

University of Jaffna



Professor
Sivapathasuntharam Mageswaran
Memorial Lecture

COMMERCIALLY USEFUL
NATURAL PRODUCTS

by
Professor S. Sotheeswaran

Senior Professor
Institute of Chemistry, Ceylon

06TH DECEMBER 2011

UNIVERSITY OF JAFFNA
SRI LANKA



Professor
Sivapathasuntharam M^ageswaran
Memorial Lecture – 2011

**COMMERCIALY USEFUL
NATURAL PRODUCTS**

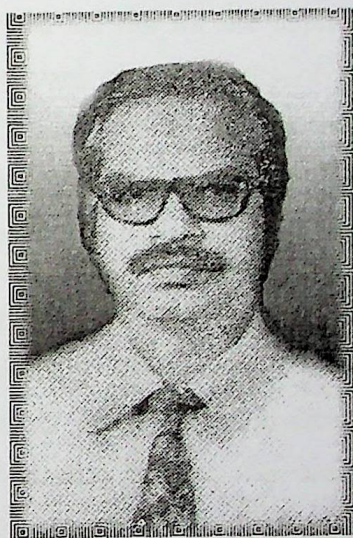
Professor S. Sotheeswaran

*Emeritus Professor, The University of the South Pacific, Fiji and
Senior Professor, Institute of Chemistry Ceylon*

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Prof. Sivapathasuntharam Mageswaran

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Vice-Chancellor's Message

Late Prof. S. Mageswaran is one of the most important pioneers of the University of Jaffna. He took major role in the development of the University, has taken immense interest and devoted his life for the improvement and upgrading the standard of the Faculty of Science and Department of Chemistry. Prof. Mageswaran has taken appropriate action to maintain the student discipline and had been the role model to many academic staff.

I am happy that Prof. S. Sotheeswaran, Emeritus Professor at University of the South Pacific, Fiji and Visiting Professor of Institute of Chemistry, Ceylon is delivering the Memorial Lecture. We are very much honored to have a such an eminent professor delivering this lecture. I thank Prof. Sotheeswaran for delivering this memorial lecture.

Prof. (Ms) V. Arasaratnam

Vice-Chancellor

University of Jaffna

06.12.2011

**Professor S. Mageswaran Memorial Lecture –
University of Jaffna – 06 December 2011.**

*By Professor S. Sotheeswaran, Emeritus Professor, The
University of the South Pacific, Fiji and Senior
Professor, Institute of Chemistry Ceylon.*

About the Late Professor Mageswaran:

I have known Professor Mageswaran since he entered the University of Ceylon in the year 1962. He started his first year studies at the Peradeniya Campus and I was based in the Colombo Campus of the University of Ceylon that year. In 1963, he moved to the Colombo Campus to start B.Sc (Honours) studies in chemistry but I was appointed as an assistant lecturer at the Peradeniya Campus. In 1964, I left for my Ph. D studies in the UK and I was away when Professor Mageswaran moved to the Peradeniya Campus for his final B.Sc (Honours) year. He graduated from the Peradeniya Campus in 1966 and was appointed as an assistant lecturer in chemistry in 1966. I was told that Professor Mageswaran took special interest in teaching chemistry at Peradeniya and one reason was that Rajes (his future wife) was a first year student at Peradeniya at that time.

I returned from my studies in the UK in 1967 and during 1967/1968, we worked together in the Chemistry Department at the Peradeniya Campus of the University of Ceylon.

Then in 1968, Professor Mageswaran proceeded to the University of Sheffield, UK for Ph.D. studies and returned to Peradeniya in 1971. During one of my visits to the UK, I met Professor W D Ollis at the University of Sheffield, who was Professor Mageswaran's Ph.D. thesis supervisor. Professor Ollis was very much impressed with Professor Mageswaran's research work.

Peradeniya lost Mageswaran when he decided to accept the post of Professor of Chemistry when the post fell vacant with the departure of Professor Thurairajah, the first professor of chemistry at the newly created University of Jaffna. Peradeniya's loss has been Jaffna's gain. Professor Mageswaran devoted much time and effort to the development of the chemistry department here at the University of Jaffna. He was fortunate in that his wife was his colleague and worked with single minded devotion to help Professor Mageswaran in nurturing a relatively young institution during difficult times.

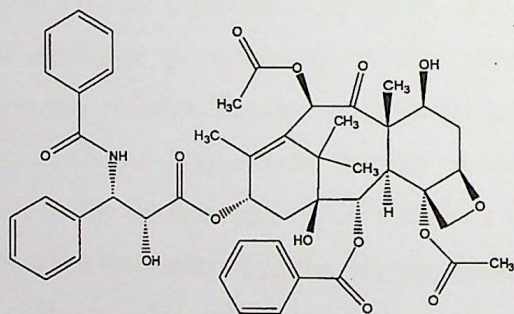
Professor Mageswaran and I continued to work together even though Professor Mageswaran was in Jaffna and I was in Peradeniya, especially in setting GCE Advanced Level Chemistry examination questions and marking answer scripts.

Jaffna University lost an eminent and dedicated staff member when Professor Mageswaran passed away prematurely.

In this Professor Mageswaran Memorial talk, I wish to speak on some Commercially Useful Natural Products. This is an area of organic chemistry in which Professor Mageswaran specialized.

Commercially Useful Natural Products

A **natural product** is a chemical compound or substance produced by a living organism - found in nature. It usually has a pharmacological or biological activity for use in pharmaceutical drug discovery and drug design. These molecules provide sources of inspiration for drug discovery. In particular, these compounds are important in the treatment of life-threatening conditions. One striking example is **Taxol**, a well-known **Anticancer Agent** of this century.



Taxol

Natural products can be extracted from the tissues of terrestrial plants, marine organisms, microorganisms or

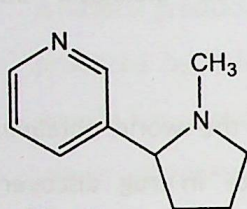
from fermentation broths. A crude (untreated) extract from any one of these sources typically contains novel, structurally diverse chemical compounds. Chemical diversity in nature is based on biological and geographical diversity.

Many researchers travel around the world obtaining samples to analyse and evaluate in drug discovery screens or bioassays. This effort to search for natural products is known as bioprospecting.

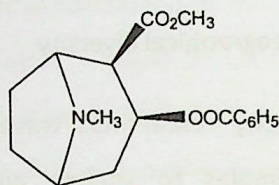
Pharmacognosy provides the tools to identify, select and process natural products destined for medicinal use. Usually, the natural product compound has some form of biological activity. That compound is known as the active principle - such a structure can act as a lead compound. Many of today's medicines are obtained *directly* from a natural source.

On the other hand, some medicines are *developed from a lead compound originally* obtained from a natural source. Plants have always been a rich source of lead compounds: (e.g. Alkaloids, morphine, cocaine, digitalis, quinine, tubocurarine, nicotine, and muscarine). Many of these lead compounds are useful drugs in themselves

(e.g. Alkaloids, morphine and quinine). Others have been the basis for synthetic drugs (e.g. local anaesthetics developed from cocaine).

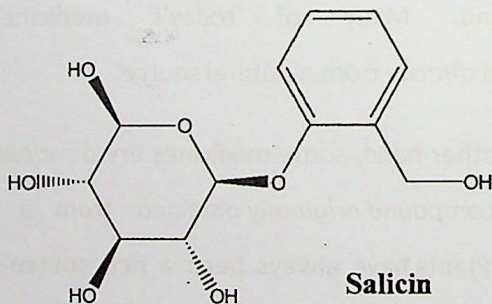


Nicotine



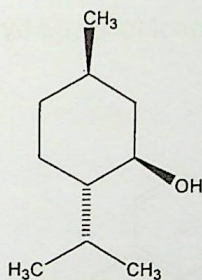
Cocaine

Clinically useful drugs which have been recently isolated from plants include the anticancer agent mentioned above, which is **taxol** from the yew tree, and antimalarial agent **artemisinin** from the Chinese plant *Artemisia annua*.



Salicin

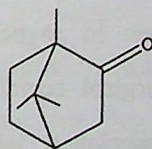
In 1897, Felix Hoffmann created a synthetically altered version of **salicin** (in this case derived from the *Spiraea* plant), which caused less digestive upset than pure salicylic acid. The new drug, acetylsalicylic acid, was named subsequently as **aspirin** by Hoffmann's employer Bayer AG. This gave rise to the hugely important class of drugs known as non-steroidal anti-inflammatory drugs (NSAIDs).



Menthol is an organic compound made synthetically or obtained from peppermint or other mint oils. The main form of menthol occurring in nature is (-)-menthol, which is assigned the (1R,2S,5R) configuration.

Menthol Menthol has local anesthetic and counter-irritant qualities, and it is widely used to relieve minor throat irritation.

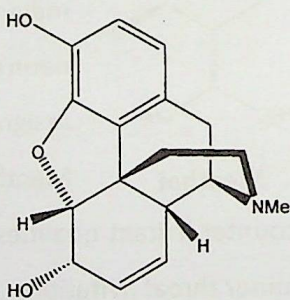
Camphor, a waxy, white or transparent natural product has a strong, aromatic odour. It is a terpenoid with the chemical formula C₁₀H₁₆O. It is found in



Camphor wood of the **camphor laurel** (*Cinnamomum camphora*),

a large evergreen tree found in Asia (particularly in Borneo and Taiwan) and also of *Dryobalanops aromatica*, a giant of the Bornean forests. Camphor can be synthesized from *alpha*-pinene, which is abundant in the oils of coniferous trees. With acetic acid as the solvent and with catalysis by a strong acid, *alpha*-pinene readily rearranges into camphene, which in turn undergoes Wagner-Meerwein rearrangement into the isobornyl cation, which is captured by acetate to give isobornyl acetate. Hydrolysis into isborneol followed by dehydrogenation gives camphor.

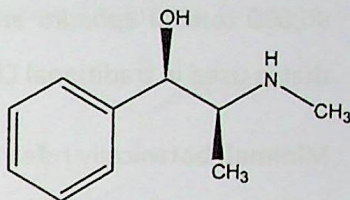
Morphine is a highly potent opiate analgesic drug and is the principal active agent in opium and the prototypical opioid. Morphine is very useful as an analgesic in hospital settings to relieve :



Morphine

pain in myocardial infarction; pain associated with surgical conditions, pre- and post- operatively; pain associated with trauma; severe chronic pain, e.g., cancer, pain from kidney stones); and severe back pain.

Ephedrine is a sympathomimetic amine commonly used as a stimulant, appetite suppressant, concentration aid,



Ephedrine

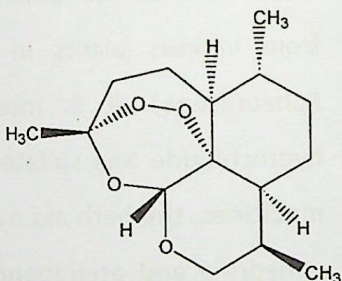
decongestant, and to treat hypotension associated with anaesthesia. Ephedrine is similar in structure to the synthetic derivatives amphetamine and methamphetamine. Chemically, it is an alkaloid derived from various plants in the genus *Ephedra* (family Ephedraceae). It is most usually marketed in the hydrochloride and sulfate forms. In traditional Chinese medicines, the herb *má huáng* (*Ephedra sinica*) contains ephedrine and pseudoephedrine as its principal active constituents. The same is true of other herbal products containing extracts from *Ephedra* species.

Nagayoshi Nagai was the first one to isolate ephedrine from *Ephedra vulgaris* in 1885. The production of ephedrine in China has become a multi-million dollar export industry. Companies producing for export extract US\$13 million worth of ephedrine from

30,000 tons of *ephedra* annually, 10 times the amount that is used in traditional Chinese medicine.

Minimal, botanically referred to as *Catharanthus roseus* (Madagascar Periwinkle), is a species of *Catharanthus* native and endemic to Madagascar. From this plant, the following commercially useful alkaloids have been produced: Vincristine and vinblastine used in cancer chemotherapy.

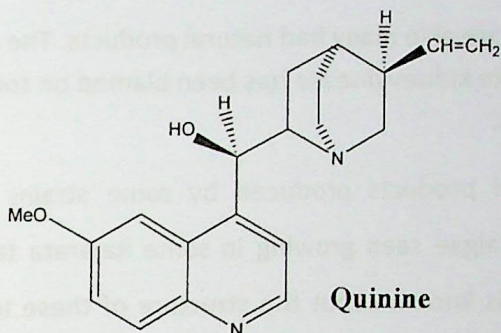
Artemisinin is a drug used to treat multi-drug resistant strains of *falciparum malaria*. The compound (a sesquiterpene lactone) is isolated from the plant



Artemisinin

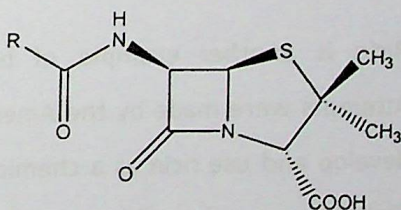
Artemisia annua used in traditional Chinese medicine. Apparently it is only produced when the plant is subjected to certain conditions, most likely biotic or abiotic stress.

Quinine was the first effective treatment for malaria



caused by *Plasmodium falciparum*, appearing in therapeutics in the 17th century. It remained the antimalarial drug of choice until the 1940s, when other drugs took over. Since then, many effective antimalarials have been introduced, although quinine is still used to treat the disease in certain critical situations.

Penicillin is produced by the fungus *Penicillium*. Penicillin is a group of *Beta*-lactam antibiotics used in



Penicillin

the treatment of bacterial infections caused by susceptible, usually Gram-positive organisms.

Are some natural products bad?

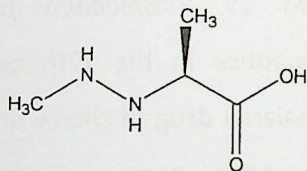
There are also many bad natural products. The cause of Rajarata kidney disease has been blamed on toxic organic

natural products produced by some strains of blue-green algae seen growing in some Rajarata tanks. Not much is known about the structure of these toxins but published reports

on the compounds produced by these types of algae,

growing elsewhere, have shown that

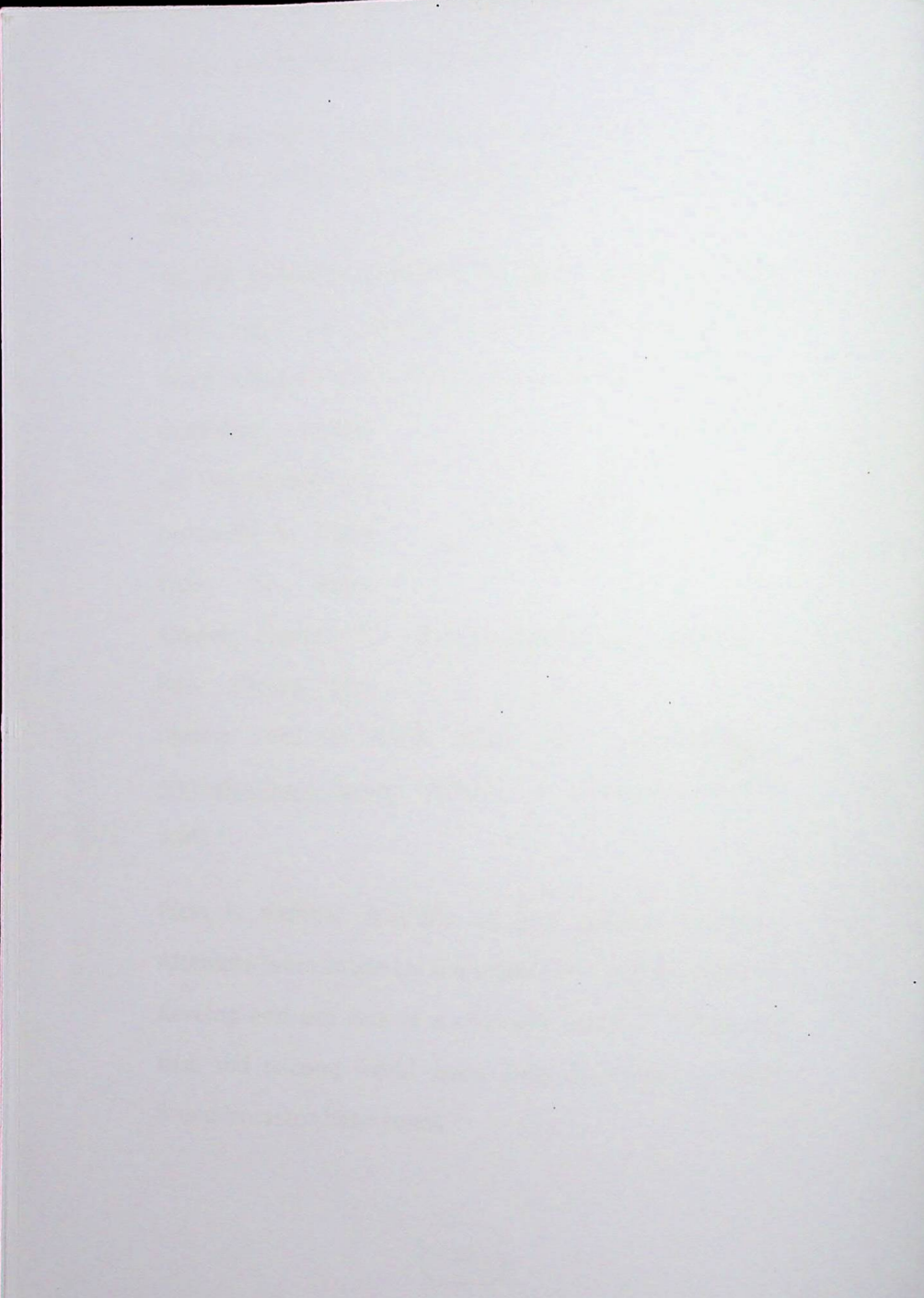
diverse taxa of these algae do produce β -N-methylamino-L-alanine (BMAA), a neurotoxic amino acid).



β -N-methylamino-L-alanine

Ricin is another example of bad natural products. Attempts were made by the Americans and Russians to develop and use ricin as a chemical weapon during the first and second world wars. Ricin is a toxic protein found in castor bean seeds.









Professor S. Sotheeswaran

Author of more than 110 publications in Refereed International Journals and more than 100 publications in Regional Journals and Regional and International Conference Proceedings, Professor Sotheeswaran is one of the foremost academics of Sri Lanka.

He graduated in 1963 with a First Class Honours from the then University of Ceylon, winning the Bhikaji Framji Khan Gold Medal for the best performance and in 1967, got his Ph.D from the University of Hull, UK. He was awarded the Doctor of Science (D.Sc.) degree by the University of Hull in 1987 for his work on Chemistry of Some Organic Natural Products.

Professor Sotheeswaran has served in the capacities of Lecturer, Senior Lecturer and Associate Professor at the University of Peradeniya before joining the University of the South Pacific, Fiji. He was a member of the team which won the Sri Lankan President's Award of a Gold Medal and a Cash Prize in 1986 for Harnessing Natural Products Resources of Sri Lanka and for developing a Center for Academic Excellence in Natural Products Chemistry at the University of Peradeniya. While at Peradeniya he also served as a Visiting Lecturer to the Chemistry Special Students of the University of Jaffna.

At the University of the South Pacific, Fiji, Professor Sotheeswaran won numerous Grants and Awards for research and has made a significant contribution to the study of natural products in the South Pacific region.

Currently he is an Emeritus Professor of the University of the South Pacific, Fiji and a Visiting Senior Professor at the Institute of Chemistry, Ceylon.