated to a small volume and treated with concentrated sulphuric acid to give the crude glycoside of glycyrrhitic acid. The glycoside is dissolved in acetone and hydrolysed with 6% sulphuric acid. The reaction mixture is extracted with hot chloroform. Removal of the solvent and acetylation of the residue with pyridine and acetic anhydride, yields the acid acetate which is crystallised from methanol chloroform.





PRODUCTION OF GLYCYRRHETIC ACID

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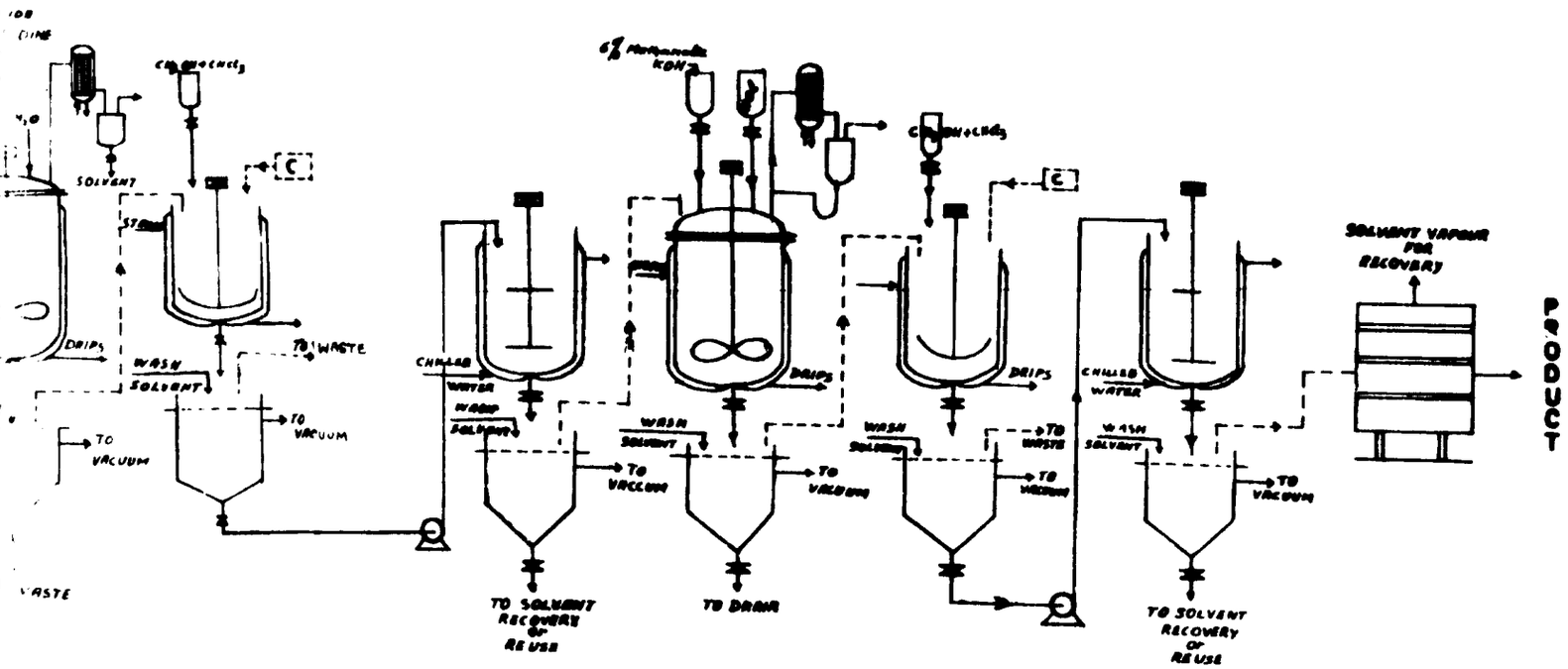
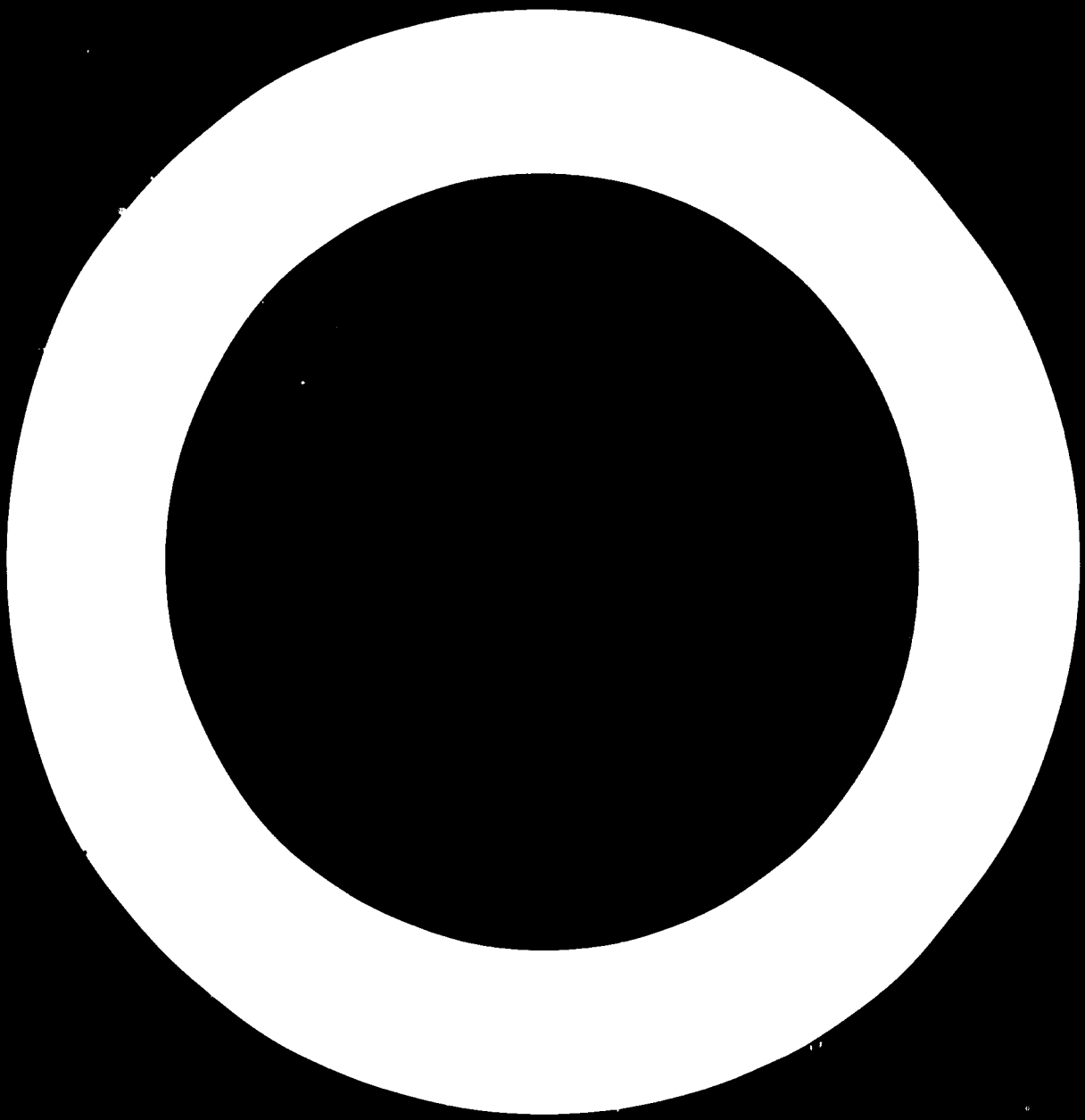


PRODUCTION OF GLYCYRRHETIC ACID

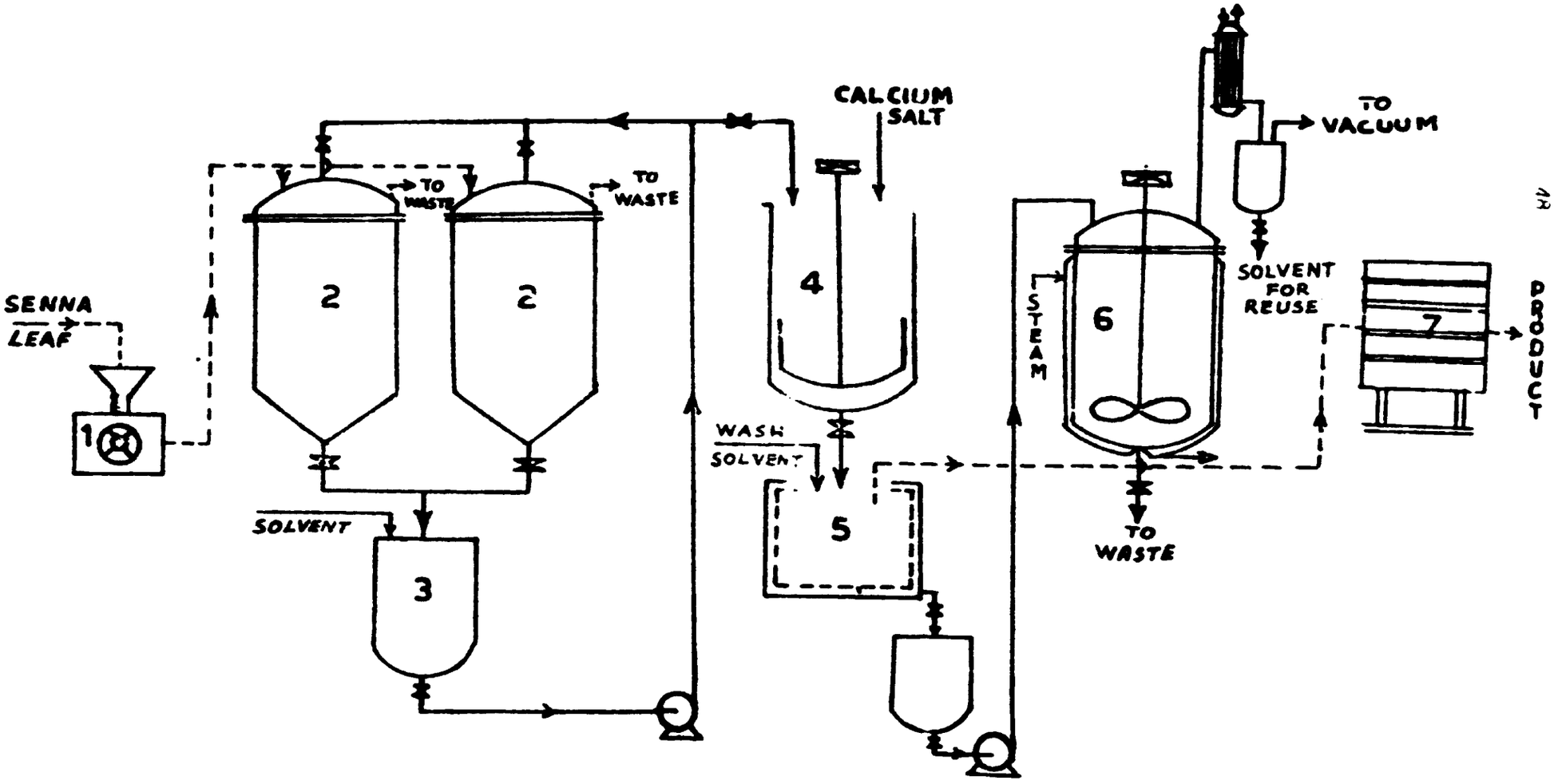


Deacetylation of this material with methanolic KOH followed by precipitation with hydrochloric acid and crystallisation from methanol chloroform gives the title compound.

5.11 SENNA

5.11.1 Senna consists of dried leaves and pods of Cassia acutifolia, (Alexandrian senna) or C. angustifolia (Tinnevelly Senna). C. acutifolia is found growing wild near the Nile river in Sudan and parts of Egypt while C. angustifolia is growing wild in Somalia, and Arabia and India. Most of the Senna comes from wild growth in Sudan or the cultivated crop in Southern India.

In India it is cultivated mostly in the district of Tinnevelly and surrounding areas, mostly as a dry land crop with or without irrigation. However, it is sometimes also cultivated in wet land after a crop of rice. Seeds are broadcasted or drilled in soil at the rate of 15 kg per hectare. As the seed coat is tough, it is generally damaged by pounding with a mixture of sand. The crop is ready for harvesting after 3-4 months. When the leaves are fully grown they are stripped by hand. Another crop of leaves is obtained after another month, after which the crop is allowed to mature and the pods are harvested at the end. The leaves are dried in thin layers in shade, while the pods are dried and beaten to remove the seed. On an average about 600 kg dried leaves and about 100 kg pods per hectare are obtained. However, under good management 800-1200 kg dried leaves and 150-200 kg pods can be obtained. The leaves and pods contain 2-2.5% glycosides. Alexandrian Senna is generally richer in glycosides than Indian Senna.



FLOWSHEET FOR THE PRODUCTION OF CALCIUM SENNOSIDES

5.11.2 Process Description : A brief description of the process to be employed for the production of Calcium sennosides from Senna leaf/pod is presented below. The flowsheet attached to this report indicates only the major equipment required for the particular product.

Senna leaf/pod is extracted at room temperature with a suitable solvent. The extract is treated with a calcium salt to precipitate calcium sennosides. The slurry is filtered and the solid cake is washed, dried, powdered and packed. The mother liquor is distilled for solvent recovery.

5.12 STRAMONIUM

Stramonium consists of dried leaves and flow top of Datura stramonium often called Jimson Weed. It is an annual herb indigenous to Caspian sea and has become naturalised in Europe and North America. The plant is also cultivated in Central Europe and South America. In India most of commercial supply comes from Kashmir Valley where the plant has been found growing wild on waste lands as a weed for a considerable period of time.

When cultivated, the crop is raised from seeds. Generally seeds are broadcasted or dibbled. After germination the seedlings are planted at a distance of 60 cms from plant to plant in rows which are 70 cms apart. The crop can also be raised by raising nursery and transplanting the seedlings after 45 days. The crop planted in March-April is ready for harvesting during June. Leaves alongwith the twigs are harvested and dried in shade. The dried leaves contain

total alkaloids upto 0.4 - 0.5%, 60-70% of which is mostly Hyoscyamine with 20-30% hyoscine. On an average about 100-800 kg of dried leaves are obtained from a hectare.

5.13 SOLANUM SPECIES : A group of Solanum species containing steroidal alkaloid Solasodine have been considered an alternate source for steroidal drugs during the recent years. The species which have been reported to contain Solasodine, belong to both temperate as well as tropical groups.

Only the temperate species have been exploited commercially to certain extent in some European countries; mostly in USSR, Czechoslovakia and Hungary. These include S. lacintium and the related species S. avicalare. In these species the alkaloid is distributed throughout the plant and both the leaves as well as berries contain appreciable amount of active constituent. Only leaves are exploited commercially for extraction of Solasodine, as 2-3 crops can be easily obtained during the cropping season.

The plant is propagated through seeds. Seeds are either directly planted in rows or seedlings are raised in autumn or spring and planted in early spring or summer. The seedlings are transplanted at a distance of 70-90 cms in rows which are 90-100 cms apart. Seedlings planted in spring give the first crop of leaves in early summer. Two more crops of leaves are obtained before the onset of Winter.

The plant requires liberal doses of nitrogenous fertilizers in order to get optimum yield of leaves. It is also affected by a large number of insect pests and effective control measures have to be taken in order to get an economic return. The plant has been tried in Kashmir Valley several times during the last ten years and it grows well in that climate. However, its cultivation on commercial scale has not been possible because of low yield of leaves and low Solasodine content, which is 1.5%. A hectare of good crop of Solanum yields 1000-1200 kg of dried leaves. The leaves contain 1-1.5% of Solasodine. Although the crop has been cultivated in East-European countries, the acreage has gone down recently because of a large number of virus diseases which are becoming a limiting factor in cultivation of this plant.

The main tropical species is S. khasianum which is found growing wild throughout the Northern Indian plains from Himachal Pradesh to Assam. It is an annual herb having thorny leaves, stem and yellow berries. The berries of this plant have been reported to contain .5% to .7% of Solasodine. However, on an average 1-1.5% Solasodine has been obtained. A large number of experiments have been carried out throughout the country for cultivation of this plant in the North as well as South and some pilot-scale plantations have already been established. However, it is not possible to exploit it commercially as a source of Solasodine because of low yield of berries and low Solasodine content of the commercial crop.

The plant is propagated through seeds. Seedlings are raised during the months of May and June and planted in the field when 8-10 weeks old, sometimes in July-August. The seedlings are planted at a distance of 45-60 cms in rows which are 60 cms apart. The crop is kept free from weeds by frequent interculture. However, very little irrigation is required in Northern India, as it is grown in rainy season. The crop is effected by a large number of insects and diseases and this is one of the limiting factors in cultivation of this crop specially in Northern India. The berries are ready for harvesting sometimes in November-December. A hectare of good crop of S.khasianum yields 800-1000 kg dried berries containing 1-1.5% Solasodine. However, there have been experimental plantations to show an yield as high as 2000 kg per hectare. One of the main limiting factors in cultivation of this crop is presence of a large number of thorns which make harvesting very difficult. Other related species which have been reported to contain Solasodine, are S.nigrum, S.incanum and S. xanthocarpum.

Conclusions

1. In view of the relatively low cost of medicaments used in traditional systems of medicine, and the dependence of large sections of the population of developing countries upon such remedies, it is necessary to take steps to include them in the medicare programmes of these countries which would require (i) standardisation of the production and quality control of important medicaments, (ii) evaluation of the safety of drugs that have to be administered for long periods, (iii) clinical and biological evaluation of drugs for which evidence regarding therapeutic activity is insufficient or doubtful, and (iv) broad spectrum biological screening of plants.

2. Since plants are an important renewable source of drugs and other chemicals of economic value, their cultivation and production of their active constituents would be of great economic benefit to the developing countries and should be promoted. About a score of such plants have been identified.

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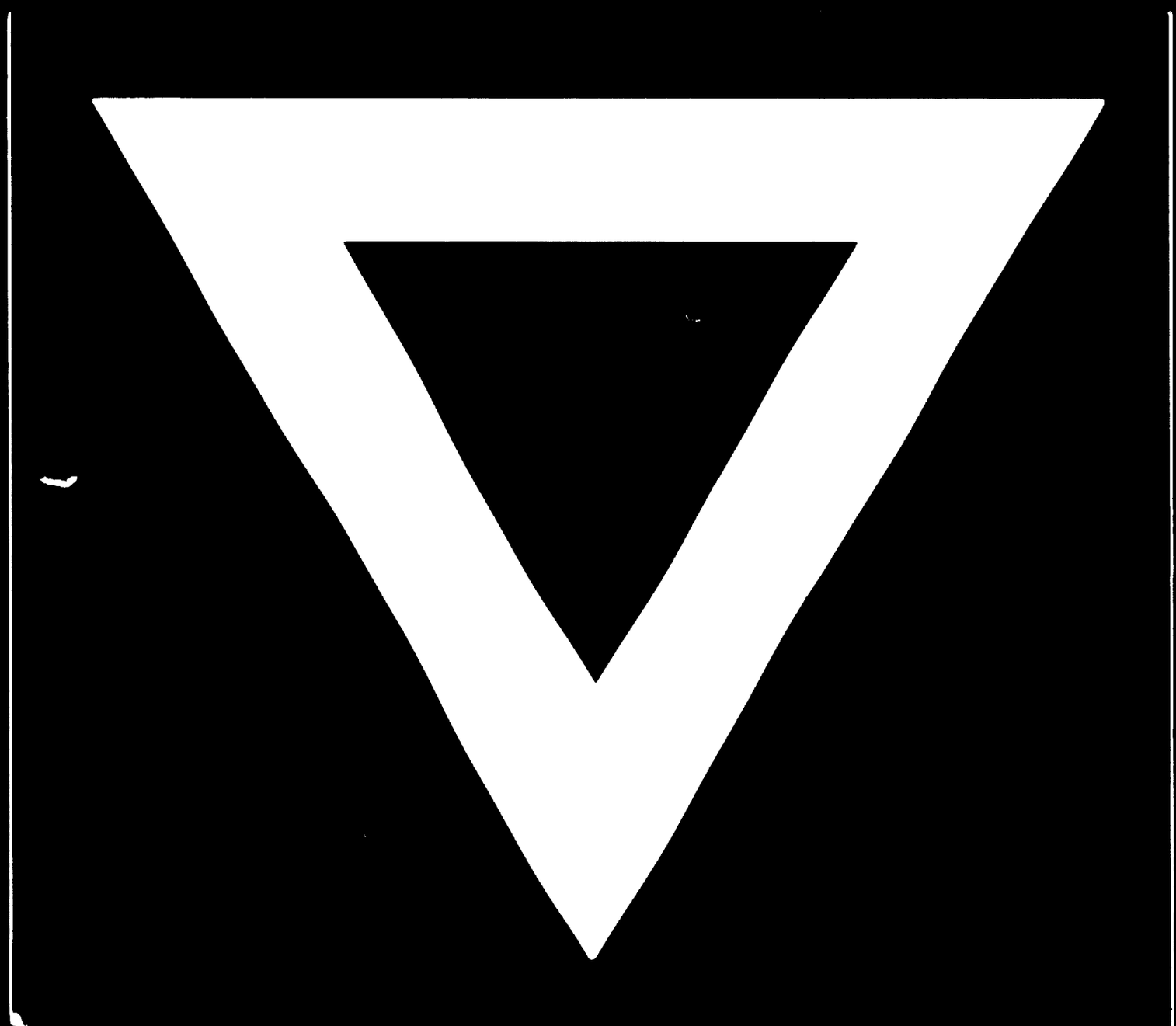

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