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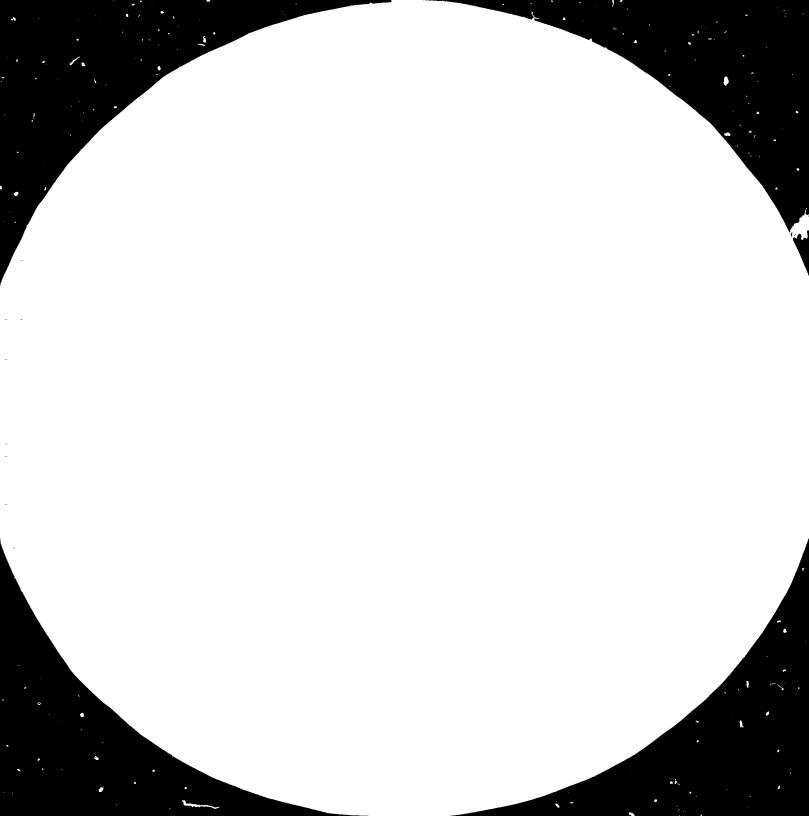
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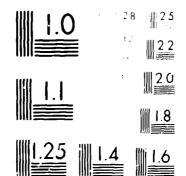
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United Nations Industrial Development Organization

Second Consultation on the Pharmaceutical Industry Budapest, Hungar, 21-25 November 1983

THE DEVELOPMENT OF DRUGS

Background paper \*

prepared by the UNIDO secretariat

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#### INTRODUCTION

1. In the last century, medicinal plants have developed new applications as raw materials for bulk drugs and intermediates, in addition to its customary use in traditional inc. cine. The genesis of interest in herbal medicines (plants constitute its major source, animals and minerals are minor sources) lies in their observed clinical benefits. The empiric performance of this natural pharmacopeia led (along with physiology), to characterize new drugs by isolating their active principles.

2. The high cost of chemical drugs encouraged a number of developing countries, in particular in Asia, to merge the modern allopatic medicine with the local traditional medicine to spread health care coverage to the majority of the population at reasonable cost.

Traditional medicine is a term customarily used in a very broad sense to cover three main groupings: (i) folk medicine, which is a tradition based on pharmacological properties, magic and ritual; (ii) traditional medicine proper, which is a comprehensive and rational body of theory and practice of an empirical pharmacological tradition held together by fundamental concepts of natural philosophy that incorporate the phenomena of health and illness; (iii) modern traditional medicine, which combine ancient diagnostics and herbal medicines with modern instruments and adjuvants.

3. A major problem in the harmonious merging of allopatic and traditional medicines is that their theoretical structures exist side by side, compartmentalized. Allopatic medicine is the result of systematic research and development work complemented by rigourous and sophisticated testing methods. Traditional medicine is the outcome of empirical methods systematically worked into a methaphysical structure that can be neither buttressed nor destroyed by experimental proof. This theoretical incompatibility is further compounded by semantic problems arising out of the use of different word to describe the same thing or the same word to describe different things.

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4. The criteria used to verify the effectiveness of a traditional treatment are very different from those of allopatic treatment. However, herbal medicines used in traditional treatments can be pharmacologically tested for efficacy. In fact, in developed countries substantial research was devoted to elaborate chemical experiments to study the physiological basis for drug action followed by rigourous clinical testing and the development of process technologies. In contrast, the fewer developing countries undertaking research and development work concentrated more on validating the efficacy of herbal medicines than to the isolation of their active principles. Hence, expediency and financial limitations have not enabled developing countries to develop adequate process technology and manufacturing know-how to obtain pure plant principles, for their research often skipped the elaborate chemical experiments required for obtaining them.

5. The three more important areas for the production of active plant principles in developing countries, are the following:

- (a) the transfer of technology for the production of active plant principles to be used as bulk drugs or intermediates.
- (b) the supply of adequate quantities of medicinal plants to ensure the required production of active principles, crude and/or purified.
- (c) the identification of the local flora and fauna characterized to contain known active principles.

Annexure A presents a list of important plant drugs suitable for production by developing countries.

#### I. THE USE OF MEDICINAL PLANTS

# A. Patterns of pharmaceutical development from plants

6. Pharmaceutical development stemming from flora and fauna mostly prevalent in developing countries, can be classified under four main groups as follows:

- a) Pharmaceuticals from plants used in traditional pharmacopeias.
- b) Pharmaceuticals from plants utilized regionally against ailments peculiar to the region.
- c) Plants as raw materials for obtaining drugs already accepted in developed and developing countries' pharmacopeias.
- d) Plants as raw materials for obtaining drug intermediates.

7. Groups (a) and (b) pertain to herbal remedies used in traditional medicines. In group (a) pharmaceuticals, there is a need to standardize compositional preparations, improved formulations and more convenient dosage forms, and carry out clinical testing to ensure safety, efficacy and acceptability.

In group (b) pharmaceuticals, they could become sources to characterize known and new drugs on the identification of active plant principles. Since the costs of isolating new active principles is high and require sophisticated chemical experimentation and clinical testing, the use of plant extracts may become the most economic option available to developing countries, depending on pharmacological evidence.

Further, it is not always necessary to undertake the expensive cost of extracting the active plant principles and formulate them into convenient dosage forms, when preparations based on total plant extracts could be both cheap and effective. Plant extracts including the active principles with other plant constituents, often show increased solubility and bioavailability. 8. Groups (c) and (d) refer to plants used as raw materials for obtaining drugs and intermediates. These are plants identified to contain widely used known drugs or intermediates and for the production of which technology is available. A list of such plants for the developing countries' regions is given in Annexure B.

In group (c) drugs, the extraction of pure active principles require transfer of the relevant production technology according to the degree of uniqueness of each plant specie, solid longer term market prospects and assurance of continuous supplies of medicinal plants for production. The technology is generally available in developed countries whilst the plant raw material is generally cultivated in developing countries.

In group (d) drug intermediates, there are fewer plants in this category which have production requirements similar to group (c) plants above. However, further transfer of technology would be required to process the plant-based drug intermediate into the drug itself.

#### B. The consumption of plant-based drugs

9. There are no comprehensive world statistics on medicinal plants and the pharmaceutical products derived from them. Such statistics would be difficult to compile. However, the national trade figures of developed countries and some developing countries contrive to give a view of world trade for economically important plant-based drugs and the trends perceived in them.

10. Over 400 botanical products are marketed internationally with Hamburg, Federal Republic of Germany acting as the main world trading centre for these products. These botanicals provide plant extracts for several industries such as feed, cosmetic, perfumery and pharmaceuticals, each with its requirements on quality, safety and efficiency.

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11. Concerning plants for pharmaceuticals, imports of the main developed countries in 1980 were the USA with 34,000 tons worth  $78 \text{ million } \frac{1}{2}$  and the European Economic Community with 80,738 tons worth  $180 \text{ million } \frac{2}{2}$ . Exports of the US and the EEC in 1980 were 4,000 tons and 7,300 tons respectively.

A recent survey on OECD countries' imports of medicinal plants estimated that imports grew from \$ 53 million in 1967 to \$ 127 million in 1976  $\frac{3}{}$ .

12. For example, in the single largest pharmaceutical market, the US, it still relies on medicinal plants as a major source of some of its most useful drugs. A national survey of prescriptions dispensed from pharmacies in 1968 revealed that 25% of those prescriptions contained one or more active principles consisting of a crude plant material, a crude plant extract or a purified active plant principle. Among those prescriptions, 76 pure active principles were found, and all of them except 7 are still comercially extracte. from plants. Further, 99 crude drugs or crude extracts from plants were encountered in the surveyed prescriptions, which represent 2.5% of the total number of prescriptions.

A computerized analysis of similar data for the period 1959-1968 revealed that the percentage of plant materials as function of the total annual number of prescriptions, remained about constant. This situation has remained also in the 1970s  $\frac{4}{}$ .

13. Market profiles for the 10 more important families of medicinal plants have been carried out recently. The trends show that the use of medicinal plants and derivatives in modern allopatic medicine would not increase much in volume or may eventually decline in developed countries, partially due to uncertainty in the availability and quality of many botanicals from developing countries.

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<sup>1/</sup> US Department of Commerce, "US imports for consumption and general imports: TSVSA commodity by country and origen" FT 246.

<sup>2/</sup> European Communities Statistical Office, "Analytical tables of foreign trade: CST", Vol. i

<sup>3/ &</sup>quot;Markets for selected medicinal plants and their derivatives", UNCTAD/GATT International Trade Centre, Geneva 1982.

<sup>4/ &</sup>quot;Herbal Pharmacology in the People's Republic of China", US National Academy of Sciences, 1975, pages 7 to 9.

Annexure B gives a list of biologically active plants which active principles are used n modern medicine and shows their individual market pctential for developing countries. Although this list was drawn up in 1978  $\frac{5}{}$ , the market potentials remain valid.

## 11. PHARMACEUTICAL MANUFACTURING FROM MEDICINAL PLANTS

#### A. <u>Production of therapeutic agents from plants</u>

14. Plant extracts have customarily been the most simple and traditional form of therapeutic agent in the world. However, the modern and systematic development of drugs based on natural pharmacopeia, has evolved a sequence of operations for its attainment which covers three main areas of activity:

- a) chemical activities, which pertain to the isolation and characterization of the chemical structure of individual phytochemical constituents of the plant. It also includes the development of quality control methods, chemical synthesis and modification of the chemical structure to obtain the desired biological activities. These chemical activities are often the preferred approach to industrial drug development.
- b) biological activities, cover two main areas:
  - biological testing designed to ensure the safety and efficacy of drug preparations in order to get the drug accepted by pharmaceutical regulatory organizations.

These activities, in particular toxicological and teratological testing, needs expensive facilities, considerable amounts of experimental animals and large

<sup>5/ &</sup>quot;Report of the technical consultation on production of drugs from medicinal plants in developing countries", Lucknow, India, 13-20 March 1973, UNIDO report ID/222.

operating budgets since drug approval often takes several years.

- ii) genetic development of plants designed to continue to obtain the drugs from plants. It requires the establishment of the respective crop, agronomic activities to increase crop yield, and genetic activities to improve the crop and yield of desirable phytochemicals.
- c) technological activities, which require technology appropriate to the degree of uniqueness of each plant specie and process development which is dependent on this factor. Hence, considerable research and development effort goes into these activities.

The processes of extraction, isolation, formulation and where relevant, synthetic manipulation, becomes the acquired knowledge and property of technology holders which have carried out this developmental effort.

Further, a considerable infrastructure would be needed for transfering this technology from one situation to another.

Figure 1 in the annexures presents a diagramatic representation of methodology for production of plant-derived pharmaceuticals.

15. Considerations of para. 14 above and in particular 14(c), point out where industrial production of drugs from medicinal plants is concerned, that the plants to a large extent are indigenous to developing countries (see Annexure B), these plants are the raw materials that supply manufacturing iacilities in developed countries, the value added to obtain pure active principles is at least 10 times the value of crude extracts, and thereafter high value plant-derived drugs are sold back to developing countries thus putting extra pressure in their scarce foreign exchange resources. 16. The technological status of different developing countries varies, a number of countries have practically no industry and can not easily obtain the solvents required for extraction, while others have a reasonably well established phytochemical industry. The two leading developing countries on phytochemical production are China and India which supply extracts, crude drugs and finished products for domestic use and export. For example, the phytochemical production of India in 1980 was US\$ 125 million. Countries without phytochemical industry could start by preparing crude extracts for domestic use and export. The production units should have wellequipped quality control laboratories; and even small units processing one ton of raw material a day could be of economic benefit.

Countries with a reasonably well established phytochemical industry could set up more sophisticated facilities which require transfer of suitable technology, to produce semi-finished and finished products for domestic use and export.

#### B. <u>Technology</u> Requirements

17. A survey of the main technologies for processing medicinal plants indicated that production processes for most of the important plant products were not covered by patents.

18. The requirements for transfer of technology for the four main groups of phytochemicals given in para. 6 are as follows:

a) Plants used in traditional pharmacopeias, require analytical quality control techniques and generally available dosage technology. The nature of the dosage form depends on several factors such as the extent of development in the region concerned and the situation of the available infrastructure. b) plants used regionally against prevailing regional ailment;, include plant species with clinical evidence of curing specific ailments but whose chemical composition of plant material is either unknown or not yet fully investigated.

Since chemical experimentation to characterize these plant species is expensive and lengthy, the use of plant extracts coupled to rigourous quality control would be the more viable alternative in particular if export is considered. The cost and time of undertaking the necessary biological testing to overcome the pharmaceutical regulatory barriers makes it prohibitive for most developing countries.

Currently the pharmaceutical industry is able to utilize plant extracts in a variety of dosage forms where the phytochem. I content is standardized. Several developed and developing countries have generated technology for the utilization of plant extracts.

The transfer of such technologies either from developed to developing countries and/or among developing countries is required, particularly if the technology is appropriate or relevant and yet the use of it is not for competing products. Developing countries would need to develop suitable regulatory requirements for acceptability and introduce medical practitioners to phytotherapy, for the employment of such products.

c) plants as raw materials for obtaining internationally accepted drugs are generally known in its major economic plant constituents and the technology for processing them into accepted drugs.

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This type of plant species requires an analytical appraisal of quality and quantity of the required drug present in the plant; the development, acquisition or adaptation of appropriate technology for obtaining pure active principles, and assurance of continuous supply of raw material for processing.

The technology is available mainly in developed countries but the raw material is primarily grown in developing countries.

 d) plants as raw materials for drug intermediates, comprise a limited number of plant species which technology requirements are similar to group (c) plants above.

However, technology to extract and isolate plant-based intermediates need to be complemented, when feasible, by methods of synthesis for conversion of the natural product to the drug itself.

### C. Supply of plant raw materials

- 19. Developing countries have a rich flora that is a potential source of known drugs and new biologically active substances. A coordinated effort would be needed to properly exploit that vast resource, in particular of pharmacological screening for the biological evaluation of medicinal plants.
- 20. A few years ago, WHO compiled a representative list of the plants most widely used in traditional medicine in the world  $\frac{6}{}$ . Only a fraction of those plants have been fully investigated concerning their phytochemical constituents and their therapeutic potential.

<sup>6/ &</sup>quot;Inventory of medicinal plants", G. Penso, WHO-DPM/WP/78-2, 1978.

- 21. Concerning plants as raw materials for drug or intermediate production, a major problem of the pharmaceutical industry is to ensure a regular supply of such plants in adequate quantity and quality. A number of these plants grow wild, but many others need to be cultivated. Annexure B shows the availability of cultivated and wild plants in developing countries.
- 22. The industrial scale cultivation of medicinal plants demand special requirements not all of which are analogous to cultivated food crops. For instance, the value of a medicinal plant crop is dependent on the high content of the required phytochemicals within it, and this may differ from standard food crop yield per hectare.

Further, there are very significant differences among plant species and geographical locations that have to be taken into account as well as agronomic requirements on soil conditions, altitude and humidity, sunshine availability, plant nutrients, good farm management practices, etc.

In addition, proper practices should be established for the cultivation, harvesting, storage and processing of medicinal plants.

#### III. CONCLUSIONS

- 23. The main features that highlight the issue of drug development based on medicinal plants are the following:
  - plants used in traditional medicine provide important leads for the development of new therapeutic agents. These plants grow primarily in developing countries.
  - ii) the technology for the systematic evaluation, analysis and processing of useful drugs from medicinal plants have generally been developed and is utilized in developed

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countries. Drugs isolated from plant raw materials supplied by developing countries are sold back to these countries at relatively high cost.

- iii) Often, developing countries are unaware of the phytochemical constituents of their flora that could give rise to industrially utilizable drug material.
- iv) there are many diseases prevailing in developing countries for which effective therapies could only be obtained through cooperation between developed and developing countries. This co-operation should cover from basic research through technology development and clinical trials.
- 24. One of the first requirements for the development of plant-derived therapeutic agents is the systematic compilation of relevant information on botanical, ethnomedical, agronomic, phytochemical, technological, etc. characteristics of plant species used in traditional pharmacopeias. Often many developing countries are unaware of a wealth of data already available on plants growing within those countries.
- 25. An examination of the patterns of drug development from plants and its techrological requirements for production indicate that developing countries are generally not in position to identify and isolate new drugs from plants on its own (see figure 1 in the annexure). However, co-operation efforts making use of ethnomedical information and promising research leads, may translate them into commercial drug production.
- 26. Technology for groups (a) and (b) of herbal medicines (see para. 6) is relatively simple to develop, adapt or transfer to a given situation. The products are not likely to be competitive with those produced in developed countries but may compete with similar products within developing countries. In the latter case, there

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is a risk to regard the newly developed formulations of traditional medicines as inferior medicines in comparison with chemical drugs, which need not to be the case if proper scientific methods are utilized.

27. However, groups (c) and (d) of plants as raw materials for drugs and intermediates respectively, require transfer of appropriate technology from developed to developing countries in order to better utilize the latter's raw materials for global benefit. For example, drugs obtained from group (c) plants such as quinine, quinitine, reserpine and related alkaloids are isolated from plant raw materials of leveloping countries but are processed in North America and Western Europe. The same applies to intermediates of group (d) plants such as diosgenin and tabersonine.

In the case of liquorice, the plant is native to Southern Europe but is commercially cultivated in several drveloping countries which export its roots to Western Europe. A developing country which is a major supplier of liquorice roots sought, without success, european technology for processing the roots into solid extract. This setback was due in part to his lack of means and expertise to negotiate acceptable terms for technology transfer.

It would be generally possible that a major portion of the processing of plants of groups (c) and (d), if not in its entirity. could be done where the raw material is grown and harvested. A further advantage of this co-operation through transfer of technology would be the redundancy of competitive chemical processes to obtain the same drug which is more economically obtained from plants. This would entail substantial savings on research and development costs for developed countries.

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# ANNEXURE A

#### INFORMAT PLANT DRUGS SUITABLE FOR PRODUCTION BY DEVELOPING COURTRIES

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	Essen	tial	Second category				
Therapeutic Group	Plant	Active constituent	Plant	Active constituent			
Ansesthetics		-		-			
inalgeoics, antipyratics,	Papaver somiferum	Norphine Codeine	Assculus Elippocastanum Assoulus indica	Asscine and total extract			
Nonsteroidal anti-inflammatory drugs and antigout drugs	Gloriosa superba	Colchicine					
Antiallergics	· <b>–</b>	. –	-	-			
Antidotes, chelating agents, cholagogue			Combretua Micranthum	Extract			
Anti-epileptics	-	-	-	-			
Anti-infective Antiprotogoal	<u>Cephaëlis ipecacumha</u> <u>Cinchona</u> sp.	Emetine Quinine	-	-			
Anthelmintic	-	-	Chenopodium ambrosicides Artemisia maritima	Ascaridol, total extract Santanin			
Antimigraine	Claviceps purpures	Ergotamine	- '	<b>-</b> ·			
Antineoplastic	<u>Catharanthus roseus</u> Catharanthus Lanceus	Vinblastine Vincristine	Podophyllus hexandrus (P.esodi) Prunus africana	Fodophyllotoxin and total extract Total extract (specific for prostate enlargement)			
Artiparkinsonisa Blood and heemtopoietic system Cardiovascular	Natural provisions	1_Dops.	-	÷			
Antihypertensive	Raumolfia serpentina Raumolfia vomitoria Raumolfia confertifloratum	Reservine	Rameolfis sp.	Deserpidine			
	Cathoranthus roseus Catharanthus lasceis Vinca minor Voscanga africana Voscanga thoursii	Raubasine Vincamine	And visnaga	Visnegin			
Anti-arrhythmic	Cinchona sp. Rauwolfia serpentina and other species	Quinidine Ajmaline					
Cardiotonio	Digitalie lanata	Digoxin and lanatosides -	<u>Strophanthus gratum</u> Thevatia narifolia Urginea scilla ( <u>Scilla maritima</u> )	Strophanthin Peruvoside Proscillaridine Rutin or bioflavanoide			
Dermatological preparations	Annti ma jao	<b>Xenthotoxin</b>	Peoralea coryli- folia	Psoralen			
	Centella asiation	Asiaticoside	-	-			
Diagnostic agents Diurstics Gastointestinal drugs	Theobross cacao	Theophylline		-			
Antispasmodica	Duboisia myoporoides Duboisia leichartii Atropa belladonna Atropa scuminota Da ra sanguinea Da, ra strasonium Dat .a metel M'_acyamus muticus b.com.umus miger Physoohlaina presita	Total alkaloide atropine or kyoscynsine					

S Provides was esterial for drug production.

#### Cathartics

Laxatives Anti-ulcar

Antidia-rhoeal

Hormones

Immunologicals

Muscle Relamants (peripherally acting) and antagonists

Ophthalmological preparations

Oxytocics

Psychotherapeutic

Drugs acting on the respiratory tract

Solutions correcting mater, electrolyte, and scid-base disturbances Vitamins and minerals

Cassia angustifolia Cassia italica Cassia acutifolia Plantago ovata Glycyrrhiza glabra

Berbevis aristata Dioscorea deltoidea

Dioscorea floribunda Dioscorea composita Costus spiciosus Solamum laciniatum

Solanum khasianum Solanum xanthocarpum

Agave sisalana -

Physostigm Venenosus

Chondrodendron tomentosum

Pilocarpus sp.

Physostigms venenosum Dubcisia myoporoides

Claviceps purpures

Sennosides R eun sp Total extract mixture or sennosides A,B Allos sp. Aloin as such and products glycyrrhetic acid and extract a Berberine Ceratonia siliqua Total extract Diosgenin a/

Solasodine a/

Hecoginin 5/

Physostigmine

d-Tubocurarine

**Pilocarpine** 

Physostigmine Atropine a/ (as hosotropine)

Irgometrine

Rauwolfia serpen-Reservine and crude ina extract Rauwolfia confertiflora+um Rauwolfis vomitoris Valeriana wallichii Valepotriate and Valeriana officitotal extract nalis

Ephedra gerardiana (Ephedra vulgaria)

Ephedra nebrodensis

Theobross cacao

Papaver somniferum

Ephedrine

Codeine

Theophylline a/

(as aminophylline)

Olycyrrhiza glabra Total extract Olycyrrhiza urslenvis Olycyrrhiza vio-Inces

Claucus flavus

Polygala sellega

Total excract

Glaucine

s/ Provides raw materials for drug production.

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## ANNEXURE B

## ILLUSTRATIVE LIST OF BIOLOCICALLY ACTIVE PLANTS

Name of plant	AL		Availability			Region		Rethod of			
	the plant used	Product	Culti- vated		Africa	Latin America	<b>As</b> ia	produc- tion s/		Export	Trend
cacia arabica)	Sten			+	•				 >	++	Steed
cacia senegal)					·			_	r		-
lconitum sp.	Root	Total extract		+			+	C	+	+	Down
	Rhizome	Essential oil and crude drug		+			÷		+	++	Stead
les lus Lippocastanum	Seeds	Aescin and total extract	+	+			+	с	+	++	Ũp
gave sisalana	Juice	Hecogenin	+		+	+	+	D	+	++	Steady
loe sp.	Leaf juice	Aloin	+	+	• +	+	-		+	++	Stead
smi mejus	Seeds	Ianthotoxin	+	+	+		+	Ð	+	++	Ūp
ami Visnägä	Fruits	Visnagin, khellin		+	+	+		C	+	++	Steady
momun subulatum	Fruits	Essential oil	+	+	÷		+	*	+	++	Ũp
anthioides	Fruits	Essential oil	+	+	+		+		+	++	Ūp
ndira araroba	Stem wood	Total extract		+	+	+		c		+	Steady
nethum sp.	Pruit	Essential oil	+			+	+		+	+	Steady
nise	Fruits	Essential oil	+		+		+		++	++	Steady
rtemisia Maritima	Flowering tops	Santonin		+	•		+	~	+	+	Steady
tropa elladonna	Leaf and roots	Total alkaloids		·	·		+			•	
erberis ristata	Root, stem bark	Berberine	·	+					++	++	Steady
erberís siatica	Root, scen bark	Berberine					+	В	+	++	Stead
erberis lycium	Root, stem	Berberine		+			+	B	+	**	Stead;
	bark	<b>.</b>		+			+	B	+	++	Stead
etula alnoides	Ster bark	Crude drug		+			+		+	+	Stead
apsicus annum	Pruits Pruits	Capsaicin oleoresin	+		+	+	+	D	+	+	Steady
arica papaya arum carvi	Pruit juice Pruit	-	+		+	+	+	B,C	+	+	Up
RESIA	Leaves and	Essential oil Sennosides	-+		+		+	•	+	++	Steady
cutifolia Assia	pods Leaves and	Sennosides		+	+.	+	+	C	+	++	Up
ngustifolia	pods		+				+	с	+	++	υp
assia italica	Leaves and pods	Sennosides		+	+			с	+		
atharanthus oscus	Leaves and roots	Vinblastine, vin- cristine, raubasine	+	+	+	+	+	D	+	++	Steady
entella siatica	Whole plant	Asiaticoside	+	+	+		+	c	+	++	Steady
entella cuminata	Roots	Enstine	+	•		+	+	D			
ephaëlis pecacuanha	Roote	Enstine	•	-		•			+	++	Up 11-
eratonia silique	Pruit	Total extract	+	▲	•	*	+	D C	+	++	Up
henopodium mbrosicides	Plowering top and	Eesential oil	Ŧ	Ŧ	*				+	++	Steady
	whole plant	<b>~</b> ,,,	+	+	+	+	+		+		Steady
inchous sp.	Stem and ' root bark	Quinine, guinidine	+	+	+	+	+	ם	++	. ++	۳p
laviceps urpures		Ergotamine, ergo- toxine, ergometrine	+			•	+	D	++	++	Steady
ola nitida	Seeds	Total extract	+	+	+	+		3	++	++	Up
mbretum	Leaves	Total extract						-			

 $\frac{1}{2}$  A = steam distillation; B = water extraction; C = Alcohol extraction; D = extraction with other solvents.

	Part of	<u></u>	Availability		Negion			Nethod of			
Name of plant	the plant used	Product	Calti- veted	Wild	Africa	Letin America	Asia	produc- tion a/		niial Expert	Trend
Commiphore multul	Resin	Gue		•			+	 D	++		
Costus speciosus Costus citratus	Rhisome	Diosganin		+		+	+	)			
Cymbopogon flexuosus	Leaves	Essential oil, citral	•••		+	+	+		+	++	Steedy
Datura sp.	Leaves	Atropine			•						
Derris elliptica	Root	Rotenome	+	<b>+</b> *	+		+	D	+	++	Up
Digitalis lanata	Leaves	Digorin and lanato- sides	+		+			C,D	++	<b>++</b> .	Steedy
Dioscorea sp.) Dioscorea leichartii	Tubers	Dicegunin	+	+	+	•	+	D	++	**	Steedy
Duboisia myoporoides	Sten	Rycocyamine, hycocine	+	+	+	+	+	D	++	++	Steedy
Ephedre gerardiana	Whole plant	1-Bpt string		+			+	D	++	++	Steedy
Ephedre vulgaris	Whole plant	1-Ephedrine		+			+	D	++	++	Steady
Ephedre nebrodensis	Whole plant	1-Ephedrine		+	••		+	D	•	++	Steedy
<u>Eucalyptus</u>	Leaves	Essential oil	+		+	+	+	A	++	++	Steedy
<u>Claucus flavus</u>	Leaves	Glancine		+	+		+	С	++	++	Steady
Claucum simpler	Rhisome	Colchicine		+	+		+	D	++		•
Gloriosa superba	Rhisome	Colchicine		+	+		+	D	++	+	Steady
<u>Clycyrrhi</u> :	Rhisome	Total extract		+			+	B	++	++	Steedy
Reracleum candicans	Roots	Xanthotorin		+	+		+	D	+	++	Steedy
<u>Hibiscus</u> sabdariffa	Flower	Dried flowers	+		+	+	+		+	++	Ūy -
<u>Holarrhena</u> florihunda	Stem bark	Concessing and total alkaloid	•	+			+	D	+		
<u>Hydnocarrus</u> kurzii	Seeds	Pixed oil, hydno- carpic acid		*			+		+		
Rydnocarpus Wightiana	Seeds	Chanlacogric acid									
Ryoscynmis sp.	Root	Ryoscymmine and other alkaloids		+	+				+		
Lippis chevatiari	Whole plant	Camphor and ensur-		+	+			4	+	+	Steedy
Lobelia pyramidalia	Leaf, flowering top	Lobeline and total extract						D		٣	٩,
Montha ep. ) (Japanese mint)) Mentha piperita)	-	Essential oil	+	•	+	•	• ·	1	+ ++	++	Ūp
lucuna pruriens	Beans	1-Dopa	•		•	•	*	3	+	•	Steely
Oncobs eclinata	Seeds	Pixed oil	•	•	<b>▼</b>	•	•	-	+	*	
Papaver somniferus		Norphize, codeine moscapine pepeverine	•		•	•		Ŀ	•	++	Ūp
Passiflora sp.		Total extract	•	+	+	•	÷	c	+	•	Steely
Pausinystalis yohimba	Stee bark	Tohimbine and totrl extract	-	•	•	÷	•	D	+	•	Steely
Physosticse venenosus	Seeds	Physostignins, stignaturol		•	•			D	• •	+	Steely
Physochlains prealts				-		•			•		
Pilocarpus sp.	Leaves	Pilocarpine						3	٠	•	Steely

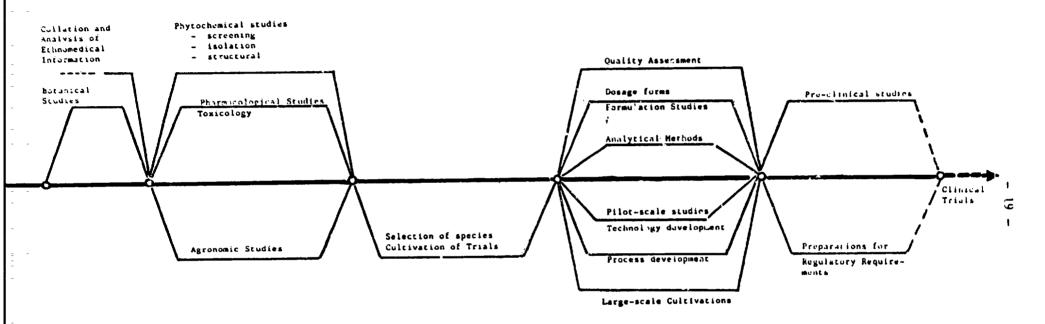
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Name of plant	Part of	Product	Availability					Nethod of	Market potential		
	the plant used		Culti- vated	Wild	Africa	Latin America	Asia	produc- tion a/		Export	Trend
Plantago ovata	Seeds, husks	Ispaghula, payllium	+				+		++	++	Up
Podophyllum hex- andrum (P.emodi)	Tubers	Podophyllin, podo- phyllotoxin		+			+	D	+	++	
Polygala senega	Roots	Resin		+	+				+	+	Մք
Prumus africana	Stem bark	Total extract		+	+			C	+	++	Steady
Peoreles corylifelia	Seeds	Peorélen		+			+	D	+	+	Steady
Rausolfia ) heterophylla ) Rausolfia ) serpentina ) uusolfia ) 	Roote	Reserpine, ajmaline, deserpidine, rescinnamine, reserpiline		•	•			D	+	+	Ūp
Phasmas	Bark	Crude extract				•		· c	•	+	Steady
purshiana	<b>D</b>			*	•	+	+	c	Ĭ	+ +	Steady
<u>Lheum emodi</u>	Rhisome Rhisome	Total extract Total extract	+	+	*		Ť	c	•		Steady
Ricinus communis	Seeds	Fixed oil	+	Ť	+		•	-	• •	++	Steady
	Berries	Solamodine	+	Ť	•	•	•	D	+	• ··· .	•
Solanum sp. Sterculia	Bark	Com	•	•	•	·	•	_	+	+	Steedy
setigers Strophanthus gratus Strophanthus	Seeds	Strophanthine, strophanthidine		•	•		·	ם	+	+	Ծջ
kombe Strychnos nux vomica	Seeds	Strychnine		+	•		+	D	+	+	Steady
Tabernanth iboga	Stem bark	Ibogaine		+	+			D		+	·
<b>Tarazacua</b> officinale	Root	Resin and total extract		+		+	+	D	+	+	Stendy
Thevetia neriifolia	Seeds	Peruvosids	<b>.</b>		+	+	+	D	+	+	Steady
Urgines indica ) Urgines scilla )	Bulbs	Proscillaridine		+	+	•	+	C	+	+	Steady
Valeriana ) officinalis ) Valeriana ) wallichia )	Rhisome	Total extract	+	+		+	+	C	+	+	Steady
Voscanga ) thoursii Voscanga ) africana )	Seed	Tebersonine		•	•			D		*	Ũp
Vinca minor	Leaves	Vincesine	•	•	+	+	+	D	+	+	Ūp

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Fig.1

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Diagramatic representation of Methodology for production of plant-derived pharmaceuticals

