

# LINK Natural Products Digest

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# EDITORIAL

## Responding to Aromas

The human sense of smell can elicit strong emotional responses. It can recall, from the depths of memory, often without conscious awareness, significant incidents from a person's past. Smells and mostly pleasant ones are a powerful link with a person's past.

It all works this way. Our olfactory system, by means of which we detect aromas, can send out chemical messages with regard to the aromas around us, via the limbic section of the brain. Instantly this message is transmitted to the central nervous system, which manages our body functions as well as our feelings, and thereby our responses to these aromas. Hence our sense of smell can determine our moods, our feelings of depression and wellbeing.



Remains of Ancient Technologies

The ancient civilizations in Arabia, Babylon, China, Egypt, Greece, Rome and the Indus valley, were aware of this from their own observations. They used the fragrant aromas from plants for purposes of wellbeing, controlling sadness, and even to heal and embalm. They felt that a dead person should be accompanied with pleasant smells which may then hasten the journey to heaven!

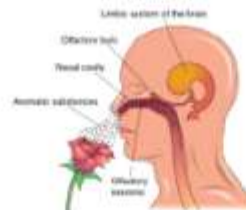
Since those early times man has harnessed scents from plants (and even animals as in the case of the civet cat), to isolate the pure essences, and to put together others from them. This was the beginning of the Essential Oils industry, from which followed the Fragrance and Perfumery industry.

Realization of the influence of aromas on the human being, and scientific studies of the phenomenon has now given rise to another health promoting industry in the form of Aromatherapy. Aromatherapy is a scientific

healing practice which uses essential oils as well as herbs to treat stress-related conditions and other problems such as muscular, circulatory, respiratory, and digestive ailments, including skin problems. Aromatherapy can foster deep relaxation which in turn can alter perceptions of pain. Essential oils also affect the seat of memory, and, that which governs emotions. Inhalation of them can give feelings of euphoria, as for example one feels when walking across a field of Ylang ylang flowers when they are in full bloom.



Flowers of ylang-ylang



Inhalation of aromas

Aromas also activate the deeper part of the brain where memories are stored. Pleasant memories serve to ease tensions.

Thus has been born a potent tool in the design of the interior of buildings such as hospitals, industrial factories, community halls even the working environment and the home. The interior designer can use the sense of smell as a potent design tool. Smell can be made an integral part of a building's design plan. Essential oils and combinations of them could be used to bring to a room a sense of nature, the fragrance of a flower garden, feelings of harmony and serenity. Introduction of aromas can instill in people the urge to work in harmony and happiness, and help them to combat the onset of tiredness.

Increasing scientific evidence backs this concept and its utilization is now in progress.



## An outline of the history of Ayurveda in Sri Lanka

*C.G. Uragoda*  
*Consultant Physician*

The earliest system of medicine that existed in Sri Lanka was *desiya chikitsa* or *sinhala vedakama*, which was a truly ingenious system of medicine that was handed down from generation to generation. In the course of time this system became integrated to a large extent with Ayurveda and is now practiced by only a few who still possess some remedies preserved exclusively in their families.

Ayurveda was introduced to Sri Lanka from North India. It was part of the cultural heritage that flowed into the country in the wake of Buddhism, which was introduced into Sri Lanka in the 3rd century BC. Ayurveda was sustained by an extensive pharmacopoeia of drugs which were mainly herbal in origin. The fact that many of these herbs grew in Sri Lanka, and therefore were readily available locally, added to the attractiveness of the system.

### **Ayurvedic medical literature**

The early Ayurveda texts used in Sri Lanka were mostly compiled in India, but in time original books were written by local authors. These volumes were inscribed on *ola* leaves, which were prepared from the talipot palm. These leaves have provided ancient Sri Lanka with a traditional medium for bequeathing their religious scientific and literary knowledge to posterity.

Sanskrit and Pali were the learned language at the time. While religious literature was written mostly in Pali, Sanskrit was the medium largely employed for medicine. Buddhist monks comprised the majority of those proficient in these two languages, and as was to be expected, some of the classical treatises were written by them. Some of these works were subsequently translated into Sinhala by later writers mainly for the use of the lay sectors.

In ancient times, in the era before printing, duplication of a book was a laborious manual procedure. With copies of medical books therefore hard to come by, practitioners of medicine adapted the method of committing their knowledge to memory. In this respect verses were more easily memorized than prose, and therefore the contents of some of these books are versified.

Since learning of medicine devolved on the question of literacy, the few who were able to read and write studied this branch of science. It became the prerogative of a few, namely Buddhist monks and people of gentle birth. There was a copious flow of medical literature from them. In fact a large proportion of *ola* literature extant today concerns medical literature, and in volume probably comes only second to religious works. The Buddhist temple played a substantive role in ancient medical education.

### **Foreign powers**

Ayurveda enjoyed its golden era during the period of Sinhala kings who built several hospitals, including the ones at Mihintale and Medirigirya. After serving the people for centuries, it faced competition from western medicine from the 16th century onward, when successive powers, namely the Portuguese (1505-1656), the Dutch (1656-1796) and the British (1796-1948) occupied the country. This foreign invasion and the resultant strife sapped the strength of the monarchy, and Ayurveda became a casualty in common with other ancient arts and crafts.

However this threat to Ayurveda was minimal during Portuguese and Dutch occupations. First western medicine itself was not sufficiently developed at the time, and secondly the Portuguese and the Dutch were themselves impressed by the knowledge of herbal medicines possessed by the local physicians.

The British, on the other hand, gradually became interested in the health of the people. They thought that their system was the best for the people, and as a result Ayurveda began to take a back seat.

### **Post-Independent period**

Sri Lanka gained her Independence from the British in 1948. By that time many western medical hospitals had been built by the British, and Independent Sri Lanka improved these efforts.

At the same time, there has been a resurgence of Ayurveda, especially after Independence. A ministry and a department of Ayurveda, together with new hospitals and dispensaries, were set up. Now western medicine and Ayurveda stand side by side, and it is left to the individual concerned to select the system he favours.

## SHARING AN EXPERIENCE

*K. Godage\**

I personally owe a deep debt of gratitude to Ayurveda — for I owe my life to it. In 1967 I suffered from Hepatitis and was compelled to spend no less than five months in hospital. I was treated with Prednisolone by a well known physician and it was not possible to stop the treatment for when the dose was tailed off my serum Bilirubin count increased. I was absolutely 'hooked' on it and as you would be aware my physical form underwent change. The Physician consulted a number of other well known physicians and even Prof. Sheila Sherlock, a specialist on the Liver in the UK but to no avail, until I had a visit from Mrs. Preeni Deraniyagala, the wife of the late Mr. PEP Deraniyagala one time Archeological Commissioner. She was quite shocked to see my state and inquired as to what I was being treated with and when told, she was very angry and asked me to throw away the Cortisone (which I was prepared to do for by then, I would try anything) and she said she would send me a 'Basne' and a 'Kanda', which she sent and I started on from the following morning and within a week my Bilirubin was under control and I was able to finally leave hospital and resume life once again. The 'kenda' which Mrs. D sent me had been made from 'Heenbowitiya', I am certain that had I continued to be on Prednisolone I may not have been alive today; I am alive today thanks to Mrs. Deraniyagala and the Ayurveda 'kanda'.

Six months after I left hospital I developed pain in the region of the left knee and I consulted the late Dr. Rienzie Peiris, the well known Orthopaedic surgeon, who examined me and stated that the pain in the knee was reflected pain and that I was developing Osteoarthritis and recommended hip replacement surgery. I must confess that it scared me no end and I preferred to live with the pain, which at times was excruciating, than undergo surgery. I lived with this for years - swallowing pain killers until I could not almost walk; most fortunately I was stationed in Japan at the time; even in this condition I was scared of having my hip replaced but two friends Prof. Monte Cassim (then a student in Japan now the only foreign Vice Chancellor of a prestigious Japanese University, Ritsumeikan University in Kyoto) and his wife Julie tricked me into going to hospital after

having made all arrangements with the senior Orthopaedic surgeon of the Tokyo University hospital, one Professor Tagawa, who in later years became a world authority on hip surgery. I was operated on within days and after I had recovered consciousness the surgeon came to see me and showed me what was left of the femur and he crushed a piece - (I live today with an 'Austin More' type replacement, that was what I was told). A few days after the operation they had done an analysis of the bone and had come to the conclusion that my condition was caused by an overdose of Cortisone!

Thirty years have elapsed and I have most fortunately not had to go under the knife again; according to a specialist, it has been, in the first instance because I have not put weight on the leg which was operated upon by using a walking stick and secondly because the surgeon who operated on me had done a perfect job. Whilst I am indeed grateful to the surgeon and his team and my friends who helped in those difficult times, I cannot forget Mrs. D and the Ayurveda Heenbowitiya Kenda which in fact saved my life.

I thought I should share with you my experience with Ayurveda; it remains my first choice after proper diagnosis.

*\* K. Godage is a retired diplomat*

### OF SIMPLICITY & BEAUTY.

"Molecules, can be beautifully simple and simply beautiful....."

But chemists and artists know that there is infinitely more to beauty than simplicity. Beauty resides, not just in simple things but in the tense edge where simplicity and complexity, where symmetry and asymmetry, where chaos and order contend with each other."

Roald Hoffman 1981 Nobel Laureate in Chemistry,

Quoted by Fiona Case, in Chem.World : 2007, Dec. p 50.



# HEPATOPROTECTIVE ACTION OF HEENBOVITIYA

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(Adapted for the Link Natural Products DIGEST,  
from a Review in Science Sri Lanka. 2000, 9-13.)

## Introduction:

Viral Hepatitis is a health problem that effects several millions of people worldwide. The current drugs of choice are the interferons and corticosteroids. Particularly in the treatment of hepatitis B and C. However these have the drawback that they produce serious side effects and further they do not possess any specific antiviral effects. Hence any agent from natural sources that would possess specific action on hepatitis would have worldwide significance. Accordingly our studies over the past few years have focused on remedies prescribed by local medical practitioners for the treatment of liver diseases.

In Sri Lanka two closely related plants of the *Osbeckia* species, *O. Octandria*, and *O.aspera*, are both referred to as Heenbovitiya, and used for the treatment of liver diseases like hepatitis. Which species is used depends on the local availability. Hitherto there has been no scientific evidence in regard to the efficacy of these plants in respect of the treatment of hepatitis and similar ailments. Since 1987, my research group has carried out a series of studies to determine in modern scientific terms the hepatoprotective potential of these species of *Osbeckia* collectively referred to as Heenbovitiya. This work [vide references] is briefly reviewed, and summarized here.



## Confirmation of Hepatoprotective activity.

### In-vivo investigations.

In-vivo experiments using the rat model or the mouse model have demonstrated that the aqueous extracts of the leaves of the *Osbeckia* species offers significant protection against acute liver injury mediated by carbon tetra chloride or paracetamol ( toxins with differing modes of action).

### Effects on Carbon tetrachloride mediated toxicity.

Within 24 hours of administration of a sub-lethal dose of carbon tetrachloride to rats there was a marked:

1. elevation in serum levels of ALT, AST, and alkaline phosphatases &
  2. histological changes in the liver similar to those seen in viral hepatitis – centrilobular necrosis with mononuclear infiltration in the portal area, fatty deposition and loss of reticular framework).
- which would be indicative of extensive liver damage.

In rats pre-treated or post-treated with the leaf extracts of either species, the alterations in the liver function and histology caused by the toxin, were found to be significantly less than the controls treated with only the toxin even though the plant extracts themselves had no significant effects on these parameters. [1,2,3]. The extent to which *O.aspera* and *O.octandria* were able to moderate the toxin-mediated changes were similar, thus helping to rationalize the use of both the species in therapy.[4].

### Effects of paracetamol mediated toxicity.

Paracetamol at a dose of 450mg/kg to mice caused extensive liver injury as demonstrated by an increased blood Normotest and and plasma AST activity accompanied by gross necrosis in the centrilobular hepatocytes and reduced total liver glutathione and GSH:GSSG ratio in comparison with untreated control animals.

By concurrent oral administration of paracetamol with extracts of *Osbeckia* (330mg/kg) a significant decrease in the mediated toxic effects were observed.[5]

Thus the carbon tetra chloride or paracetamol mediated alterations in liver function and in liver histology could be significantly reduced by pre or post treatment of animals with the plant extracts, although the extracts alone did not display any effects on any of the above parameters.



#### **In-vitro investigations.**

In-vitro investigations consisted of the assessment of the ability of the plant extracts to protect freshly isolated rat hepatocytes or Hep G cells, (an immortalized human hepatoma cell line) against cell damage mediated by a variety of toxins with different modes of action. The toxins used were: N-galactosamine, (N-gal), t-butylhydroperoxide (TBH), bromobenzene, and 2,6-dimethyl-N-acetylparaquinoneimine, (an analogue of the toxic paracetamol metabolite.

#### **Effects on the NG and TBH mediated toxicity.**

The extract gave a dose dependant protection against N-gal (10mM) and TBH 0.75 mM mediated alterations in hepatocytes, with a maximum protection at 500ug/ml concentration in the incubation medium. At this concentration it protected against the N-gal mediated decrease in protein synthesis, TBH-mediated increase in lipid peroxidation, as assessed by MDA generation, increased leakage of cellulose LDH mediated by N-gal and TBH and also the enhanced leakage of AST. Significant protection was also observed when the extract was added to the incubation medium up to 30 min after pre-exposure of hepatocytes to either N-gal or to a lesser extent TBH. [6].

#### **Effects on 2,6-DMNAPQI**

*Osbeckia* extract (500ug/ml) when added to rat hepatocyte incubation medium together with 2,6-DMNAPQI displayed significant changes in cell viability, cell reduced glutathione (GSH) level, and reduced release of LDH after incubation for 1 hour as compared with 2,6-DMNAPQI by itself.[7]

#### **Effects in HepG2 cells.**

Similar beneficial effects were also observed.[8]

Thus the effects noted in the in-vivo experiments were endorsed by the in-vitro experiments. The results also demonstrate that the hepatoprotective effects of *Osbeckia* is due in part to direct effects on liver cells. It is evident that both *Osbeckia* species possess a common active ingredient.

#### **Mechanisms of Action.**

We have also examined the mechanisms of action of the *Osbeckia* extracts.[8,9,10] These have been studied relative to established mechanisms such as the following:

- \* Hepatocyte membrane stabilization
- \* Stimulation of hepatocyte regeneration
- \* Immunomodulation
- \* Direct viral effects

The following conclusions may be drawn from these studies:

- \* In-vivo studies with rats and in vitro studies with HepG2 cells indicated the presence of a powerful anti-lipoperoxidative and anti-radical activity in the leaf extract suggesting that anti-oxidant activity could be one of the mechanisms involved in the beneficial effects demonstrated by the extract.
- \* Both in -vivo and in-vitro studies further demonstrate the presence of compounds with radical scavenging and anti-radical effects. These are in all probability polyphenolic in nature.
- \* Quenching of free radicals may be a contributory mechanism of action
- \* In-vitro inhibitory on activities of the human complement system and also luminal-induced chemiluminescence of human polymorphonuclear lymphocytes



indicates that immunomodulation could indeed be a mechanism of action by which the *Osbeckia* extract exerts its hepatoprotection.[11]

- \* The effects of the extract on Woodchuck hepatitis virus was significant and this demonstrates that the plant constituents include anti-viral compounds.
- \* The overall results indicate that the hepatoprotection by *Osbeckia* leaf extract is more likely to be due to a combination of direct effects on hepatocytes and immunomodulatory effects rather than direct anti-viral action.

### Isolation of Active Principles.

Activity guided sequential fractionation of a crude methanolic extract of *Osbeckia octandra* leaves followed by chemical screening of fractions indicated the presence of three possible active compounds belonging to the flavanoid, and general polyphenol category. Investigations are ongoing. Large scale cultivation of this plant is warranted due to its demonstrated utility and intense chemical work is called for.

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### EXPERIENCE

There are some things which cannot be learned quickly and time which is all we have must be paid heavily for their acquiring. They are the very simplest things, and because it takes a man's life to know them, the little new that each man gets from life is very costly, and the only heritage he has to leave.

*Ernest Hemmingway*

### WOMEN IN SCIENCE

Responding to a question if she had felt very strongly about the position of women in science Dame Professor Dorothy Crowfoot-Hodgkin FRS Nobel Laureate says:

*"No! I think it is because I did not really notice it very much that I was a woman amongst so many men. — I am a little conscious that there were really moments when it was to my advantage. My men colleagues at Oxford were very often nice and helpful to me as the lone girl. At the time just after the war and the first elections to the Royal Society were made it probably got me in earlier than one might have as a man."*

### THE AGE OF NOISE

The twentieth century is, among other things, the age of noise: Physical Noise, Mental Noise and the Noise of Desire. All the resources of our miraculous technology have been thrown into the current assault against silence.

*Aldous Huxley*

# An Introduction to :- Hazard Analysis & Critical Control Point System - (HACCP)

R.O.B.Wijesekera

## 1. What is "HACCP"?

The "HACCP" or, Hazard Analysis & Critical Control Point system is derived from a concept in engineering which aims to detect what could possibly go awry during processing of raw materials into finished products. It examines each stage of the protocol of operations, and places suitable control mechanisms to detect errors. The system is now recognized by bodies such as the WHO, FAO, WTO, ISO, and is internationally accepted by the Food & Pharmaceutical Industries. HACCP is now regarded as a Safety Management System and the main objective is to ensure prevention of hazards by putting into place the appropriate control measures. It is defined as a **system which identifies, evaluates, and controls hazards, which are significant for ensuring product safety.**

## 2. HACCP, in Industry.

HACCP is now mainly used in industries such as Food Processing, and processing of Pharmaceuticals and what are now termed "Nutraceuticals" or Over-the-Counter, OTC healthcare products. This includes for all purposes the Herbal products industry as well. The rationale is that consumers have the right to expect the products they have to consume or even topically use, to be safe and suitable for the purpose they are meant to serve. Illnesses resulting from consuming or applying unsafe products can have serious consequences to entire groups of people or even populations. These consequences can be costly in terms of medical care or even human lives. International trade is a major business activity and many products are produced in developing countries so that it is important for them too to have such safety management programs like HACCP.

In addition to product safety HACCP has the following advantages.

- \* It provides a note of confidence to the consumer/customer/enforcer
- \* It adds a preventive approach to the otherwise purely retrospective end-product testing methodology.

- \* It provides a control for any possible hazards in a cost-effective manner.
- \* It uses technical resources within critical areas of the production process.
- \* It can support inspection by regulatory authorities
- \* It facilitates trade by enhancing the confidence in regard to product safety.
- \* It facilitates both local and international legal requirements



## 3. The Seven "Principles" of HACCP

Basically, there are seven "principles" that are recognized as important steps in the institution, and maintenance of an HACCP system, within a processing industrial organization. They are:-

1. Conducting a hazard analysis. A hazard is any biological, chemical or physical property that could cause a product to be unsafe.



2. Determining the critical control points (CCP's). A CCP is a point, step, or procedure in a production process at which control can be applied, and as a result, a product safety hazard can be prevented, eliminated, or reduced to an acceptable minimum level.
3. Establishing critical limits. A critical limit is the maximum or minimum value to which, a physical, biological, or chemical hazard must be controlled at a CCP to prevent, eliminate, or reduce, to an acceptable level.
4. Establishing systems to monitor control of CCP's. These systems are needed to ensure that the system is under control at each CCP.
5. Establishing corrective measures to address flaws in the CCP's. These are necessary when a deviation from an established critical limit has been noted in the monitoring. Corrective action as specified in the HACCP Plan has to be taken to ensure that no unsafe product enters the market.
6. Establishing validation mechanisms to ensure that the HACCP system is working as intended. Validation ensures that the manufacturing system functions in the way that it was designed to do. This means that the safety of the products is ensured.
7. Formulating the necessary documentation in respect of all procedures relevant to the above and their application. The HACCP regulations require that certain documentation is maintained. These include: a Hazard Analysis and the HACCP Plan; and records documenting the monitoring of CCP's, critical limits, verification activities, and the handling of processing deviations.

#### 4. Pre-requisites, for HACCP, and an HACCP Plan.

Pre-requisite programs form the foundation for the implementation of HACCP.

For example, it is evident that the maintenance of an appropriate HACCP system within a processing company requires that the company possesses the relevant multi-disciplinary expertise in-house. Accordingly care must be exercised in the development of relevant pre-requisite programs. These are defined as "practices and conditions needed prior to and during implementation of HACCP".

In addition it must be ensured that within the company the following basic pre-requisites are met.

- \* Acquisition of detailed knowledge of the products being processed

- \* Acquisition of reliable knowledge of the raw materials used in the processing.
- \* A thorough understanding of the process protocols employed.
- \* A review of any possible or likely hazards to the consumer or the processing personnel.
- \* A concept of any possible health risks.

The HACCP system must be summarized in a document called the "HACCP plan". This document must be readily accessible to all relevant personnel, and it should contain all the information related to the CCP's, the operating standards, and the critical limits. The document must also indicate data such as the following:-

- \* Which individual or group is responsible for the monitoring, and what the mandated periodicity of monitoring is?
- \* The corrective measures to be instituted in case something goes awry.
- \* The potential hazards that are to be addressed. (Here besides the classical hazards, physical, biological & chemical, hazards introduced from the raw materials, from micro-organisms, hazards from equipment, environment, personnel or equipment should be evaluated.)
- \* A flow diagram of the process protocol; and/or a stepwise drawing of each step of the process.

#### 5. The Need for HACCP and the Role of Management.

Overall there must be the realization within a company that HACCP is by no means a once-and-for-all-time, precise code. It is a changing feature and should be regularly modified and updated in the light of gathered experience, and newly acquired knowledge, so that it may serve the purpose of monitoring possible hazards and dangers to company personnel and customers.

In the context of the present day, consumers are more aware of the need to ensure safety of the products they acquire. The print, as well as electronic media, keep a watchful eye on tales related to: suspect products, and processing conditions, where hazards may be manifest. Accordingly manufacturers need to be prepared to respond to questions, even if sometimes they are unreal and bear little relevance to the actual state of affairs. Complete documentation in the form of efficiently maintained HACCP records may be necessary to counter any hostile propaganda.

Although the consumer or retailer may hardly be aware of what HACCP means, they may expect the producer company to implement HACCP plans.

All inspections carried out on production premises nowadays include an assessment of the competence of management. An effective HACCP system is a prerequisite in demonstrating that the producer company understands the management of product safety hazards,



## 6. Some Guidelines for the Application of an HACCP plan.

The application of an HACCP plan will contain the following steps:

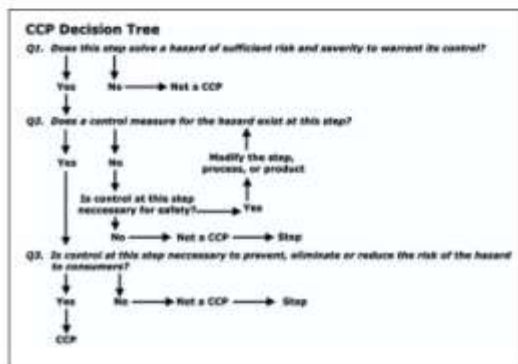
- \* Assembling an appropriate multidisciplinary HACCP team. This will be dependent on the nature of the final products, the processing technology and the measures needed for quality assessment and management.
- \* Defining the terms of reference of the team. This is a necessary measure and will ensure that there will be no confusion.
- \* Elaborating the HACCP plan. The plan after elaboration will need to be discussed with all participants in its execution.
- \* Constructing a flow diagram of the process protocol. A Flow Diagram will ensure that the basic features of the protocol will be clear to the processing personnel. The

secrecy of the protocol may be safeguarded with the necessary measures.

- \* In situ verification of the flow diagram. Since many protocols are based on practical trials the verification is important to ensure that the original concepts and practices remain valid. Where several products are processed there may be the need for a flow diagram for each product.
- \* Verification in accordance with each of the seven HACCP 'principles'

The final step and this may be one that must be determined from time to time, will be to ascertain that the seven principles of the HACCP continue to be reviewed, with respect to the actual operations, and if needed the relevant changes made and documented.

## 7. Concluding Observations.



The application of HACCP principles should be the responsibility of the management. However it is recognized by governments, regulatory bodies, and industrial organizations there could arise, difficulties in the effective application of HACCP by individual operators. This will be evident mostly in the case of small scale businesses. The flexibility of application of HACCP should therefore take into consideration the nature and size of the operation, including its customer base, human and financial resources, infrastructure, the nature of products and the processes, and also the knowledge and experience base of the company or business operator.

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### SERENDIPITY AND EAU DE COLOGNE.

A fragrance born by accident survives the vicissitudes of time.

The story goes that a Perfumer in the City of Cologne fell down the flight of stairs of his studio one day whilst in the act of carrying a tray of several extracts of flowers. The resultant "spill" brought forth a remarkably pleasant fragrance. Furthermore the mixture was ever so much stronger than any of the individual extracts in the tray which the perfumer accidentally spilt. The collective fragrance of the extracts spilt proved that it was far more acceptable, stronger and more lasting than the component flower extracts. The sum total of the components therefore proved to be greater and more appealing than the individual flower odours.

So a new fragrance was born serendipitously, and together with it, the modern fragrance industry.

S.J.Herman  
In Fragrance Application  
- A survival Guide- Carol Stream, Illinois.  
Allured Publishing Co. 2002

Source:  
[www.cosmeticsandtoiletries.com/articles](http://www.cosmeticsandtoiletries.com/articles)

### WINE.

"Like rain for plants, wine promotes the growth of the body. Like fire grading gold, it also shows up people as superior, average, or inferior, in terms of their response to drinking. For, those who drink wine with due attention to propriety in method, quantity, food and time, wine is a nectar.

To others who act in total disregard of propriety, wine is better than poison"  
Archarya Charaka. Chikitsa 24, 26-28.

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### SCIENCE & THE PUBLIC MIND.

"Science really is great but only when it is shared. .... Securing people's trust in Science has been one of the key goals of outreach activities. And yet scientists often ask why an appreciation of the benefits of science still seems as distant as ever in the public mind. There are many factors effecting this;

- \* Education
- \* Development of a generally differential society, unwilling to placidly follow whatever "experts" tell them.
- \* A tendency towards secrecy.

(A Lack of transparency in some areas of science can play a significant part in limiting public confidence in science.)

- Mark Peplow
- Chemistry World (2008).  
April Editorial.

# Society, the Pharmaceutical Industry, and, the Ethical Dimension. - A Point of View.

R.O.B.Wijesekera.

## Introduction

In the modern context, and given the present global situation, the pharmaceutical industry remains one of the most formidable of industries. People with widely different discipline areas, with diverse backgrounds, and different experiences and perspectives are participants in the industry from their varied standpoints. Within them all, the ethical dimension of the industry must indeed loom as most important, for the industry impacts so closely with human lives.

The word "ethics" in the times of the zenith of Greek civilization, was defined as "beliefs of the people". - a study of what is right and good in human conduct and the justification of such claims. Introduced to the complexity of the modern pharmaceutical industry, and what is health care in the modern age, it is no easy task to identify what is "right and good" and what exactly are "the beliefs of the people"

Those who will enter the debate or what is the judgment scenario will come from government, and industry, from medical and scientific organizations, from social regulatory, and advocacy organizations, trans-national organizations, from financial and insurance organizations, and even schools of business. The question begs itself: Can there possibly be a consensus opinion on the direction the industry should take? The industry is profit driven. Yet its products must seek to address illnesses of human kind, and thus fulfill its social objective. Can we identify a middle-path to follow?

## The Dominant Issues & Contending Perspectives

Given the powerful force that is globalization today, every individual standpoint will reflect different national, regional, and social perspectives. Hence there will be a broad spectrum of issues that will dominate the pharmaceutical industry, and the society that it serves. First of all let us define what we mean by the very broad term "Pharmaceutical Industry". There will undoubtedly be several different categories of the industry, which could be broadly identified as follows:

1. The giant multinational pharmaceutical companies.
2. Smaller companies which are primarily national.
3. Companies of the Developing World.
4. Small Manufacturers of Herbal Pharmaceuticals
5. Major manufacturers of Herbal Health Care Products (OTC)
6. Small Manufacturers of specialized items of Healthcare.
7. Manufacturers of Products for complementary Medicine.

It will not be feasible to identify every relevant issue in regard to the ethical dimension, but some general issues could be common to all these types, There could and will arise, disagreements both collegial and fundamental, depending on the perspectives adopted

The ethical dimension in the pharmaceutical industry, and the dominant issues will have developed in accordance with the differing perspectives of the stakeholders. The major perspectives may be judged to be the following:

- \* The contention that healthcare is a commodity, which has to be purchased by the individual, or society provision being made by, for example, with insurance.
- \* Health care viewed as a fundamental human right, that even circumscribes the exercise of intellectual property rights, such as in the case of critical drugs such as vaccines for diseases of epidemic level, HIV/AIDS.
- \* The role of Governments to ensure that the economically disadvantaged have access to healthcare.
- \* The free choice of the patient to decide the type of healthcare delivery eg Complementary Medicine, Ayurveda, Chinese Accupuncture.

These contending perspectives give rise to the dominant issue as to how much government regulation will be needed and or whether the market place forces themselves, can address the social issues.



The perspective that deems that healthcare is a commodity must of necessity derive from the experience within relatively opulent societies such as the US, and Europe. Yet there too there is room for disagreement and debate. However living in the US even temporarily and fortified by the institutional social insurance, failed to convince the writer that there is justice in this concept. One came across hordes of ordinary folk who were not so blessed who live, quite simply put, in constant fear of falling ill. For this to be socially equitable it must be combined with the concept that it is the role of government, to ensure that the economically and socially disadvantaged have adequate access to healthcare.

Such an issue, does prevail, and find resolution, sometimes within richer societies, for example: in a country such as Austria where there is a government sponsored health insurance and healthcare service in addition to privately managed institutions.

The other perspective of Healthcare viewed as a human right will be endorsed by many who come with experience in the developing world. Immediately following the end of World War II, the then Socialist government in Britain established their National Health Service, which institutionalized the practical framework of this form of a service. However as time went by and healthcare became more and more expensive, the Governments that followed found it politically expedient to abandon sole responsibility for national healthcare.

Even those who believe in the free market, and healthcare as a commodity, will sometimes endorse the need for stronger government regulation of the pharmaceutical industry. There are many who believe that this is inevitable as the dictates of the market too often drive pharmaceutical companies to maximize their profits, in a manner that fails to deploy social resources optimally to provide the best healthcare for people. Yet it must be admitted that the Pharmaceutical companies pay for the bulk of the R & D and this is formidably costly. The money has to come from some source and continue to be available for R&D.

For those who believe in the alternative perspective of health as a human right there remains the dilemma of how the ever escalating

funds deemed vital for R&D in the search for new therapeutic agents to combat disease can be got.

Many of the above issues apply to the larger companies, including those that cater for herbal healthcare products as well, for they too belong to the pharmaceutical industry. In many of the developing countries the added issue of the choice of healthcare methodology is of consequence. More than ever nowadays there is increased faith in complementary medicine even among those in the industrialized nations. And herbal healthcare products as OTC's are increasingly in demand.



*Catharanthus roseus* ( Minimal)



*Centella asiatica* (Gotukola)

*Two plant species that are used worldwide in the Industrial Production of phytopharmaceuticals.*

The herbal products industry, worldwide is estimated to have climbed over the 90 billion dollar mark. This estimate however could not include the industry's turnover in countries such as India, China, and the Latin American region.

## A new Paradigm

The different perspectives that characterize the approach to healthcare should in practice therefore, be dominated by the ethical dimension. Whether the differences of opinion are merely philosophical or real, one thing is clear. All people should be entitled to, and should be served with affordable products and services, that will save, enhance, improve, and prolong and enhance their quality of life. At the same time new and better products arise only from consistently good research and the multi-disciplinary nature of pharmaceutical research makes this one of the most costly exercises.

There should be a dialogue on the issues between the research scientists, the healthcare industries and the regulatory authorities and governments as to what is best within a given situation. It has been noted that the renowned physicist Professor Abdus Salaam classified the diseases of the World as belonging to two groups viz: the Diseases of the Rich and the Diseases of the poor. It was the case that pharmaceutical companies largely focused their R & D on delivering therapeutic agents for the diseases of the rich North, on the basis of profitability. The disease of the South came to be relatively neglected in this regard as the poorer nations of the poor South, were not deemed to be sufficiently affluent to generate large profits. However, in the disease patterns of the today it would appear that the divide is fusing. Diseases such as HIV/AIDS, SARS, and the multitude of stress related problems now common to both north and south, bring in another dimension. Yet R&D in the modern context is dependent on a variety of sophisticated and expensive instrumental hardware. The expenditure is beyond the capability of small and medium scale institutions or companies and even Universities have to be heavily endowed with high quality personnel and laboratory and pilot plant facilities to be able to make any impact.

Agreement on issues such as the ethical aspects, and the need for adequate access to healthcare, for all of the world's population, and, how best the industry could serve in this scenario, will be the determinants of the needed new paradigm of effective healthcare delivery. The public as well as the private sectors are both stakeholders. The medical and scientific communities have also their share of responsibility.



Research & Development in all areas is heavily dependent on modern instrumental hardware, and skilled, well-trained personnel. It is prohibitively costly but still all new technology is dependent on R&D

Neutral international organizations, such as WHO, and UNIDO, have their special facilitating role to play. The need is a concerted effort to develop technologies that add quality, value and cost-effectiveness to healthcare systems. In this in particular, the value of traditional medicine and complementary systems, must be harnessed. It is when new technologies, derived from new and innovative R&D, can engage in the system of healthcare delivery to the fullest, that the pharmaceutical industry whatever the type can fully participate and indeed profit in the wider sense as well, albeit, within the ethical dimension. Clearly a paradigm change in healthcare delivery is a burning need.

Natural abilities are like natural plants that need pruning by study.

- Sir Francis Bacon.



# ALOE VERA – “The Plant of Immortality”

Shamila Wickramaarachchi and R.O.B.Wijesekera.  
Link Natural Products

## 1. INTRODUCTION

*Aloe vera*, is certainly one of the truly universal medicinal plants. Man's recognition of aloe as a therapeutic agent dates back to over 4000 BC. Its first written record of medicinal use is on a Sumerian clay tablet dated 1750 BC. Its therapeutic benefits have also been described in the Ebers Papyrus around 1500BC. [1] Aloe is also known to have been associated with the beauty of such historical figures such as Cleopatra and Nephrites. It is believed that even Alexander the Great was aware of the value of this plant and that is long before modern science began to confirm its medicinal value.



Today, its universality, and versatility is proven in a number of areas of application where its efficacy is scientifically recognized. [2-6] Aloe has been used in Ayurvedic medicine too, for a long time, and indeed its value has been amply noted in it being called the Ayurvedic Miracle plant.[8]. Ancient Egyptians have called it the “**Plant of Immortality**”, and used it for bathing to acquire health and wellness, and for embalming.

It remains one of the most studied plants in the modern pharmacopoeias. [9-16]. Aloe is a semi-tropical plant and there are over two hundred or more species recognized the world over.[1,5,17] The plant species to which aloe belongs is recognized as originally being native to Africa., although it is now ubiquitous within the temperate tropical regions. It is a perennial succulent plant with thick fibrous roots. Its

leaves are fleshy, and grow upwards from its base. Each leaf is edged with spikes along the margins. The leaf colour, varies from a grey-blue to a bright green and sometimes under stress conditions may take on reddish tones. The flowers are generally yellow to red and are mounted on a slender central stalk. Each mature leaf weighs between 0.5-1.5 kilograms and it is from the leaf that the medicinal properties are derived. Aloe vera is a xerophytic plant - ie. resistant to drought. Botanically it is identified as a xeroid, which means that if the leaf is cut it seals off to retain fluid. The *aloe vera* plant could grow to man-height or more depending on the conditions.

*Aloe vera* is assigned to the botanical family the Liliaceae. It has also acquired the name *Aloe barbadensis*, following its domestication in the island of Barbados.

## 2. HISTORICAL USES

The historical uses of aloe are now well documented. [2, 3, 12-18] They include such a wide variety of uses and are summarized below. The dried leaf latex has been traditionally used as a laxative, and as a vermifuge to combat intestinal worm infestations. Traditional topical uses of Aloe vera gel include:

- \* Treatment of minor burns, cuts, and, lacerations.
- \* Healing of wounds
- \* As a poultice for cuts, and to remove thorns.

Traditional medicine also employs aloe in preparations for treatment for the following conditions:

Fevers, constipation, gonorrhoea, jaundice, rheumatic conditions, hemorrhoids, sciatica, lumbago, retention of urine, indigestion, chronic flatulence, abdominal tumors, carbuncles, muscular spasms during menstruation, ulcers, colitis, inflammatory conditions, vaginitis, cervicitis, And ailments of the liver, and spleen.

Aloe has also been widely employed in personal care down the ages. The popularity of the plant in an amazing variety of personal care products available as OTC's today derives largely from traditional usage as a popular agent in skin care and cosmetics.

### 3. DOCUMENTED MODERN USAGE & PHARMACOLOGY

In modern times the use of this plant in preparations for personal care dominates its market popularity. There are OTC preparations for every nature of skin condition in forms such as creams, gels, ointments, ranging in use from burns, cuts and abrasions to sunburn and frostbite. It has been a most popular plant for scientific research on account of this prolific market usage. Scientific evidence to a phenomenal extent underscores the traditional values attributed to it as some evidence cited below will indicate.[3-7, 15-19]

- \* Acceleration of the healing of wounds:

Aloe promotes wound-healing presumably by directly stimulating the activity of macrophages and fibroblast. Fibroblast activation increases both collagen, and proteoglycan synthesis, thereby promoting tissue repair. Some of the active agents are polysaccharides. Also responsible are several monosaccharides like mannose-6-phosphate the principal sugar of aloe. The complex carbohydrate acemannan in Aloe leaves is also an aid in wound healing.

- \* Reduction in radiation-induced skin reaction

Acemannan, is a contributor to this effect. It acts in a twofold manner. Firstly, acemannan is a potent macrophage-activating agent and thus will stimulate the release of fibrogenic cytokines. Secondly the growth factors will directly bind to acemannan, promoting their stability, and prolonging the stimulation of granulation tissue.

- \* Prevention of progressive dermal ischemia, caused by burns, frostbite, electrical injury, intra-arterial drug abuse,

Aloe vera gel acts as an inhibitor of Thromboxane A, a mediator of progressive tissue damage

- \* Anti-inflammatory role.

Aloe vera appears to exert an anti-inflammatory effect through bradikininase activity and thromboxane B2 and prostaglandin F4 inhibition. The specific plant steroids in Aloe also contribute to its anti-inflammatory activity.

- \* Treatment of Burns

The existence of diverse components in aloe gel each of which and/or all together may be instrumental in the healing of burns is now well recognized. The gel possesses an anaesthetic effect, a bacteriocidal action, and an anti-thromboxane effect. The gel has been shown to be able to penetrate tissues, relieve pain, reduce inflammation, and increase blood supply by inhibiting the synthesis of thromboxane A2, a potent vasoconstrictor.

- \* Microbiological effects.

Aloe vera is known to kill *Mycrobacterium tuberculosis*, the organism responsible for TB., and also the herpes virus responsible for, *Herpes genitalis*. It also inhibits the growth of other many common organisms, such as yeast, fungi, and the bacteria associated with wound infections.[19].

- \* Therapy for HIV/AIDS.

A Polysaccharide fraction from aloe gel, accmannan, had also been used in the treatment of AIDS patients. A 70% reduction in the symptoms had been recorded, presumably due to stimulation of the immune system.

- \* Effect on the gastrointestinal tract. & Laxative Effects

A series of trials on humans had revealed a tonic effect on the intestinal tract, with a reduction in the transit time. Protein digestion and absorption also showed improvement. The laxative effect is due to 1:8-dihydroxyanthracene glycosides, Aloin A and Aloin B, formerly designated as Barbaloins. Following oral administration of Aloin A and B, they are hydrolysed in the colon by intestinal bacteria, and then reduced to the active metabolite aloe-emodin-9-anthrone. This acts in similar fashion to the sennosides.

- \* Effect on Peptic ulcers.

Oral administration of Aloe gel had proved useful in the case of peptic ulcers. This could be due to the inhibition of causative bacteria, *Helicobacter pylori*. The gel is reported to have a soothing effect on the ulcers.



\* Anti-diabetic activity.

A clinical trial conducted in India, where in about 3000 mildly diabetic patients were fed with bread in which the gel had been incorporated, showed a 90% reduction in the blood sugar levels.

\*Rheumatoid Arthritis.

Aloe vera, administered orally as a juice, or applied as a gel to the painful joints, has been shown to be effective in pain reduction in the repair of damaged tissue and the regeneration of cells.

\* Cancer treatment.

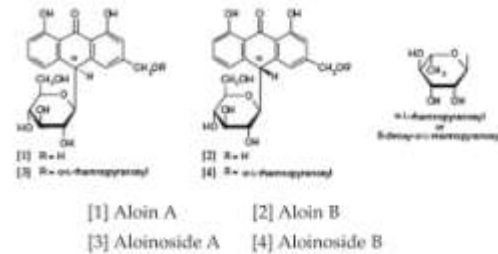
The claims in the treatment of cancers have yet to be fully substantiated.

#### 4. CHEMICAL CONSTITUENTS OF ALOE

Aloe contains an amazing array of constituents and it is perceived that it is the collective action of many of them that accounts for its curative functions. The inner surface of the leaf contains a bitter yellow sap, which when dried and powdered forms the "bitter aloes", which has been used as a purgative. Within the leaf itself is the clear semi-liquid pulp or paracyma, This contains the aloe gel and juice.

The major constituents are hydroxyanthrone derivatives, of the aloe-emodin-anthrone 10-C-glucoside type. The major constituent is known as Aloin or Barbaloin. [3].

The content of aloin varies from 15-40%. It also contains hydroxyl aloin ( about 3%). Aloin which is also referred to as barbaloin, is chemically a mixture of two compounds Aloin A(1) and Aloin B(2), which interconvert via the anthranol form. The variety Aloe ferox, contains: Aloinosides A and B, (3 and 4), which also interconvert like the aloins A and B and which are responsible for the gel's pronounced anti-inflammatory and pain killing effects. It also contains mucopolysaccharides. It is thought that these mucopolysaccharides boost the immune system especially acemannan, which is an abundant component.[3].



#### 5. PROCESSING OF ALOES

The technology for the processing of Aloe gel is schematically represented in the flow diagrams. [Charts 1,2,&3].

Chart number 1. TTS ALOE PROCESS

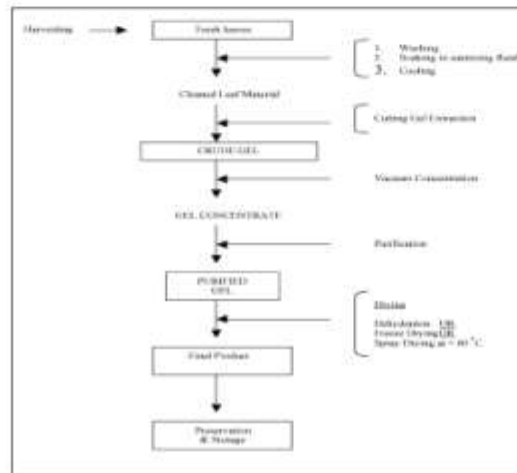


Chart number 2. MECHANICAL PROCESS

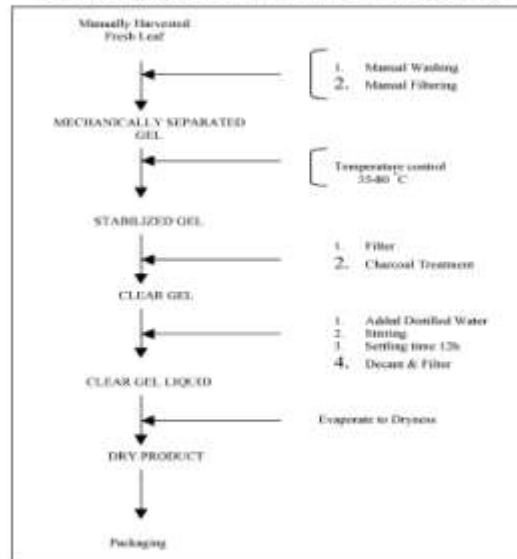
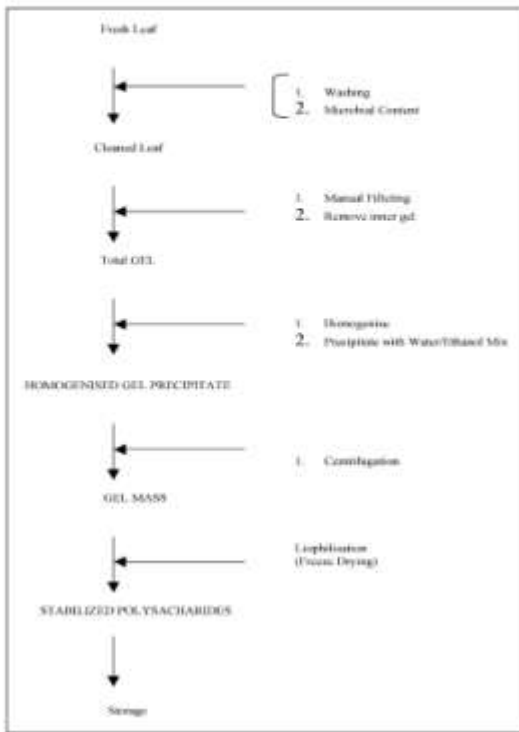


Chart number 3. PROCESS FOR PRODUCTION OF MUCILLAGINOUS POLYSACCHARIDES



There are a number of variations and the method adopted depends very much on such factors as:

- \* The biological nature of the aloe variety
- \* The products that are to be made
- \* The quantity of material available
- \* Temperature and logistic factors.

Many of the methods are the intellectual property of the processing companies and the scale of operations vary from very large operations by transnational companies such as in The United States, Australia, Central America and the Caribbean, to almost cottage-scale operations in Asia and Africa. Each type of process technology has merit in respect of the given situation and need.

Some typical process types are represented by the flow diagrams. The TTS method, Chart #1, (which stands for "Time, Temperature, Sanitation, Method"), is one that is typical for large scale operation for specific requirements. The Mechanical Method represented in Chart #2 is typical of one used in smaller operations, such as in Asia, where the gel is the main industrial product. Also when the main product required is

derived from the mucilaginous polysaccharides, and the scale is larger, the simpler method in Flow chart # 3 is typical

### Large - scale Processing of Aloes



Large-scale processing of Aloes  
Aloe leaves being washed prior to processing.



Aloe leaves on the conveyor belt,  
being processed

## 5. COMMERCIAL CULTIVATION

Commercial cultivation for large scale processing of Aloes is conducted generally in close proximity to the processing centres. Indeed processing is conducted always alongside the cultivations. Aloe is swiftly oxidized after harvesting and hence transportation of the raw material for long time periods is not feasible.

Major cultivation for commercial purposes now takes place in several countries across the world. In Australia, which is a relatively recent large-scale producer, the regional city of Bundaberg, in Queensland is a major centre. The region between Cairns in the North and Brisbane further south is an area that has a climate ideally suited for aloes. This is one of the major modern centres of aloe cultivation.



In India *Aloe barbadensis* is cultivated in the Nu Tech Farm in the Great Kutch region of Gujerat. Once again the climate is most suitable, and hence the choice of region.

In countries of the Central America, and the Caribbean for example: Costa Rica, and Mexico, large farms of aloe are supported with equally large processing centres, all owned and managed by large companies.. One of the largest aloe producing areas is the California Valley Center. The scale of operations here, will be illustrated by the following facts The number of adult plants are of the order of 600,000, during the peak crop time, and these are changed within a seven year cycle. The crop age is around 18 months and the leaf capability is 14,400,000, leaves/year. At the centre there are over 18 million baby plants awaiting introduction.

For such large and medium scale plantations attention to the following requirements are crucial

- \* Selection of the best species
- \* Selection of the most suitable location for cultivation & Processing
- \* Knowledge of farming methodology and Good Agricultural Practices.
- \* Developing the most suitable process technology.
- \* Adequate irrigation facilities.
- \* Methodology for quality assessment of products.

Smaller scale cultivations for situations that are specific, also need the heed the above factors prior to embarking on cultivation.



A large-scale plantation of Aloe in California.



A single plant of Aloe in a garden

A small-scale plot of Aloe

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# Value Addition at Link Natural's Supply Chain - an Operations Management Perspective

Tharanga Perera,  
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Link Natural has devoted itself for ensuring a healthy long life to people at large, by providing innovative healthcare solutions embedded in a range of herbal formulations. It is a company specific, operations management process that enables such innovative products to become realistic and competitive, with the integration of traditional knowledge with modern science & technology and modern management practices.

Operations Management is the proValue Addition at Link Natural's Supply Chain- an Operations Management Perspective

**Operations Management is the process of designing, operating and improving the systems of an organization that create and deliver the firm's primary products or services. Therefore it is a vital component of any organization's management strategies.**

## Operations Management System of Link Natural

Operations Management System of Link Natural has evolved through out its quarter century history from a primitive stage to its present status, having undergone significant reforms with the development of the organization. Having started as a small manufacturer with a limited staff and limited resources, careful application of Operations Management strategy has developed Link Natural to a medium scale organization, establishing 'quality' as the prime objective in its value chain. Today the organization enjoys improved technological capabilities, enhanced innovation capability, higher competitive advantage in market and sound employee-employer relationships.

The following model illustrates the components of Link Natural's Operations Management system.

Natural herbal material,  
Other factors of production,  
Supporting Raw material

(Inputs)

Chemical Processing  
Physical Processing  
Biotechnological Processing

Transformation Process

Herbal healthcare Products,  
Herbal Cosmetics  
Food ingredients

(Outputs)

## Operations Management Strategy

Link Natural carefully manages all these components considering both long term and short term impacts of the Operations Management system to the development of the organization. This is facilitated by few vital management decisions, which encompass all operational aspects of the value addition processes.

1. Strategic decisions - Concerns location of plants & facilities, capacity and improvements.
2. Tactical decisions - Concerns the number of people required, arrangement of shifts, overtime and inventory levels.
3. Operational planning & control decisions. - Concerns jobs to be done daily / weekly, assigning workers and prioritizing jobs.

All these decisions collectively outline the operations strategy of Link Natural, which leads to development and maintenance of processes, infrastructure and capabilities. The Operations Management system developed in accordance with this strategy, gives an edge to Link Natural in the competitive business environment. Operations Management practices ensure conformity to specifications, customize to



needs, on time delivery and competitive price, as the core services embedded in products of Link Natural. Thus the company aims to achieve high quality, flexibility towards customer requirements, fast approach to market and high profits with its Operations Management system.

### Competitive Priority

All competitive factors mentioned above helps in gaining a competitive advantage in the industry, but it is pivotal to define and establish a priority factor, which the company can achieve through its core competency. Accordingly Link Natural has selected 'ensuring the consistency of products with strict conformance to standardized procedures' as the competitive priority, which establishes 'quality advantage' as the performance objective, over the other competitors in the industry.

Following practices help to achieve the performance objective

1. Planning of production consistent with existing capacity.
2. Using raw materials of high quality and consistency
3. Effective verification methods of vital stages of process. (E.g. Raw materials, intermediate products & final products)
4. Machinery, with required capacity and operational reliability. (also the effective maintenance practices.)

### Other Competitive Factors

Link Natural, apart from its competitive priority, also considers many other competitive factors which result in competitive advantage in the dynamic market environment. Other prominent competitive factors are,

1. Higher degree of dynamism in all its functional areas- material sourcing, manufacturing, distribution etc. - resulting a 'fastness' ahead of the competitors, to gain speed advantage.
2. Ensuring establishment and achievement of realistic targets by individuals and teams resulting in completion of tasks on time, to gain dependability advantage.
3. Ability to modify certain stages of existing value addition processes within the standard framework to gain flexibility advantage.

4. Cost conscious approach towards value addition, focusing on cost effective methods and machinery, to gain profitability advantage.

### Towards Business Excellence with Operations Management

Historical development in Operations Management has contributed an array of management concepts and tools, which lead the businesses of different types, through generations. In fact, business excellence of almost all successful organizations was achieved by being abreast with such paradigm shifts of managerial aspects.

Link Natural, having recognized the importance of effective handling of Operations Management concepts to continue its efforts to become a world class organization, has implemented a number of such concepts together with related management tools developed during the recent past.

Concept	Tools
i. Manufacturing strategy	Performance controls for high quality
ii. Application of computer technology	Inventory control, forecasting, scheduling
iii. Total Quality Management	ISO 9001, Quality Function Deployment
iv. E-commerce	Web based trading

Link Natural has been successful in its capacity to be in line with many other successful organizations, implementing these concepts and tools. Also, the company is setting its eyes and gradually developing infrastructure to implement modern Operations Management tools such as ERP, JIT and Six Sigma, though it is challenging due to limited resources and specific constraints affecting the herbal products industry.

The greatest compensation of old age is its freedom of spirit.....  
another compensation is that it liberates you from envy, hatred, and malice.

Somerset Maugham.

## TURKISH ROSE OIL: The Queen of Essential Oils



K. Husnu Can BASER & Mine KURKCUOGLU  
Anadolu University, Eskesehir, Turkey.

The history of the rose is as old as human history. The strong and pleasant fragrance attributed to roses has been known to mankind since ancient times. Reference is made in old Chinese and Sanskrit texts to rose fragrance. It is widely believed that the so-called "Rose Oil" mentioned in these ancient texts was prepared by macerating fresh rose flowers in a liquid fixed oil.



*Rose damascena*

According to Hippocrates during the 4th century B.C. "Rosaceum oleum" (Rose Oil) was prepared in Anatolia by macerating fresh roses in olive oil. A similar description of rose oil manufacture was given by Dioscorides in the 1st century AD in his *Materia Medica*. To the best of our knowledge, these are the earliest reports of rose cultivation and its use in Turkey (1-3).

Ibni Haldun mentioned the production and the use of rose oil and rose water for the first time in his books. He reported that the best quality rose oil was obtained by hydrodistillation. The distillate waters were used as rose water

which was traded to India and China as an important commodity in the 8th and 9th centuries (3-5).

Although no definite information exists, in our estimation the production of rose oil by distillation probably originated in Iran. By the 17th century, rose cultivation had spread from Iran to India and Turkey. There is evidence of rose cultivation for the production of rose water in European Turkey dating to the 17th century. Towards the end of that period, rose cultivation was introduced by a Turkish merchant to Bulgaria, which was then a province of the Ottoman Empire. By the middle of the 18th century, Bulgaria had already become a world center for the cultivation of roses and the production of rose oil. A variety of fragrant rose species was used for oil production until, finally, *R. damascena* established itself as the singularly desirable source. In late 19th century, rose oil cultivation was initiated in several provinces of Turkey through a royal decree. Over time, however, the Isparta and Burdur provinces in southwest Anatolia have become the only cultivation and production sites.

Since 1934, a cottage industry of rose oil production has been replaced by modern factories (3, 6).

Anatolia's first rose oil and rose water were produced in Bursa in 1885 followed by Cavusbasi Farm owned by Sultan Abdülhamid II in 1886. Towards the end of the century a royal decree was issued for the spread of rose cultivation, and with the backing of Melhame Selim Pasha several other Turkish provinces began to grow roses for rose oil. In time some provinces abandoned rose farming, leaving the provinces of Isparta and Burdur in Southwestern Anatolia to become the country's only region cultivating roses for rose oil production. Prior to World War I production levels of rose oil here rose to 800 kg (7).

Rose oil is produced in Turkey and Bulgaria by water distillation of fresh flowers of *R. damascena* Miller (damask rose). It is a cultivated hybrid of *R. gallica* L. and *R. phoenicia* Boiss. Both of these parents grow wild in Turkey. The cultivated variety is called "trigintipetala," meaning "having 30 petals." The characteristic scent given off by these flowers is highly regarded by perfumers (6).



Rose oil is produced by water distillation of the freshly picked flowers. Oil is generally obtained in 0.02 percent yield; the aqueous distillate, which is left out of distillation, is sold as rose water. Rose concrete is produced by n-hexane extraction of fresh rose flowers. Annually, an average of 7,000 tons of roses are processed to produce about 1,600 kg of rose oil and about 2,400 kg of rose concrete. To produce 1 kg of rose oil via distillation, 3,500-4,000 kg of fresh roses are needed. One kg of rose concrete may be solvent extracted from 400 kg of fresh roses. Rose absolute production has also started in Turkey in recent years. It is obtained by ethanol-extraction of the rose concrete (6, 8-11). Table 1 shows the production figures for rose oil and concrete in Turkey for the years 2003-2007.

### Cultivation and Distillation



Picking the roses for distillation

In December and January, rows of ditches 50 cm in depth and 50 cm in width are prepared and manured. Rose twigs cut at the soil level are placed in the ditches which are then covered with soil. It takes at least three years for a rose plant to attain maturity. A mature rose field normally yields 5 tons of fresh roses per hectare. However, in a carefully nurtured field the yield may go up to 7-8 tons per hectare. It is normal for a field to be productive for up to 20-30 years. Once in every six years, plants are cut to soil level to rejuvenate the field. Blossomed flowers are hand picked during the early hours of the day. A skilled worker can pick about 40 kg of roses in 8 hours (3, 12).

In cottage scale production, the rose petals are distilled in galvanised iron or copper retorts with a capacity ranging from 150 to 1,000 litres, but most with a capacity of 300 litres. The

body of the retort has carrying handles on either side, and is wider at the base than at the rim. The spherical head attached to the rim can be easily



Rose oil distillery

removed. A condenser in the form of a pipe passing through a cooling tank of warm water connects the head of the retort to the glass receiver, which has a volume of 9 litres (7).

In the case of a 300 litre retort, it is filled with 10 kg of petals and 60 litres of water, which are heated for one hour, producing two bottles (18 litres) of distillate. At this stage the distillate is not sufficiently concentrated for the oil to separate out. When 100 kg of petals have been distilled, producing 200 litres of distillate, this is distilled for a second time, producing 20 litres of the distillate. This time the rose oil rises to the surface and is drawn off. The remaining liquid is diluted with distilled water and sold as rose water (7).

The current industrial rose oil distillation in Turkey is as follows: The process is a batch operation. Fresh rose flowers (400-500 kg) and water (1,500- 2,000 L) are charged into 3,000L jacketed stainless steel or copper stills. Distillation lasts for 1.5 h. Condenser temperature is kept at 35°C to avoid solidification of the oil due to paraffins. The distillate is collected in stainless steel separators called Florentin flasks. Rose oil starts separating in the distillate only after the third or fourth batch. When enough oil separates, it is decanted and kept separately. This greenish yellow oil is called "crude oil," "first oil" or "direct oil." Distillation waters are accumulated in 5,000 L stainless steel tanks and redistilled in 3,000 L stills to yield "second oil" — also called "indirect oil" or "cooked oil." The distillate of this second distillation, after removal of oil, is diluted with distilled water and sold as rose water. The first and second oils are mixed to produce Turkish rose oil (3, 5, 13).



Rose oil in Florentine flask

**Table 1.** Rose flower, rose oil and rose concrete production in Turkey.

	2003	2004	2005	2006	2007
Rose Oil* (kg)	454,00	488,45	694,60	613,29	623,84
Average price (\$/kg)	4.150	5.600	5.700	4.100	6.000
Rose Concrete* (kg)	1.137,54	604,62	703,77	476,97	877,00
Average price (\$/kg)	650	725	650	400	600
Rose Flowers** (kg)	6.000.000	6.000.000	6.500.000	7.500.000	6.500.000
Average price (\$/kg)	1.39	1.41	1.54	0.81	1.14

\* Processed volume and price of Gülbirlik, the major rose oil manufacturer in Turkey

\*\* Estimated total (Turkey).

**Table 2.** Twenty one years of Gülbirlik rose oil (1986-2007)

Compound	Main components (%)	
	Min.	Max.
citronellol	30.9	43.9
geraniol	9.3	19.1
nonadecane	8.3	14.7
nerol	5.2	8.7
1-nonadecene	2.4	4.9
methyl eugenol	2.4	4.0
heneicosane	2.5	4.2
geranyl acetate	1.0	2.2
linalool	0.6	2.1
phenylethyl alcohol	1.2	1.9
b-caryophyllene	0.7	1.6
citronellyl acetate	0.7	1.4
germacrene D	0.7	1.4
(2E, 6E)-farnesol	0.6	1.4

Main components of Turkish rose oil are terpene alcohol such as citronellol, geraniol, nerol, linalool and phenylethyl alcohol. Methyl eugenol, geranyl acetate, citronellyl acetate and sesquiterpenes like b-caryophyllene, germacrene D and (E, E)-farnesol are also characteristic constituents. Rose oil solidifies below room temperature. This is due to the occurrence of paraffins such as nonadecane, nonadecene, heneicosane, etc. Limits of main constituents of Turkish rose oil can be seen in Table 2.

Damask rose (*Rosa damascena*) is a delicate plant requiring very special soil and climate conditions. In Turkey and Bulgaria it grows only in certain regions to yield oil which is profitable. Although attempts have been made to cultivate

it in Iran, India, China and Morocco, those oils have not been appreciated. Iran produces rose water and Morocco produces rose concrete.

Indian and Chinese rose oils are used domestically.

Rose oil is an ingredient of highly esteemed perfumes and is a highly precious material for a creative perfumer. It is regarded as a perfume of its own. Due to extremely complex nature of rose oil its synthetic version is not so easy to produce. Therefore, rose oil is regarded as the "Queen" of essential oils.

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### RELATIVITY.

**There was a young lady named Bright,  
Who travelled much faster than Light,  
She started one day in a relative way,  
And returned the previous night.**

(A limerick written to commemorate the Theory of Relativity of Albert Einstein when it became experimentally validated during a solar eclipse in 1919)

### DEMOCRACY

Democracy is not just an electoral ritual, but the power of people to shape their destiny, determine how natural resources are owned and utilised, how water, food, and energy are distributed, and how children are educated.

Dr. Vandana Shiva.

### SCIENCE & THE PUBLIC MIND.

"Science really is great but only when it is shared. .... Securing people's trust in Science has been one of the key goals of outreach activities. And yet scientists often ask why an appreciation of the benefits of science still seems as distant as ever in the public mind. There are many factors effecting this;

- \* Education
- \* Development of a generally differential society, unwilling to placidly follow whatever "experts" tell them.
- \* A tendency towards secrecy.

(A Lack of transparency in some areas of science can play a significant part in limiting public confidence in science.)

- Mark Peplow
- Chemistry World (2008).  
April Editorial.

### WINE.

"Like rain for plants, wine promotes the growth of the body. Like fire grading gold, it also shows up people as superior, average, or inferior, in terms of their response to drinking. For, those who drink wine with due attention to propriety in method, quantity, food and time, wine is a nectar.

To others who act in total disregard of propriety, wine is better than poison"  
Archarya Charaka. Chikitsa 24, 26-28.  
Quoted in: M.S.Valianathan (2003): The Legacy of Charaka. Chap 58. p.41. Orient Longmans Pvt. Ltd., Chennai, India. (2004).

# “PEPPER” ROSE` (*Schinus terebinthifolius* Raddi) or Brazilian Pepper - an unusually pretty ornamental tree.

By Vikrama



## 1. Introduction.

It is called Pepper Rose, but strictly speaking it is not a pepper. It does not belong to the true pepper family, the Piperaceae (For a description of True Pepper, vide LNP Digest 2006, vol 2 issue2, pgs 20-24).

From a botanical standpoint, Pepper Rose, is a member of the Cashew family the Anacardiaceae, understandably because it is a tree, and not a vine. The pepper-corn-like-fruits resemble the real pepper when ripe though not so red, instead they have a bright pink colour. Hence the appellative Pepper rose or Pink Pepper.

## 2. Sensory qualities

The sensory qualities of the Pepper rose are quite different. There is no pungency, but they do possess a sweet aromatic flavour somewhat similar to juniper, though of course identifiably different.. The sweet taste is attributed to considerable amounts of sugar and the striking aroma to the presence of an array of volatile compounds of the terpenoid category. [1-3].

## 3. History and Natural Habitat.

The plant is native to Argentina, Paraguay and Brazil, and is related to the species *Schinus molle* L., which is referred to as Peruvian Pepper tree.

It is regarded as a strong invasive species and produces shady habitats that repel other plant species.[1]

Brazilian pepper is an evergreen tree 3-7 meters in height. The leaves when crushed also possess an aroma which is described as “turpentine -like”. [1]. It has many uses, as an ornamental shade tree, and its bark is a source of tannins. The bright pink berries are used in Christmas decorations and also in salad decorations, and called pink pepper corns.

Many medicinal properties have been attributed to the plant such as anti-oxidant, wound healing, anti-tumor, anti-microbial, and the bark is also reputed to have the property of cicatrizing wounds.[1,4-6].

Despite its benefits, the plant is considered undesirable in many situations. It was introduced to the United States in the late nineteenth century to Florida and Hawaii. It is categorised as an exotic invasive plant that out-competes indigenous species..[1] It is deemed to be able to alter the structure and function of native communities of plants.[7].. The occurrence of deleterious interactions due to chemical metabolites among higher plants is referred to as allelopathy. This is generally considered to be a significant ecological factor in determining the structure, variety, and composition of plant communities. A variety of “ allelochemicals” have been identified, some of them components of essential oils, which are known to inhibit seed germination as well as plant growth.

## 4. Use of Pink Peppercorns.

Though never a substitute for the traditional peppercorns, these pink peppercorns are used in French cuisine. They are a valued addition to fresh salads where they offer a gentle aroma and a liquorice-like flavour, and impart a lovely pink colour. They are employed in Vinaigrette or recipes for salad dressings. In popular French cooking port mignon is rolled in coarsely ground pink peppercorns before roasting or grilling. However allergic reactions to pink pepper have been recorded. Accordingly it has to be used in moderation.

It is also used to flavour fish and asparagus dishes. (Vide Recipes below)



## 5. Chemical Characteristics.

The steam-distilled essential oil of the pink berries has been extensively studied.[3,4]. The oil is composed of an array of terpenoids and the main components are: alpha-pinene, alpha-Phellandrene, Delta-3-Carene, beta-Phellandrene, Germacrene, Elemol and alpha-Cadinol. Over 27 compounds have been identified altogether [2,3]

Recent studies on berries of a single tree in the campus of Link Natural Products at Dompe revealed the same pattern of terpenoids. [5]

## 6. Medicinal Uses.

Virtually all parts of the tree have found uses in traditional medicinal systems. This includes its leaves, bark, fruits, seeds and resin. It has been found useful as a treatment for respiratory and urinary infections and as a topical antiseptic application.[6,7]

Some Chilean wines incorporate extracts of pink pepper corns and are attributed with medicinal properties.

## 7. Recipes using Pink Pepper corns [8]

### (A) Pink Peppercorn Sauce.

#### Ingredients:

Butter 2-3 tsp  
Pink peppercorns (crushed) 1 tsp  
Pimentos = All spice (finely chopped) 1 tsp  
Tomatoes (sun-dried & chopped) 1 tsp  
Heavy Cream 4 ozs.

#### Method:

Melt the butter in a saucepan. Add ingredients and cook to desired thickness. Served warm.

### (B) Pink Peppercorn Chicken.

#### Ingredients:

Boneless chicken breasts 4  
White wine - dry 2 cups  
Leeks (rinsed and cut in 1 in strips)  
5 medium sized.  
Pink Pepper corns 2 tsp  
Rosemary spice 2 tsp  
Butter (fresh) 2 tsp

#### Method.

Trim chicken breasts of excess fat. Flatten breasts to an even thickness. Marinate for 1

hour in white wine. Place leeks under the flattened chicken breasts in a shallow pan, sprinkle peppercorns and rosemary and bake at 350 degrees till done.

### (C) Pink Peppercorn Vinaigrette.

#### Ingredients.

Red wine vinegar 1 Table sp.  
Fresh Lemon juice 2 Table sp.  
Olive oil 3 Table sp.  
Shallots very thinly minced. 2  
Pink Pepper corns (ground) 2 Table sp.  
Freshly ground black pepper'  
Parsley finely chopped.

#### Method

Whisk together lemon juice, vinegar and olive oil.

Add parsley and pink peppercorns.  
Add salt and black pepper to taste.

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### NORMAN R. FARNSWORTH - Inventor of NAPRALERT.

*R.O.B.Wijesekera.*



*Norman R. Farnsworth*



*Norman Farnsworth (right) with the author, (left),  
And Dr.Won Sik Woo (Centre) in Seoul in 1980.*

Anybody who has had anything to do with research on Medicinal Plants and Herbal Pharmaceuticals could not in any way have failed to hear of the irrepressible Norman R. Farnsworth. Norman's domineering presence as perhaps the most prolific researcher in this field the world over, is acknowledged by many other researchers widespread in many lands. Norman bestrides this field like a veritable colossus. He even looks the part. He is silver haired, stands over six feet tall, has perhaps given up his inevitable cigar, which he only chewed, but never actually smoked. By his own admission, (but this could be apocryphal), he painted his hair grey during his times as a young debonair pharmacist, as customers mistook his freshness

of face for inexperience. But there can be no mistake about the quality of the man, and his stupendous contribution over the years and across the globe, in the field he has served, and deservedly acquired a unique reputation.

This author first met this colorful American in 1975, when he came to Sri Lanka as a member of a team of natural products researchers to participate in a joint US-Sri Lanka workshop on Natural Products, sponsored by the National Academy of Sciences of the US. Carl Djerassi was the leader of the US team, and the author was the counterpart Sri Lankan team leader. One recalls Norman coming through customs at the airport with his characteristic, heavy leather document case, and explaining interminably the features of his computerized data base, since then known to all as NAPRALERT. By any standards that was a great idea and an even greater accomplishment.

Later, perhaps as a result of that first meeting in Colombo, the author and he were colleagues in the WHO task force on "Plants for Research on Fertility Regulation". Norman, through NAPRALERT, and also his own part, and, together with his inseparable colleagues Harry Fong and Doel Soejarto, was to play a leading role in the work of that task force.

One recalls traveling a great deal together with Norman during the period one had stewardship of the task Force. We were in the countries where the task force had some of its collaborating centres, such as in Peradeniya, in Seoul and in Hong Kong. One incident strikes a chord as to the generous nature of the man himself. We were on a train from Peradeniya to Colombo. Norman will not recall this as one of his most comfortable journeys. The train was crowded and the compartment had many children. By the time we reached Colombo, Norman had distributed, one by one, the innumerable pens he carried, (and he carried enough to open a small shop), to all the children in the compartment. Finally there was a single child who had missed out, and was without a pen. Norman smiled at him in a sort of mock helplessness, and then pulled out the only pen he had left with him,



and the most expensive one, and gifted it to the flabbergasted kid.

One great characteristic of Norman was his indefatigable temperament. He could work without grumbles in many a difficult situation. Today he has had bestowed on him, many titles and honors. President Clinton appointed him to serve on the White House Commission on Dietary Supplement Labels, in 1995. He has received the Annual Research Achievement Award of the American Society of Pharmacognosy, which has now been named the "Norman R. Farnsworth Research Achievement Award in Natural Products Research" in 2006. He remains on the WHO Expert Advisory panel on Traditional Medicine. He has been awarded the E.K.Janaki Ammal Medal from the Lucknow based Society of Ethnobotanists, in recognition of his distinguished services. In 2001 he was named a Distinguished Professor, for "scholarship, creativity and leadership" at the University of Illinois at the Chicago, where he still serves as a Research Professor of Pharmacognosy, the Director of the Pharmacognosy Graduate Program, and Director of the Program for Collaborative Research in the Pharmaceutical Sciences, and Senior University Scholar. His accomplishments are indeed so numerous.

He is also, a co-founding Editor of the Journal of Phytomedicines.

Norman's research interests have covered the widest range of natural products, including, information - both biological and chemical, and the nature of biologically active natural products. He continues his association with the WHO.

However above all these honours one feels that his greatest contribution is in regard to the assistance he has rendered to fellow scientists around the world, especially those in the developing countries, and consequently, their appreciation of him is his finest merit award. He is a legend in the developing countries of Asia, Africa, and Latin America, and is noted for his wealth of knowledge, the generous assistance he renders and, without any doubt, also for his colorful expressions.

Among the Sri Lankans who have worked with him in his multi-disciplinary research laboratories at the University of Illinois at the Medical Center in Chicago, are such well known chemists like Leslie Gunatilake, and Sarath Gunasekera.

## HISTORY OF SCIENCE

"I think the history of Science has a very invigorating influence on students. If you want to have success in science my advice is simple: aim right but hard. In order to aim right you have to develop an intellectual taste. To do this history of science is crucial, because it shows you what ideas turned out to be important in the long run. Another thing which is also fun is to see that these scientists were also human, as human as you and me."

Pekka Pyykka,  
Professor of Chemistry, University of  
Helsinki  
Finland.

### N.B.

Prof. Pyykko in Turku, the site of the first University in Finland founded in 1640. Chemistry was studied there since 1761. He lived at the exact address where Johan Gadolin, the famous Finish chemist lived and since 1984 he occupies a recent version of the original Chair of chemistry of Professor Gadolin in Helsinki.

Native ability without education is like a tree without fruit.

- Aristippus

Good ends can be achieved only by the employment of appropriate means.

- Aldous Huxley

There is only one thing that age can give you and that is wisdom.

- S.I.Hayakawa.

### PAPAYA - (PAPAW) - A VERSATILE HEALTH-GIVING FRUIT.

*Ayesha Tanya*

The original habitat of papaya is not too well known. Some authorities hold the view that its native habitat was in Mexico, Today it is almost ubiquitous, as a fruit, and found in the markets of Hawaii, Florida, Mexico, Central and South American regions, India, Sri Lanka, Malaysia and the Far east. It is a popular and tasty fruit with many varieties now grown for their special characteristics. Mostly it is green on the outside and yellow or orange inside with multiple seeds. However some varieties are red inside, or yellow outside when ripe. Some are large in size like elongated pumpkins, and are referred to as the Mexican type, while others like the Hawaiian type, also referred to as "Solo," are as small as a larger mango. Both types are also found in Central American countries like Costa Rica. The smaller or Solo variety, has sweetness and flavour and is very tasty. The Malaysian variety is reddish inside and referred to as the "Red Lady" type. It has a different flavour and is also very acceptable. The very large types are juicy, and makes for a refreshing papaya puree or drink. In Viet Nam a bulky variety with lesser fruity flavour, is consumed in the form of an iced puree as a cocktail with a little added



vodka. In Sri Lanka there are a large variety of papayas due to massive hybridization, resulting in a variety of sizes and flavours.

The papaya is a fruit that enjoys universal acceptance, and its versatility does not end with that. Some varieties are cultivated for the extraction of the industrially utilized enzyme papain, which is a meat tenderizer.

**Papayas are a rich source of the vitamins A and C. Therefore it follows that in countries where it is readily available, there is no need for anyone to indulge in daily intakes of these vitamins. One quarter of a medium sized papaya, or a 4cm slice, can provide well over the recommended dietary intake of vitamins A and C.**

This would be a pleasant method of ensuring the needed intake.

Papayas are also low in calories, fat free, cholesterol free, and a good source of potassium, folate, and fibre. It is also recommended as an agent to ensure against constipation. Ayurvedic physicians recommend papayas among other fruits to ensure satisfactory bowel movement particularly in children.

#### TRUTH THE WINNER

"In Science Truth always wins"

Max Perutz. 1914-2002  
Nobel Laureate in Chemistry 1962.



## ARTIMISININ - THE NEW GOLD STANDARD FOR THE TREATMENT OF MALARIA

by Keara.

Every year 1-2m people, mostly children die of malaria. Artemisinin, (1), is the most effective treatment against this dreaded infectious disease.



*Artemisia annua* plants, from which artemisinin is extracted



Female mosquito - Anopheles  
(The carrier of the Parasite)

Once again it is a natural product that has given humankind a much needed breakthrough. Long ago it was the versatile Quinine from the Peruvian cinchona bark that conquered the dreaded malaria. Then, as quinine became rarer and rarer, and World War II complicated matters, there was a push towards cultivating the cinchona tree whose bark it was that generated this valuable natural product. But the tree, whose valuable property of being able through its bark, to generate a potent anti-malarial drug, took long to grow. Meanwhile chemists like the great Sir Robert Robinson O.M. spent decades unraveling the chemistry of quinine. And others like him spent a deal of time imitating its chemistry to generate such synthetic substitutes such as: Chloroquine.(2).

Chloroquine was the major tool of malaria treatment, after the celebrated quinine. But it was not long before the malaria parasite was able to overcome its lethal effects by developing resistance to quinine as well as the other synthetics. Malaria which was thought to have been almost eradicated by the use of insecticides like DDT and the WHO initiatives, began, with time to show signs of re-emergence. Fortunately then, there appeared the Chinese drug Qinghasu, which had been used in China for over 2000 years.

The new gold standard of treatment of malaria is based on the natural product from this plant, viz: *Artemisia annua*, which the Chinese chemists had isolated in the 1980's. It had been extracted and developed as an anti-malarial drug by the Chinese government to protect soldiers from malaria during the Vietnam war.

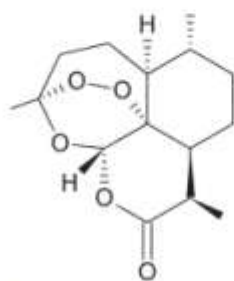
The story began thus. Following the failure of the synthetic anti-malarials that had been employed to save the lives of soldiers from the scourge of malaria during the Vietnam War, there was a worldwide search for new anti-malarials. The Chinese government too joined in this search. They commenced with a systematic examination of plants used in the Traditional Chinese pharmacopoeia. The herb *Artemisia annua*, or "qinghao" was among the several hundred species listed to be tested. In terms of Chinese medical theory *Artemisia annua* is classified as belonging to the yin category, that corresponds to "cool". It could therefore be employed to treat internal conditions classified as due to "heat" or yang. The very first recorded instance of the use of qinghao, for yang conditions, appeared in 1596 AD. This was in the Chinese Materia Medica, Bencao Gangmu, where it was recommended for treatment of intermittent fevers. The treatment according to the traditional method was to collect a bunch of leaves in spring or summer, and pound the material, together with added water, with a pestle and mortar to express the juice, which contained the active ingredient. It was not long after 1970 that Chinese scientists studying the old texts were successful in isolating and characterizing the crystalline substance artemisinin, (1), which they called, qinghaosu, meaning the principle from qinghao. During the 1970's clinical studies conducted using the extract of the plant leaves on members of the Chinese army infected with the Plasmodium parasite, demonstrated a spectacular therapeutic activity in almost all the treated patients. Furthermore there was none of the toxicity that characterized the other

anti-malarials that were used at the time. Qunghasu proved to be completely effective in treating chloroquine-resistant falciparum malaria, as well as the often fatal complication, cerebral malaria.

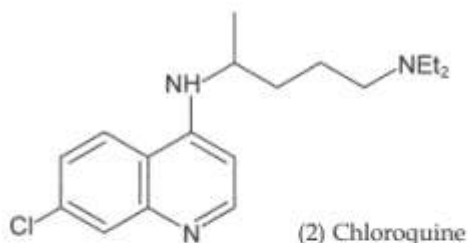
However even though Chinese scientists had proved conclusively that quinghasu, could clear the blood completely of the malarial parasite more swiftly than any other drug, western scientists were skeptical. There was the usual bias against herbal medicine, and the vision was characteristically through the western-medical-centric blinkers. There were all sorts of theories concocted to explain why such a molecule particularly one with a 1,2,4-fqioxane ring embedded in the structure could be stable and useful as a drug. Furthermore at the period the wars dragged on and access to the drug, and the herb was denied to organizations such as WHO which were able to harness the resources to develop it as a drug for global use.

Then in 1982, UNIDO staged a Symposium with the active participation of the Government of the People's Republic of China at which Chinese scientists together with those of the other nations of the world discussed in open forum the merits of the drug among a host of other factors within the framework of Traditional-Modern Pharmaceutical Research & Technology Development. Qinghasu was now available for global use in the name of human wellbeing with the blessing of the government of China. Western scientists and organizations such as UNIDO and WHO joined in the development of artemisinin and new anti-malarials based on the unique discovery from the Chinese Traditional Medical Arsenal. Once again Traditional medicine had provided modern medicine with a new tool.

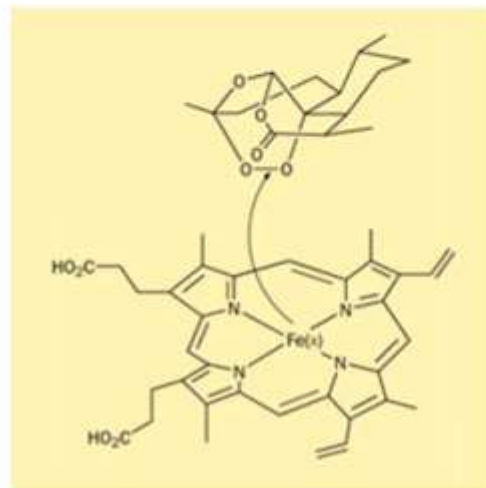
Like its predecessor Quinine, Artemisinin, also operates in the malaria parasite's food vacuole, with the breaking open of the characteristic endoperoxide bridge, in the molecule, a reaction with the iron present in haemoglobin, to give substances which are toxic to the malaria parasite. (Scheme 1)



(1) Artemisinin



(2) Chloroquine



**Scheme 1 Cleavage of the endoperoxide bond in artemisinin by iron (II) in a haem group**

The reaction also releases a burst of free radicals into the parasite, which finally kills the parasite. It is this new mode of action, which bypasses changes that have allowed resistance to chloroquine(2) and Quinine, to develop, is what makes artemisinin(1), so powerful.

Soon synthetic organic chemists were able to develop analogues of the new molecule with modifications commencing with the lactone group. Several such analogues are now in use and some are injected intravenously or even administered orally. Current malaria therapy is dependent on two such synthetic derivatives artemether and artesunate.

However the WHO is now in favour of "Artemisin Combination Therapy", (ATC), having noted from previous experiences with chloroquine, that a single antimalarial may run the risk of one powerful genetic mutation overcoming the action of the drug.

None of the large pharmaceutical companies were at first interested in artemisinin. There was no financial incentive, as they perceived that either there was little malaria at the



time, or the disease was confined to remote third world nations. (Vide Article entitled: Society, the Pharmaceutical Industry & the Ethical Dimension, in this issue.)

In the 1990's the situation had changed and the conglomerate of companies that merged to form Novartis, for one, had approached the Chinese government, and consolidated their interest. Now these companies are offering their best resources to Anti-malarial drug development which is boosted by the sponsorship from the Gates Foundation. The resulting Medicines for Malaria Venture gets about 60% of its funding from the Gates Foundation, and is a non-profit organization dedicated to research into new malarial treatments. The key focus is on ACT's. They are artemisinin based drugs which are combined with drugs with entirely different modes of action

There is without doubt a major thrust now into research on Artemisia-derived drugs and into other species of Artemisia the world over. So far Artemisinin, remains the sole natural product found that possess the 1,2,4-trioxane ring system. *Artemisia annua* continues to be the sole natural source. However its wide availability in China, Vietnam, Myanmar, India, and other countries of the region makes it still suitable as a cheap industrial source. The method of production of the drug as till now practiced, even on a very large industrial scale, is based on plant material cultivated in China and Vietnam. Accordingly many believe that on account of its cheapness (One kg costs about a few hundred USD), Artemisinin will be a good starting material for the synthesis of the improved derivatives that have been now developed. Thus cultivations of the plant would still be the final basis of obtaining valuable anti-malarials.

**However the key point that must be underscored is that once again, a natural product derived from a traditionally used treatment has come to the rescue of humankind in a dire situation. Can there be a stronger case for the value of Research into the world's traditional medical systems?**

Funds directed towards preservation and sustainable utilization of these should be a major global trust for maintenance of healthcare.

#### Sources:

1. Chemistry World. (2008) April: 50-55.
2. Brown, G.D., (2006): Educ.Chem. Artemisinin & a New Generation of Antimalarials.

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## CHEWING GUM IS AN OLD CONFECTIONARY

By Ayesha Tanya

Chewing gum is probably the world's oldest confectionary. The chewing cult commenced when pre-historic man first discovered the pleasant tasting exudates, (gums), from the bruises inflicted on the trunks of trees. The edible exudates from, for example, the sapadilla tree, seemed to have been a popular one.

In time, many other pleasant tasting and flavorful exudates came to be popular. Then as in many other instances, the gums which were harmless and non-toxic were recognized and used. Some of them though ideal for chewing were without any specially attractive aroma or flavor, and so such naturally well recognized flavors like, mint, thyme, cardamom, sage and such like, came to be added to the natural exudates to make the "chew" more attractive. This habit of chewing was common to the Indian sub-continent and particularly to the region of central Asia, and the Mediterranean countries. Reports reveal that the habit appeared to be common in central and south America and the Caribbean, as well as the regions of Oceania.

Similar developments appear to have taken place with the oriental habit of betel chewing giving rise to what is now referred to as the "sahra bulath".

Along the same pathway, of exotic flavoring of "chews", and in recent times, came the introduction of synthetic substances particularly in the western world. Firstly, there was introduced a petroleum-derived paraffin wax as the base. Thomas Adam was credited with introducing "chick gum".

An average American is supposed to chew 700g of chewing gum per year. Today, synthetic rubber, a styrene-butadiene type or substances related to polyethylene, polyvinyl acetate are used as the base and natural latex is also sometimes incorporated. A variety of synthetic and natural flavoring agents are extensively employed in the chewing gum industry which has reached gigantic proportions. Here again, as in other instances a "back to natural" trend is discernible in respect of flavorings. The variety in market trends is

bewildering.. There are chewing gums to refrain from smoking, for protection of teeth, as well as to deliver vitamins. There are gums to ensure mood regulation as well. It could very well become a means of introducing medicaments particularly for children, but there are dangers too particularly when unscrupulous producers are involved.

**Sources:**

Chem.& Eng. News. (2007), 85.(32), p.36.

### PEPPERMINT MYTHOLOGY !



Persephone with Hades



*Mentha piperita* (Peppermint)

Persephone, the Greek Queen of the underworld is reputed to be responsible for the herb Mint - (*Mentha piperita*). The story goes that Persephone was so jealous of her husband Hades' romantic inclination towards the Nymph Minthe, that she converted the nymph to the eponymous plant now known as mint and which produces peppermint oil and menthol.

### HANDICAPPED PLANTS RACE FOR THE SUNLIGHT

By Annissa

In the natural state why do some plants grow thin and tall seemingly racing for a share of the sunlight? New research has revealed the reason and the mechanism. Plants that have been deprived of their share of the sunlight, either by the leaves of competing plants, or the shade cast on them by taller trees shoot skywards. This can be easily seen in any rain forest. The reason is, according to a group of scientists, these deprived plants feature the phenomenon now known as "shade avoidance" This phenomenon triggers off a rapid synthesis of the **growth hormone auxin** to fuel the spurt to get a better share of the sunlight. The plant's response to the phenomenon of "shade avoidance" is driven by particular wavelengths of red light which are caused by white light being filtered through the interfering leaves of other species of plants. The auxin is transferred to the stem of the plant causing it to grow tall and spindly. Research scientists led by Joanne Chory of the Salk Institute for Biological Studies, in La Jolla, California, USA, have been able to map out a molecular pathway for the biosynthesis of auxins, in a model plant namely *Arabidopsis thaliana*.

Source: *Chemistry World* May 2008, 4.



Photo © Vimukthi Weeraratunga



## *Of Molecular Shapes, Odours and the "Hotness" of Chillies ... ..*

### **FOR PLEASURE OR FOR PAIN - IT'S THE SHAPE THAT OFTEN MATTERS**

*Annissa*

Molecular shapes have important bearings on their bioactive properties, as odours, pungency, spicy-character, bitterness, taste, and even their effectiveness as medicaments. Molecules with specific shapes are recognized by specific "receptors" in human or animal systems in a manner analogous to keys fitting into mechanical locks.

For instance, when the shape of a drug molecule is altered it alters the manner in which it fits into the receptors. If the drug molecule is tenaciously bound, by tight fit, it could be very effective. If, on the other hand, it is loosely bound, the enzymes responsible for the body's clean-up operations may easily dislodge the enzyme from the receptor, rendering the drug less effective. It all depends on the molecular shape.

This lock-and-key type of model is also used to explain, for example, why different substances have different odours, and different tastes.

#### ***Stereochemical Theory of Odours***

What is known as the "Stereochemical Theory of Odors" implies that the molecules of an odoriferous substance latches on to an "olfactory receptor", and thus can stimulate the nerve cells. This ultimately results in the perception of a particular odor.

This theory first proposed by John Amoore, (summarized in *Nature* (1971) vol.,233, p270.), recognizes five basic types of odors associated with the shapes of molecules. It is noted for instance that football-shaped molecules fit into a receptor that perceives an odor similar to that of camphor. Molecules shaped like a necklace are said to fit into a receptor that perceives a musky odor. Wedge-shaped molecules are said to generate the odor of peppermint, while tadpole-shaped molecules give off odors like that of flowers. An ethereal odor is said to be that generated by long and thin ether-like molecules. Different "special odors" are the result of molecules fitting into groups of receptors. John Amoore's theory postulates that molecules that can lock into more than one receptor will gener-

ate the more complex odours. Amoore explains the smell of almonds generated by the molecule benzaldehyde as being due to its ability to lock into the postulated shapes for the camphoraceous, and the pepperminty receptors. Amoore's theory is without doubt a simplification of the actual bioactive system. There are over a thousand olfactory receptors. The odor-giving molecule is able to move through tissue containing layer after layer of receptors and this would determine the final odor that is perceived. Perfume chemists know how to use the physiological basis to get the best value for the synthetic molecules they produce in terms of the final odor perception..



Odoriferous flowers of ylang ylang.



Fragrance of Roses

#### **The Hotness Factor in Chillies**

An analogous mechanism is postulated for the perception of other biological effects, for instance for the perception of the "hotness factor" of chillies.

Most chillies, and there are hundreds of different types, contain the molecules capsaicin, and dihydrocapsaicin, which are responsible for the hotness factor. The molecule of capsaicin contains a long hydrocarbon tail, which enables it to bind very securely with the lipoprotein

receptors on the mouth, tongue and throat. It can also slip through the fat-rich cell membranes making the perceived burning sensation more severe and persistent. Capsaicin is not soluble in cold water, but freely soluble in alcohol and fatty oils. So a drink of water will not reduce the burning sensation. For relief from a chillie "burn" one may drink milk. Milk contains a lipophilic (fat-soluble) protein, casein, which can help dissolve away the offending capsaicin, in the manner a detergent washes away greasy matter.

Those who relish spicy foods rich in capsaicin can build up a tolerance to the effects.. Capsaicin can excite the nervous system into producing endorphins, which can in turn bring about a sense of well being. The endorphin-effect makes spicy foods in a sense addictive or even sometimes an obsession. However too much of it can and will cause problems. Capsaicin in high concentrations is indeed toxic. It can prevent nerve cells from communicating with each other by blocking the production of certain neurotransmitters, or even when in very high concentrations destroying them.



Chillies – Colours & "Hotness"

This is the reason why the early Mayans, who found chillies to be an agreeable food additive, also discovered its effectiveness in weaponry. The Mayans burnt chillies to create a repelling smoke-screen. This they used in battle. They also filled various gourds with chillies and flung them at the enemy - a kind of "Chillie-Bomb."

It is ironical that a similar technique is even employed in modern times when capsaicin sprays are employed to ward off muggers or aggressive dogs.

Capsaicin is in a sense a mysterious natural product. As a food-additive, in moderation it is a spice. It excess it can cause pain and damage. Its ability to cause pain is used in modern therapy to alleviate pain. Exposure to capsaicin is believed to lower sensitivity to pain. It is thus employed in applications to alleviate pain in

rheumatoid arthritis, and other inflammatory conditions. In this its main function is that of a counter-irritant.

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1. Amooore, J. (1971) Nature vol 233. 270-271.
2. UCSF (1990) Chilli Peppers & Capsaicin
3. Wood, J.: Capsaicin in the Study of Pain. Academic Press.
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### ARCHIBALD SCOTT COUPER – Earliest structural organic chemist?

#### *Annissa*

Not many chemists, even modern students of organic chemistry would have heard of a chemist by the name Archibald Scott Couper. Yet he it was who made an indelible contribution to structural organic chemistry way back in 1858. He was indeed the first chemist to deploy structural chemical formulae in the manner that is recognized now. Yet like many an epoch-making fundamental idea his colleagues of the day were not too ready to recognize his novel idea. Barely 32 years following his epoch-making publication, the unfortunate Couper, was dead, and his pioneering idea forgotten.

During the period chemical theory was untidy and not coordinated and the senior chemists of the time were unable to recognize the merits of the novel propositions presented by the young Couper. The controversial presentation was made in his third paper to the Paris Academy of Sciences namely: "sur une nouvelle theorie chimique"

In it he proposed the existence of carbon to carbon chains a unique idea at the time.

This paper was instrumental in his now being recognized as a pioneer of structural chemistry.

Couper was born in Glasgow, Scotland in 1831. He had a scattered chemical education in Berlin University in Germany and finally went over to Paris to work under Charles Adolphe Wurtz. It was a period when the discrepancies in the determination of atomic weights, the evolving theories of atoms, their modes of combination and their spatial distributions, caused bitter controversies.

Wurtz, who was Couper's supervisor had been lethargic in the submission of his paper and so the publication was unduly delayed, and appeared in print only on June 14th 1858. Meanwhile the now celebrated German chemist Auguste Kekule, who was responsible for the unique idea at the time that the six carbons in benzene were in the form of a hexagonal ring. Kekule



himself had submitted a similar paper which was published a few weeks earlier.

Kekule in response to Couper's article, dismissed it as lacking, clarity and originality. He claimed for himself the priority for the discovery of carbon chains. The concept of valency or "bonding" or "saturation" capacity had not yet emerged and it was not until the mid 1860's that the word valency was coined. Yet chemists accepted that this factor whatever it was called, was four for carbon, normally. Yet although Couper was posthumously recognized as a founder of modern structural chemistry his contribution was down-played at the time. Part of the reason for this lay in the personal qualities of Couper himself. His paper was aggressively critical of others and expressed scorn at earlier chemical theories and their adherents. This was an era where rivals often degenerated into personal exchanges; and Kekule and Couper were no exceptions.

So, even the greats have had their times of descent from the norms of ethics. Ethical practices, are so often unknowingly attributed to those of bygone times.

Source : M. Sutton Chem. World 2008. May

## ODOUR AND THE PERCEPTION OF WOMEN'S WEIGHT

(Summary of a Study conducted by A. R. Hirsch, J. R. Hoogeveen, A. M. Busse, & E. T. Allen published in *Int.J.Ess.Oil.Therapeutics*, (2007) 1, p.16-20.)

A Study was conducted to make an assessment of the effects of odorants on men's perception of the weight of a woman. A white, sales woman of cosmetic products, served as a model in the study. She measured 1.75m or 5'9" in height, and weighed 111kg or 245lb in weight. She was made to wear, successively:

1. A *floral spicy* odorant (a 1:1 combination of floral & spicy)
2. A *citrus floral* odorant
3. A *sweet pea and lily of the valley* odorant (1:1 Mixture)

In the assessment 199 males ( a strange number it would seem), were employed and they had to make their own perceived assessment of the weight of the woman. A non-odorant control was used to obtain the blank assessment or "Control Perceived Weight" designated "CPW"

The model had no knowledge of the hypothesis or details of the study. She was also instructed, for each day of the study:

- \* To refrain from speaking
- \* To display minimal effect

- \* Wear the identical clothing for each evaluation
- \* Wear the same hair style make up and accessories
- \* Avoid fragrances, scented soaps & shampoos

The 199 male volunteers used for the study were between the ages of 12 years to 61 years. They were: 93% White (186), 02% Black (04), 03% Hispanic (06), and 1.5% Asian (03).

The three test odours were selected by a ten-person mixed-gender panel of the "Smell & Taste Research Foundation". They were judged to be hedonically positive by the panel and were supplied by IFF.

Each test odour was sequentially applied at non-irritant threshold levels, over separate days, to scarves worn by the model. The model was made to stand at a distance of 3 meters from the subjects (males) making the assessment, a distance which had been pre-determined as adequate for those to be able to detect the odorant.

The subjects were asked to make an assessment of the weight of the model. A written format was used. The model was not told anything of the estimated value. The subjects were then queried on their detection and hedonics of the scents.

Experiments were performed each day with the control trials without any odour, and the experimental trials with the designed odour. The results were analysed by the University of Illinois School of Public Health. Comparisons were determined for each odour against the control, as well as sub-groupings based on age and hedonics.

The results were most interesting.

Of 50 males tested with the model and odorant Floral & Spicy there was a significant reduced perception of weight ie. 1.86kg or 4.1 lbs. a 2.4% reduction.

In the case of some of those males who perceived the odour as hedonically positive (16 in number) the perceived weight of the model was even more substantially lower, ie. 6.4kg or 12 lbs less - a 7% reduction; the weight being assessed by 49 males to be 78.38kg or 172.8 lbs.

The conclusion that can be deduced is consistent with the research which has demonstrated that:

- \* Odorants have a diverse impact on human behaviour and moods.
- \* Can affect learning rate, insomnia, migraine, headaches, and aggression.

Modern society recognises the importance of aroma, image and mood. It is true that over 19 billion US dollars are spent annually on fragrance products in the US. However theories as to how they act and the mechanisms are still in the theoretical realm.

*Kenneth de Silva / Johann de Silva*

### IMPETUS TO VANILLA CULTIVATION IN SRI LANKA



Further to our article on vanilla, in our issue of LINK NATURAL PRODUCTS DIGEST, Vol 3 issue 1, 2007). We are pleased to know of the efforts of the Ceylon Cold Stores Ltd., together with the Kandy Vanilla Growers Association, who have initiated a joint project to promote the cultivation of Vanilla in the Central province. (SOURCE Sunday Island (Date) April 2008 p VI, Business Section).

**Permit me to quote:**

President of the KVGA, Mr. M. Madugalle said: "that in today's profit oriented corporate world, it was encouraging to see how CCS was actively involved in uplifting and

developing the local vanilla industry and also using locally grown produce in ice-creams.

When our members initially went into mass scale production, we did not know anything about vanilla processing techniques. It was the personnel from CCS who patiently taught the finer points and even went further to purchase our entire produce. The fact that CCS has taken its Elephant House ice-cream to the world is an endorsement of the quality of locally grown vanilla beans. 100% natural vanilla essence is a key ingredient in the world renowned Elephant House ice-cream. A project to extract essence from processed vanilla beans was first initiated at its factory in Ranala, Kaduwela, in 2002. Local vanilla cultivation was up until then promoted by the Agri-business Council. The national yield was 30kg in 2002. CCS identified the KVGA, a small group of 30 farmers, as partners in the revival of the local vanilla industry. Today six years later, farmers are engaged in the profitable cultivation of vanilla in Matale, Kandy, Kurunegala, Kegalle, and Nuwara Eliya In addition to providing assistance to farmers, the KVGA also buys the raw beans at a pre-guaranteed price, processes and cures the beans, and supplies the processed beans to CCS., for extraction. Of 5000kg produced annually, 3000kg are produced for CCS. In addition 600kg of processed beans, are sold to CCS by farmers at Rupees 5500/- per kg. The KVGA has plans to further increase its production of processed vanilla beans for wide distribution."

*Vickrama*

**Note by Editor.**

Also see Letter to the Editor by Dr. A. L. Jayewardene, of Walnut Creek, California USA in DIGEST vol.3 issue 2. Dr. JAYAWARDENE'S HOPES SEEM TO HAVE BEEN REALISED!



## A RASAYANA - IN A TEA BAG.

- Keera

This is a story for the present not even for a not too distant future. It is just like the one that changed an ensconced traditional habit, the British habit of tea drinking. Truly, tea drinking began in China, and from the Chinese, tea saplings were smuggled by design, and planted in Assam; which too had some few indigenous tea plants. The British planted tea in Assam on a large scale and followed it up with plantations in Ceylon as Sri Lanka was then known. In 1900 there were 384,000 acres or 600 square miles of plantation tea in Ceylon, which made the island's tea industry almost as large as that of India. And all this was for export to the "mother country", which was Britain. During the World War II, tea was regarded as an essential commodity and hence was subject to rationing. However exports from Ceylon dropped due to the German Blockade and tea became a precious commodity till the war was over. More than this, tea had become part of British cultural practice. The ritual of tea time engaged even a methodology; in scientific nomenclature one may call it a protocol, in respect of the making of a "good cuppa tea". In Ceylon too one may remember the Tea Propaganda Board putting out "Charlie's Golden Rules" for Tea making. Then with a bang came a new paradigm change. Tea drinking and marketing in the twentieth century was dramatically changed by the American invention of the "tea bag". It is stated that in about 1908 the New York Tea dealer, Thomas Sullivan, started to send out samples of tea to his clients in small silk bags. Some clients thought they were meant to be infused by immersing the bag itself in hot water. They told Sullivan that the silk was not satisfactory as the mesh was too fine. So he subsequently issued the tea in gauze sachets. So the tea bag was born soon afterwards, following experimentation with different materials.

Yes, undoubtedly after much Good Old fashioned, R & D.

Yet in Britain where most of the tea was consumed hard tradition was not easy to overcome. The tea bag was introduced to Britain in 1935 by Tetleys. By 1970 the market share was only 10%. Today it is well over 90%. The tea bag has caught on because it has adapted to usage, and matched

the requirement of convenience. Now tea is attributed at the present with so much health maintaining and disease controlling properties that it has become a virtual "Rasayana in a Tea bag". The properties are even scientifically confirmed and documented

Some Ayurvedic preparations too, have now donned the Tea bag as their preferred attire, both convenience and efficacy, not to mention the supreme requirement of dose control, being assured. Many Ayurvedic physicians have approached institutions that make herbal preparations, and posed the issue whether many of the Ayurvedic Preparations in the Sri Lanka Ayurvedic Pharmacopoeia, could be rendered in the form of Tea bags for dispensation to their patients. So another paradigm change may be round the corner, if not perhaps a revolution. But much R&D, more than that which Sullivan was engaged in, would be needed and that is the rough passage to the goal. The need is certainly there.



## The Digest Mail Bag

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### Letter 1

To the Editor-in-Chief

*I write to congratulate you on the Digest you produce and also to thank you for sending me a copy of same. I need also to congratulate you on your own article in the current issue on the occasion of the Silver Jubilee of your organization. The Digest is most informative and well produced.*

*Mr. K. Godage  
Retired diplomat.*

### Letter 2

*We thank you for sending us a copy of your Link Natural Products Digest Magazine which is a very well compiled and an informative journal. We are enclosing our request in order to receive this journal in the future.*

*We would like to reproduce 01 or 02 articles from this magazine in our next issue of the Sri Lanka Exporter Magazine and before doing so; we would like to have your consent. We would give credit to "Link Natural Products Digest".*

*Mr. Rasa Weerasingham  
Executive Director  
National Chamber of Exporters of Sri Lanka.*

### Letter 3

To the Editor-in-Chief

*Thank you for the latest issue of the Digest, it looked good and after reading it cover to cover I found it most informative. Well-done editors. Do you have access to any library databases, if not it is something to pursue. You may be able to put a young officer to look for at least a specialized db. For medicinal and aromatic plants journals and also trade journals.*

*Dr. Anura L. Jayawardena*

## NOTE TO POTENTIAL CONTRIBUTORS

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### Link Natural Products Digest

The DIGEST is a popular publication, albeit a scientific one, dedicated to medicinal plants, herbal healthcare and personal care products, essential oils, aromatherapy, herbal therapy and Ayurveda, and related healthcare systems. It is published bi-annually.

The DIGEST welcomes contributions in English in the category of reviews, brief communications, ethno reports in brief, phytomedical and phytochemical communications, book reviews, and reports on safety and efficacy of phytomedicines.

Potential authors may consult the Editor-in-Chief prior to dispatch of communications, reports and reviews.

Authors may submit manuscripts by post or e.mail to :

**Dr. R.O.B. Wijsekera,**  
Editor-in-Chief  
Link Natural Products Digest  
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Please forward to the editor one original hard copy and a soft copy in the form of a PC compatible diskette (Microsoft Word).

#### All manuscripts must include the following :

Title (in brief), author(s), address(es) of affiliated institutions. The authors' names must include initials and/or forenames as required in publication. All papers and submissions are subject to peer review, but the editors reserve the right to regulate the content. No proofs can be sent prior to publication. The decision of the Editor-in-Chief will be final in all matters.