AYURVEDA TOMORROW

Voice of the Ayurveda Fraternity of Kerala

Confederation for Ayurvedic Renaissance - Keralam Ltd.
A Project under Dept. of AYUSH, Govt. of India

CARe KERALAM

July - September, 2012

Printed and Published by:
Karimpuzha Raman, Managing Director , CARe KERALAM LTD, KINFRA Small Industries Park, Nalukettu Road, KINFRA Park P.O, Koratty – 680 309, Thrissur, Kerala – Tele: 0480-2735837/2735757, Email: md@carekeralam.com

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(for Private Circulation only)

CARe KERALAM

CARe KERALAM Ltd
KINFRA Small Industries Park, Nalukettu Road, KINFRA Park P.O,
Koratty – 680 309, Thrissur, Kerala – Tel: 0480-2735837 / 2735757

Message from the Chairman

Ayurveda, the sacred knowledge of life, is the oldest medical system in the world. Medical traditions were prevalent in other parts of the world also. But most of them disappeared, unable to withstand the test of time. Conceived by the *rishis* of ancient India, Ayurveda continues to serve the humanity. Ayurveda has seen many ups and downs during the course of its long history. The arrival of western colonialism inflicted much damage to its fabric. Ever since the introduction of western medicine in the 16th century by the Portuguese, Ayurveda was relegated to the background.

Nevertheless, a major shift in global health care management policy was instrumental in renewing interest in Ayurveda. To encourage national and international action to develop and implement primary health care throughout the world, the World Health Organization (W.H.O.) convened the International Conference on Primary Health Care (6-12 September, 1978) at Alma Ata, in the former Soviet Republic of Kazakhistan. The conference adopted the famous Alma Ata Declaration which called upon member nations to formulate national policies, strategies and plans to launch and sustain primary health care. The members were especially encouraged to mobilize their own national resources. The Western world was thus encouraged to study in depth the various traditional medical systems of the world. The Alma Ata Declaration was largely instrumental in kindling western interest in Ayurveda.

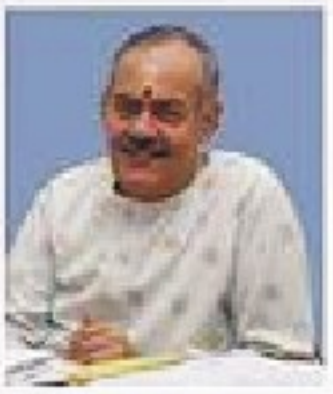
Ayurvedic therapy is natural and cost-effective. It is safe, as it does not provoke newer disorders. But we have not been successful in taking it to the western market. This is mainly due to lack of rigorous testing and certification procedures. The use of inferior raw materials and the absence of controlled clinical trials have also worsened the situation.

Therefore, it was timely that a band of progressive ayurvedic entrepreneurs joined together to found a consortium, with the assistance of Government of Kerala and Kerala Industrial Infrastructure Development Corporation (KINFRA). The Government of India has also contributed generously to this project. We are grateful to all of them.

CARe KERALAM Ltd envisages rendering all possible assistance to the Ayurveda industry of Kerala. It will address problems like lack of validated analytical procedures to test ayurvedic medicines, problems in the supply of raw materials, paucity of information on the clinical efficacy of products and difficulties in the export of ayurvedic medicines. As the Chinese say, journey of a thousand miles begins with a single step. I call upon the Ayurveda fraternity of Kerala to join us in this noble mission!

Padmasri P.R. Krishna Kumar

Board of Directors of CARe KERALAM Ltd



Padmashree Shri P.R. Krishnakumar
(Chairman of the Board of Directors)
The Arya Vaidya Pharmacy [CBE] Limited
P.B. No: 3769, 326, Perumal Koil St.,
Ramanathapuram
Coimbatore : 641 045, Tamil Nadu
Mob: 9843064401

Shri Karimpuzha Raman
MD. CARe KERALAM Ltd.
KINFRA Park PO,
Koratty-680 309

Dr. K. Anil Kumar
Kerala Ayurveda Limited
Athani: 683 585, Aluva,
Ernakulam. Tele: 0484 - 2476301
E-mail: anilk@keralaayurveda.biz
Mob: 9846014176

Dr. E.T. Neelakandhan Mooss
Vaidyaratnam Oushadhasala
Thaikkattussery : 680322,
Ollur,Thrissur
Mob: 9447025338

Shri M.C. Balachandradas
Sree Sankara Community
for Ayurveda Consciousness Ltd
Sree Sankara Buildings , Mannam Road,
Perunna, Changanacherry : 686 102
Mob: 9846031480

Shri Ajay George Varghese
Bipha Drug Laboratories
XIII/804, Pallipurathukavu Jn.,
Kottayam : 686 039
E-mail: ajay@bipha.com;
Mob: 9447186644

Shri Hari N. Namboothiri
Sreedhareeyam Eye Hospital &
Research Centre P. Ltd,
Nellikkattu Mana,
Kizhakombu, Post Box No: 25
Koothattukulam : 686 662, Ernakulam
Mob: 9447033928
E-mail: hnamboothiri@sreedhareeyam.com

Dr. D. Ramanathan
Sitaram Ayurveda Pharmacy Ltd
4th Floor, Pathayapura Buildings
Round South, Thrissur : 680 001
Mob: 9846020540

Shri Michael Joseph
Nagarjuna Herbal Concentrates Ltd
Kalayanthani : 685 588,
Thodupuzha, Idukki Dist.
Tele: 04862 - 276112/276113/276114
E-mail: michael_joseph@nagarjun.com

Shri Prasad C. Ninan
Relax Herbals & Exports P. Ltd
2nd Floor, Menathottam Chambers
Pattom
Thiruvananthapuram : 695 004
Mob: 9847061743
E-mail: prasad.ninan@gmail.com

Dr. S. Sajikumar
Dhathri Ayurveda Pvt. Ltd
Adappilly Road
Vennala : 682 028, Ernakulam
E-mail: drsajikumar@vedacure.com

Shri Anandan Ramasami
[Nominee Director [IL& FS] - CARe Keralam Ltd]
Sr. Manager, IL & FS CDI Limited
E-mail: anramasami@ilfsindia.com
Mob: 9790002422

Shri K.P. Wilson
Kandamkulathy Ayurveda Hospital
Kuzhoor : 680 734, Thrissur Dist.
E-mail: ayurveda@kandamkulathy.com
Mob: 9447233279

Dr. Satheeshkumar Nampoothiri
Dhanwanthari Herbal Products
Thodupuzha : 685 584, Idukki Dist.

Dr. Raghu Arackal
[Nominee Director [AYUSH] - CARe Keralam Ltd]
Asst. Adviser [Ayu.] Department of Ayush
Ministry of Health & Family Welfare,
Govt. of India
E-mail: a.raghu@nic.in

CARe KERALAM Ltd –

A Model for Cluster Development Initiative in Ayurveda

Karimpuzha Raman, Managing Director

A sector study on ayurvedic industry conducted during 2003 by the Kerala Industrial infrastructure Development Corporation (KINFRA) revealed that Kerala's contribution to the All India turnover of 4000 Crores was only a meager 5%. Considering Kerala's hoary Ayurveda heritage and the presence of 200 GMP certified Ayurveda companies, this is indeed a low figure. The study also brought to light the problem of manufacturing spurious medicines using sub-standard raw materials. It was felt that a concerted action should be initiated to promote the State as a sourcing centre to ayurvedic products and services of high standard.

In this backdrop KINFRA, ayurvedic product manufacturers and service providers of the State arrived at a consensus to form a consortium with the objective of jointly promoting Kerala as a global destination for sourcing ayurvedic products and services of impeccable standards. Thus was born CARe KERALAM Ltd.

The Project

CARe KERALAM Ltd is a Special Purpose Vehicle (SPV) for setting up a centralized infrastructure for standardized manufacture of ayurvedic medicines and services to the cluster of ayurvedic companies in the State. The common facilities include raw material distribution, quality control laboratory, R&D division and media centre for branding of Kerala Ayurveda. The company will also work on documentation of various ayurvedic products. This is a pre-requisite for the marketing of Ayurveda products in the overseas market. This innovative project, sponsored by the Department of AYUSH, Govt. of India, under the scheme for development of AYUSH clusters, is established on two hectares of land in KINFRA Park, Koratty, Thrissur District.

Objectives

- To upgrade the process technology of ayurvedic medicines, so as to make them acceptable in the international market
- To develop R&D in the field of ayurvedic medicine
- To overcome the obstacles to export of ayurvedic products
- To develop a Centre of Excellence for research in Ayurveda
- To establish a Kerala brand of ayurvedic products
- To impart training to the manufacturers on safety, quality and efficacy of medicinal plants
- To protect Ayurveda from adulteration and sub-standard products and services
- To protect the intellectual property of ayurvedic manufacturers
- To enrich the resource base by encouraging farmers to take up cultivation of medicinal plants
- To improve the livelihood of communities dependant on medicinal plant cultivation and post-harvest processing

Facilities offered

The small and medium scale industries engaged in the manufacture of ayurvedic medicines do not have enough resources to upgrade the quality of their products. KINFRA's cognizance of this fact and timely intervention led to the establishment of the

present project, the first of its kind in the country, thus making it possible to set up R&D and quality control laboratories for the benefit of a cluster of ayurvedic, herbal drug, health food manufacturers and service providers.

The facilities include a full-fledged quality control and R&D laboratory for herbal and ayurvedic products. These consist of QC and R&D laboratories, toxicology study centre, process validation lab for scale-up operations, a raw material warehouse with mini lab, IT & marketing infrastructure, a common facility centre for production and packaging, as well as a nursery for herbs. The facilities are described in detail below:

1) Analytical Lab:

This well-equipped laboratory with all modern facilities for analytical testing, method development and contract research will provide reliable, dependable, economical and rapid analysis of samples submitted by entrepreneurs.

Working with GC-MS

2) Toxicology Study Centre:

Evaluation of the toxicity and adverse drug reactions of herbal preparations has been a neglected area . Often the safety of herbal products is taken for granted in the absence of scientific reports. Lack of information makes it difficult to compare the benefit-risk profile of herbal medicines. Long-term toxicity, mutagen city and genotoxicity also need to be studied extensively, as they are not easily evident in clinical practice. Clinical validation, as done for modern medicines, is the need of the day.

It is in this context that a toxicity study centre is established at CARe KERALAM Ltd. The design and scope of the studies in this centre will be in accordance with traditional use and modern standards. The studies will be on direct toxic effects, allergic reactions and other side-effects, effects from contaminants and or interactions with drugs and other herbs. The benefit-risk ratio of herbal drugs will also be addressed. An animal house with high standards of hygiene and husbandry conditions forms part of this centre.

3) Process Validation Lab:

This is an age of increasing health consciousness and desire to return to nature. This is evidenced by all kinds of holistic treatments and products advertised regularly in the media. Consequently Ayurveda is finding more followers in India and abroad. The process validation lab will augment the introduction of a whole range of health supplements and specific curative medicines that that will find widespread acceptance in the society.

The main purpose of the process validation lab is to offer laboratory facilities for R&D to small and medium enterprises for innovation. This will indeed revitalize the industry. Facilities are also available for scaling up of various processes developed through process validation. The process validation lab has all the state-of-the-art equipments required for carrying out the necessary scale-up activities.

4) Raw Material Store & Mini Lab :

CARe KERALAM Ltd will procure and supply to the member industries all the raw materials and crude drugs required for production of medicines. This intervention is expected to liberate small and medium scale manufacturers from the clutches of middlemen. It is not an exaggeration to state that this step will enhance the quality of the

medicines. A well-designed raw material warehouse has already become functional.

The mini lab attached to the warehouse will ascertain the quality of the raw materials procured. As soon as consignments arrive, samples will be drawn and brought to the mini lab for testing of quality. Only those raw materials that pass the quality test in the mini lab will be accepted for purchase.

5) IT & Marketing Infrastructure:

The lineages of the rishis of yore have vanished. Many valuable manuscripts which describe the nuances of the healing arts have disappeared. Due to wanton modernization and destruction of the ecosystem, many herbs with miraculous healing powers have become extinct. Many reputed families of hereditary *vaidya*s could not perpetuate their tradition.

It is in this context that an IT& marketing infrastructure for Ayurveda is set up in the ambience of traditional Kerala architecture. This IT infrastructure, the first of its kind in the country, will have a database on the long and vibrant history of Ayurveda and exhibits illustrating the history of Ayurveda.

The database will depict the origin, development, and application of traditional Ayurveda and its role in the history of medicine. It will serve as an excellent education tool to the lay public on healthy living. The visitors can gather detailed information on herbs, formulas, and all aspects of the ayurvedic health system. Information in plant taxonomy and the ayurvedic plant classification system will be an additional feature.

The marketing infrastructure division will collect, preserve and exhibit the traditional medical heritage. Around 1250 plants are currently used in various ayurvedic medicinal preparations. The IT & marketing infrastructure will have a vast collection of these medicinal plants preserved in their natural form.

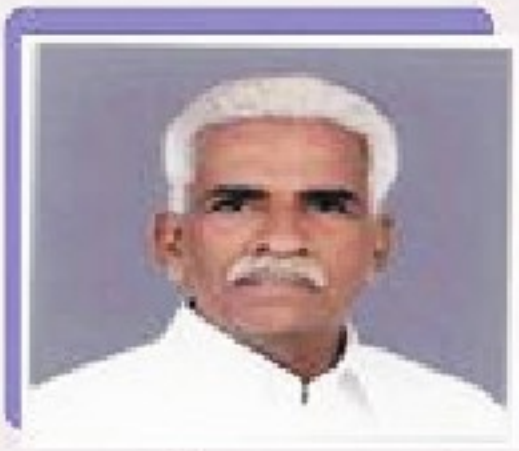
6) Common Facility Centre for Production & Packaging:

Hardly any ayurvedic product satisfies the western standards applicable to medicine. The common facility centre at CARe KERALAM Ltd for the production and packaging of ayurvedic products is in tune with the standard norms. The centre is equipped with state-of-the-art equipments to carry out testing and certification, measurement, quality and safety certification and certain key processes, which are not affordable to small manufacturers. The common facility centre can be used by entrepreneurs to manufacture high quality products that meet international standards of hygiene, product specification and quality.

Production Facility

The establishment of these facilities will ensure the standardization of raw materials, manufacturing process and finally the end products. These medicines with enhanced quality will be brought under the umbrella of a common label, while retaining the brand name of the individual manufacturers. Therefore, they will be easily recognized in the market as products conforming to high standards, thus gaining acceptance as "quality products" in Ayurveda. Kerala's ayurvedic products shall thus gain wider acceptance in national and overseas markets on account of their high quality standards.

Government of India, through the Cluster Development Programme of Department of AYUSH, granted Rs. 10 Crores for this project. CARe KERALAM Ltd. has 110 share holders as members. CARe KERALAM Ltd keeps its door wide open to the Ayurveda industry of Kerala.



Alzheimer's Disease

Dr. C.I. Jolly
Research Advisor, CARe KERALAM Ltd

Alzheimer's disease is a steadily progressive neuropsychiatric condition that is mainly characterized by cognitive deficit and debility. There is a disturbance ion many higher cortical functions such as memory, speech, learning, thought orientation and judgment. Alzheimer's disease is normally observed in the elderly. It is a mental deterioration in the elderly that cannot be explained by normal ageing. Earlier it was erroneously attributed to hardening of arteries. But now it is established that the condition arises from degeneration of nerve cells.

This condition is characterized by twisted, tangled nerves and hardened deposits of chemical plaques in the brain. Throughout the world it is assuming epidemic proportions in persons above 70 years of age. Dementia which is a characteristic feature of Alzheimer's disease is defined as an acquired deterioration in cognitive abilities that impairs the successful performance of activities of daily living. Memory is the most cognitive ability lost with dementia. This results in decreased central cholinergic transmission.

Symptoms

There is gradual memory loss, disorientation and loss of language ability. This will result in devastating personality changes over the years. Neuropsychiatric and social deficits developing in many dementia syndromes result in depression, withdrawal, hallucinations, delusions, agitation, insomnia and disinhibition.

Conventional treatment

Conventional or modern medicine has very little to offer. Currently the only available treatment option is a drug called Tacrine (tetrahydroaminoacridine). It slows down the deterioration to a very little extent and exhibits dangerous side-effects. Most of the drugs are given to ease pain and agitation. Women who take hormone replacement therapy are found to have lower risk. As no effective drug is available, the focus is on cholinesterase inhibitors, symptomatic management of behavioral problems, antipsychotic drugs and building rapport with the patient, family members and other care givers. Donezepil, Galantanine and Rivastigmine are selective cholinesterase inhibitors used in the treatment of Alzheimer's disease.

The natural approach

One should avoid foods that contain heavy metals including mercury, aluminum or lead. The blood-brain barrier is intended to keep most of the toxins out of the brain. But unfortunately those which get in are prevented from getting out. This phenomenon continues to build up over the years progressively blocking brain and nerve function. These days mercury fillings are the possible chief source of danger that is released into the body by chewing. Finally the dangerous elements end up in brain.

Ayurvedic therapy

Ayurveda does not correlate Alzheimer's disease to any of the diseases mentioned in

the treatises. The very fact that this disease is not described in Ayurveda suggests its recent origin. But based on the theory of Ayurveda one can logically choose herbs that will improve memory, intellect, judgment and abstract thinking.

Recently it came to light that a small dose of Turmeric (*Curcuma longa*) powder reverses the disease to a larger extent. *Brahma Rasayanam, Amalaki Rasayanam, Brahmi Ghrtam* and *Kalyanaka Ghrtam* are some of the ayurvedic formulations found to be effective in the early stages of Alzheimer's disease.

Ginkgo, the oldest tree species in Chinese medicine is beneficial to the brain. Evening primrose oil along with zinc (90 mg) and selenium (2 g) is also found to be useful. A study conducted with the extract of *Gikgo biloba* reported effective control of dementia.

Diet and other regimen

A nourishing diet with plenty of fruits, vegetables, olive oil and fish oil should be consumed. The patient should remain free from worries and live amidst pleasant surroundings and companions. Yogic procedures and meditation can also improve the condition. Chelation treatments and home remedies are also useful in removing heavy metals from tissues. Homoeopathic chelation is reported to offer good relief.

Some folklore remedies

* Almonds improve and strengthen memory. A combination of almond oil and milk taken together before going to bed sharpens memory.
* Apples and grapes have high level of quercetin which protects from Alzheimer's disease.
* Eggs are excellent source of choline that helps in brain function and enhances thought processes.
* Red onions contain anthocyanin and quercetin which are excellent for brain.
* Lycopene from tomato is excellent for dementia.
* Omega 3 fatty acids present in fish oil are good for memory retention. For vegetarians the source is flax or linseed oil.
* Researchers from Innsbruck University in Austria found that caffeinated coffee can temporarily sharpen a person's memory.

Validation and Standardization of Ayurvedic Formulations

Dr. Joy T. Verghese & Ajay Jagan*

Executive Director (Technical) & Head Production*, CARe KERALAM Ltd

Ayurveda offers remedies for age-related diseases like memory loss, osteoporosis, diabetic wounds, etc. for which no efficient medicine is available in modern therapy. Even though Ayurveda has a sound theoretical background, its share in the global medicinal market is very less (0.5%). This is due to lack of standardisation and validation of ayurvedic medicines.

In ayurvedic classic texts like *Charaka Samhita* and *Susruta Samhita* the use of plants and polyherbal formulations was documented based on the fact that the therapeutic efficiency of the herbal constituents of plants is enhanced by their synergistic efficacy. Various metallic compounds like cinnabar, gold pyrites, lead salts, mercury, copper salts, borax and iron pyrites are also used in ayurvedic formulations. Several pretreatments including sand heating, boiling, smoking, steam heating, sublimation, evaporation, condensation and oxidation are carried out on these chemical ingredients prior to their addition in herbal formulations. The commonly used ayurvedic drugs are *churnam, kashayam, lehyam, arishta, asava, gulika* and *taila* or oil extractives. The concept of *anupanam* or vehicle for drugs is quite significant in ayurvedic treatment. Various vehicles like milk, honey, cold water, etc. are used in Ayurveda. The same ayurvedic formulations can be used with different *anupana* for different diseases. They accelerate circulation, absorption and assimilation (bioavailability) of the drug in the body and enhance therapeutic efficiency. There is significant difference in processing steps, even for drugs of the same class. Each step in drug preparation is stringent because a simple error can affect the efficacy of the formulation. Though Ayurveda industry adopted modern pharmaceutical technology in manufacturing process quite well, the impact of this on polyherbal formulations is yet to be studied scientifically. This has resulted in the core ingredient losing its therapeutic effect in the final product. Formulations can be modified or standardized utilising this concept in modern dosage forms like soft gels, which is a relatively recent development in pharma technology. When efficacy and validity of traditional medicines are evaluated with clinical studies quality and safety aspects of ayurvedic formulation are also matters of concern.

A typical example is with relation to shelf life of products. The table below gives the comparison between that given in the text and the one recommended in the recent notification in gazette. Modern packing technology has contributed much in improving shelf life. However the other aspects like leaching and interactions with polythene packs, pet bottles, and polyurethane containers are yet to be studied in detail.

This can be brought about only by validation of the manufacturing process of each formulation, using modern technology.

Class of formulation	Shelf Life	
Dosage Form	According to Yoga Ratnaker	As per 161B of Ayush
Kvatha	3 hrs	2 yrs
Kalka	3 hrs	
Swarasa	3 hrs	
Anjana	3 months	
Churna	3 months	
Vati(Gulika) with	1 year herbs only	2 yrs 5yrs with
	Guggulu and drugs	
Avaleha	6 months	3 years
Ghrta & taila	1 year	
Asava	Indefinite	Indefinite
Rasa	Indefinite	Indefinite

Though work is being initiated on classical drugs by developing monographs, the patent and proprietary products need to validated and standardised.

Concept of Validation

According to GMP definition validation is "Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes."

Appropriate and complete documentation is recognized as being crucial to the validation effort. Standard operating procedures (SOPs), manufacturing formulae, detailed batch documentation, change control systems, investigational reporting systems, analytical documentation, development reports, validation protocols and reports are integral components of the validation philosophy. The validation documentation provides a source of information for the ongoing operation of the facility and is a resource that is used in subsequent process development or modification activities.

All validation activities will incorporate a level of impact assessment to ensure that systems, services and products directly influenced by the processing have been identified.

A revalidation program should be implemented based on routine equipment revalidation requirements and on the change control policy.

What Gets Validated

1. General

- All process steps, production equipment, systems and environment, directly used for the manufacture of sterile and non sterile products must be formally validated.

- All major packaging equipment and processes should be validated. This validation is less comprehensive.

- All ancillary systems that do not directly impact on product quality should be qualified by means of a technical documentation of the extent of the system and how it operates.

2. Facility

- Manufacturing area design.
- Personnel and material flow

3. Method Validation (MV)

MV provides documented evidence that internally developed process methods are accurate, robust, effective, reproducible and repeatable. The validation protocols should reference background documentation relating to the rationale for the determination of limits of detection and method sensitivity.

4. Process and Equipment Design Utility Systems Design

Raw/purified steam, purified water, compressed air, air conditioning system, vacuum, power supply, lighting, cooling water, waste etc

5. **Computerized Systems Design**

Information system, Laboratory automated equipments, manufacturing automated equipments, Electronic records etc

6. **Cleaning Validation (CV)**

CV provides documented evidence that a cleaning procedure is effective in reducing to pre-defined maximum allowable limits, all chemical and microbiological contamination from an item of equipment or a manufacturing area following processing. The means of evaluating the effectiveness of cleaning involves sampling cleaned and sanitized surfaces and verifying the level of product residues, cleaning residues and bacterial contamination.

7. **Computer Validation**

Computer validation provides documented evidence to assure that systems will consistently function according to their pre-determined specifications and quality attributes, throughout their lifecycle. Important aspects of this validation approach are the formal management of design (through a specification process), system-quality (through systematic review and testing), risk (through identification and assessment of novelty and critical functionality) and lifecycle (through sustained change control).

Types of Validation

1. **Prospective validation**

Establishing documented evidence that a piece of equipment/process or system will do what it purports to do, based upon a pre-planned series of scientific tests as defined in the Validation Plan.

2. **Concurrent validation**

It is employed when an existing process can be shown to be in a state of control by applying tests on samples at strategic points throughout a process; and at the end of the process. All data are collected concurrently with the implementation of the process until sufficient information is available to demonstrate process reproducibility.

3. **Retrospective validation**

This is establishing documented evidence that a process does what it purports to do, based on review and analysis of historical data.

Performance Qualification (PQ)

The purpose of PQ is to provide documented evidence that the process steps and equipment description. i.e. dispensing, formulating, packaging, equipment washing and cleaning etc can consistently achieve and maintain its performance specifications over a prolonged period to produce a product of pre-determined quality.

The performance specification will reference process parameters, in-process and product specifications. PQ requires three product batches to meet all acceptance criteria for in-process and product testing.

The PQ documentation should reference standard manufacturing procedures and batch records and describe the methodology of sampling and testing to be used.

Conclusion

Even though India has a rich traditional knowledge and heritage, its share in the international market is very negligible. There is a growing demand for products from traditional medicinal systems in the present global market. In order to compete in the global traditional medicine market, India should lay more stress on standardization and quality proofing of its drugs. Development of Ayurveda and other traditional Indian systems of medicine will help to tap the traditional ethnopharmacological knowledge through modern approaches.

Need for the Use of Quality Raw Materials in Ayurveda

Mariya Paul, Botanist, CARe KERALAM Ltd

Quality of a product or ingredient needs to be defined first in terms of its characteristics. For ayurvedic raw materials, parameters such as physical and chemical characteristics, medicinal quality and microbial load are important. The approach to the quality assurance varies greatly in large and small factories in different countries. In some places control hardly exists while in others there are laboratories carrying out many analytical tests. Production of goods set to a certain standard demands close control of raw materials. The increase in demand of medicinal plants for the commercial herbal medicine led to the indiscriminate and unscientific collection with total disregard for quality of the material collected. Rare and important medicinal plants have almost become extinct, leading to the emergence of adulteration. It is therefore important to establish quality parameters of medicinal plants by undertaking in-depth investigations on the traditional treatises. In modern times, quality awareness in every aspect of life is increasing both on physical and psychological planes. The recent trend of implementation of good and efficient policies of quality management like ISO 9000 certification, Good Laboratory Practices, Good Manufacturing Practices, Total Quality Management and Accreditation of Testing and Calibration Facilities has helped to provide better quality of life.

For standardization and quality control of ayurvedic drugs various steps can be adopted like physical description, tests of physical parameters, pharmacognosy techniques etc. In this way the correct identity of the herb in question and its usefulness in medicinal preparations can be ascertained. It is needless to state that the quality of ayurvedic products is fully dependent on the quality of raw materials. The acceptance or rejection of raw materials is normally the duty of the pharmacognosy department. Their duty is to decide whether the material is to be accepted for production or not. Inspection combined with sampling is most important. A sampler must be reliable. The sample must be checked for rodent contamination and the presence of insect fragments. Careful physical examination and sieving tests will reveal foreign matter present. Raw materials received in sacks, wooden cases or paper-lined cartons may easily become contaminated during opening.

Knowing the supplier's method of processing the raw material and quality control greatly influences the degree of inspection to be carried out at the receiving end. It is necessary for a purchase executive to visit the supplier and to agree on specifications, type of packing, batch codes and sticking to schedules. In many cases supplier will give a certificate of analysis with every consignment.

A specification is the minimum requirement according to which a product is delivered to the customer. The clearer the specification better will be the possibility of delivering quality products. In setting

specification limits, the following should be considered:

1) Requirements of product safety and health hazards provided in the statutory and regulatory requirements

2) Requirements provided for in national and/or international standards.

The following factors need to be considered before accepting the consignment in question:.

1) Authentication (stage of collection, parts of the plant collected, regional status, botanical characteristics like phytomorphology, histological details, taxonomical status, etc.) (Figure 1).

2) Foreign matter. Herbs collected should be free from soil, insect parts or animal excreta.

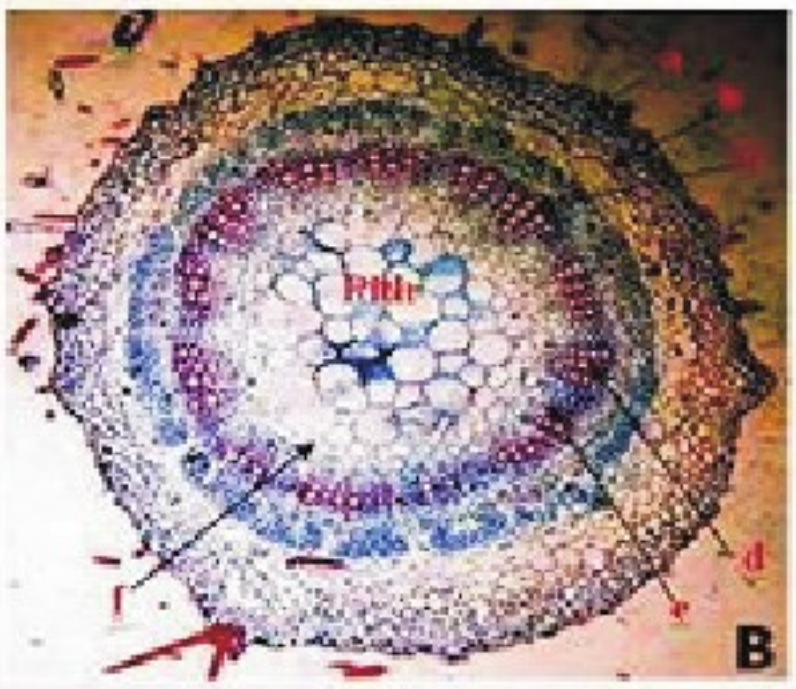
3) Organoleptic evaluation (sensory characters like taste, appearance, odor, feel of the drug, etc.)

4) Tissues of diagnostic importance present in the drug powder.

5) Ash values and extractive values.

6) Volatile matter

7) Moisture content



Photomicrograph of T.S. of *Sida cordifolia* stem

The raw materials comprising medicinal and aromatic plants, essential oils, fixed oils, extracts etc are authenticated with the help of pharmacognostical specifications. A crude drug museum has been set up at CARe KERALAM Ltd. It has a myriad display of preserved crude drugs including Herbaria. Herbaria of a wide range of plants from different parts of the country. Are available here. This crude drug museum is an integral part of a Pharmacognosy laboratory that serves the purpose of authentication. To verify the identity of the supplied raw materials the museum preserves control samples of raw materials for at least 2 years and 6 months. Pharmacognosy laboratories of Ayurveda companies can utilize the more classical chemical techniques and bring them into current use robustly so that analysis of crude drugs and detection of adulteration become easier tasks.

To summarize industrial pharmacognosy in Ayurveda companies, the raw materials are first subjected to macroscopic and microscopic examination. Thereafter, physicochemical parameters such as ash values, alcohol soluble and water soluble extractive values and fluorescence characteristics of herb powders are studied. Alongside these phytoconstituents like total tannins, glycosides, alkaloids, resins and sugars of the raw materials can also be estimated. Data accrued from all these studies form the basis of the certificate of analysis, on the basis of which the consignment in question is accepted or rejected.

On the Quality Control of Natural Products

Dr. D. Suresh Kumar, Head (R&D), CARe KERALAM Ltd

Our country is home to about 47,000 species of plants. Out of them 7500 species are considered as medicinal plants. Among them only 800 species are in actual use and 120 species are used in high volumes. This shows that there is an untapped potential for scientific exploration.

Interest in natural products arises out of two reasons. First of all, medicinal plants are used in traditional systems of medicine, as phytomedicines and as food or beverages. This sector is growing fast. Secondly, natural products are the main source of new drug discovery. It is accepted all over the world that new chemical entities can be discovered by screening natural products.

There is a growing trend all over the world in the use of natural products and traditional medicines. In spite of the several obstacles created by regulatory agencies of many countries, there is an upward trend in the export of traditional medicines and other natural products. The major hurdle in improving our export performance is the lack of standardization and quality control of natural products.

Authentication of herbs

Standardization of natural products is a complex task due to their heterogeneous composition. To ensure batch-to-batch consistency in the quality of herbal products, there should be proper control of the starting material. Authentication of the starting material is the first step in this direction.

Most of the crude drugs traded in the country is collected from the wild by illiterate and poor tribals regardless of botanical identification or authentication. Therefore, the material supplied in many cases is adulterated intentionally and unintentionally. Every medicinal herb has several vernacular names. Local trade is based on these local names and Latin names are confined only to the scientific community.

There is much controversy about the correct botanical identity of many plants. For example, there are more than 550 species of *Phyllanthus*. Among them *Phyllanthus amarus* and *Phyllanthus debilis* are of great medicinal value, as they only contain high amounts of the hepatoprotective phyllanthin and hypophyllanthin. Other *Phyllanthus* species are totally devoid of these compounds.

Similarly, the ayurvedic drug *Sariba* has become controversial since many plants are sold in this name. Important among them are *Ichnocarpus frutescens*, *Hemidesmus indicus*, *Decalepis hamiltonii* and *Cryptolepis buchanani*. Authentication of crude drugs is presently carried out by NISCAIR, New Delhi.

Adulteration

When fully dried many crude drugs look the same. The stem bark of *Holarrhena antidysenterica* is often adulterated with that of *Wrightia tomentosa* and *Wrightia tinctoria*. In the same way what is being sold in the name of *Saraca indica* is mostly the bark of *Polyalthia longifolia*. Unscrupulous traders are also known to substitute root of *Moringa oleifera* with root of *Carica papaya*! As crude drugs are sold in gunny bags by weight, consignments often contain good amount of

sand, fine pebbles, metal pieces, small stones and unwanted foreign organic and inorganic material.

Phytochemical variations due to environmental factors

Many intrinsic factors govern the growth and quality of herbs. Standardization of herbs becomes most important on account of these inherent, uncontrollable variations. Seasonal changes in rainfall and photoperiodism affect the chemistry of *Adhatoda zeylanica* and *Holarrhena antidysenterica*. Many species of *Garcinia* are influenced by geographical location. Similarly, age of the plant at the time of harvest is important in the case of *Ginkgo biloba*. Chromosome number and variety affect the quality of *Acorus calamus*. Quality of the much-used *Andrographis paniculata* is affected by edaphic factors like soil pH, soil chemistry and nutrient status.

Lack of reference standards

Reference standards are required to ascertain the authenticity of crude drugs and their content in formulations. However, the marker compounds for many plants are not known. In cases where they are known , the standards are unavailable, making quantification difficult.

Lack of pharmacopoeia

Pharmacopoeias serve as guides in analytical work. Nevertheless, very few pharmacopoeias are available for botanical drugs. More work needs to be initiated in this direction.

Some solutions

Botanical reference material

An authentic reference standard of a particular crude drug is required for its correct identification. This can be achieved by generating authentic botanical reference materials. Samples of fresh plants are to be collected from the wild, at the right geographical location, at the right season and at the right age. Thereafter their taxonomical identities should be verified on the basis of herbarium sheets and documentation of the collection data. Thereafter, the parts intended for use should be carefully collected, dried under controlled conditions and stored appropriately to serve as authentic botanical reference material.

TLC Fingerprinting

A major problem encountered in herbal medicine industry is the identification of crude drugs. Many of the crude drugs look alike and after pulverization it becomes impossible to set aside the genuine ones. It is at this stage that thin layer chromatography (TLC) comes to help. It is one of the easiest and cheapest tools for Phytochemical analysis and is widely used in crude drug authentication. Co-TLC is done using the authenticated botanical reference material. The TLC fingerprint of the sample under test is compared with the TLC fingerprint of the authenticated botanical reference material. Thus the availability of authentic botanical reference material is very important in quality control of crude drugs.

Quantification of markers

Markers or reference standards are compounds unique to the plant in question, are present in detectable amounts and can be easily isolated. A marker compound can be quantified whenever the actual bioactive are not known. The concentration of markers in a particular drug could be appropriately fixed and each batch of the drug produced should conform to these limits. Quantification can be achieved by high performance thin later chromatography (HPTLC) or high performance liquid chromatography (HPLC).

In case of plants for which markers are not known, Phytochemical profiling of the category compounds like alkaloids,

terpenoids, glycosides, saponins, flavonoids, tannins etc can be carried out.

Biological standardization

Traditional medical systems like Ayurveda adopt a holistic approach to health and disease. Therefore, a single chemical entity cannot be held responsible for the whole biological activity. Quantification of actives can be misleading in judging the efficacy of crude drugs or their formulations. Therefore, a new concept of biological standardization has been introduced in medical research. Many enzyme assays can be used in this regard.

Conclusion

The healing power of Ayurveda and other forms of herbal medicine is fast unraveling before the world and there is great market potential for medicinal plants their value-added products, both in the national and international markets. The global market needs superior quality medicinal formulations. Therefore, it is essential to ensure their quality at all levels of standardization, efficacy, safety and consistency.

WHAT TOXICOLOGISTS STUDY

Dr. P.Yuvaraj
Department of Toxicology, R&D, CARe KERALAM Ltd

Toxicology has become a science that builds on and uses knowledge developed in other related medical sciences, such as physiology, biochemistry, pathology, pharmacology, medicine, and epidemiology, to name only a few. Given its broad and diverse nature, toxicology is also a science where a number of areas of specialization have evolved as a result of the different applications of toxicological information that exists within society today. It might be argued, however, that the professional activities of all toxicologists fall into three main areas of endeavor- descriptive toxicology, research/mechanistic toxicology, and applied toxicology.

Descriptive toxicologists are scientists whose work focuses on toxicity testing of chemicals. This work is done primarily at commercial and governmental toxicity testing laboratories, and the studies performed at these facilities are designed to generate basic toxicity information that can be used to identify the various organ toxicities (hazards) that the test agent is capable of inducing under a wide range of exposure conditions. A thorough "descriptive toxicological" analysis would identify all possible acute and chronic toxicities, including the genotoxic, reproductive, teratogenic (developmental), and carcinogenic potential of the test agent. It would also identify important metabolites of the chemical that are generated as the body attempts to breakdown and eliminate the chemical, as well as analyze the manner in which the chemical is absorbed into the body, distributed throughout the body and accumulated by various tissues and organs, and then ultimately excreted from the body.

Hopefully, appropriate dose–response test data are generated for those toxicities of greatest concern during the completion of the descriptive studies so that the relative safety of any given exposure or dose level that humans might typically encounter can be determined.

Basic research or mechanistic toxicologists are scientists who study the chemical or agent in depth for the purpose of gaining an understanding of how the chemical or agent initiates those biochemical or physiological changes within the cell or tissue that result in the toxicity (adverse effect). They identify the critical biological processes within the organism that must be affected by the chemical to produce the toxic properties that are ultimately observed. Or, to state it another way, the goal of mechanistic studies is to understand the specific biological reactions (i.e., the adverse chain of events) within the affected organism that ultimately result in the toxicity under investigation. These experiments may be performed at the molecular, biochemical, cellular, or tissue level of the affected organism, and thus incorporate and apply the knowledge of a number of many other

related scientific disciplines within the biological and medical sciences (e.g., physiology, biochemistry, genetics, molecular biology). Mechanistic studies ultimately are the bridge of knowledge that connects functional observations made during descriptive toxicological studies to the extrapolations of dose–response information that is used as the basis of risk assessment and exposure guideline development (e.g., occupational health guidelines or governmental regulations) by applied toxicologists.

Animal house of CARe KERALAM Ltd.

Applied toxicologists are scientists concerned with the use of chemicals in a "real world" or non-laboratory setting. For example, one goal of applied toxicologists is to control the use of the chemical in a manner that limits the probable human exposure level to one in which the dose any individual might receive is a safe one. Toxicologists who work in this area of toxicology, whether they work for a state or federal agency, a company, or as consultants, use descriptive and mechanistic toxicity studies to develop some identifiable measure of the safe dose of the chemical. The process whereby this safe dose or level of exposure is derived is generally referred to as the area of risk assessment. Within applied toxicology a number of subspecialties occur. These are: forensic toxicology, clinical toxicology, environmental toxicology, and occupational toxicology. Forensic toxicology is that unique combination of analytical chemistry, pharmacology, and toxicology concerned with the medical and legal aspects of drugs and poisons; it is concerned with the determination of which chemicals are present and responsible in exposure situations of abuse, overdose, poisoning, and death that become of interest to the police, medical examiners, and coroners. Clinical toxicology specializes in ways to treat poisoned individuals and focuses on determining and understanding the toxic effects of medicines and simple over-the-counter (non-prescription) drugs. Environmental toxicology is the sub-discipline concerned with those chemical exposure situations found in our general living environment. These exposures may stem from the agricultural application of chemicals (e.g., pesticides, growth regulators, fertilizers), the release of chemicals during modern-day living (e.g., chemicals released by household products), regulated and unintentional industrial discharges into air or waterways (e.g., spills, stack emissions, NPDES discharges, etc.), and various nonpoint emission sources (e.g., the combustion byproducts of cars). This specialty largely focuses on those chemical exposures referred to as environmental contamination or pollution. Within this area there may be even further subspecialization like ecotoxicology, aquatic toxicology, mammalian toxicology and avian toxicology. Occupational toxicology is the sub-discipline concerned with the chemical exposures and diseases found in the workplace.

Regardless of the specialization within toxicology, or the types of toxicities of major interest to the toxicologist, essentially every toxicologist performs one or both of the two basic functions of toxicology, which are to (1) examine the nature of the adverse effects produced by a chemical or physical agent (hazard identification function) and (2) assess the probability of these toxicities occurring under specific conditions of exposure (risk assessment function). Ultimately, the goal and basic purpose of toxicology is to understand the toxic properties of a chemical so that these adverse effects can be prevented by the development of appropriate handling or exposure guidelines.

Regulatory agencies insist on toxicity data of ayurvedic formulations. Therefore, CARe KERALAM Ltd is equipped to carry out all kinds of toxicity studies. However, special attention is paid to acute oral toxicity, LD_{50}, sub-acute toxicity, sub-chronic toxicity, chronic toxicity and acute dermal irritation.

The animal house of CARe KERALAM Ltd makes use of forced ventillated cages, for housing experimental animals. In traditional animal houses, small animals are housed in plastic or metallic cages having a metallic grill on the top. However, in such animals houses the animals do not have any protection from contamination within the room, from surrounding animals or attending personnel. The odour in the room cannot be eliminated due to open cages. The forced ventillated cage system has a ventilator unit, individually ventillated cages with air distribution ducts. Clean air passes through the cage and contaminated air is evacuated from the cage. CARe KERALAM Ltd is the first institution in Kerala to install individually ventillated animal caging system. With state-of-the-art facilities in the toxicology centre, CARe KERALAM Ltd is all set to undertake toxicological studies of ayurvedic medicines.

Individually Ventillated Cages

News in Brief

To enrich the pool of trained analysts in Kerala, CARe KERALAM Ltd has initiated a six months-long training programme on industrial laboratory practices. Four young biotechnologists are currently undergoing this training which began on 23 March. They are receiving hands-on training in analytical instruments like HPTLC, HPLC, LC-MS, GC-MS, ICP-MS, UV spectrophotometer and FTIR spectroscope. Additionally they will undergo training at our sophisticated toxicology and microbiology laboratories. CARe KERALAM Ltd plans to conduct many more of such training programmes.

Ayurvedic manufacturing units often complain of souring of *arishtas* and *asavas*. Considering the importance of this problem CARe KERALAM Ltd organized a one-day workshop on souring of *arishtas* during production process . It was held on 8 May 2012 at CARe KERALAM auditorium. The workshop attended by 37 delegates, was inaugurated by Dr. C.I. Jolly, Research Advisor, CARe KERALAM Ltd., presided over by Sri. Karimpuzha Raman, Managing Director, CARe KERALAM Ltd. Dr. K.C. Chacko, Administrator, welcomed the participants and resource persons. Following the inaugural session, Sri. V.V. Venugopal, Scientist, NIIST (C.S.I.R.), Thiruvananthapuram delivered a lecture on fermentation technology. This was followed by another one on re-examination of manufacture of *arishtas* and *asavas* by Dr. D. Suresh Kumar, Head, R&D., CARe KERALAM Ltd. Dr. C.I. Jolly also made a presentation bringing out the technological issues related to these fermented products. The delegates actively participated in the post-lunch session and shared their experiences. The workshop concluded at 3.30 pm with a vote of thanks by Dr. Joy T. Verghese, Executive Director.

Workshop on Souring of Arishtas

To familiarize the industry with analytical testing methods CARe KERALAM Ltd intends to conduct a series of training workshops. The first of this series, a workshop on pharmaceutical botany was conducted on 25 and 26 April, 2012. It was inaugurated by Sri Karimpuzha Raman. Dr. C.I. Jolly and Mrs. Mariya Paul, botanist of CARe KERALAM Ltd demonstrated the preparation of herbaria and permanent slides of herbs, powder analysis, fluorescence analysis, histochemistry and *Lycopodium* spore method of enumeration of well-defined particles like pollen grains, starch grains and single-layered tissues. The workshop was attended by 4 delegates from the industry and 16 students from Ayurveda colleges.

High Performance Thin Layer Chromatography (HPTLC) is increasingly being used in the evaluation of ayurvedic herbs and detection of adulterants. A one-day industrial workshop on application of HPTLC for herbal drug analysis was

conducted on 31 May. The workshop was inaugurated by Sri Karimpuzha Raman. It was followed by addresses by Dr. C.I. Jolly, Dr. Joy T. Verghese and Dr. D. Suresh Kumar. Mr. K.S. Jayachandran, Application Specialist from Anchrom, Mumbai delivered a slide show on the application of HPTLC technique to herbal materials. The remaining part of the workshop was devoted to evaluation of a typical ayurvedic *kashayam* by HPTLC. Mr. K.S. Jayachandran and Dr. C.I. Jolly demonstrated the entire process of this interesting chromatographic technique. The workshop was attended by 20 delegates from the Ayurveda industry.

A workshop on Inductively Coupled Plasma Mass spectrometry (ICP-MS) was held on 7 June. Two experts from Agilent Technologies India Pvt Ltd demonstrated the process of analyzing the elemental content of *Nisakatakadi kashayam*. The aspects of sample preparation, injection of sample into the instrument and interpretation of the results were demonstrated by the team, under the direction of Dr. C.I. Jolly. The workshop was attended by 10 delegates from the industry.

CARe KERALAM signs MoU with Coconut Development Board

From left to right: Mr. Karimpuzha Raman, Mr. T. K. Jose I.A.S. and Dr. K. Muraleedharan

Coconut Development Board, Kochi and CARe KERALAM Ltd signed a Memorandum of Understanding on 27 July, to work jointly for the promotion of coconut-based R&D activities. The MoU was signed between Mr. T.K. Jose, Chairman of Coconut Development Board and Mr. Karimpuzha Raman, Managing Director of CARe KERALAM Ltd. CARe KERALAM Ltd will source research projects to be submitted to Coconut Development Board for funding. These research projects will be on themes of interest to Coconut Development Board. Coconut Development Board has developed several technologies for manufacturing value added products from coconut. CARe KERALAM Ltd will identify entrepreneurs who are willing to invest in such technologies and submit well-documented detailed project reports for consideration for assistance under Technology Mission on Coconut (TMoC). Additionally, CARe KERALAM Ltd will act as a focal point of Coconut Development Board activities on a national basis.

Coconut Development Board is associating with CARe-KERALAM Ltd on research studies, product development, validation and commercialization in areas such as clinical studies on use of virgin coconut oil as oral supplement to infants to improve immunity, pharmaceutical studies to develop a product based on tender coconut water against urethral stones, production of antibiotics using tender coconut water, preparation of RTS Products against diarrhea and validation/ patenting.

CARe KERALAM signs MoU with Dhathri group

From left to right: Mr. Karimpuzha Raman, Sri P.R Krishna Kumar and Dr. S. Sajikumar

CARe KERALAM Ltd has entered into a collaboration with Kochi-based Dhathri group for manufacturing tablets, conducting clinical trials, process validation and new product development in the ayurvedic treatment space. The MoU was signed at Kochi on 21 June, between Sri P.R. Krishna Kumar, Chairman of CARe KERALAM Ltd and Dr. S. Sajikumar, Managing Director of Dhathri group.

The tie-up which will involve an investment of Rs. 5 Crores in the first year will focus on developing remedies for life style disorders like diabetes and cardiovascular diseases, besides maladies like arthritis and spondylitis. The collaboration will enable joint research, procurement of raw materials and quality screening procedures for the final product. This joint R&D effort will bring down development costs and help the consumer as well.

Ayurveda Tomorrow invites for publication articles on Ayurveda in general and Ayurveda renaissance in particular. Please send in your contributions (2-3 pages in Word format) to: Editor, ***Ayurveda Tomorrow*** E.mail: carekeralam@ymail.com

We also look forward to your valuable views and opinions.

Analytical Services of CARe KERALAM Ltd

Equipped with state-of-the-art analytical instruments like High Performance Thin Layer Chromatography (HPTLC), High Performance Liquid Chromatography (HPLC), Liquid Chromatography- Mass spectrometer (LC-MS), Gas Chromatograph- Mass spectrometer (GC-MS), Inductively-Coupled Plasma- Mass spectrometer (ICP-MS), Fourier Transform Infrared Spectroscope (FTIR) etc, we undertake analysis of ayurvedic raw materials, ayurvedic products and nutraceuticals. Additionally, we also carry out toxicological and microbiological studies of products. For details contact:

Dy. Manager (Business Development)
CARe KERALAM Ltd
KINFRA Small Industries Park, Nalukettu Road
KINFRA Park P.O.- 680 309
Koratty, Thrissur District
Mobile: 8129688999

CARe KERALAM

We offer to the Ayurveda industry a wide range of crude drugs at competitive rates:

Honey
Jaggery
Katukurohini (*Picrorrhiza kurroa*)
Raktachandanam (*Pterocarpus santalinus*)
Manchatty (*Rubia cordifolia*)
Ayamodakam (*Trachyspermum ammi*)
Satakuppa (*Anethum graveolens*)
Kattupatavalam (*Trichosanthes lobata*)
Arjuna bark (*Terminalia arjuna*)
Jeerakam (*Cuminum cyminum*)
Nagapoovu
Nellikka
Katukka
Thannikka
Chukku and many more!

For details contact:- Shamjith Shajahan
Executive Business Development
CARe KERALAM Ltd
KINFRA Industries Park, Nalukettu Road,
KINFRA Park P.O – 680309
Koratty, Thrissur District
Mob- 8129688999
Phone- 480 2735837, 2735737
Email: bd@carekeralam.com