

CHEMISTRY

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44TH ANNUAL SESSIONS OF THE INSTITUTE OF CHEMISTRY CEYLON



Prof. H D Gunawardhana delivering the Presidential Address.



Mr. Athauda Jayawardena, Chief Guest delivering his address.



Dr. Upali Samarajeewa, Guest of Honour delivering his address.



Prof. P A Paranagama receives the Dr. C L de Silva Gold Medal Award



Dr. V M Thadhani receives the Chandrasena Memorial Award



Mr. S C D Fernando receives the Kandiah Memorial Graduateship Award



Mr. N I N S Nadarasa receives the Special Service Award



Ms. H L Anoma Champanie receives the Special Service Award



Mr. U J Nishan Chandana receives the Special Service Award



Winners of the all Island interschool chemistry quiz competition 2014/2015



Chemistry in Sri Lanka

ISSN 1012 - 8999

The Tri-Annual Publication of the Institute of Chemistry Ceylon

Founded in 1971, Incorporated by Act of Parliament No. 15 of 1972

Successor to the Chemical Society of Ceylon, founded on 25th January 1941

Vol. 32 No. 3

September 2015

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Theme for the year -

Ethics and Responsibilities of Professional Chemists for the National Development

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Outline of our Institute

The Institute of Chemistry Ceylon is a professional body and a learned society founded in 1971 and incorporated by act of Parliament No. 15 of 1972. It is the successor to the Chemical Society of Ceylon which was founded in 1941. Over 50 years of existence in Sri Lanka makes it the oldest scientific body in the country.

The Institute has been established for the general advancement of the science and practice of Chemistry and for the enhancement of the status of the profession of Chemistry in Sri Lanka. The Institute represents all branches of the profession and its membership is accepted by the government of Sri Lanka (by establishment circular 234 of 9-3-77) for purposes of recruitment and promotion of chemists.

Corporate Membership

Full membership is referred to as corporate membership and consists of two grades: **Fellow (F.I.Chem.C.)** and **Member (M.I.Chem.C.)**

Application for non-corporate membership is entertained for four grades: **Associate (former Graduate) (A.I.Chem.C.)**, **Licentiate (L.I.Chem.C.)**, **Technician (Tech.I.Chem.C.)** and **Affiliate Member**.

Revision of Membership Regulation

All Special Degree Chemists can now apply directly to obtain **Associate (Graduate) Membership**. Three year B. Sc. Graduates (with an acceptable standard of Chemistry) can

- directly become **Licentiate**
- obtain corporate membership in a lesser number of years.

Tech.I.Chem.C.

Those who have passed the DLTC examination or LTCC examination or have obtained equivalent qualification and are engaged in the practice of Chemistry (or chemical sciences) acceptable to the Council are entitled to the designation **Tech.I.Chem.C.**

Members/Fellows are entitled to the designation of **Chartered Chemist (C.Chem.)** on establishment of a high level of competence and professionalism in the practice of chemistry and showing their commitment to maintain their expertise.

All corporate members (Members / Fellows) are entitled to vote and become Council/ Committee members whether Chartered Chemists or not.

Membership Applications

Any application for admission to the appropriate class of membership or for transfer should be made on the prescribed form available from the Institute Office.

Current Subscription Rates

Fees should be paid on 1st of July every year and will be in respect of the year commencing from 1st July to 30th June

Fellow	Rs. 1500
Member	Rs. 1500
Associate	Rs. 1200
Licentiate	Rs. 1000
Technician	Rs. 500
Affiliate	Rs. 1000
Membership for Life	Rs. 15000

Entrance Fee

All the grades	Rs. 1000
Processing Fees*	Rs. 500
Processing Fee for Chartered Chemist designation	Rs. 1000
Institutional Members	Rs. 2500

*per application for admission/transfer to any grade

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Dr. (Mrs) R Kandiah

CHEMISTRY IN SRI LANKA

Chemistry in Sri Lanka is a tri-annual publication of the Institute of Chemistry Ceylon and is published in January, May and September of each year. It is circulated among the members of the Institute of Chemistry and students of the Graduateship/DLTC course and libraries. The publication has a wide circulation and more than 1000 copies are published. Award winning lectures, abstracts of communications to be presented at the annual sessions, review papers, activities of the institute, membership news are some of the items included in the magazine.

The editor invites from the membership the following items for publication in the next issue of the Chemistry in Sri Lanka which is due to be released in January 2016.

- *Personal news of the members*
- *Brief articles of topical interests*
- *Forthcoming conferences, seminars and workshops*
- *Latest text books and monographs of interest to chemists*

All publications will be subjected to approval of the 'Editorial and Publicity Committee' and the Council of the Institute of Chemistry Ceylon.

Further, prospective career opportunities for chemists, could be advertised in Chemistry in Sri Lanka at a nominal payment. The editor welcomes from the members suggestions for improvement of the publication.

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Message from the President



The year 2015 began with a hive of activity, mainly focused on the graduation ceremony / convocation of the College of Chemical Sciences, the most eagerly looked forward to event in any given year. It was held on 19th February at Eagle Lakeside, Attidiya; the success of the event was a

tribute to Emeritus Professor J N O Fernando (JNOF) for his untiring efforts, meticulous care and efficiency. It was well attended and indeed, a very happy occasion. However, a couple of weeks later (2nd March 2015), we were shocked to learn about the sudden demise of Prof JNOF. We were dumbfounded and in a state of shock for quite some time. In the end, the whole Institute Community rose to the occasion in giving a fitting farewell to the man who stood tall at all occasions, fought tooth and nail for the benefit of the Institute at all times.

The untimely death of Prof. JNOF has created a void that no single person can fill. His commitment and vision for the ICHEMC was extraordinary which saw the Institute grow from infancy to what it is today. Hence, I consider this year as one of the most, if not the most, challenging period for the ICHEMC, as we are entrusted with the task of taking forward the objectives of the Institute; the mantle of leadership has fallen on the shoulders of the present Council members under my leadership, a tough task indeed.

In January 26th of 1941 Ceylon Chemical Society was established; it was then transformed to Institute of Chemistry Ceylon in the year 1971 by an act of Parliament in 1972. Hence, the year 2016 would be quite significant as we celebrate 75 years of our existence. I consider it as a singular honour for me in more ways than one as I am the first graduate chemist to

hold the prestigious position of President, ICHEMC and that too, in its 75th Year. I am one the few who joined the very first batch of students offering the Graduateship Course in Chemistry in 1979. It is most unfortunate, therefore, that Prof. JNOF is not there to celebrate my Presidency as it was he who groomed me to take on the role of President, ICHEMC.

Among the many goals set for this year, my first priority is to carry forward the vision / ideas of late Prof JNO Fernando. He tried his best to ensure that our own graduates are recognized locally and internationally; certain issues in this regard are being addressed at the moment.

Chemistry has contributed immensely towards the new technological developments; chemical industries serve the global population with new products and formulations with added advantages in terms of affordable prices. However, the role played by chemists who developed these products remain unknown to the vast majority of end users. Majority pharmaceuticals that we use today are chemical compounds developed by chemists involved in the drug development industry. Hence, gaining recognition for the chemist should be one of the primary but long term objectives of ICHEMC and its Members. On behalf of the Institute of Chemistry, may I appeal to all of you to give your fullest support in this regard.

Theme of the Council this year is “Ethics and Responsibilities of Professional Chemists for the National Development” in line with some of the statements mentioned above. As an institution commemorating 75 years I trust that the above theme is a reminder to encourage all our members to act with a sense of purpose and vision, to build an image for the chemists in our society and to play a role in the transformation of the present for a better tomorrow.

K R Dayananda

Grad.Chem., F.I.ChemC, C.Chem., M.Phill.

President, Institute of Chemistry Ceylon.

Cover Page

Food safety is a scientific discipline describing handling, preparation and storage of food in ways that prevent food borne illnesses. This includes a number of routines that should be followed to avoid potentially severe health hazards. On the other hand, food security can be defined as “When all people at all times have access to sufficient, safe and nutritious food to maintain a healthy and active life”.

pages 6 -18 for more details.

Role of Professional Chemists for National Development

Dr. Piyal Ariyananda

Regional Head of Research and Development, Midas Safety – Sri Lanka



More than ever before in the world, science and technology dominate in every corner of the society. From the diaper we dress to our newborn to the hundred year old man who takes his last breath, science and technology makes their lives comfortable, livable, and touches in all other requirements. Out of all sciences, chemistry is regarded as the “Central Science” due to this sole reason. Those who engage in this central science are scientists, engineers, technicians, chemists, even artists. The term Chemist has a very vague meaning. It can be a true scientist who deals with Chemical substances, or a druggist at a pharmacy who mixes daily doses of medicine to the patients. Be it whatever it is, Chemists are an important part of the modern society. Chemists do more than just being a part of the Society. They are educators, investigators, scientists and trend setters.

Chemistry and chemical formulae, are not new to the chemists, but sciences are highly specialized and alienated areas from general public. Even in developed countries, general public is distanced from these areas because of the specialties involved with the subject areas and the general public has tendency to stay away from unknowns. Animals are scared of unknowns, so do the humans. Chemistry, Chemicals are scary things for most of the general public, even educated ones make wrong assumptions on chemicals.

What makes a Good Chemist?

The answer is that the same materials that makes a good citizen. A good Chemist must indeed be armed with sufficient knowledge to tackle or handle the related issues. However, thanks to the misconceptions in the society which think a Scientist/Chemist knows all the answers to any chemical related problem, we get all the problems in the world to solve: which is good in one way. The other part of the answer comes with the responsibility. A Good Chemist must be as Ethical and Responsible as any other good citizen, or better than them. This is however, difficult to measure.

Ethics, integrity, honesty, responsibility go hand-in-hand with a good citizen. A Chemist is a responsible

person in the society; his or her decisions might alter someone's life, or society's thinking pattern. We encounter many ambiguities in the society related to chemical issues. Integrity of a chemist plays a major role in biasness and honesty for the respective parties. Unfortunately, ethics is also an alienated word in the vocabulary for many easterners in the world. Especially south Asia, Ethics are not well received in the society. Whether it's on the road, at work or any public place, it's hard to find someone who follows ethics or the norms of the society: Pity, but true.

What could we do, as chemists, for the national development? Chemists, as I pointed out, have enormous amount of knowledge in many fields. Whether it is Food safety, consumer safety, public knowledge, communal diseases, or environmental issues, chemists have a major role to play. Recent CKDU episodes showed the real situation in the society. Several research groups claimed that they have discovered the cause of the CKDU and argued to establish their own findings. It's one thing that you need to fight for what you believe in, and also you should give in to consider other opinions as well. The society could have been in much better place if all these groups got together shedding all their differences for a common cause: a permanent cure for the CKSU issue.

Sri Lanka, as a middle income country needs a lot of reforms. With the new governments playing a huge role in new ideas, while the president himself being the minister of environment, Sri Lankan Chemists and scientists have an open invitation to contribute for the development of the country. Sri Lanka still doesn't have any clear Chemical, Environmental, or Drug policies. Illicit drugs, illicit medications float through the society without any regulation, eventually kills many innocents knowingly or unknowingly. Sri Lanka needs a clear Consumer safety policy and regulations. All these institutions require qualified, recognized and ethical chemists to make policies, regulate them and execute the plans. Unfortunately, Sri Lankan Chemists are cornered as technicians due to lack of interest or lack of direction.

Media spreads a lot of unwanted information and public knowledge on Chemicals and related subjects is next to nothing. Chemists have a major role in Media,

correcting the substandard information and educating the general public in rightful manner to educate them in chemical knowledge. Many of the poisoning in Sri Lanka occurs due to lack of knowledge: Usage and prevention both.

In the west, there are chemists in almost all the major institutions. Research programs, analytical laboratories are managed by professional chemists. There are many voluntary organizations run by the chemists to help out the less knowledgeable public on poison control, proper usage of chemicals, and correct chemical practices. Even transportation department in the USA have more sophisticated laboratories and anything in Sri Lanka. There are large number of TV programs on Astrology, Feng-Sui, and numerous

interesting subjects to target the curiosity of the general public, but unfortunately only less than a handful of people talk about sciences in all these. Chemists need to step into their lab coats and start educating the public on proper chemical usage, proper food practices, healthy lifestyles and many other issues that can be addressed through their knowledge.

We all are born equally and survived up to now due to the contributions of many others around us. Chemists are a unique breed of the society, and we all have a mission to accomplish during our short lifespan on this planet. Chemists have a huge responsibility and an obligation to serve the society to make it a better place.

Forty Fourth Annual Sessions and Seventy Fourth Anniversary Celebrations 2015

Presidential Address

Chemical Sciences in Food Safety and Food Security

Professor H D Gunawardhana

Emeritus Professor of University of Colombo

Immediate Past President, Institute of Chemistry Ceylon

The safety of air we breathe, water we drink and food we eat plays an important role for a healthy nation. A healthy nation is an invaluable asset for the economic development of a country. Institute of Chemistry Ceylon, therefore, selected "The role of Chemical Sciences in Food Safety and Food Security" as the theme for the year 2015.

Chemical science is defined as the science of matter, the branch of the natural sciences dealing with the composition of substances and their properties. Using Chemistry as a basis one can understand the structure, organization and functions of living matter. Biochemistry is useful to understand the metabolism and the chemical reactions of the living systems. While plants obtain its energy requirement from sunlight, living beings derive energy from food. The processes underlying these can be understood by using chemistry and the principles of thermodynamics. Chemical and biological structures; amino acids, sugars, lipids, nucleotides, vitamins, minerals and hormones form the basis of food, the backbone of human survival and evolution. Chemical sciences are therefore necessary to understand our food and nutritional needs in modern times.

However, today we find the food remains an issue. The world is facing a food crisis, considering the food

supply and security faced by the developing countries. The strain on food supply is aggravated by the climate change and the non-availability of land for cultivation of food due to the competition for industrial and domestic use of land. The Global demand for food has increased due to population and economic growth especially in the developing countries such as India and China. In the developed world the food supply chain has improved with the use of petrochemical based energy and chemicals in agriculture, manufacture and distribution. The advances in chemistry and biology have greatly helped to increase the availability of relatively cheap food in plenty. This may not be sustainable with the increased population expected over the years. The greatest technological challenge that humanity faces in the future is the improvement of food security without permanently damaging the environment. The application of chemistry and engineering is a key to solve this problem.

The chemical sciences will be needed to supply adequate food security in the future, and to increase production efficiency in all stages of the food supply chain. The demand placed on the environment must be taken into account. Use of land, sea, and air, use of fresh water and the treatment of waste must be sustainable to secure a lasting supply of food. Application of chemical

sciences and advancing technology will assist in global sustainability of food in the long term.

Food Safety

Food safety is a modern concept. Food safety is a multifaceted subject, using microbiology, chemistry, standards and regulations and risk management to address issues involving bacterial pathogens, chemical contaminants, natural toxicants, additive safety, allergens and more. In short food safety refers to the science of keeping food safe. Remarkably, it is only in the last 200 years that such concepts as food borne germs and the means of combating them, such as antiseptics and refrigeration, have been popularized. Yet in the 21st Century consumers in the developed world do not accept that the food which they purchase and continue might carry a risk of making them ill. Our food should be safe, is something we will take for granted.

Food safety is a scientific discipline that describes the handling, preparation and storage of food resulting in the prevention of food borne diseases. Food borne diseases are usually either infections or toxic in nature, caused through the food taken. They could be microorganisms or other agents including chemical products.

The science of keeping food safe is described under various quality management systems. They are: Hazard Analysis and Critical Control Points (HACCP); ISO/IEC 17025-Laboratory Accreditation; ISO 15189-Medical Laboratory Accreditation; the International Organization for Standardization (ISO); the International Electro-technical Commission (IEC); Asia Pacific Laboratory Accreditation Co-operation (APLAC); International Laboratory Accreditation Cooperation (ILAC); Determination of food contaminants; Chemical analysis and accuracy of analytical results ISO/IEC 17025; ISO 17043-New standard on proficiency testing; Inter laboratory comparisons; Internal audit and ISO 22000.

ISO 22000 are protocols used in food safety. ISO and its member countries used the Quality Management System approach, and tailored it to apply to Food Safety, incorporating widely used and proven HACCP principles into the quality management system. The resulting standard is ISO 22000.

ISO 22000:2005 specifies requirements to enable an organization to: Plan, implement, operate and maintain and update a food safety management system aimed at providing products that according to their intended use

are safe for the consumer; to demonstrate compliance with applicable statutory and regulatory food safety requirements; to effectively communicate food safety issues to their suppliers, customers and relevant interested parties in the food chain; to ensure that the organization conforms to its stated food safety policy; to demonstrate such conformity to relevant interested parties; to seek certification and registration of its food safety management system by external organization or make a self-assessment or self declaration of conformity to ISO 22000:2005; to ensure that the organization conforms to its stated food safety policy; to demonstrate such conformity to relevant interested parties; to seek clarification or registration of its food safety management system by an external organization or make a self-assessment or self-declaration of conformity to ISO 22000:2005; to demonstrate such conformity to relevant interested parties.

Food Security

The food security was defined at the 1996 World Food Summit. It states that “Food security exists when all people at all times have both physical and economic access to sufficient food to meet their dietary needs for a productive and healthy life”. Food should be nutritious, safe and culturally appropriate. They should be produced in an environmentally sustainable and socially just manner, and that people are able to make informed decisions about their food choices. Food security also means that the people who produce our food are able to earn a decent living wage by growing, catching, producing, processing, transporting, retailing and serving food. The concept of food security should address both hunger and under-nutrition. A normal growth requires a diet rich proteins, essential fatty acids and micro nutrients.

The achievement of food security depends on three interconnected factors. They are the availability of food, access to food and utilization of food. The availability of food ensures sufficient quantity and variety of diverse foods for consumption from many sources. The access to food is determined by households obtaining appropriate foods for a nutritious diet. The households must have physical and financial resources required to obtain nutritious diet. For most people ability to do so depends on the price of food. The utilization of food needs the capacity and resources necessary for the appropriate use of food. Appropriate use of food provides healthy diets which include sufficient energy and essential nutrients. This also includes the quality of potable water and adequate sanitation. Effective

utilization of food requires knowledge of food storage, processing techniques, and basic principles of nutrition. The nutritious food must have adequate protein, energy, vitamins and minerals at all times.

The core of food security is access to healthy food and optimal nutrition for all. Food access is closely linked to food supply, so food is dependent on a healthy and sustainable food system. The food system includes the production, processing, distribution, marketing, acquisition, and consumption of food.

The state of having reliable access to a sufficient quantity of affordable nutritious food and food security has declined dramatically in many developing countries. A healthy, sustainable food system is one that focuses on environmental health, economic vitality, human health and social equity. Environment health ensures that food production and procurement do not compromise the land, air, or water now or for future generations. Economic vitality ensures that the people who are producing our food are able to earn a decent living wage in doing so. This ensures that producers can continue to produce our food. Human and social equity ensures that particular importance is placed on community development and the health of the community making sure that healthy foods are available economically and physically to the community and that people are able to access these foods in a dignified manner.

Generally food security means the enhancing the availability of food. This is linked to innovations in agricultural production. In many developing countries, agriculture remains the backbone of the rural economy. Increasing agricultural outputs impact economic growth by enhancing farm productivity and food availability.

This provides economic and employment opportunities. In the 1970s and 80s, large investments in agriculture, technology, roads and irrigation led to major improvements in production. Chemical sciences were at the heart of some of these tools and technologies.

From a historical perspective it is clear that Chemistry has played a central role in the production of nutritious food. This covers the production of food from planting stage to the final stage of seed production and also from pest control to human nutrition. Chemistry plays a vital role in contributing to improve the post harvest storage loss. Chemistry also contributes to bio-fortification by incorporating essential micronutrients into staple food, food processing and essential medicines. Chemistry has contributed much to the development of food security for increasing population.

Food safety and food security are complex and require efforts from governing authorities, scientists, industrialists and others engaged in food production to enhance food availability with increasing access and utilization. In the past, agriculture was revived through the use of chemistry and the development of connections between chemistry and other disciplines. Food safety and food security require multidisciplinary and interdisciplinary approaches to address issues such as agriculture, health, water, sanitation, infrastructure, gender and education, many of these rooted in the science of chemistry. Such an approach builds on the knowledge and capacities of local communities would help to transform and improve the quality of diet for better health and nutrition. It is widely believed that chemical sciences will become more important in all aspects of food safety, security and nutrition in the future.

Call for Nominations for Institute of Chemistry Gold Medal 2016 by 31st March *(Under Revised Rules)*

This Gold Medal was the very first of such awards to be donated to the Institute and was made possible through a generous donation made by **Mascons Ltd** in memory of their founder **Mr A Subramaniam** in 1978/79. It recognised contributions made to National Development through research and development involving Chemical Sciences. The Gold Medal Fund was supplemented recently through a further contribution from Mascons Ltd. This criteria governing the award were changed in 2011 since there were no applicants since 2007 in order to enable the award to be made to a mid-career Chemist in recognition of honorary services to the Institute.

Nominations are now being invited for the 2016 Award from amongst **Corporate Members** of the Institute who have fulfilled the following minimum criteria;

- Nominees should be not more than 55 years of age and should have been Corporate members of the Institute for at least 10 years on 1st of June 2016
- Nominees should have made significant contributions towards the activities of the Institute through yeoman services in an honorary capacity during the period of membership. These activities could include holding office, membership in committees, coordination of events such as workshops, social events etc.

Nominations could be made by any **corporate member** of the Institute and should include the consent of the nominee and details of the contributions made by the nominee in accordance with the above guidelines. The Award will be presented at the 45th Annual Sessions. **Nominations should be forwarded to reach the Hony. Secretary, Institute of Chemistry Ceylon not later than 31st March 2016.**

Chief Guest's Address

Chemical Sciences in Food Safety and Security

Mr. Athauda Jayawardena

President, Organisation of Professional Associations of Sri Lanka

Chemical Sciences play a major and critical role in production, processing, packaging, transport and storage to ensure food safety and security. In the context of changing environment, life styles and food habits, Chemical Sciences will face more complicated challenges in the years to come.

Food safety is a scientific discipline describing handling, preparation and storage of food in ways that prevent food borne illnesses. This includes a number of routines that should be followed to avoid potentially severe health hazards.

On the other hand, food security can be defined as "When all people at all times have access to sufficient, safe and nutritious food to maintain a healthy and active life".

At present, the entire world faces a huge challenge related to sustainability of food supply and its security. The demand for food is increasing primarily due to the growth in population and improving economic prosperity. By the year 2050, the World's population will have increased to over 9.00 billion. The situation will be further aggravated by increase in demand, from more affluent people of emerging economies, for high value-added meat and dairy products. The total meat consumption at the global level has gone up from 139 million tons in 1983 to 229 million tons in 1991/2000. It has also been estimated that consumption of meat would be about 303 million tons by the year 2020.

In the above context, the global food production has to be increased by about 70% by the year 2050 to meet the Millennium Development Goal of Eradication of Hunger.

The challenge has to be met in an environment where the available extent of land for cultivation is increasing only marginally by about 5% by the year 2050 and available water for irrigation is declining. According to estimates of the World Bank, one hectare of land will have to feed 5 people by the year 2025. In the year 1960, one hectare was required to feed only 2 people.

Though 71% of the Earth's surface is covered in water, about 97% of this water is saline. Further, 90% of the balance 3% of fresh water is locked away in glaciers and ground water. Then only 0.3% of the Earth's total water is available for irrigation and drinking purposes.

With the increase in population there will be a proportionate increase in demand for potable water. This results in further reduction of water available for irrigation for cultivation of crops.

Climate change will also have negative impacts on agriculture by changing the weather patterns and by shifting pests.

In view of the above, the only alternative available is to increase agricultural productivity to ensure food security. As some section of the society advocates, resorting to traditional varieties and organic farming to ensure food safety and security is only an illusion. Before 1950s the average yield of traditional varieties of rice was about 1 ton per hectare. Today new improved varieties produce about 4 tons per hectare.

Development and adoption of new technologies are the key to effectively handle this situation. Chemical Sciences can play a major role in ensuring supply of healthy, safe and affordable food for all.

At present, there are some agricultural lands where the yield levels are still below the average. In these areas, agricultural productivity can be increased by applying currently available technologies such as use of improved high yielding varieties, better farming practices, agro chemicals and recently developed biotechnology.

In order to meet the increasing demand in the future, the currently available technologies developed by the Chemical Sciences have to be applied in every activity related to production, processing, storage, marketing, etc. Increased precision in agricultural activities such as application of plant nutrients, target application of agro chemicals can improve the quality and yields of crops while minimizing the use of inputs.

Up to about 40% of agricultural production will be lost if crop protection chemicals are not used. Development of new high-potency, pest specific pesticides with new modes of action will help overcome pest resistance. Pesticides that are more safer to the user with less persistency in the environment and required in small quantities per unit area of land cultivated, have to be developed using Chemical Sciences. Development of pheromones to attract insect pests is another area that requires new technologies.

Chemical Sciences in association with

biotechnology can improve efficiency of utilization of plant nutrients by understanding the metabolic pathways and role of growth regulators to increase crop yields.

Further, new inorganic fertilizer formulations should also be developed to ensure that the nutrients such as nitrogen, potassium, phosphorus and micro nutrients are efficiently delivered. Loss of these nutrients to the environment should also be minimized.

By understanding the complex soil structure, chemical and microbial composition of soil and its interaction with the plant roots and the environment, fertilizers can be formulated to ensure optimum uptake by plants while minimizing losses to the environment and improving retention in soil. Development of technologies to prevent emission of methane gas is also vital. Decomposition of organic matter in soil during land preparation under wet conditions for cultivation of crops emits toxic gases like methane. Another aspect is the development of in situ bio sensors to monitor soil quality and nutrient contents for optimum use of fertilizers.

As household, agricultural and industrial demands for water is increasing, conservation of water through more targeted delivery system such as drip systems, and use of grey water, reuse and recycling of used water becomes essential.

Chemical Sciences have to play a major role in devising of new inexpensive methods of treating water including desalination. Development of portable technologies for analyzing and treating contaminated ground water will help local populations have access to potable water.

Biochemical rapid detection methods should also be developed to identify pathogens in potable water. Setting standards for rain and grey water enables localized treatment of harvested rain and grey water for secondary use.

Contamination of water with various chemicals occurs due to human activities. Some chemicals are available in nano particles. More chemical research is required to measure the amounts and to understand their fate and the impact on the environment, human health and the biological systems.

Proper nutrition plays a very important role in promoting health, preventing and treating diseases and ensuring quality of life. Moreover Chemical Sciences can modify the available food to ensure control release of macro and micro nutrients while removing the unhealthy contents. By understanding the satiety signals, fat and sugar can be replaced with safe fats and

sweeteners, respectively while maintaining the texture of real fat. Fortification of food items to meet specific needs of the body to lead a healthy life is another role that can be played by Chemical Sciences.

Chemical Sciences have to ensure that food is safe for consumption. Food safety is the safe handling, preparation and storage of food in such a manner that prevents food borne illness and covers the activities from farm to plate.

Microbial contamination of food is the most common health problem for consumers. Spoilage and adulteration are two major problems in this area. Chemical Sciences have to develop intelligent packaging to improve the control of food spoilage, hygiene and food safety. Innovation of new irradiation methods to remove pathogens, as well as new more efficient refrigerant chemicals that will have no harmful effects on the environment with less energy consumption is vital.

Increase in efficiency of refrigeration at every stage in the supply chain by resorting to super chilling as an alternative to freezing is also of paramount importance.

In order to reduce energy use scaling down and combining of process steps in production of food can be adopted. To recover valuable materials and reduce wastes through new routes for bi-products and co-products use high pressure processing and pulsed electric fields at all stages of production of food. Development of surface coating technologies for cleaning of food preparation surfaces with antifouling properties will also contribute towards ensuring food safety.

Designing of improved food preservation methods for liquids and solids by rapid chilling, heating and salting is another important area that requires research activities. Development of technologies pertaining to flexible thin films made of corn starch, polypeptic acid and cellulosic materials that withstand the chill chain handling and storage is also vital. Another opportunity for Chemical Sciences is the development of new food additives like natural preservatives and antioxidants. Development of food packaging that is compatible with anaerobic digesters and packaging of biodegradability or recyclability is also essential.

Convenient methods to detect industrial chemicals, residues of pesticides and fertilizers, allergens, toxins, veterinary medicines, growth hormones and microbial contamination should be developed. Suitable processes and devices should also be developed to measure food quality, safety, ripeness,

etc.

In view of the above, it is clearly evident that there is enormous opportunity for Chemical Sciences to devise ways and means to improve agricultural productivity and food safety while protecting the environment.

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Guest of Honour's Address

Chemists and Professionalism

Professor Upali Samarajeewa

President, Institute of Food Science & Technology Sri Lanka

Past President, Institute of Chemistry Ceylon

Professionalism is defined as the skill, good judgment, and polite behavior that are expected from a person who is trained to do a job well. Professionalism reflects degree of excellence or competence that is expected of a person.

The Institute of Chemistry Ceylon, along with Royal Society of Chemistry has along history of professional development in Sri Lanka. We all as members of the Institute of Chemistry have been responsible for achieving great heights in our profession. The Institute to its credit has the first graduateship programme established and operated successfully for many years producing graduates for the industry and the academia. The Institute encouraged research, recognized research through awards, and have been working with many researchers of reputation in the Universities and research institutes. The graduates of the Institute are holding key positions in industry ensuring quality of products and serving the consumers.

In the current day context, the professionals are faced with the problem of balancing ethics, politics and policy.

Describing the roles and responsibilities of professionals, an eminent chemist Professor Owen R Fennema, who had written many books during the last century, which are used even today as standard text books in the field of food science, and particularly food chemistry writes;

“If food chemists do not become involved in techno-societal issues, the opinions of others –

scientists from other professions, professional lobbyists, persons in the news media, consumer activists, charlatans and anti-technology zealots- will prevail. Many of these individuals are less qualified than food chemists to speak on food-related issues and some are obviously unqualified.

Types of activities to fulfill societal obligations;

- a) *Participate in pertinent professional societies*
- b) *Serve on governmental advisory committees*
- c) *Undertake personal initiatives of public service nature*

The third point involves letters to newspapers, journals, legislators, government regulators, company executives, university administrators, and others, and speeches / dialog with civic groups, including sessions with students, and all other stakeholders. All these should lead to improve the ability of public to intelligently evaluate information on topics”.

Chemophobia (the fear of chemicals) has afflicted a significant portion of the population. To many of their minds, food additives represent hazards and only hazards. Chemophobia has made them move away from well researched and scientifically established facts. There are persons mostly among non-chemists, continuously ingraining the brains of the public with false notions through electronic and print media. If the public is to believe such persons, they should first establish their credibility and authoritativeness by exhibiting complete knowledge against partial knowledge, their ability to weigh risks against needs of the society in relation to foods, and a high degree of

honesty in their expressions.

Professor Fennema continues to describe the characteristics of persons who should be discussing food safety issues as, *“Credibility is founded in formal education, training, practical experience, scholarly contributions to the body of knowledge, to which a particular dispute is linked. Scholarly activity can take the form of research, discovery of new knowledge, and review and interpretation of a body of knowledge. Credibility is also found in the authors in being objective, which requires alternate point of view and as much as existing knowledge of the subject as feasible, instead of only pointing out facts and interpretations that are supportive of a preferred view point”*.

As against chemophobia related to foods, there is no chemophobia related to medicines. Medicines are all chemicals taken directly in full dose, against chemicals added in recommended safe doses to foods. They both

are tested for their safety applying the same principles, technologies and interpretations. I believe some of the persons talking of food chemistry have miserably failed, because of their unprofessional approaches, and the greed for cheap publicity created by public media.

It is time that the Institute of Chemistry Ceylon as a professional organization, with a large number of members, young and old, and especially the graduates passing out and in the field, takes the responsibility of taking a brave step of addressing the societal obligations based on sound science and not incompetent interpretations as happening around us today. Mr. President of the Institute of Chemistry Ceylon and President Elect, I am sure you will address the issue of appropriate and scientific societal interactions, which is an obligation of chemists, more seriously in time to come.

Theme Seminar on

“The Role of Chemistry in Food Safety and Food Security”

18th June 2015

Venue: PPGL Siriwardene Auditorium, Adamantane House, Rajagiriya

Chief Guest's Address

Food Safety

E G Somapala

Former Government Analyst, Member of Food Advisory Committee

All foods are complex mixtures of chemical substances which are organic and/or inorganic. The major constituents of food are moisture, mineral matter, carbohydrates, proteins and oils & fats (lipids). Also there are minor components such as pigments, flavor compounds, vitamins and toxic substances (not in all foods) naturally present in foods in trace levels. In addition to the above there are food additives and food contaminants and in some instances there may be food adulterants and these foreign substances play an important role in safety of food.

Safety aspects of food

Food to be safe for consumption, shall be free from toxic substances and pathogenic organisms. Safety means practical certainty that illness or injury will not result from the consumption of food (either short term or long term). In other words, food shall be free from hazards which arise from the presence of undesirable matter in the food from primary production, harvesting, handling and various stages of processing and

preparation.

Hazard is a biological, chemical or physical agent or factor with the potential to cause adverse health effects. Examples of hazards are;

- Biological hazards which include pathogenic microbes, toxin plants and animals, and products derived from biochemical reactions and toxic chemicals produced by microorganisms.
- Chemical hazards which include natural toxins, pesticides, veterinary drug residues (antibiotics), heavy metals, non permitted food additives and excessive levels of food additives.
- Physical hazards which include objects such as metal fragments, glass pieces, stones and similar substances.

Food becomes unsafe due to the presence of any hazard and they are introduced to food mainly by contamination. Food contaminants are undesirable

substances inadvertently added to food during the various stages of production, distribution, transport, storage, sale, offer for sale and consumption. Food becomes unsafe due to the presence of pathogenic microorganisms such as Salmonella, Vibrio, shigella, staphylococcus, clostridium etc.

There may be toxic substances produced by microorganisms such as fungal toxins (Aflatoxins, patulin, islatodotoxin, ochratoxin, hepatotoxin etc), bacterial toxins (botulin, enterotoxin, staphylococcal toxin etc).

Certain naturally occurring chemicals in plants will make the food unsafe. Among them, the protease inhibitors, phytates, goitrogens, cyanogenic glucosides, trypsin inhibitors, saponnins, solannins and gossypol are main chemicals. Certain fish species and poisonous mushrooms are also considered as hazards to food.

Among the chemical hazards, heavy metals, pesticide residues, veterinary drug residues, packaging materials and man made chemicals play an important role in the food safety. Heavy metals such as Pb, As, Hg, Cd, Sb, Sn are introduced to food through various roots such as agrochemicals, machinery involved in the production, polluted water, packaging material, solders, pottery, pipes, paints, soil and plants. Pesticide residues gain entry to food mainly due to mis-use by the stake holders. It has been observed that over dosing is the main reason to have unacceptable levels of pesticide residues in food. Similar situation is found where the animals treated with veterinary drug residues are being used for milking and meat production.

Poly Chlorinated Biphenyls (PCB), Polycyclic Aromatic Hydrocarbons(PAH), Asbestos and Dioxin etc are the man made chemicals contributing to the food hazards.

Hazards through Food Additives

Food additives are safe substances intentionally introduced to food in small quantities but do not consume as it is. The basic functions of the food additives are,

- (a) to improve the keeping quality of food, eg Preservatives and Shelf life extenders such as Antioxidants, Emulsifiers & Stabilizers, Sequestrants
- (b) to improve organoleptic properties such as colouring substances, sweeteners, flavours and flavor enhancers
- (c) to facilitate preparation such as enzymes, pH regulators etc.

The use of food additives is well regulated in Sri Lanka. The maximum permissible level is specified in the Food regulations and implemented. In spite of these there had been occasions where these levels were exceeded specially in food preservations. For example, excessive levels of sulphur dioxide has been reported in ready to drink beverages.

The food becomes unsafe due to the use of non permitted toxic chemicals as food additives. It has been reported that the use of formaldehyde to preserve fish, malathion to prevent insect infestation during the storage of cereals and pulses, carcinogenic dyes Metanil yellow and Rhodamine B in confectionery, Sudan colours in chillies, hydrogen peroxide to preserve liquid milk.

The food also becomes unsafe due to the adulteration. Use of paddy husk and saw dust in condiment powder adulteration, contaminated water in liquid milk adulteration are few examples.

Food safety in Sri Lanka

Implementation of the Food Act No 26 of 1980 and its subsequent amendments is the main legal frame work to ensure the food safety in Sri Lanka. There are number of Food Regulations published under the section 32 of the Act and the implementation of them is the responsibility of the Ministry of Health. The main features of the Act is to control the importation, distribution, transportation, storage, sale and offer for sale of food. The apex body under the Food Act is the Food Advisory Committee (FAC) chaired by the Director General of Health services who is the Chief Food Authority (CFA). Authorized Officers have been appointed to implement the Act. Public Health Inspectors, Food & Drugs Inspectors, Medical Officer of Health and Food Inspectors are included in this category. They are authorized to take samples, inspect premises and prosecute as and when necessary. Analytical services are provided by the approved analysts gazetted under the Act.

Some important Regulations relevant to the food safety are on Preservatives, Antioxidants, Colouring substances, Sweeteners, Irradiated food, Hygiene, Packaging materials, Shelf life of imported food, Formaldehyde content.

In spite of the implementation of Food Act in Sri Lanka, we still come across unhygienic restaurants, eating houses, mobile food stalls, manufacturing establishments and incidents of food adulterations. We will not be able to achieve the total safety in food by the

implementation of laws alone. It is necessary to improve the knowledge based food related activities. We need to change the attitudes of those who are involved in food related activities. The importance of the certification systems such as Good Agricultural Practices (GAP), Good Hygienic Practices (GHP), Good Manufacturing Practices (GMP) and Hazard Analysis Critical Control Point (HACCP) should be emphasized. These systems must be implemented throughout the food chain and necessary training be provided to all sectors involved in manufacture and handling of food.

To improve the food safety activities in Sri Lanka, it is necessary to improve the analytical services,

specially in the detection of trace levels of contaminants. Use of newer techniques and modern instruments, accreditation of laboratories, instrument calibration, use of Certified Reference Materials (CRM) and Reference Materials (RM), engage in Inter Laboratory testing, and participation in Proficiency Testing (PT) programmes are useful to improve the analytical capabilities of laboratories. There is an urgent need to establish a reference laboratory, specially for method validation and development of methods suitable for local food products. Finally, we need to provide correct scientific information to the public on various issues by qualified in food and food safety issues.

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Food Security and Water Quality

Professor H D Gunawardhana

Emeritus Professor of Chemistry, University of Colombo

Immediate Past President, Institute of Chemistry Ceylon

Water is the most important natural resource vital for life. Water is a public good and, the state is only the custodian of water resources. The need for a POLICY on water was emphasized in all deliberations and discussions at the Theme Seminar. Since the draft of the "Water Policy" was met with some criticism, it was proposed to have following three policies related to the use of water.

Water for Human use	}	Irrigation Policy
Water for Food Security		Ground water Management
Water for Industrial		Policy
Water for recreation		Surface water Management
		Policy

The largest quantity (more than 80% of withdrawal) of water in Sri Lanka is used for irrigated agriculture. Therefore, a separate policy is emphasized. However, little or no consideration is given for irrigation water quality in Sri Lanka which is evident in the approved National Agricultural Policy in Sri Lanka. In the management of irrigation water, the quantity required by the farmers is always being given the highest priority. The personnel who deal with the management of irrigation water do not seem to be aware of the so called '**irrigation water quality**' which is stated in the documents published by the Food and Agriculture Organization of the United Nations (FAO). The elements of irrigation policy of FAO includes, national needs in the irrigation, achieve a national irrigation plan, adopt appropriate technological advancement.

Water resources can be categorized into ground water resources and surface water resources. The ground water and surface water management should also be geared towards water for drinking (potable water), for irrigation agriculture, for industries and for recreation. Over 60% of Sri Lankans use ground water for their living. Since the state does not own water resources, a need for a sound National Policy on the management of groundwater resources is emphasized. A proper plan for the management of flood, drainage and waste waters should also be a part of the National Policy on surface water management.

The elements of the Ground water management policy include, establish a national policy on groundwater, prevent the pollution of groundwater, protect equal water right to everybody and regulate the industrial use of groundwater (bottling).

The surface water policy includes elements such as improve drainage facilities for flood management, prevent the pollution of surface waters, encourage the reuse of water especially by industries and encourage the harvesting of rain water.

Importance of water quality in food security

The knowledge of the quality of irrigation water is important in judging its suitability for irrigation. Suitability of irrigation water depends upon several factors associated with characteristic of water, soil, plant and climate.

The irrigation water flows through a system of tunnels, streams, reservoirs ("Wewa"), canals etc.

before it reaches the field where crop is grown. During this flow some soluble salts are always dissolved in and the water becomes saline containing high dissolved salts. Man's activities such as industries, deforestation etc. in and around water flow also enhance the dissolution of salts. In the fields, the water will undergo evapotranspiration, resulting the accumulation of dissolved salts, which will affect the soil properties, especially the soil permeability and subsequently crop growth. It has been reported that in countries such as Afghanistan, Pakistan, Egypt etc. millions of hectares of irrigated lands have been abandoned due to the loss of soil permeability which affects the crop growth.

Some consideration is given for the quality of "potable" (drinking) water, since there is an obvious undesirable effect of the potable water of poor quality. However, as mentioned above little or no consideration is given for the quality of irrigation water used in Sri Lanka. In the ancient time the available water undoubtedly was suitable for the purpose of its use such as drinking, agriculture etc. Therefore, the need to check the 'suitability' for use did not arise and also was not a factor to be considered. Therefore, the ancient concept of the availability of water for economic prosperity is not valid for today.

Today, not only the quantity, but also the suitability of water for the purpose, i.e. quality, should be significant. For example, if water containing harmful chemicals is available in large quantities, then the people who drink the water will be sick thus affecting the economy. Even if there is a plenty of water of poor quality is available for irrigation it would lead to a crop failure affecting the economy. With the assistance of regular water quality monitoring programmes there is a need to develop water quality criteria for all projects which involve water management. These criteria will provide guidance for irrigation water management problems.

The operation of the "water cycle" in the earth is affected and will be affected due to anthropogenic inputs. The regular monitoring of the quality of water in all parts of the island will be helpful to take timely remedial measures leading to a meaningful integrated development in 21st century. It is suggested that the water - quality testing should be carried out at provincial levels even as a part of school curriculum. The data - even through may not be very accurate, will be useful in the water management programmes.

Management of Irrigation Water and Food security

Two main objectives in the conservation of water

are, to provide water for irrigation during the dry season such that an uninterrupted agricultural activity with the production of food is maintained and to improve the health of the people by making the water available for domestic purposes.

Ancient Sri Lankans realized the importance of the conservation of water and constructed reservoirs (Wewa) to collect rainwater for the subsequent use in irrigation and other purposes. It seems that an economic prosperity of ancient Sri Lankan was dependent on the conservation and subsequent continuous availability of water for human needs. Eventhough, it is not the agricultural economy today, the conservation of water still plays a significant role in economy of the country. Therefore, the two terms "water" and "economic development" cannot be separated from one another.

The history of the conservation of water in Sri Lanka could be traced to the reign of King Pandukabhaya (380 – 310 B.C.) who constructed the first reservoir (Wewa) at Anuradhapura. Thereafter, several hundred of reservoirs have been constructed mainly to conserve the rain water. Very little evidence could be gathered on the construction of reservoirs by building dams across flowing streams or rivers. In such instances a forest cover was maintained in an around the streams carrying water to the reservoirs and also the canals which supplied water to paddy fields. The belief such as divine being living in trees assisted to preserve the forest cover. In addition, powerful dictatorship and good governance prevented people even to clear a forest. One method of achieving sustainability in the ancient irrigation projects is to maintain the forest cover. The modern science reveals that clearing of forest increases the sodium ion concentration of irrigation waters thus making the water unsuitable ultimately leading to lost of soil permeability. The ancient water management was based on this type of ancient scientific views (unwritten science).

Kalawewa is one such reservoir constructed by King Dathusena (6th Century A.D.) by building a dam across a stream (presently Dambulu Oya – Kala Oya). He may have constructed this to fulfill his wishes and may have gone against the opinion of his advisors in making the decision. Three or four hundred years after the continuous use of Kala Wewa waters for irrigations, the Anuradhapura kingdom was shifted to Polonnaruwa. One could attribute, reason for the shift is a crop failure due to the lost of soil permeability. The administrative failure during the period 6 – 9 century resulted the poor water management which ultimately

led to the crop failure. The continuous irrigation with poor quality water and consequent crop – failure affected the agricultural economy in the Anuradhapura area resulted the shift of the kingdom to Polonnaruwa in the 10th century.

The recurrence of a large scale crop - failure can not be ruled out today. However, it is now impossible to shift the population in the affected area unlike in the 10th century. A possible crop failure today will lead the disaster and the destruction of the development achieved during last two decades. A proper water management programme guided by the results of continuous monitoring programme and water quality criteria undoubtedly, prevent such disasters.

The recent studies in the Kala-oya basin proved the poor water quality in Rajangana region. Since cultivation of paddy involves the use of extensive amount of water of poor quality in the lower Rajangana region, it is recommended an immediate change of crop pattern such that lesser amount of water is used. If this is not done the loss of soil permeability is imminent with a major crop failure. In a discussion with the representatives from farmer organizations in the area, it was revealed that there is substantial alteration of the crop pattern especially in the lower zone. The farmers

are inclined to cultivate crops which require lesser amount of water. There is a need to encourage the farmers continue with this healthy aspect of the crop pattern which will ultimately reduce the anticipated salt danger of the area. This could even be a temporary effect associated with heavy rainfalls in recent past. However, it is essential to be watchful especially during the period of drought as well as the period during which the water flow is curtailed. There is a need to take adequate measures to maintain this desirable feature.

The sustainable development could only be achieved if we take steps to continue this operation today. This was not the problem in the past 2000 years due to the wisdom of the ancient concept of “Respect Water”. The smooth implementation of the above requires the application of scientific principles to technological needs.

Irrigation Policy

Policy element	Strategy	Actions
1.1 National needs in the irrigation	1.1.1 Consider the Heritage. (Ancient hydraulic civilization which is an example of sustainable development.	1.1.1.1 Study the ancient method of maintaining irrigation systems. 1.1.1.2. Modify the ancient methods to make them suitable for present conditions.
	1.1.2 Classify irrigation activities	1.1.2.1 Assess the large scale irrigation projects. e.g. Mahaweli 1.1.2.2 Assess the exiting anicut systems
	1.1.3 Implement the rules on irrigation.	1.1.3.1 Improve the awareness on irrigation rules among the people. 1.1.3.2 Conduct training camps for farmers.
	1.1.4 Monitor irrigation water quality	1.1.4.1 Provide facilities for water quality testing even at school level. 1.1.4.2 Establish regional laboratories for the testing of water quality.
1.2 Achieve a National irrigation plan.	1.2.1 promote water use efficiency	1.2.1.1 Incorporate irrigation in the school curricula. 1.2.1.2 Incorporate irrigation water quality in the chemistry curricula at all levels.
	1.2.2 Establish an equity on the distribution of irrigation waters.	1.2.2.1 Encourage the establishment of farmer societies.

contd. 17

1.3 Adopt appropriate technological advancement	1.3.1 Increase the water use efficiency by the application of modern techniques.	1.3.1.1 Use drip irrigation system. 1.3.1.2 Make finances available for investment in modern techniques such as drip irrigation.
	1.3.2 Improve the fertility of the land	1.3.2.1 Classify the land based on the fertility. 1.3.2.2 Select crops required to improve fertility of the land. 1.3.2.3 Reduce the excessive drainage of irrigation waters. 1.3.2.4 Monitor the loss of nutrients by drainage waters.
	1.3.3 Enhance productivity	1.3.3.1 Select high yielding varieties. 1.3.3.2 Provide adequate amount of water of suitable quality. 1.3.3.3. Minimize the loss of nutrients by drainage.
	1.3.4 Implement remedial measures if there is a danger of the deterioration of water quality	1.3.4.1 Assess the quality of irrigation waters 1.3.4.2 Predict the possible danger with respect to the loss of the permeability of soil. 1.3.4.3 Report the possible deterioration of the quality of irrigation waters. 1.3.4.4 Advise farmers to implement remedial measures such as crop rotation. 1.3.4.5 Monitor the water quality after the implementation if the remedial measures.

Ground water Policy

Policy element	Strategy	Actions
2.1 Establish a national policy on groundwater.	2.1.1 Assess the capacities of aquifers.	2.1.1.1 Use modern methods to estimate the aquifer capacities.
	2.1.2 Assess the recharging abilities of aquifers.	2.1.2.1 Monitor the quantity used for recharging.
	2.1.3 Allow large scale extraction based on capacities.	2.1.3.1 Develop a legal frame work on large scale extraction of groundwater.
2.2 Prevent the pollution of groundwater.	2.2.1 Achieve community participation in the maintenance quality of groundwater.	2.2.1.1 Introduce awareness program on groundwater pollution even at school level. 2.2.1.2 Incorporate this aspect in the school curricula. 2.2.1.3 Conduct regular discussions on causes of groundwater pollution and the mitigation aspects at Vidatha Centres, Rural Development Societies etc.
	2.2.2 Incorporate potable water quality criteria in Education.	2.2.2.1 Introduce potable water quality standards (WHO, SLSI) to school curricula.
	2.2.3 Encourage communities to establish regional groundwater management.	2.2.3.1 Develop regional groundwater management plan. 2.2.3.2 Obtain views from the communities in the implementation and the revision of the regional groundwater management plan
2.3 Protect equal water right to everybody.	2.3.1 Ensure the idea that water is a public property.	2.3.1.1 Give equal opportunity for every person to use groundwater.
2.4 Regulate the industrial use of groundwater (bottling)	2.4.1 Introduce legislation on the use of groundwater for bottling.	2.4.1.1 Monitor the bottling process.

Surface Water Policy

Policy element	Strategy	Actions
3.1 Improve drainage facilities for flood management.	3.1.1 Assess the rainfall in different parts of the country.	3.1.1.1 Calculate the quantity of water flow with respect to rainfall. 3.1.1.2 Predict the dimensions of the drainage system based on the quantity of water.
	3.1.2 Survey the drainage system	3.1.2.1 Assess the capacity of the drainage system to hold the quantity of water.
3.2 Prevent the pollution of surface waters.	3.2.1 Strictly enforce the environmental laws/standards for the discharge of effluent into public waters.	3.2.1.1 Conduct regular monitoring of the water quality of the surface water bodies. 3.2.1.2 Ensure that all industrial effluents conform to standard prior to the discharge.
	3.2.2 Introduce rules and regulations for domestic waste waters	3.2.2.1 Ensure that no domestic waste water is discharged directly into surface water bodies. 3.2.2.2 Prevent water pollution with human waste including faecal matters.
	3.2.3 Impose regulations on the solid waste disposal	3.2.3.1 Introduce sanitary land fillings to prevent dumping of solid waste.
3.3 Encourage the reuse of water especially by industries.	3.3.1 Apply science and technology in the reuse of water.	3.3.1.1 Develop quick methods check the quality of to be reused. 3.3.1.2 Introduce incentives (e.g. tax benefits) for those industries which reuse water.
3.4 Encourage the harvesting of rain water.	3.4.1 Promote rain water harvesting in rural as well urban/sub-urban areas	3.4.1.1 Create awareness and educate the general public on rainwater harvesting. 3.4.1.2 Promote the development devices and appropriate technology on rainwater harvesting



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- (ii) Registering a Patent or
- (iii) where the contribution has already resulted in a positive impact in the development and innovation in the industry.

Dr. C L De Silva Gold Medal Award 2015



Professor Priyani Paranagama

Professor Priyani Paranagama is the Chair of Chemistry and a Senior Professor in the Department of Chemistry, University of Kelaniya and a Visiting Lecturer of the Institute of Chemistry at present. She has been teaching Organic Chemistry and Biochemistry to undergraduate and postgraduate students for the past 24 years. She obtained her BSc and MPhil degrees in Chemistry from University of Kelaniya. She received her PhD degree in Chemistry from the University of Glasgow, UK and continued Post-Doctoral studies at University of Arizona, USA. She is also involved in conducting research on biopesticides, isolation and identification of bioactive compounds from plants and fungi in addition to her teaching and other commitments.

She is the author of over 40 peer-reviewed national and international publications and over 71 conference papers. She has been the supervisor of over 14 successful postgraduate degrees. She has also authored and edited about 7 books and monographs related to organic chemistry.

Her work has won many national and international awards; Professor M U S Sultanbawa Memorial Oration Gold Medal Award – 2008, Presidential awards, 2009 & 2008, Merit award from National Research council, 2014, Merit certificate for Scientific Research at Young Scientists Forum – 2007, National Science and Technology Commission, Ministry of Science and Technology. She was selected as one of the best 10 scientists by the Third World Academy of Science, Italy in 2003. The results of her research led to obtain a number of patents and she is a recipient of local and international research grants from funding agencies; National Research Council (2015, 2008 and 2001), National Science Foundation (2008, 2003, 2000 and 1997), International Foundation of Science, Sweden (2003), Third World Academy of Science, Italy (2001 and 1998), Council for Agriculture Research Policy (CARP) (2000), University of Kelaniya (2014, 2008 and 1997) and Institute of Chemistry Ceylon (2014 and 2015).

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Exploring Endolichenic Fungi in Sri Lanka as a Potential Treasure Trove for Bioactive Small Molecules; A Journey through the Fascinating World of Endolichenic Fungi

Professor P A Paranagama

Chair of Chemistry and Senior Professor, Department of Chemistry, University of Kelaniya

The demand for new and safe bioactive compounds from natural resources is increasing due to emergence of new diseases, development of drug resistant to pathogenic bacteria and development of toxic viruses etc. (Newman & Cragg, 2010). This situation has forced researchers to explore new natural sources with potent novel bioactive compounds as they continue to deliver a great variety of structural templates for drug discovery and encounter the challenges of the twenty first century. Fungi are an

important resource of novel natural bioactive compounds with their potential applications in agriculture, pharmaceutical industry and food industry. The first milestone in the field of drug innovation research from fungi was started with the discovery of penicillin, the first natural antibiotic discovered from a fungus, *Penicillium notatum* (Fleming, 1929). Thereafter, exploration of microbial diversity has been encouraged by the fact that microbes are essential for sustainable development of bioactive compounds.

Importance in the discovery of new bioactive compounds from fungi has greater attention than that of plants by the fact that fungi can be grown using fermentation methods or solid cultures and need insignificant amount of raw material indicating it does not affect the biodiversity of the country. Since over 60 % of the approved drugs available in the market are of natural origin, there is a great demand for bioactive secondary metabolites isolated from fungi with unique structural diversity in order to strengthen the drug discovery programs (Dias, *et al.*, 2012). Examples for isolation of biologically active molecules from fungal extracts with anticancer, antifungal and antibacterial activities are monocillin, radicicole and curvularin (Paranagama *et al.*, 2007a). Subsequently, there is a growing interest to identify new fungal species and isolate their secondary metabolites in order to obtain naturally occurring structurally diverse new bioactive compounds.

Discovery of endolichenic fungi (ELF), microorganisms asymptotically live in lichen thalli are one of the largest unexplored reservoirs forming a warehouse of natural bioactive compounds on the earth (Arnold, *et al.*, 2007, Arnold & Lutzoni, 2007, Miadikowska *et al.*, 2004 and Li *et al.*, 2007). The host ELF relationship is believed to be complex and different from the fungi that form symbiotic association with algae / cyanobacteria in lichens. The diversity and prevalence of ELF have not been reported in Sri Lanka. Until 2007, there was no report on isolation of bioactive compounds from ELF. The first global report on isolation of secondary metabolites from an endolichenic fungus was initiated in USA and published by Paranagama *et al.* (2007a). It was reported that the EtOAc extract of an endolichenic fungus, *Corynespora* sp. isolated from the lichen *Usnea cavernosa*, exhibited significant cell migration inhibitory activity and two new heptaketides, corynesporol and 1-hydroxydehydroherbarin along with herbarin were isolated (Paranagama *et al.*, 2007a). Thereafter, search for new bioactive compounds from ELF was continued and two leading research groups from USA and China had conducted their research on bioactive compounds in ELF and reported several publications on new bioactive compounds isolated from ELF (Wijeratne, *et al.*, 2012, Wu *et al.*, 2011, Wang, *et al.*, 2013, Zhang, *et al.*, 2012).

In Sri Lanka, a new research program on searching bioactive compounds from ELF was initiated by myself at the Department of Chemistry, University of Kelaniya

in 2009. Sri Lankan forests contain higher diversities of many varieties of lichen species such as fruticose, foliose and crustose. *Usnea* sp., *Parmotrema* sp and *Pseudocypellaria* sp. are some of the dominant lichen species in the lower elevation (1750 m) of Knuckles forest and Hakgala botanical garden in Sri Lanka were used in the present study to isolate ELF. The lichens were processed according to the method described by Paranagama, *et al.*, (2007) and endolichenic fungi (ELF) growing from each lichen particle were isolated into pure cultures. The endolichenic fungus, *Chrysosporium* sp. 2 was common to all three lichens and isolated at higher percentage frequencies of 21%, 19% and 13% respectively from *Usnea* sp., *Pseudocypellaria* sp. and *Parmotrema* sp. (Table 1).

Substrate utilization of endolichenic fungi;

Evaluation of substrate utilization potentials of the endolichenic fungi using cellulose, starch, pectin and lignin, revealed that all the fungal strains utilized starch (plate 1) except *Cladosporium* sp. and *Curvularia* sp. The cellulose utilization ability was demonstrated by *Phoma* sp., *Penicillium* sp. *Chrysosporium* sp. 1 and 2. *Chrysosporium* sp. 2. *Curvularia* sp. and *Penicillium* sp. showed the ability to produce both polygalacturonase and pectate lyase enzymes. *Broomella* sp., and *Nigrospora* sp. (plate 2) produced the enzyme, polygalacturonase whereas *Cladosporium* sp., *Chrysosporium* sp.1 and *Phoma* sp. were able to produce pectate lyase enzyme. Only *Broomella* sp. showed the ability to produce all the lignases (Table 2, plates 3, 4, 5).

Antifungal activities

The growth of *Fusarium* sp. was inhibited by *Cladosporium* sp., whereas *Nigrospora* sp. inhibited the colony growth of *Botrytis* sp. (plate 6) and *Colletotrichum* sp. *Chrysosporium* sp. 1 and sp. 2 were able to inhibit the colony growth of *Colletotrichum* sp. Similarly *Chrysosporium* sp. 1 was also able to inhibit the colony growth of *Fusarium* sp. (Table 3).

The results were published in journal of applied microbiology in 2009 as the first publication on investigation on endolichenic fungi in Sri Lanka (Kannangara *et al.*, 2009).

contd. 21

Table 1: Mean percentage frequency of occurrence of the endolichenic fungi isolated from *Usnea* sp., *Pseudocyphellaria* sp. and *Parmotrema* sp.

Fungal strains	%frequency of occurrence		
	<i>Pseudocyphellaria</i> sp.	<i>Parmotrema</i> sp.	<i>Usnea</i> sp.
<i>Curvularia</i> sp.	14	-	10
<i>Fusarium</i> sp.	-	-	5
<i>Nigrospora</i> sp.	-	-	11
<i>Cladosporium</i> sp.	11	18	8
<i>Chrysosporium</i> sp. 1		20	10
<i>Chrysosporium</i> sp. 2	19	13	21
<i>Phoma</i> sp.	11	-	-
<i>Penicillium</i> sp.	16	-	-
<i>Aspergillus</i> sp. 1	5	-	-
<i>Aspergillus</i> sp. 2	6	-	-
<i>Broomella</i> sp.	-	18	-
<i>Acremonium</i> sp.	-	10	-
<i>Periconia</i> sp.	-	5	-
Sterile sp. 1	-	-	6
Sterile sp. 2	-	-	6
Sterile sp. 3	-	-	11
Sterile sp. 4	-	-	4
Sterile sp. 5	-	-	5
Sterile sp. 6	-	7	-
Sterile sp. 7	-	11	-
Sterile sp. 8	5	-	-
Sterile sp. 9	6	-	-
Sterile sp. 10	3	-	-

Table 2.: Substrate utilization patterns of frequently isolated endolichenic fungi from *Pseudocyphellaria* sp., *Parmotrema* sp. and *Usnea* sp.

Fungal species	Cellulose	Starch	Pectin		Lignin		
			Polygalac turanase	Pectate Lyase	L	P	T
<i>Broomella</i> sp.	-	+	+	-	+	+	+
<i>Cladosporium</i> sp.	-	-	-	+	-	-	-
<i>Chrysosporium</i> sp. 1	+	+	-	+	-	-	-
<i>Chrysosporium</i> sp. 2	+	+	+	+	-	-	-
<i>Curvularia</i> sp.	-	-	+	+	-	-	-
<i>Nigrospora</i> sp.	-	+	+	-	-	+	-
<i>Penicillium</i> sp.	+	+	+	+	-	+	+
<i>Phoma</i> sp.	+	+	-	+	-	+	-

Number of replicates = 03
+ = able to show activities

L = Laccase P = Peroxidase
- = not able to show activities

T = Tyrosinase

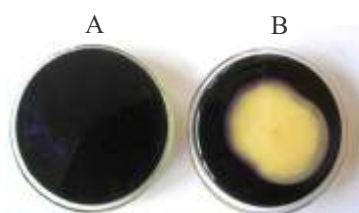


Plate 1 : Starch utilization
A: Control
B: Plate with the test fungi, *Broomella* sp.



Plate 2: Pectin utilization
A: Control
B: Plate with the test fungi, *Nigrospora* sp.

Table 3: Antifungal activities of frequently isolated endolichenic fungal species on the growth of selected plant fungal pathogens

Test fungi	Pathogenic fungi				
	<i>Sclerotium</i> sp.	<i>Colletotrichum</i> sp.	<i>Botrytis</i> sp.	<i>Pestalotiopsis</i> sp.	<i>Fusarium</i> sp.
<i>Broomella</i> sp.	-	-	-	-	-
<i>Cladosporium</i> sp.	-	-	-	-	+
<i>Chrysosporium</i> sp.1	-	+	-	-	+
<i>Chrysosporium</i> sp. 2	-	+	-	-	-
<i>Curvularia</i> sp.	-	-	-	-	-
<i>Nigrospora</i> sp.	-	+	+	-	-
<i>Penicillium</i> sp.	-	-	-	-	-
<i>Phoma</i> sp.	-	-	-	-	-

Number of replicates = 03

+ = able to show antifungal activities

- = not able to show antifungal activities

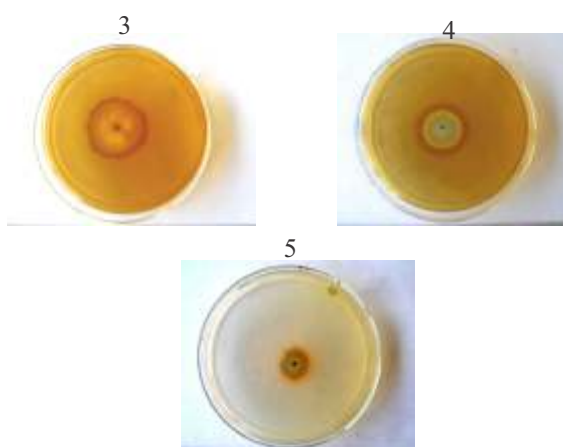


Plate 3: Development of violet colour indicates the production of laccase by *Broomella* sp.

Plate 4: Development of yellowish brown colour indicates the production of peroxidase by *Nigrospora* sp.

Plate 5: Development of orange brown colour indicates the production of tyrosinase by *Penicillium* sp.



Plate 6: Inhibition of the growth of *Botrytis* sp. (B) by *Nigrospora* sp. (A)

Bioactive compounds in the endolichenic fungi

The EtOAc extracts of selected endolichenic fungi exhibited antifungal activity against *Colitrotricum*

musae, a pathogenic fungus that causes anthracnose disease in banana and extracts of *C. trifoli* and *Chrysosporium* sp.1 on PDA showed the highest inhibitory effect. (Figure 1).

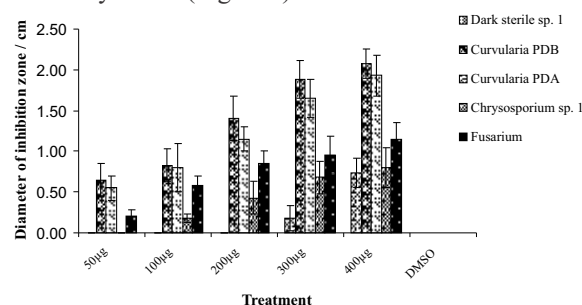


Figure 1: Antifungal activity of secondary metabolites extracted from the endolichenic fungi against *C. musae*

The results of insecticidal, anti-inflammatory, anticancer and antioxidant bioassays revealed that the crude EtOAc extract of *C. trifolii* showed a strong inhibitory activity. Therefore the EtOAc extract of *C. trifolii* was further purified using bioassay guided fractionation and led to isolation of **two new polyketides** (PP-CT-01 and PP-CT-02). PP-CT-01 was the major compound present in the EtOAc extract of *C. trifolii*. In the insecticidal assay, 100% mortality of *Callosobruchus maculatus*, a stored grain pest in cowpea was observed at the dose of 50 µg of PP-CT-01 and MIC and MLC values of PP-CT-01 were 20 µg and 40 µg against *Colletotrichum musae* respectively. The new compounds, PP-CT-01 and PP-CT-02 showed radical scavenging activity with IC₅₀ values of 4.0±2.6 mg/mL and 1.3±0.2 mg/mL respectively in DPPH

antioxidant assay and antioxidant activity of the compound PP-CT-02 was comparable to the standard antioxidant compound, BHT. Moreover, the new compounds, PP-CT-01 and PP-CT-02 were evaluated for their anti-inflammatory activity and PP-CT-02 exhibited significant activity comparable to the standard anti-inflammatory drug, Aspirin. The compound PP-CT-01 was evaluated for inhibition of cell proliferation in a panel of five cancer cell lines, NCI-H460, MCF-7, SF-268, PC-3M, and MIA Pa Ca-2 and exhibited >90% inhibitory activity at 5 $\mu\text{g/mL}$ with all the above cell lines. The structures of the new compounds were determined on the basis of their 1D NMR, 2D NMR and FABMS spectroscopic data (Figures 2 & 3).

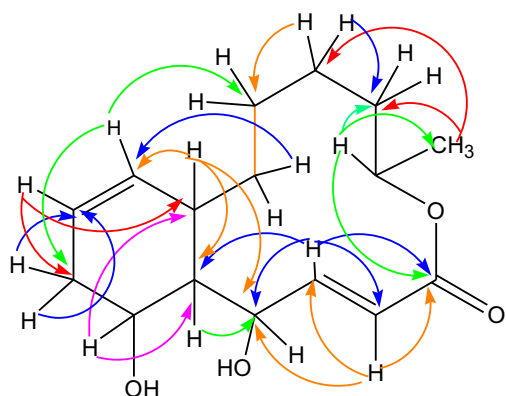
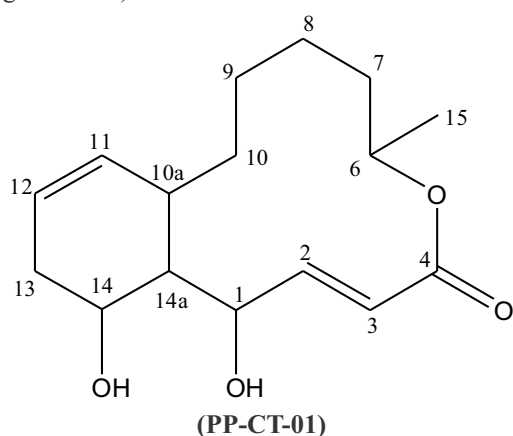


Figure 2. Selected HMBC correlations for (PP-CT-01)

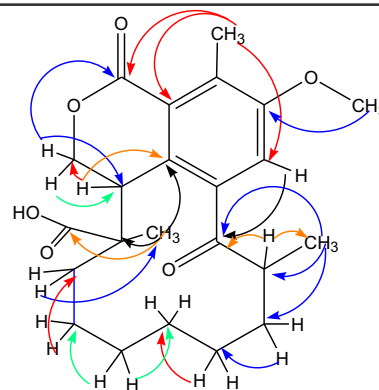
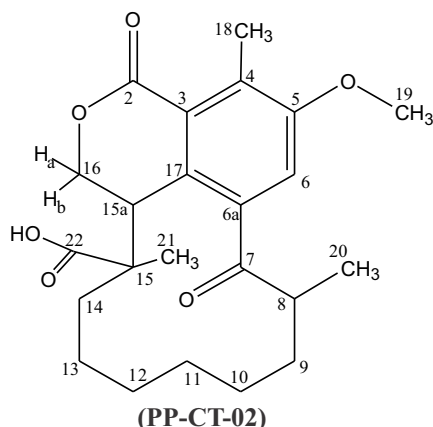


Figure 3. Selected HMBC correlations for PP-CT-02

Isolation and identification of bioactive compounds in *Penicillium citrinum*

Penicillium citrinum was isolated from *Pamotrema sp.* and grown in large scale. The results of the antioxidant assay of hexane (US/01/11/03), CHCl_3 (US/01/11/02) and 50% MeOH (US/01/11/03) fractions obtained after partitioned with the EtOAc extract revealed that the CHCl_3 fraction had the highest activity (figure 4). Bioassay-guided fractionation of the antioxidant active CHCl_3 fraction was purified sequentially with normal-phase, gel permeation column chromatography and preparative TLC, furnished two pure compounds PP-PC-01 and PP-PC-02 (figures 5 and 6). Compounds PP-PC-01 and PP-PC-02 were isolated as white amorphous solids determined to have the molecular formulas $\text{C}_{18}\text{H}_{16}\text{O}_7$, $\text{C}_{18}\text{H}_{18}\text{O}_7$ and $\text{C}_{19}\text{H}_{16}\text{O}_7$, respectively and the structures of three new compounds, PP-PC-01 and PP-PC-02 were fully established by a combination of FABMS and NMR data with 11 and 10 degrees of unsaturation respectively.

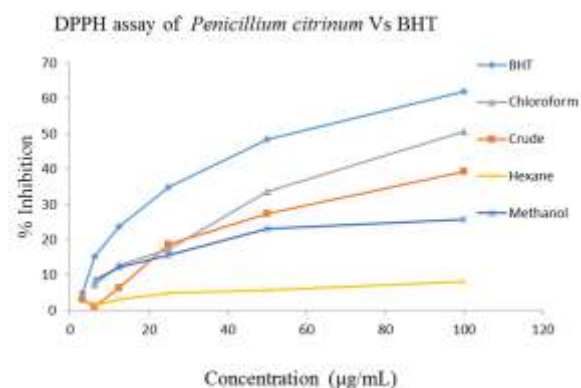


Figure 4. Antioxidant activity of the hexane, CHCl_3 and aq.MeOH fractions of EtOAc extract of *P. citrinum* against standard synthetic antioxidant BHT

PP-PC-02 and PP-PC-03 showed moderate antioxidant activities with IC_{50} values 159.6 ± 22.3

$\mu\text{g/mL}$ and $120.1 \pm 11.7 \mu\text{g/mL}$ (Figure 7) and PP-PC-01 showed strong radical scavenging activity in the DPPH assay with IC_{50} value of $68.6 \pm 4.3 \mu\text{g/mL}$ (Figure 7).

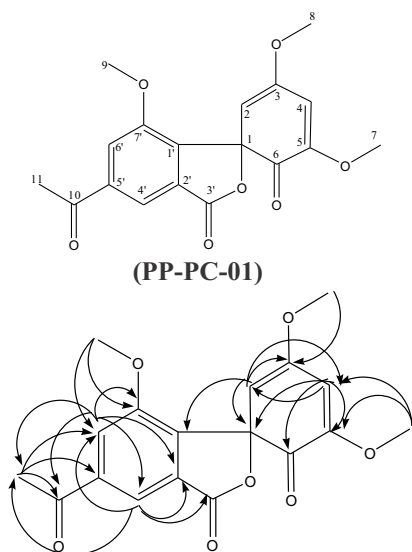


Figure 5. Structure and selected HMBC correlations for PP-PC-01

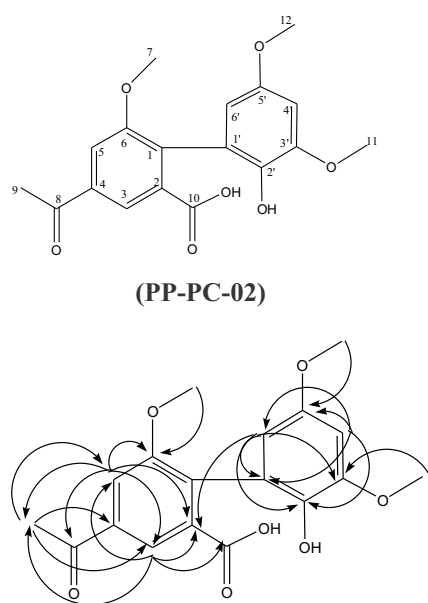


Figure 6. Selected HMBC correlations of PP-PC-02

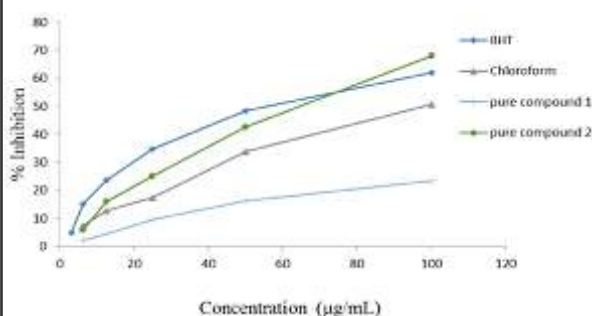
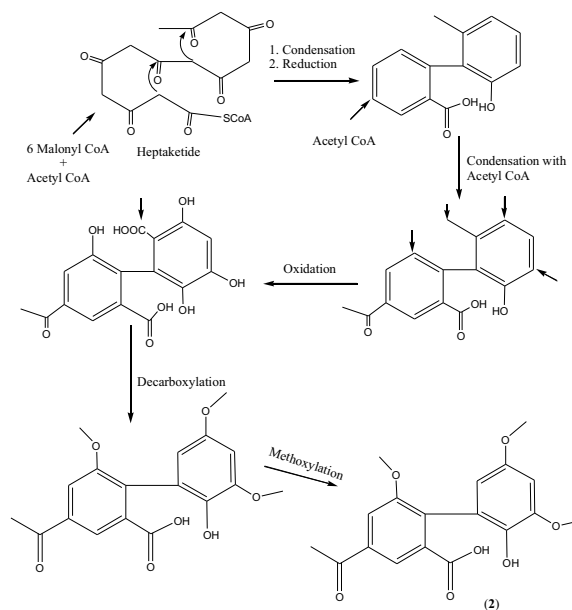


Figure 7. The DPPH radical scavenging activity of the chloroform fraction, and the pure compounds (PP-PC-01, PP-PC-02 and PP-PC-03) isolated from the

chloroform extract of *P. citrinum* compared with the positive control, BHT. Each value is expressed as mean $\pm$ SD (n=3)

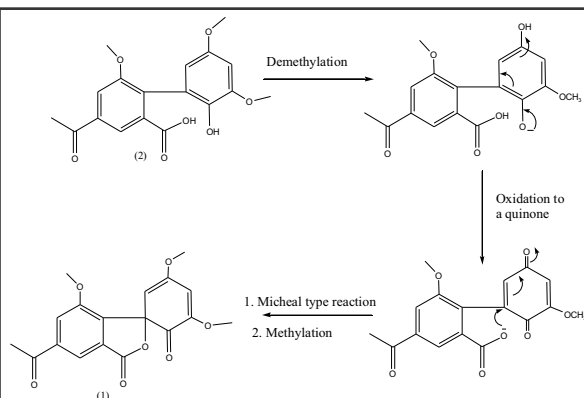
A plausible biosynthetic pathway for two new polyketides (PP-PC-01 and PP-PC-02) is proposed in Scheme 1 and 2. The compound, PP-PC-01 contains a similar carbon skeleton as PP-PC-02 except for the absence of the carboxylic acid group attached to C-2. From the structural features of PP-PC-01 and PP-PC-02, it implies that both compounds have the same polyketide origin and the biosynthetic pathway proposed in scheme 1 suggesting that PP-PC-02 is the precursor for PP-PC-01. The proposed biosynthetic pathway given in scheme 1 indicates that PP-PC-02 originated from a heptaketide via condensation, reduction, oxidation, carboxylation and other reactions to form the final polyketide product 2. Compound 2 is the precursor for compound PP-PC-01 as PP-PC-02 could undergo oxidation to a quinone to which the carboxylate group can add in a Michael-type reaction as proposed in the scheme 2.



Scheme 1: Postulated biosynthetic pathway of 2

Antioxidant, antibacterial and anti-inflammatory activities of *Daldinia eschscholzii*, *Aspergillus fumigatus* and *Daldinia cf. loculatooides* extracts

The antioxidant bioassays revealed that the crude extract of *D. eschscholzii* has significantly high antioxidant activity with DPPH, ABTS, and FRAP assays (figures 8 – 10) and high anti-inflammatory activity with NO scavenging activity (figure 11).



Scheme 2. Postulated biosynthetic pathway of 1

The crude extract of *D. eschscholzii* was partitioned with hexane, chloroform and aqueous methanol. Each fraction was then subjected to the HRBC membrane stabilizing method. The results revealed that the chloroform fraction (IC_{50} - 0.086 ± 0.007 mg/mL) possess a significantly high anti-inflammatory activity when compared with the standard, Aspirin (IC_{50} - 0.117 ± 0.007 mg/mL). Therefore the chloroform fraction was subjected to bioassay guided fractionation in order to obtain active pure compounds (figure 12).

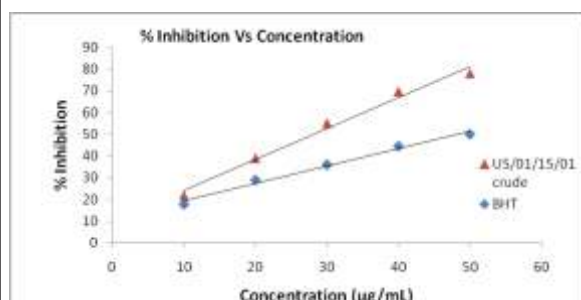


Figure 8. Antioxidant activity of crude extract of *Daldinia eschscholzii* compared to standard (BHT) as determined with the DPPH free radical scavenging (DPPH) assay.

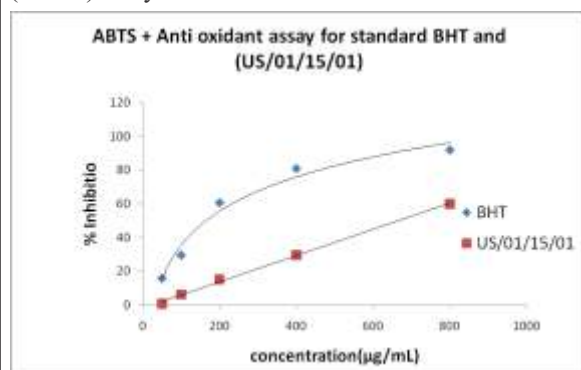


Figure 9. Antioxidant activity of ethyl acetate extract of *Daldinia eschscholzii* compared to standard (BHT) as determined with the ABTS assay.

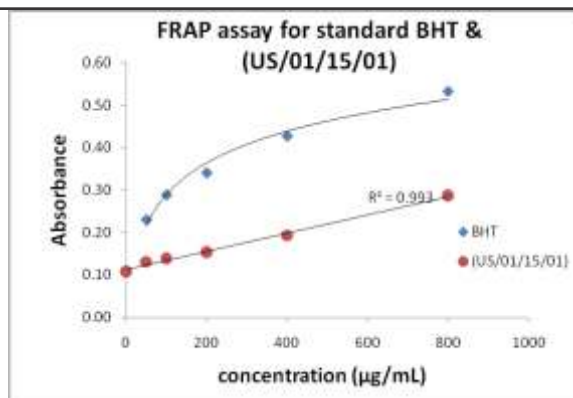


Figure 10. Antioxidant activity of ethyl acetate extract of *Daldinia eschscholzii* compared to standard (BHT) as determined with the Ferric Reducing Antioxidant Power (FRAP) assay

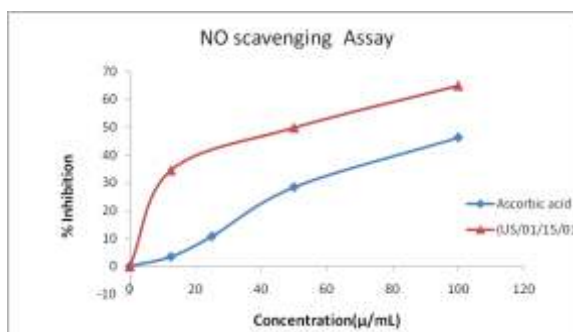


Figure 11. Anti-inflammatory activity of ethyl acetate extract of *Daldinia Eschscholzii* compared to standard Ascorbic acid determined with the NO radical scavenging assay.

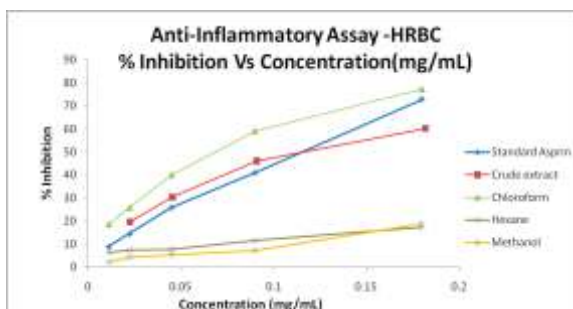


Figure 12. Anti-inflammatory activity of ethyl acetate extract of *Daldinia eschscholzii* compared to standard drug, Aspirin in Human Red Blood Cell Membrane Stability test.

The three fractions, hexane, chloroform and aqueous methanol obtained from crude ethyl acetate extract of *Aspergillus fumigatus* were evaluated for radical scavenging activity reducing power ability and the results showed that methanol and chloroform fractions of *A. fumigatus* were active against DPPH and FRAP assays (figures 13 & 14). These active fractions will be further analysed to isolate bioactive compounds.

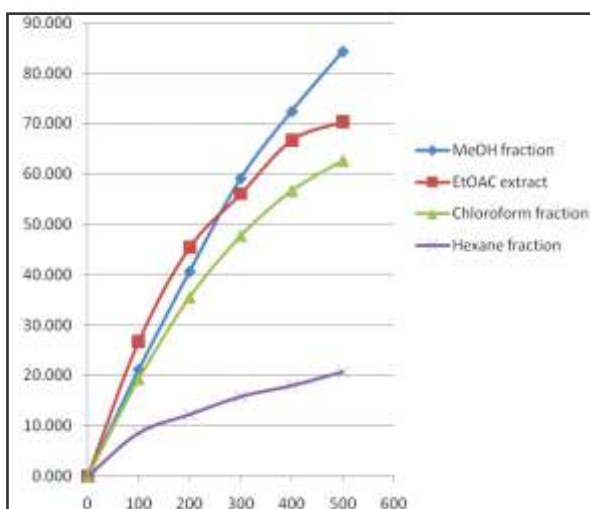


Figure 13. DPPH antioxidant activity of fractions of *Aspergillus fumigatus*

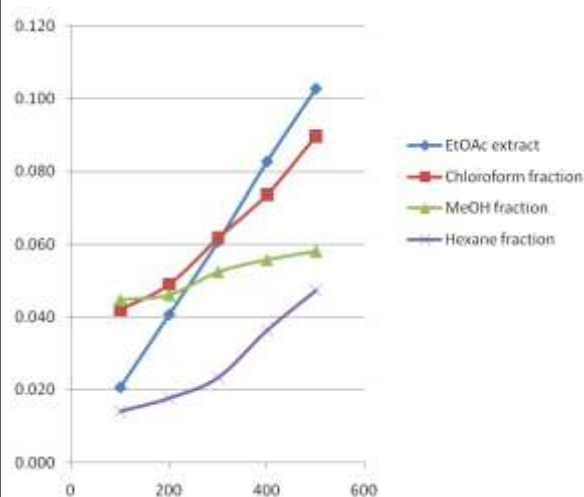


Figure 14. FRAP antioxidant activity of fractions of *Aspergillus fumigatus*

Antioxidant activity of EtOAc extract of *D. cf. localatoides* was determined by DPPH radical scavenging assay. The CHCl_3 fraction obtained after partitioned of the crude extract of *D. cf. localatoides* has the highest antioxidant activity with DPPH assay and both CHCl_3 and aqueous MeOH fractions showed the antibacterial activity against *Staphylococcus aureus* (figures 15, 16 & 17).

Bioassay-guided fractionation of the bioactive CHCl_3 fraction with normal-phase and gel permeation column chromatography and preparative TLC, furnished three pure compounds PP/01/39/04, PP/01/47/01 and PP/01/46/02. Structure elucidation of the pure compounds are in progress

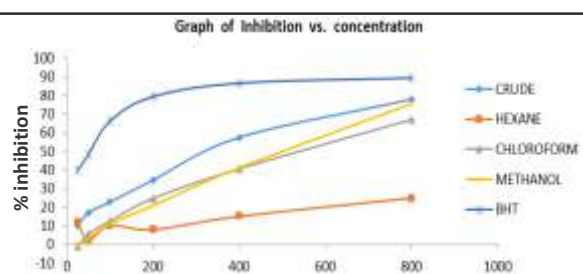


Figure 15. The DPPH radical scavenging activity of crude extract of *D. cf. localatoides* and hexane, chloroform, methanol fractions compared with the positive control, BHT. Each values is expresses as mean $\pm$ SD (n=3)

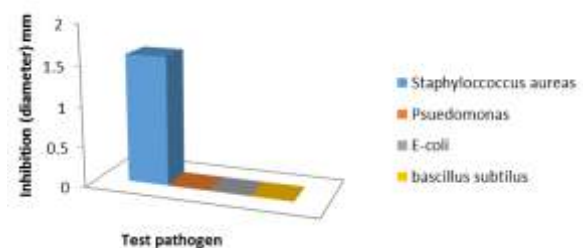


Figure 16. The antibacterial activity of crude extract of *D. localatoides* against four test pathogens compared with the positive control, Aspirin. Each value is expressed as mean $\pm$ SD (n=3)

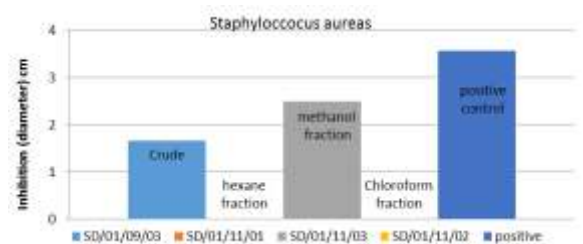


Figure 17. The antibacterial activity of crude extract of *D. localatoides*, hexane, chloroform and aq. methanol fractions against *Staphylococcus aureus* compared with the positive control, Aspirin. Each value is expressed as mean $\pm$ SD (n=3)

In the present study, it was confirmed that endolichenic fungi continue to provide a diverse and unique source of bioactive compounds which can be used for drug discovery programs. Moreover, the young researchers, postgraduate and undergraduate students who were trained on isolation and identification of endolichenic fungi and analytical techniques involved in the field of natural product chemistry to isolate bioactive compounds. Therefore this research program made a significant contribution to human resource development of the country and thereby provide an impetus to the study of bioactive compounds in endolichenic fungi in Sri Lanka. Further,

advances in this field was helped to strengthen the multi-institutional collaboration and pharmaceutical industry contributing to national economic development of the country.

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List of Publications and communications resulted from the above research program on bioactive compounds from ELF are given below

1. Samanthi, K. A. U., Wickramaarachchi, S., Wijeratne, E. M. K., Paranagama, P. A. (2015) Two New Bioactive poliketides from *Curvularia trifolii*, an endolichenic fungus isolated from *Usnea* sp., in Sri Lanka, *Journal of the National Science Foundation*, 43(3), 217-224.

2. Samanthi, K.A.U., Wickramaarachchi, S., Wijeratne, E. M. K., Paranagama, P. A (2015) Two New bioactive polyketides from *Penicillium citrinum*, endolichenic fungus isolated from *Parmotrema* sp., in Sri Lanka, *Journal of the National Science Foundation*, 43(2), 119-126.
3. Kannangara, B. T. S. D. P., Rajapaksha, R. S. C. G. and Paranagama, P.A. (2009) Nature and bioactivities of endolichenic fungi in *Pseudocypellaria* sp., *Parmotrema* sp., and *Usnea* sp. at Hakgala montane forest in Sri Lanka, *Journal of Letters in Applied Microbiology*, 48, 203-209.
4. Devpura, S.N., Samanthi, U , Paranagama, P A, (2014) *Proceedings of the 70th annual sessions of Sri Lanka Association for the Advancement of Science*, Sri Lanka, 1 – 5 December, 66.
5. Samanthi, K. A. U., Wickramaarachchi, S., Wijeratne, E. M. K., Paranagama, P. A. (2014) *In vitro* anti-inflammatory activity of organic extracts of endolichenic fungus, *Daldiniaeschscholzii*, occurring in lichen, *Parmotrema* sp. in Sri Lanka, *Proceedings of International Conference on Chemical Education and Research*, Institute of Chemistry Ceylon, Adamantane House, Rajagiriyi, Sri Lanka, 3-4 April, 109.
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Chandrasena Memorial Award

Awarded for an exceptional research contribution of an original nature in the field of Organic Chemistry and/or related areas such as Biochemistry, Pharmacognosy, Molecular Biology and Bioactivity studies.

Chandrasena Memorial Award 2015



Dr. Vinitha M Thadhani

Dr. Vinitha M Thadhani obtained her BSc (Chemistry - second class upper) and MPhil from the University of Sri Jayewardenepura, and PhD from the University of Peradeniya. She was a lecturer at the University of Sri Jayewardenepura and a senior lecturer at the College of Chemical Sciences, Institute of Chemistry Ceylon. Currently she is working as a Senior Research Scientist at the Sri Lanka Institute of Nanotechnology (SLINTEC). Dr. Thadhani was awarded the “Chandrasena Memorial Award 2015” in recognition of her research on “Lichens as a Treasure Chest of Bioactive Metabolites”.

Lichens as a Treasure Chest of Bioactive Metabolites

Dr. Vinitha Thadani

Senior Research Scientist, Sri Lanka Institute of Nanotechnology

The challenges for today's pharmaceutical industry lies in discovery and development of new pharmacologically active molecules. Natural products have been a rich source of compounds for drug discovery. Lichens represent taxonomically and physiologically a very diverse group as it consists of a symbiotic association between members of three different plant kingdoms (fungi, algae and / or cyanobacteria). Similar to higher plants lichens have been used since antiquity as medicines. Lichens are well known for their diversity of secondary metabolites, which are characteristic and unique compounds restricted to the lichenized state and are not found in higher plants. The medicinal utility of lichens is ascribed to the presence of these secondary compounds. The commonest among them are the mononuclear aromatic compounds, depsides, depsidones, diphenyl ethers, and dibenzofurans. However these natural products have received scarce attention, with respect to its biological activities. During this study abundant lichen specific compounds were isolated, and subjected to numerous biological activities including antioxidant, α -glucosidase inhibitory, urease inhibitory, anti-microbial, immune modulatory & toxicological studies which has led to several publication and patents. Further studies on α -glucosidase inhibitors were carried using animal models. Saturation Transfer Difference, NMR spectroscopy was used to determine the actual binding epitopes with the active site of the urease enzyme.

This study also reveals the possibility of conversion of major lichen specific secondary metabolites into new compounds through biotransformation and semi-synthesis.

Semi-synthesis and biotransformation of lichen metabolites

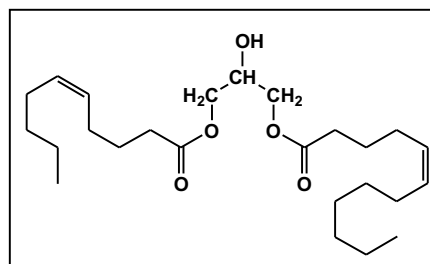
Secondary metabolites of lichens occur exclusively in these symbiotic organisms and only approximately 1050 lichen metabolites have been isolated to date. Most of the biochemical research on lichen concerns the discovery and study of new substances. However even with the advances of analytical methods, there is comparatively less isolation of new lichen metabolites may be due to the

limited biosynthetic pathways.

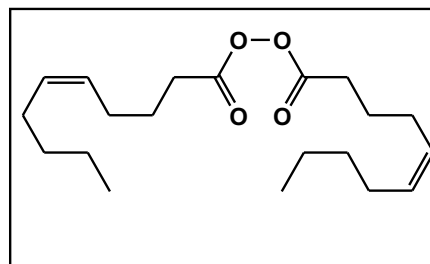
This study reveals the possibility of conversion of major lichen specific secondary metabolites into new compounds through biotransformation and semi-synthesis.

Erythrin isolated in 7.3% yield, gave a new diphenyl ether *via* Smiles rearrangement and subsequent novel decarboxylative oxidative cyclisation in the presence of Pd(OAc)₂, in three steps produced new 5-decarboxydibenzofurans in high yield (Thadhani et.al, 2010).

Biotransformation of zeorin isolated in 3.4% yield from the lichen *Cladonia sp.* through *Cunninghamella elegans* fungus, yielded 1,3-diacylglycerol and a diacylperoxidename 1-(5-dodecenoyl), 3-(5-decanoyl)glycerol (I) and 5-decenoic acid-1,1-diacylperoxide (II), respectively. *C. elegans* was grown in media containing 1 gm of zeorin for 14 days. The solution was extracted into ethyl acetate, and subjected to repeated silica column chromatography in gradient elution of hexane and acetone led to isolation of compounds (I) and (II). The 1-D and 2-D NMR data analysis and mass spectral analysis led to the following two structures.



Structure I



Structure II

To the best of our knowledge, this is the first report on formation of 1,3-diacylglycerol and a diacylperoxides through biotransformation from any

fungus. Neither of these compounds have been reported from a natural source.

Bioactivities of lichen metabolites

Antioxidant activities

Antioxidant activity of several classes of lichen metabolites were comprehensively assessed in the in vitro superoxide radical (SOR), nitric oxide radical and 2,2-diphenyl-1-picrylhydrazil (DPPH) radical scavenging assays. The depsidessekikaic acid and lecanoric acid showed promising antioxidant activity in SOR assay with IC_{50} values of 82.0 ± 0.3 mmol and 91.5 ± 2.1 mmol, respectively, while the depsidoneobaric acid exhibited an IC_{50} value of 97.9 ± 1.6 mmol, all relative to the standard, propyl gallate ($IC_{50} = 106.0 \pm 1.7$ mmol). One of the most abundant mononuclear phenolic compounds, methyl- β -orcinolcarboxylate was found to be a potent NO scavenger ($IC_{50} = 84.7 \pm 0.1$ mmol), compared to the standard rutin ($IC_{50} = 86.8 \pm 1.9$ mmol). (Thadhani et. al., 2011).

α -glucosidase inhibitory activity

Ubiquitous triterpenoid zeorin showed potent in-vitro α -glucosidase inhibitory activity with a IC_{50} value of 100.0 ± 0.3 μ M, which is seven times lower than that of acarbose, ($IC_{50} = 700.0 \pm 10.4$ μ M), a widely prescribed drug in the management of type II diabetes, and four fold more active compared to the potent α -glucosidase inhibitor, 1-deoxynojirimycin ($IC_{50} = 425.0 \pm 8.9$ μ M), which led to USA patent (Thadhani et. al., 2011).

In-vivo studies to determine the anti-diabetic studies of zeorin was performed using female wistar rats. Diabetes was induced by treating streptozotocin (45 mg/Kg of body weight). Diabetes status of animals were verified after the 7th day of injection. Rats with sugar levels > 250 mg/dL were considered as diabetic induced rats and used for further studies.

Grouping were done as follows with six animals per group. Group 1 - normal glycemic (80-130 mg/dL); Group 2 - Streptozotocin induced diabetic rats; Group 3 - Diabetic rats treated with standard acarbose (25 mg/kg); Group 4 & 5 - Treated with 50 & 100 mg/kg of zeorin respectively. Glucose level after treating with maltose (2 g/Kg) were measured at 0, 30, 60, 90 and 120 minutes. As illustrated in Figure 1, zeorin proved to be effective as anti-diabetic agent in *in-vivo* studies as well.

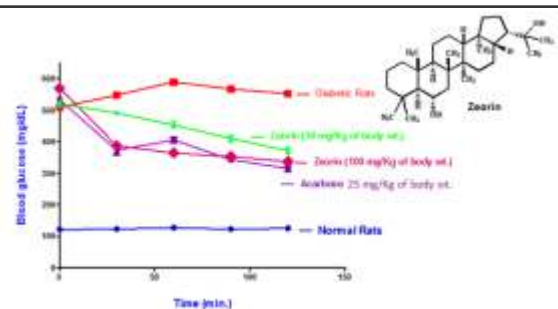


Figure 1: Reduction of blood glucose levels by zeorin with comparison to acarbose

Urease inhibitory activity

Urease (urea amidohydrolase) is a nickel containing enzyme that catalyzes the hydrolysis of urea into ammonia, and CO_2 . Production of NH_3 causes a significant increase in pH, and are responsible for negative effects of urease.

Activity of urease is not only considered as an important virulence determinant in the pathogenesis of many clinical conditions, but as a serious problem in agriculture practices. Application of urea in conjunction with urease inhibitors is an important technique used to mitigate the disadvantages associated with widespread increase of urea based fertilizers.

Medically the pH elevation, due to urease activity, directly leads to the formation of infectious stones and also plays an important role in the onset of gastric and peptic ulcers, which may lead to cancer. Targeting urease for treating pathogenic disorders, caused by urease-producing bacteria has been recognized as an approach towards the treatment for infections, caused by such bacteria. Indeed more effective and potent compounds are required with a high level of safety and specificity. We have reported the urease inhibitory activity of several phenolic lichen compounds (Thadhani V.M., 2007) (Figure 2 and 3).

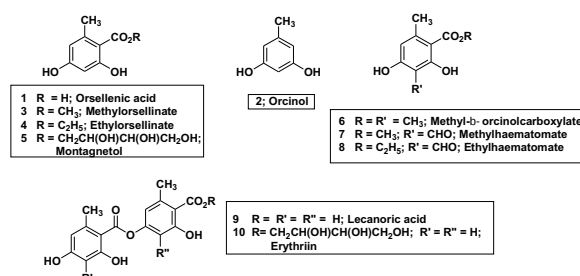


Figure 2: Polyketides subjected to Structure Activity Relationship studies for urease inhibitory activity

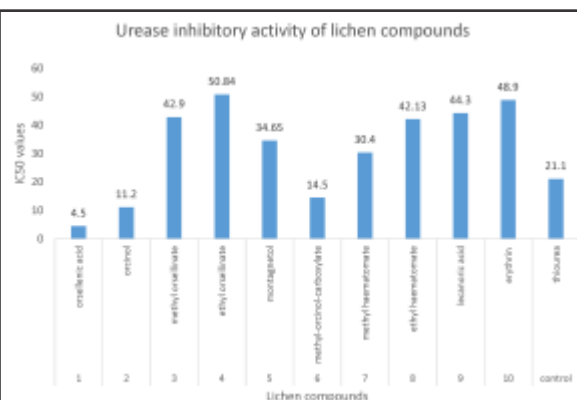


Figure 3: Comparison of IC₅₀ values of lichen compounds with standard thiourea

Saturation Transfer Difference- NMR studies of urease inhibitors

Followed by biochemical assay, the epitope mapping of compounds, which were active in urease inhibitory assay, was carried out to determine their interaction with the protein using STD-NMR spectroscopy (Thadhani et al., 2015).

During the current study, STD-NMR techniques were used for the identification of structural features responsible for inhibition of urease enzyme at the atomic levels. STD-NMR is a robust method for the study of the epitopes, responsible for their interaction with the receptor site. Due to the binding interactions between the urease enzyme and its inhibitors, the protons of the inhibitors which are in proximity to the active site of the urease enzyme, receive higher degree of radiofrequency saturation, which leads to strong signals in STD-NMR spectrum. This enhancement in signal intensity is a credible indication of affinity potential between small molecular ligands and receptor proteins.

In the given test conditions, compounds **1**, **3**, **4**, **6**, **8** and **10**, showed a significant STD effect, which indicated their interactions with the catalytic protein. A common binding mode was observed for these compounds in the STD-NMR study. All the protons and methyl groups on the aromatic ring experienced a saturation transfer from the protein, and therefore predicated to be in close contacts with the protein.

Simultaneously the compounds were also subjected to molecular docking studies using Jack bean urease to predict the interaction of these compounds with the enzyme.

The binding epitope study on orsellinic acid (**1**) with the highest urease inhibitory activity (IC₅₀ = 4.5 ± 0.14 μM) revealed that both aromatic

protons (H-3 and H-5) showed strong interactions with the enzyme. Similarly the C-8 methyl protons were interacting with the urease enzyme. The difference spectra showed enhanced signal of these protons (Figure-4).

The docked conformation of compound **1** showed the ligand co-ordinates with both Ni atoms. Both carboxylate oxygens co-ordinate with Ni 842, whereas Ni 841 co-ordinates with one of the carboxylated oxygen. The strong interaction of these carboxylated oxygen with both Ni atoms could be attributed to the strongest urease inhibitory activity of orsellinic acid (**1**) in the series. In addition, the C-2 phenolic OH, interact with the Arg (609) and Gly (550) residues of the active sites through hydrogen bonding (Figure-4).

Esterification of the free carboxylic of orsellinic acid (**1**) as in methylorsellinate (**3**) and ethylorsellinate (**4**) decreased the activity about tenfold. STD Difference NMR spectra showed that due to esterification it did not fit into the active site of enzyme, as inferred from the STD-NMR spectra both aromatic hydrogens showed very weak peaks. Molecular docking studies revealed that it binds to one Ni center, rather than two Ni centres as in case of orsellinic acid (**1**). Thus, this indepth

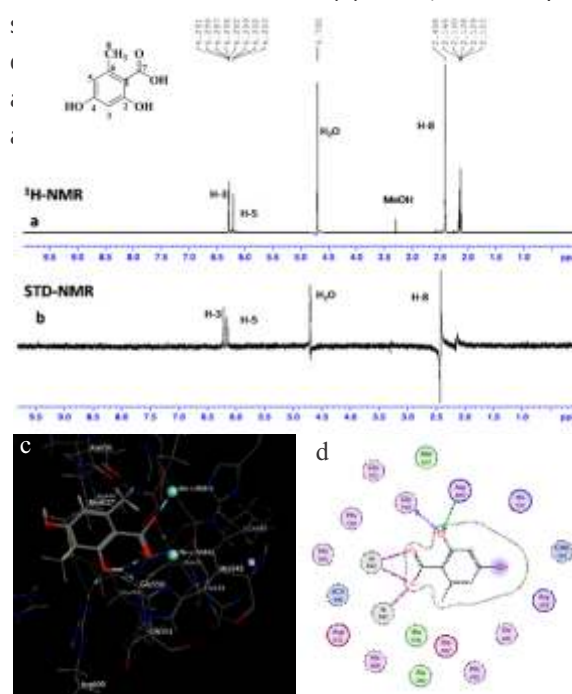


Figure-4: (a) ¹H-NMR Spectrum of compound **1**. (b) The STD-NMR spectrum of urease in the presence of

compound **1**. Both (a) and (b) were carried out at 298 K on Bruker 600 MHz NMR spectrometer equipped with cryogenic probe. (c) and (d) Modes of interaction of compound **1** with the active site of jack bean urease.

Antimicrobial & toxicological activities

Natural products have provided the starting points for most of the major classes of antibiotics. Since 2000, 22 new antibiotics have been launched for treating infections in humans, and 56 antibiotics are undergoing clinical trials in 2013. Still there is a pressing need for new and better anti-infectives. Unfortunately lichens which demonstrate exceptional metabolic adaptability and thrive in even the most extreme environmental conditions, remains scarcely explored for its anti-infective properties.

During the current studies the antimicrobial activity of some common depsides, were tested against six human and plant pathogenic bacteria and six fungal species (*with respect to standards*) to evaluate their medical efficacy as pharmacophores. In addition, toxicological studies of lichen metabolites were carried out using brine shrimp cytotoxicity assay.

The depsides ekikaic acid and the depsidone lobaric acid showed potent activity against *Escherichia coli*, *Bacillus subtilis* and *Salmonella typhi* compared to the standard imipenem. Although the depsides atranorin, lecanoric acid and erythrin showed insignificant antimicrobial activity, their hydrolytic products such as methyl orsellinate and methyl- β -orcinolcarboxylate showed significant antifungal activity (Thadhani *et al.*, 2012). The study signifies the importance of lichens as a good source of anti-infective agents.

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Kandiah Memorial Awards

Awarded for the best research contribution in Chemistry carried out by a postgraduate student registered for a postgraduate degree by either course work or/ and research at a Higher Educational Institute in Sri Lanka and for work carried out in Sri Lanka, with the exception of special analysis that cannot be done in the country. Such results should be less than 20% of the findings from the work. Sandwich programs carried out partially abroad do not qualify for the award.

Kandiah Award for Basic Chemistry: For research predominately in basic Chemistry (Organic, Inorganic, Physical, and Analytical).

Kandiah Award for Applied Chemistry: For research in Chemistry related areas such as polymer, food, biochemistry, biotechnology, where interdisciplinary research is involved and provided that chemistry has a central role and comprises at least 50% of the content.

Kandiah Memorial Graduateship Award: For the best piece of research in the Chemical Sciences carried out by a Graduate Chemist of the College of Chemical Sciences/Institute Chemistry Ceylon registered with a Higher Education Institute for a Post Graduate Degree.

Kandiah Memorial Graduateship Award 2015



Mr. S C Dilanka Fernando

Mr. S C Dilanka Fernando, a Graduate Chemist has been awarded the “Kandiah Memorial Graduateship Award - 2015” in recognition of his research on “Time course variation of nutraceuticals and antioxidant activity during steeping of CTC black tea (*Camellia sinensis* L.) manufactured in Sri Lanka”.

Mr. S C Dilanka Fernando obtained Graduateship in Chemistry in 2010 with a First Class Honours. He obtained his Master's degree in Biochemistry & Molecular Biology from the Faculty of Medicine, University of Colombo. His research work was focused on the area of pharmacognosy and bio-activity studies of various plant based medicaments under the supervision of Prof. S S S B D Preethi Soysa. He is a Corporate Member of the Institute of Chemistry Ceylon and an Associate Member of the Royal Society of Chemistry, UK. Currently, he works as a Senior Teaching Assistant at the College of Chemical Sciences, Institute of Chemistry Ceylon.

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Time Course Variation of Nutraceuticals and Antioxidant Activity during Steeping of CTC Black Tea (*Camellia sinensis* L.) Manufactured in Sri Lanka

Chamira Dilanka Fernando and Preethi Soysa

Department of Biochemistry & Molecular Biology, Faculty of Medicine, University of Colombo, Colombo 08

1. Introduction:

Oxidation is an essential biological process for energy production reactions in living organisms. However, excessive *in vivo* production of reactive oxygen species (ROS) leads to lipid peroxidation and development of a variety of physiological conditions such as cellular aging, mutagenesis, carcinogenesis, coronary heart disease, diabetes and neurodegeneration [Moskovitz *et al.*, 2002]. Recently an increasing number of scientific publications suggest that certain edible plants may offer protection or treatment against some chronic diseases. In general, these beneficial effects can be attributed to their antioxidant constituents like vitamin C, vitamin E, carotenoids, flavonoids, catechins, anthocyanins, etc. (Podsdek, 2007).

Tea is the most consumed beverage in the world only second to water. CTC (Crush, Tear, Curl) tea is manufactured in Sri Lanka from the two leaves and the bud and young leaves of the shrub *Camellia sinensis* (Shapiro *et al.*, 2006). The estimated amount of 18-20 billion tea cups consumed daily worldwide (Fernandez Caceres *et al.*, 2001) elicits its economic and social interest. Most of the tea produced worldwide is black tea, which represents 76-78 % of the tea produced and consumed worldwide (McKay and Blumberg, 2002). The production of black tea involves allowing tea leaves to wither where the moisture content of the leaves is reduced nearly to half of the original weight

followed by rolling and crushing to initiate fermentation (Carloni *et al.*, 2013).

The chemical composition of tea includes polyphenols, alkaloids (caffeine and theobromine), amino acids (mainly L-theanine), carbohydrates, proteins, chlorophyll, volatile compounds, minerals (aluminium, manganese and fluoride) and other unidentified compounds. Among these, polyphenols are the main bioactive compounds in tea (Cabrera *et al.*, 2003). The major polyphenolic compounds in tea are the flavan-3-ols (catechins) which include: (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG), (-)-epigallocatechingallate (EGCG), (-)-gallocatechins (GC) and (-)-gallocatechin gallate (GCG) (Peterson *et al.*, 2005). During the manufacturing process of black tea, the colourless catechins present in fresh tea leaves are oxidized both enzymatically and nonenzymatically to give two major groups of pigments: theaflavins and thearubigins which are responsible for the colour and sensory properties of black tea brew (Gupta *et al.*, 2002). The different manufacturing processes affect the chemical composition of teas and give rise to the commercially available vast selection of teas with unique aroma and taste (McKay and Blumberg, 2002; Mukhtar and Ahmad, 2000).

The flavonoids and other polyphenols present in tea have shown to possess a wide range of biological and pharmaceutical benefits, including prevention of

cancer (Yuan, 2013), obesity (Grove and Lambert, 2010) and type 2 diabetes (Deka and Vita, 2011), insulin-enhancing activity (Anderson and Polansky, 2002), antioxidative (Sajilata *et al.*, 2008), hypolipidemic (Yang, 1999), antimicrobial (Hamilton-Miller, 2003), immunostimulatory (Matsunaga *et al.*, 2002), antiinflammatory (Sano *et al.*, 2004) activities, neuroprotective effects (Kakuda, 2011), bone mineralization effect (Shen *et al.*, 2011) and protection against cardiovascular diseases and cerebral ischemic damage (Stangl *et al.*, 2007). These beneficial effects may be attributed to antioxidant activity possessed by the polyphenolic compounds in tea (Cabrera *et al.*, 2003). Gallic acid has proven cytotoxic activities against cancer cell lines (Inoue *et al.*, 1995). Epidemiological studies have found a positive association between dietary flavonoid intake and overall good health (Scalbert, *et al.*, 2005).

Carefully followed stirring and steeping conditions for an appropriate time and temperature are critical to extract catechins or theaflavins from teas (Khokhar and Magnusdottir, 2002). The traditional method of making a cup of tea in Sri Lanka is to place loose leaves directly, or in an infuser, into a pot or cup and pour hot water over the leaves. After a couple of minutes the leaves are usually removed using a strainer. Although there are certain reports on polyphenols and antioxidant activities of different black teas from various geographic regions as well as records on total polyphenolic levels and antioxidant activities of black tea under various brewing temperatures and times, little or no information is reported on the time course variation of polyphenolic and flavonoid profiles during brewing of black tea. Therefore this research aims to investigate the variation in the levels of polyphenols and the tea components: gallic acid, caffeine, epicatechin and epigallocatechin gallate with time during steeping of CTC black tea using a validated HPLC/UV method.

2. Materials and Methods:

2.1. Reagents and chemicals

HPLC grade acetonitrile was purchased from BDH (BDH Chemicals Ltd. Poole, England). β -hydroxyethyltheophylline, caffeine, gallic acid, epicatechin, (-)-epigallocatechin gallate, Folin ciocalteu reagent, 1,1-Diphenyl-2-picrylhydrazyl (DPPH) and aluminium chloride were purchased from Sigma Chemicals, USA. Sodium nitrite was purchased from Riedel De Haen Ag, Wunstorfer Strasse 40, SEELZE1, D3016, Germany. Crush, Tear, Curl (CTC)

low grown pure Ceylon black tea was obtained from Danduwangalawatta Tea factory, Millawitiya, Kuruwita, Sri Lanka.

2.2. Equipment

Shimadzu UV-1601 UV Visible spectrophotometer (Shimadzu Corporation, Japan) was used to read the absorbance. HPLC was performed with Shimadzu LC 10AS solvent delivery system equipped with UV/VIS variable wavelength detector Shimadzu SPD 10A (Shimadzu Corporation, Japan) and an integrator Shimadzu C-R8A (Shimadzu Corporation, Japan). Chromatographic resolution of components in tea was achieved on a 2.1 x 150 mm, betasil phenyl HPLC column (Thermo scientific) attached to a 10 x 4.6 mm Spherisorb guard column (Waters, USA). Samples were injected with a syringe loading injector fitted with 100 μ l loop.

Shimadzu Libror AEG-220 analytical balance (Shimadzu Corporation, Japan) was used to prepare standard solutions. Purified deionized water was obtained from Labconco Water Pro-PS UV ultra filtered water system (Labconco Corporation, Missouri) and distilled water was obtained by Aquatron A4S water system. Micro-centrifugation was performed using a BioFuge-Pico D-37520 centrifuge (Heraeus Instruments, Germany).

2.3. Preparation of tea brews

Deionized water (500 ml) was boiled in a glass beaker placed on a magnetic stirrer. At the onset of boiling, heating was stopped and tea leaves (5.0 g) was added to boiled water and the beaker was covered with watch glass continuing stirring at a constant speed. Samples (1.0 ml) were withdrawn at different time intervals (0, 1, 2, 4, 6, 8, 10, 12, 14, 20 min) and filtered through cotton wool plugs and the filtrates were collected. These filtrates were assayed for their phenolic and flavonoid contents by spectrometry. Gallic acid, caffeine, epicatechin, epigallocatechin gallate were quantified by Reversed Phase High Pressure Liquid Chromatography (RP-HPLC). Antioxidant activity was assayed by DPPH radical scavenging method.

2.4. Determination of Phenolic Content

The phenolic content of the samples were determined by Folin Ciocalteu method (Makkar *et al.*, 1993). Samples (25 μ l) were diluted up to 1500 μ l with deionized water. Folin Ceocalteu's phenol reagent (1 N, 250 μ l) was added to the samples (500 μ l), and the

mixtures were allowed to stand at room temperature for 2 minutes. Sodium carbonate solution (10%, 1250 µl) was added and samples were incubated for 45 minutes in the dark at room temperature. The absorbance of the resulting solutions was measured at 760 nm against a blank prepared in same manner but adding deionized water instead of tea infusion. Calibration curve was constructed using gallic acid standards (6-30 µg/ml) and the total phenolic content expressed as w/w % gallic acid equivalents (GAE) was plotted with time. Tea samples brewed independently were analyzed in replicates (n=6).

2.5. Determination of Flavonoid Content

The flavonoid content was measured by the aluminium chloride colorimetric assay (Zhishen *et al.*, 1999). A volume of 25 µl of tea samples collected at different time intervals were diluted with deionized water up to 500 µl and mixed with sodium nitrite (5%, 30 µl). After 5 minutes aluminium chloride (10%, 30 µl) was added to the mixture followed by sodium hydroxide (1M, 200 µl) at 6th minute. The total volume was adjusted to 1000 µl with deionized water and absorbance was measured at 510 nm against a blank prepared in similar manner but adding deionized water instead of tea infusion. Calibration curve was plotted using (-)-Epigallocatechin gallate (EGCG) standards (0.3-1.0 mg/ml) and flavonoid content expressed as w/w % EGCG equivalents was plotted with time. Tea samples brewed independently were analyzed in replicates (n=6).

2.6. Determination of antioxidant capacity by 1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical assay

Free radical scavenging ability of the samples was assayed by DPPH radical scavenging method described by Blois, (1958) with slight modification. Samples (50 µl) were diluted up to 1000 µl with deionized water. DPPH reagent prepared in absolute ethanol (100 µM, 950 µl) was added to the test sample (50 µl) and the mixture was allowed to stand for 30 minutes in the dark. The scavenging activity was quantified by measuring the decolourization of the resulting solutions at 517 nm. Deionized water was used as the blank. The control was prepared by mixing deionized water (50 µl) with DPPH (950 µl). Results were expressed as percentage scavenging of DPPH radical calculated from the given formula:

$$\% \text{ Scavenging of DPPH free radical} = \frac{\text{Abs. of control} - \text{Abs. of sample}}{\text{Abs. of control}} \times 100\%$$

Percentage scavenging of DPPH radical versus time was plotted. Independently brewed tea samples were analyzed in replicates (n=6) for antioxidant activity.

2.7. Determination of Gallic acid, Caffeine, Epicatechin, and (-)-Epigallocatechin gallate using Reversed Phase High Pressure Liquid Chromatography (RP-HPLC)

Chromatographic resolution of components in tea was achieved on a betasil phenyl HPLC column. The Mobile phase constituted of isocratic elution system of 8% Acetonitrile, 1% glacial acetic acid and 91 % deionized water at a flow rate of 0.5 ml/min. The detection wavelength was at 280 nm. β –hydroxyethyltheophylline prepared in deionized water (10 µg/ml) was used as the internal standard. Calibration curves were obtained using gallic acid, caffeine, epicatechin and (-)-epigallocatechin gallate mixtures (2.5 – 25 µg/ml) prepared in deionized water. Tea samples were diluted 5 times for the quantification of gallic acid, epicatechin and (-)-epigallocatechin gallate and 50 times for the quantification of caffeine. Diluted test samples/standards (100 µl) was mixed with β –hydroxyethyltheophylline (10 µg/ml; 100 µl), centrifuged (2000 rpm; 5 min) and the supernatant (25 µl) was injected to the column. The peaks were identified by comparing the retention times of these components in tea with that of the authentic standards. The HPLC method was validated for accuracy, intraday and interday precision, linearity, limit of detection (LOD) and limit of quantitation (LOQ) according to FDA guide lines (Food and Drug administration, Guidance for Industry: Bioanalytical Method Validation).

2.8. Evaluation of kinetics of releasing phytochemicals from tea leaves

Kinetics of solid liquid extraction of polyphenols, flavanoids, gallic acid, caffeine, EC and EGCG mixtures were studied.

Second-order rate law for extraction of compounds from tea leaves is considered (Chan *et al.*, 2014);

$$\frac{dc}{dt} = k_1(c - c_\infty)^2 \dots\dots\dots \text{Equation 1}$$

k_1 = the second-order extraction rate constant (g g⁻¹min⁻¹)

C_∞ = the extraction capacity (concentration of tea constituents at saturation in g L⁻¹)

C = the concentration of tea constituents in the solution at any time (g L^{-1}), t (min)

By considering the boundary condition $t = 0$ to t and $C = 0$ to C , the integrated rate law for a second-order extraction was obtained.

$$C = \frac{C_{\infty}^2 k_1 t}{1 + C_{\infty} k_1 t} \quad \dots\dots\dots \text{Equation 2}$$

By linear transformation of the above equation, the rate constant k_1 can be determined by fitting the experimental data.

$$\frac{t}{C} = \frac{1}{k_1 C_{\infty}^2} + \frac{t}{C_{\infty}} \quad \dots\dots\dots \text{Equation 3}$$

2.9. Statistical Analysis

Results are presented as mean $\pm$ standard deviation (Mean $\pm$ SD) of six independent experiments. Statistical analysis, student's t -test and calculation of Pearson's correlation coefficient (r) were done using Microsoft Excel. Value of $p < 0.05$ was considered as significant.

3. Results and Discussion:

Gallic acid, caffeine, EC, EGCG and the internal standard β -hydroxyethyl-theophylline were eluted at 1.96, 5.89, 12.21, 15.49 and 4.21 min respectively (Figure 1). The calibration curves were linear over 2.5–25 $\mu\text{g/ml}$ with R^2 exceeding 0.995 for gallic acid, caffeine, EC and EGCG (Figure 2). The method showed repeatability, interday and intraday precision (CV %) less than 6.0 % and accuracy was 96–103 % for all the compounds studied.

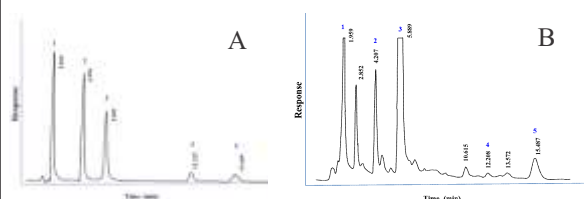


Figure 1: The HPLC chromatograms of standard samples (1– Gallic acid, 3- Caffeine, 4– Epicatechin, 5- Epigallocatechin gallate) each at a concentration level of 8 $\mu\text{g/ml}$, 2- internal standard ie, β -hydroxyethyl-theophylline (10 $\mu\text{g/ml}$) [Figure 1A]. The HPLC chromatogram of CTC black tea sample (1– Gallic acid, 3- Caffeine, 4– Epicatechin, 5- Epigallocatechin gallate) with the spiked internal standard, β -hydroxyethyl-theophylline (2) [Figure 1B].

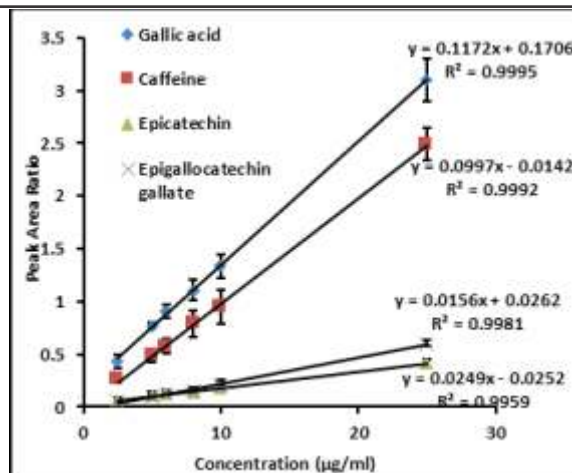


Figure 2: Standard curves obtained for gallic acid, caffeine, epicatechin and epigallocatechin gallate over the concentration range of 2.5 – 25 $\mu\text{g/ml}$. (Peak area ratio = Area under curve of the analyte / Area under curve of internal standard).

Concentrations obtained for all the compounds tested were fitted with the second order kinetics. Linear curves ($R^2 > 0.99$) were obtained for time against time/concentration (t/C) as described by many authors (Peleg, 1988; Lafka, 2013) for all individual set of data ($n=6$) for solid liquid extraction of each compound investigated. Curves obtained from the mean values of each compounds are illustrated in the Figure 3. The gradient and intercept values of the curves were used to determine the extraction capacity (C) and second-order extraction rate constant (k_1). These kinetic parameters were calculated from the data obtained during first 5 minutes of tea brewing, assuming the change of temperature to be negligible during this period. However the effect of temperature has not affected the linearity of the curves (Figure 3). The calculated values with the observed values are listed in Table 1.

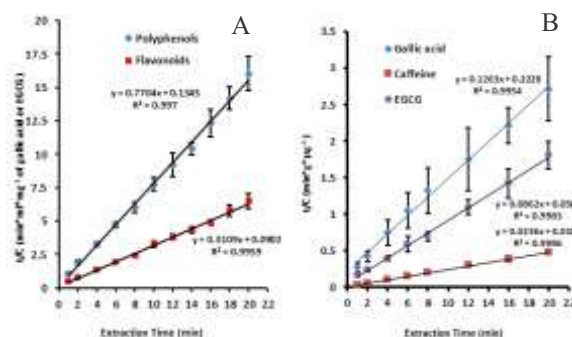


Figure 3: Correlation between t/C and extraction time for polyphenols and flavonoids (Figure 3A) and correlation between t/C and extraction time for gallic acid, caffeine and epigallocatechin gallate (Figure 3B).

Table 1: Kinetic parameters for the extraction of nutraceuticals from tea infusion

	C _∞ (mg/g)	C ₂₀ (mg/g) (observed)	k _t (g mg ⁻¹ min ⁻¹)
GA	8.0 ± 1.2	7.6 ± 1.9	7.8 × 10 ⁻² ± 0.2 × 10 ⁻²
Caffeine	42.2 ± 2.7	42.1 ± 1.9	4.1 × 10 ⁻³ ± 0.3 × 10 ⁻³
EGCG	11.8 ± 0.4	11.2 ± 1.1	1.4 × 10 ⁻² ± 0.8 × 10 ⁻²
Polyphenols	131 ± 8*	124 ± 6*	2.4 × 10 ⁻² ± 0.7 × 10 ⁻²
Flavanoids	322 ± 22**	310 ± 26**	5.8 × 10 ⁻⁴ ± 0.1 × 10 ⁻⁴

* Concentration is expressed in mg/g GAE and ** Concentration is expressed in mg/g EGCG equivalents
C_∞ = the extraction capacity, C₂₀ = the concentration of the tea constituent in the solution at 20th minute, k_t = the second-order extraction rate constant)

Rapid extraction was observed for gallic acid, caffeine, EC, EGCG within first two minutes and slowly increased with time (Figure 4A). The release of compounds from tea leaves depends on the amount present and their solubility. All the compounds investigated in the present study are water soluble. Caffeine is soluble in polar and non polar solvents and efficient release can be expected as observed in the present study. Furthermore caffeine present in the tea leaf is higher compared to the other three compounds investigated. The release of total phenols and flavonoids also showed rapid and slow release phases but comparatively slower than caffeine, gallic acid and other two catechins (Figures 4A and 4B). Total polyphenolic and flavonoid compounds extracted increased with the time and reached to a maximum concentration at 6-8 minutes (Figure 4B). The values which represent total polyphenolic content (TPC) and flavonoid content account for all the polyphenolic substances present in tea leaves having different solubility which could be responsible for slow release of TPC with time. The maximum concentrations observed for total phenols and flavonoids were 13.28 ± 0.86 w/w % GAE and 33.53 ± 2.26 w/w % EGCG equivalents respectively. At low temperature caffeine complexes with polyphenols and forms insoluble complexes (Yin *et al.*, 2009). It is observed that the temperature decreased from 100 - 75 °C during the first twenty minutes, but complexation of polyphenols with caffeine was not visible.

Most of the health benefits of tea are based on its antioxidant activity. According to DPPH assay, the antioxidant activity was increased with the steeping time (Figure 5). A significant correlation ($p < 0.001$) was observed between the antioxidant activity with

polyphenols, flavonoids and EGCG (Figures 6A – 6F). A moderate or low correlation was observed between antioxidant activity and gallic acid, EC and caffeine present in the tea brew. Though the antioxidant capacity of gallic acid and EC is high (Table 2), their contribution in tea brew to scavenge DPPH is low since their concentration is relatively low when compared with EGCG and phenols. Present study reveals that polyphenols and EGCG are major constituents responsible for antioxidant activity. Although caffeine is not considered as a polyphenolic compound, its capability to inhibit lipid peroxidation has been reported (Brezová *et al.*, 2009). However the authors suggest that its contribution to antioxidant activity in coffee and tea does not seem to be as important as the contribution of phenolic compounds. This is in agreement with the results obtained in the present study.

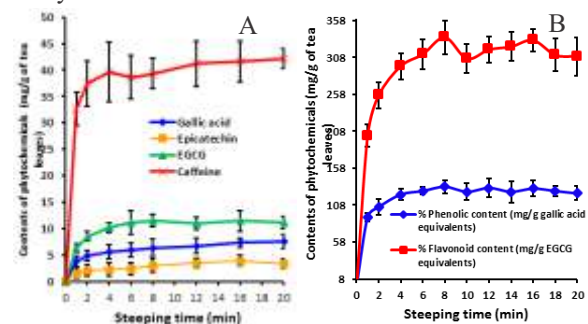


Figure 4: Kinetics of caffeine, gallic acid and catechin extraction from CTC tea leaves (Figure 4A) and kinetics of polyphenol and flavonoid extraction from CTC tea leaves (Figure 4B).

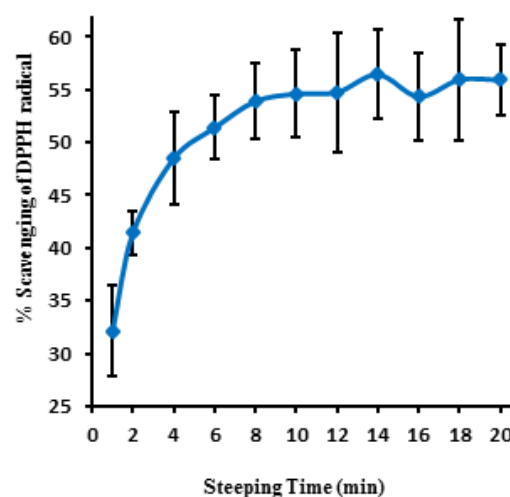


Figure 5: Variation of % scavenging of DPPH free radical with time.

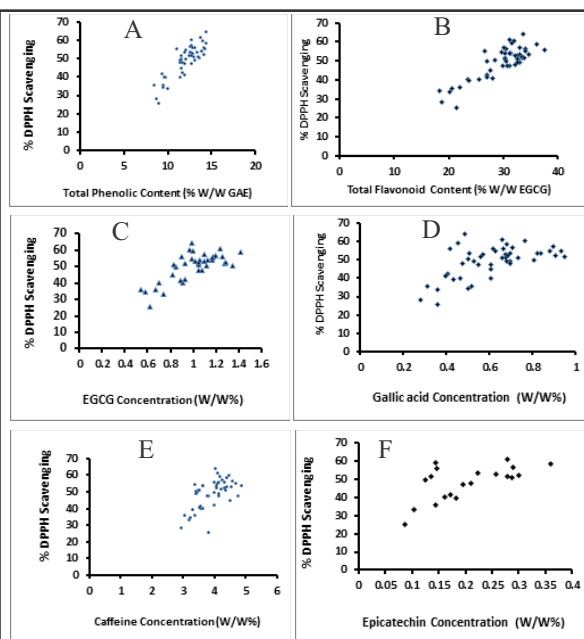


Figure 6: Correlation of antioxidant activity with the concentration of polyphenols (Figure 6A), flavonoids (Figure 6B), EGCG (Figure 6C), gallic acid (Figure 6D), caffeine (Figure 6E) and epicatechin (Figure 6F).

Table 2: EC₅₀ values obtained in the DPPH assay for authentic tea constituents and the standard antioxidant

Compound	EC ₅₀ for DPPH Assay
Gallic acid	1.38 ± 0.04 i g/ml
Epicatechin	2.30 ± 0.06 i g/ml
Epigallocatechin gallate	3.24 ± 0.07 i g/ml
L-Ascorbic acid	3.30 ± 0.27 i g/ml
Caffeine	> 1.25 mg/ml

4. Conclusion

The traditional method of preparing a CTC tea brew has influence on the extraction of total phenols, flavonoids and major phytoconstituents such as gallic acid, caffeine, EC and EGCG. The antioxidant capacity of CTC black tea significantly correlated well with levels of EGCG, flavonoids and total phenolics during steeping of the black tea. A very weak correlation was observed between caffeine content with antioxidant activity. Releasing of caffeine, gallic acid, EGCG and EC into the tea brew was much faster than the release of polyphenols and flavonoids. The minimum brewing time required to release tea constituents from CTC tea leaves is 2-8 minutes after tea is prepared according to the traditional method. Since tea is one of the major beverages consumed worldwide, studying the effect of preparation of tea on the extractability of various health beneficial phytoconstituents is highly valued.

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The Asymmetric [C+NC+CC] Coupling Reaction: Development and Application to Natural Product Synthesis

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Introduction

Highly functionalized pyrrolidine ring is a unique structural motif present in many biologically active natural and unnatural compounds. Develop amenable methodology to access these structurally diverse pyrrolidines for both target- and diversity-oriented synthesis is one of the most productive fields in current synthetic organic chemistry. Figure 1 shows three structurally diverse pyrrolidine architectures that attract the synthetic community with their structural complexity as well as biological activity.

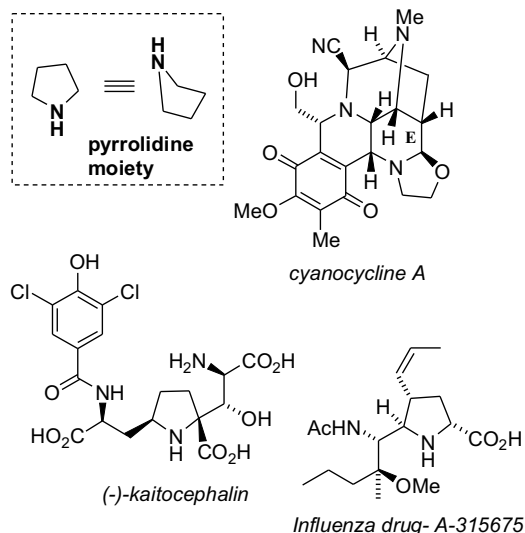


Figure 1: pyrrolidine targets.

The asymmetric [C+NC+CC] reaction

The asymmetric [C+NC+CC] coupling reaction is a union of an aldehyde (C-component), a chiral amine species (NC-component) and activated alkene (CC-component) to make a substituted pyrrolidine ring (figure 2).

The effective [C+NC+CC] multicomponent cascade is outlined in Figure 3. The hallmark of this reaction is the use of Oppolzer's glycylsultam as the reaction-enabling amine bound chiral auxiliary. Most of the azomethine ylide cycloaddition methodologies employ an external base to promote the dipole formation by deprotonating the α -proton. The external base could be one cause for the unwanted side reactions. Unlike other existing methodologies, the step (I) of [C+NC+CC] cascade is operating without an

external base. This prevents the destructive pathways such α -epimerization, imine isomerization and the self-aldol condensation of aliphatic chiral aldehydes. The *N*-acyl Oppolzer's sultam moiety not only enforces the stereochemistry of the pyrrolidine ring but also facilitates the dipole formation by lowering the pH of the glycyl α -proton ($pK_a \sim 4$). Therefore the lack of external base does not affect the dipole formation in step (III). The high equilibrium concentration of ylide facilitates the step (IV) to effectively form the cycloadduct in high yield.

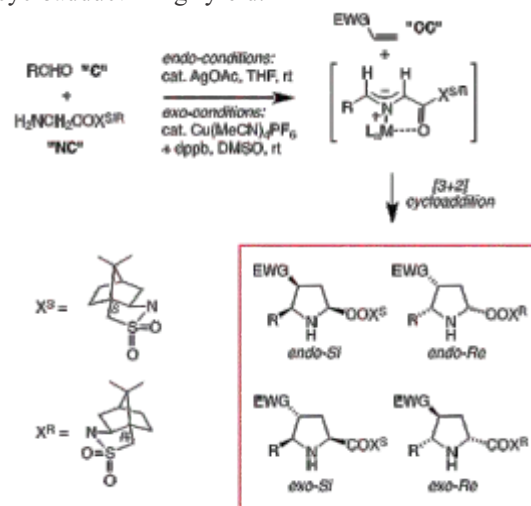


Figure 2: [C+NC+CC] reaction

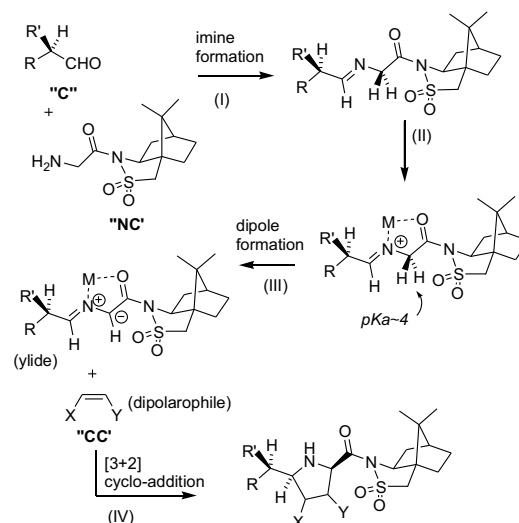


Figure 3: Proposed [C+NC+CC] coupling reaction cascade

Stereochemical modes

The *endo*-selective version (all *cis*) of this reaction is generally operated by combining the aldehyde, chiral amine and desired dipolarophile at once in the presence of 10 mol % of AgOAc in THF. The high *endo* selectivity of this reaction can be rationalized using the pre-transition state model (A) shown in Figure 4. The W type azomethine ylide shows two possible dipolarophile approaching faces. The carbonyl and SO (Pro-S) opposing dipoles forced the direction of SO (Pro-R) more towards the *endo-Re*-face. When the dipolarophile approaches toward the ylide, *endo-Re* face attack is unfavorable under the influence of forcing steric effects of dipolarophile and Pro-R. While facial selectivity is governed by the Pro-R *endo*-selectivity is presumably arises from the coordination of incoming dipolarophile with Ag(I). The mild *endo* selective reaction was demonstrated with wide variety of aliphatic aldehydes and dipolarophile to prove its versatility for highly complex pyrrolidine synthesis and anticipated to be serving as a cornerstone in multi-step synthesis applications.

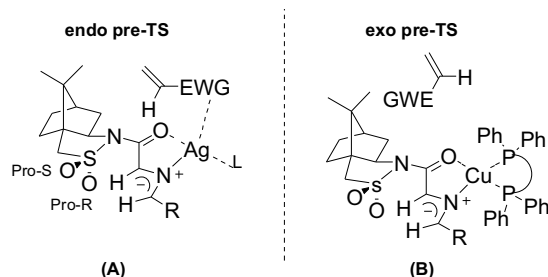


Figure 4: Pre TS-model

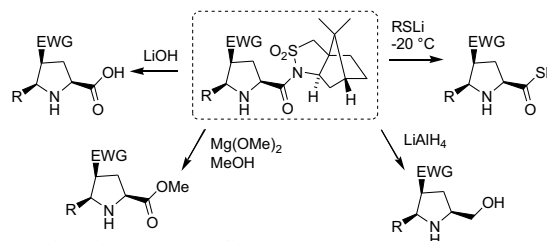
A preference for the *exo* (2, 4-*trans*) mode of the cyclo addition using copper-based catalysis is well known in the literature. Based on our understanding of the pre-TS model, the *endo* selective mode of the Ag(I) catalyzed cyclo addition is initiated with the coordination of Ag(I) with the dipolarophile. Coordination of Cu(I) with bisphosphine ligands would favour the *exo*-transition state due to the added steric factors within the system (Figure 4-(B)). The optimized conditions for the *exo*-selective reaction involve pre-forming the catalytic mixture by combining 5 mol% Cu(MeCN)₄PF₆ with 5 mol% dppb in DMSO at ambient temperature in the dark prior to combining with aldehyde, chiral amine and dipolarophile mixture.

Removal of the chiral director

The diastereofacial selectivity of the [C+NC+CC] reaction is governed by the chiral amine moiety in both *endo* and *exo* selective modes. Chemoselective

removal of the chiral auxiliary upon serving its purpose is an essential part of the auxiliary mediated reactions. The following general auxiliary removal strategies shown in scheme 1 were employed to remove the auxiliary after the successful reaction. The Oppolzer's sultam can be recovered and reused after acylation.

Scheme 1.

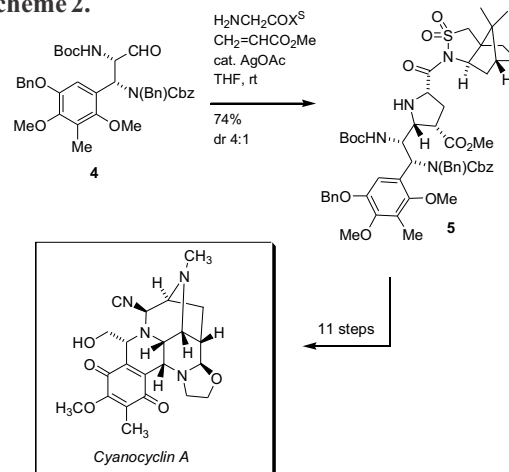


Application to Total Synthesis

Total synthesis of Cyanocycline A

Cyanocycline A is a unique small molecular inhibitor of cell migration which could be used to develop small molecular anticancer drugs. The key complexity-building reaction in the synthesis of cyanocycline A uses the Ag^I catalyzed *endo*-selective [C+NC+CC] coupling reaction to provide the target's highly functionalized pyrrolidine ring (Scheme 2). This novel strategy reduces the number of steps previously needed to assemble this complex molecule by one-third.¹⁴

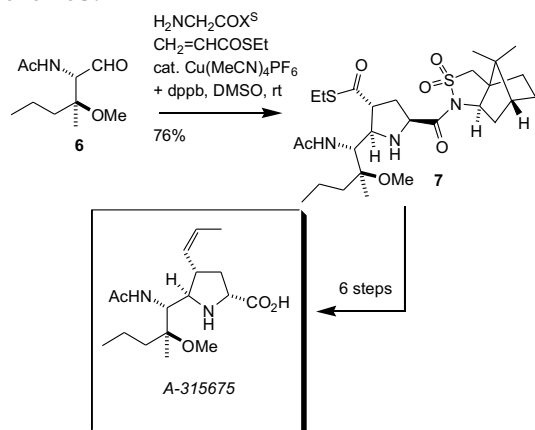
Scheme 2.



Total synthesis of anti-viral drug

Neuraminidase inhibitor A-315675 is a novel anti-viral drug developed at Abbott Laboratories. This compound exhibits superior activity against certain influenza virus strains when compared to Oseltamivir (Tamiflu). The fully-functionalized pyrrolidine ring was assembled via a Cu^I catalyzed *exo*-selective asymmetric [C+NC+CC] coupling reaction (Scheme 2). As a result of this novel strategy, most efficient total synthesis of the drug was achieved in six liner steps.

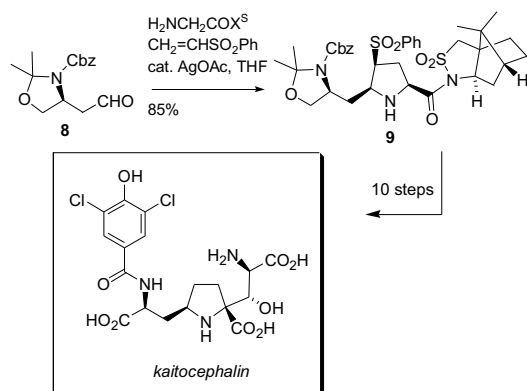
Scheme 3.



Total synthesis of kaitocephalin

Kaitocephalin is an amino acid-based natural product originally isolated from the fungus *Eupenicillium shearii*. This compound is the first naturally occurring glutamate receptor antagonist and displays different affinity for subtypes of ionotropic glutamic acid receptors. The highly substituted pyrrolidine ring was assembled *via* an *endo*-selective asymmetric [C+NC+CC] coupling reaction (Scheme 4). Among the nine total syntheses of this popular target, short most efficient synthesis was achieved in 15 steps using [C+NC+CC] strategy.²⁴

Scheme 4.



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Targeted Imaging Probe from a Natural Compound in Turmeric

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Natural compounds play a vital role in chemistry and medicine either as therapeutics or imaging probes. Majority of medicines are discovered through screening of natural compounds from plant materials, bacteria, fungi, and algae. These isolated and identified compounds are derivatized by modifying existing functional groups or introducing new functional groups to enhance their effectiveness. The number of natural products that have been identified as therapeutics or compounds with potential to be therapeutics for various diseases is immense. From this huge pool of naturally occurring therapeutically active compounds, this article focuses on curcumin, a phenolic compound found in turmeric.

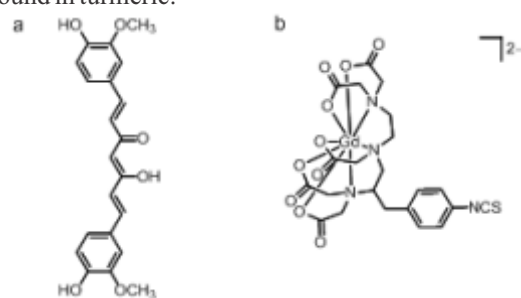


Figure 1. Chemical structures of (a) curcumin and (b) Gd^{III}DTPA-BnSCN.

Curcumin (1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is a natural compound long known for its medicinal potential (Figure 1a). Recent research have demonstrated its ability to act against perilous diseases including cancer, HIV and Alzheimer's disease. Furthermore, curcumin is a biologically safe, non-toxic compound and can be obtained by extracting from its natural source, turmeric rhizome, or synthesizing using Pabon method. Also, curcumin is an inexpensive, commercially available compound that has several sites to react with different functional groups. However, because of its hydrophobic nature, bioavailability of curcumin is limited as it is not water soluble. Additionally, underivatized curcumin is reported to be unstable under higher pH values and light. To enable the full potential of curcumin, derivatization with and conjugation to other therapeutic and diagnostic molecules are critically important. The chemical structure of curcumin

contains two phenol moieties linked through a β -ketone group. The molecule contains a conjugated system leading to the bright yellow color of the compound and its bright fluorescence. The inherent fluorescence of curcumin allows it to be used as a fluorescent dye to image biological samples. These therapeutic and imaging potentials of curcumin make it a widely using compound in medicinal and biological research fields.

Curcumin is known to interact with amyloid plaques, and the planar hydrophobic aromatic structure of the molecule is considered to be the key feature for its interaction with β -amyloid fibrils. β -amyloid plaques are a characteristic diagnostic of Alzheimer's disease, which is one of the leading neurodegenerative diseases in the world, and detection of β -amyloid plaques is important in Alzheimer's disease diagnosis, treatment monitoring, and related research. Because curcumin interacts with β -amyloid plaques and have demonstrated the ability to inhibit plaque formation, it has been studied as a therapeutic and an imaging agent to detect amyloid plaques.

Inherent fluorescent properties of curcumin and conjugation of curcumin with radiolabels are being exploited in imaging amyloid plaques. However, fluorescent imaging suffers with limited tissue penetration, and use of radiolabels and harmful radiation is not desired with live imaging. Therefore, there is a need of using other efficient and harmless imaging techniques to detect β -amyloid plaques. Magnetic resonance imaging (MRI) is a non-invasive imaging technique with excellent tissue penetration and high spatial resolution (25–100 μ m) that has the potential to overcome the limitations of fluorescence and nuclear imaging with respect to the detection of amyloid aggregates. Several imaging studies of β -amyloid plaques have been reported with MRI. In these studies, both transverse relaxation time (T_2)-weighted and longitudinal relaxation time (T_1)-weighted imaging methods were reported. However, the T_1 -weighted methods are more desirable because unlike T_2 -weighted methods, T_1 -weighted imaging can distinguish plaques from hemorrhages and blood vessels. Although T_1 imaging is desirable, it suffers from poor contrast enhancement of β -amyloid plaques. Therefore, there is a widespread interest in

synthesizing β -amyloid plaques targeted contrast agents for MRI. Examples of amyloid-targeting groups that have been reported with MRI contrast agents include amyloid peptides, monoclonal antibodies, and amyloid-binding dyes. While contrast agents composed of conjugates of these targeting groups are capable of labeling amyloid plaques, possible amyloidogenesis, toxicity, and the large size of these contrast agents limit their usefulness. These limitations reveal the need of new β -amyloid-targeted contrast agents with higher efficiency, smaller size, and non-amyloidogenic and non-toxic properties to develop MRI as a useful technique in β -amyloid imaging. To address this need, Allen and co-workers have reported a contrast agent using curcumin as the targeting unit. Because curcumin is a small, non-toxic, and non-amyloidogenic compound it can address the limitations reported with previously synthesized β -amyloid plaques-targeted contrast agents for MRI. Target-specific metal complexes can be achieved using two synthetic strategies, either conjugation or structure mimicking strategy, and Allen and co-workers have used the conjugation strategy to synthesize their β -amyloid plaques-targeted contrast agents for MRI using curcumin. To obtain efficient targeting and imaging, these metal complexes need to fulfill several requirements regardless of the synthetic strategy that is being used, including (1) enabling interaction with the target, (2) maintaining kinetic stability under the conditions of imaging, (3) having no interference of function between the targeting and imaging components, and (4) being synthetically feasible. Thus, addressing these requirements is an essential step in ligand design to achieve efficient target-specific contrast agents.

The contrast agent that was chosen for the conjugation with curcumin is a Gd^{III} -containing complex of diethylenetriaminepentaacetic acid functionalized with an isothiocyanate group (Gd^{III} DTPA-BnSCN) (Figure 1b). Gd^{III} DTPA is a clinically approved contrast agent for MRI, and the isothiocyanate group imparts the ability to conjugate to various nucleophilic functionalities. Furthermore, benzyl-isothiocyanate-containing DTPA is commercially available. To synthesize the β -amyloid plaques-targeted contrast agent (Figure 2a), an amine linker has been introduced to one of the phenol group of the commercially available curcumin. The rationale behind the introduction of an amine linker included facilitating the reaction of isothiocyanate group of Gd^{III} DTPA-BnSCN with curcumin and incorporating

space between the targeting moiety and the imaging unit to avoid potential interference of function. The synthesized curcumin-conjugated complex is water soluble unlike the curcumin itself which is not water soluble thus making this complex more bio-available than curcumin. The cell viability studies has shown that the compound has no toxicity on living cells. However, the penetration through blood brain barrier has shown some limitations due to the overall negative charge of the molecule. This limitation however, can be easily addressed by using an isothiocyanate derivative of neutral Gd^{III} complex such as Gd^{III} 3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triacetate (Gd^{III} PCTA, Figure 2b) for the conjugation.

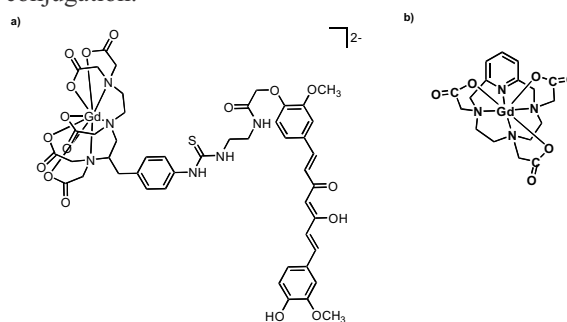


Figure 2. Chemical structures of a) Curcumin-conjugated β -amyloid plaques-targeted contrast agent. b) Gd^{III} PCTA

The efficiency of β -amyloid plaques-targeted, curcumin-conjugated contrast agent was determined by measuring the relaxivity of the compound at a clinically relevant magnetic field (1.4 T) and it was 2.6 times higher than that of clinically approved Gd^{III} DTPA under the same conditions. The high relaxivity of the curcumin-conjugated complex demonstrates that it is an efficient contrast agent for MRI. In vitro studies with β -amyloid fibrils demonstrate that curcumin-conjugated contrast agent interacts with β -amyloid fibrils resulting in a shortening of T_1 . Furthermore, the fluorescence intensity of the curcumin-conjugated complex increased by 43% in the presence of 2 equiv of β -amyloid aggregates relative to in the absence of amyloid aggregates (Figure 3). This observation also indicate that the curcumin-conjugated complex interact with β -amyloid aggregates and can also be used as a fluorescence probe. The changes in T_1 relaxation time and emission wavelength and intensity make the curcumin conjugated complex a multimodal imaging agent for β -amyloid plaques. Multimodal agents enable the use of two or more different imaging modalities to image targets using a single probe.

Importantly, these probes allow for validation of results using the different modalities: The multimodal nature of the curcumin-conjugated complex enables the validation of MRI results with fluorescence studies.

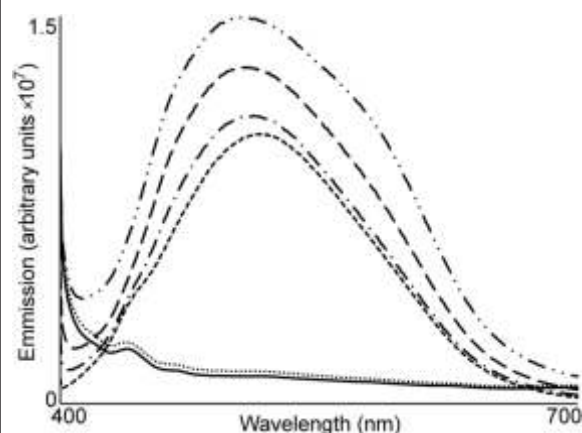


Figure 3. Emission spectra ($\lambda_{ex} = 385$ nm) of **1** and $Gd^{III}DTPA$ incubated with β -amyloid aggregates (βA) in PBS: 2 equiv βA + **1** (— · — · —); 1 equiv βA + **1** (— — —); 0.5 equiv βA + **1** (— · — · —); **1** (— — —), 2 equiv βA + $Gd^{III}DTPA$ (· · · · ·); and βA (—). The maximum emission of **1** undergoes a 9 nm blue shift and 43% increase in intensity upon interaction with 2 equiv of βA .

The curcumin-conjugated contrast agent synthesized by Allen and co-workers using a natural compound from turmeric rhizome demonstrate that it is water soluble, non-toxic, and interacts with β -amyloid plaques leading to a promising future for amyloid plaque imaging using MRI. Ease of synthesis of the curcumin amine linker is helpful for synthesis of many other conjugates with curcumin that are stable under biological conditions. Further, fluorescent properties of the curcumin make curcumin-conjugated contrast agent a multimodal imaging agent that is important for *ex vivo*, *in vitro* and *in vivo* studies of β -amyloid aggregates.

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Guest Article 03

New Era in Computational Chemistry – Graphic Processing Units (GPUs) to Accelerate Molecular Dynamics, Simulations and Molecular Modeling

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Ever increasing computational power and sophisticated hardware have been a great advantage for recent developments in computational chemistry. One such hardware is graphics processing units, commonly known as GPUs. High capacity GPUs were originally developed for computer gaming, but today these are widely used for the scientific computing as well. Such applications are known as general purpose computing on GPUs (or GPGPU). GPUs have now become a phenomenal tool to accelerate computational chemistry codes and perform many tasks which have not possible earlier. Currently many quantum chemistry and molecular dynamic codes support GPUs. This article is focused on how GPU acceleration benefit molecular dynamic (MD) simulations and molecular visualization. A general introduction to molecular dynamic simulations is also included.

Why computational chemistry?

Computational chemistry uses computers to model atoms and molecules based on theoretical methods. It is an important tool to understand chemical and biological processes and design new chemical reactions and materials. Importance in computational simulations as a complimentary tool for experiments has been well reflected by many examples where simulations provided satisfactory solutions which cannot be explained by the experiments alone. Computational chemistry methods are generally divided into *ab initio*, semiempirical, and molecular mechanics.

Ab initio methods use pure quantum mechanics, where as molecular mechanics are based on classical mechanics. Though *ab initio* techniques are the most accurate methods to study chemical processes at atomistic level, they are computationally expensive, which limits such calculations to small molecules (less than 500 atoms). On the other hand, molecular mechanics is computationally less demanding and can handle large systems containing thousands to millions of atoms. In molecular mechanics, energy and properties are calculated based on the nuclear positions and electrons are not properly accounted. Therefore, reactions involving bond breaking and forming cannot be simulated by molecular mechanics. However, a hybrid approach of quantum mechanics and molecular mechanics known as QM/MM, which introduced by 2013 chemistry Nobel laureates Michael Levitt and Arieh Warshel enables to overcome this problem to a certain extent. Semiempirical methods use parameters derived from experimental data to reduce the cost of quantum mechanical calculations. Density Functional Theory (DFT) is also a very popular quantum mechanical technique to calculate the molecular properties.

Molecular Dynamics (MD) Simulations

MD simulations are widely used to study time dependant properties of various bio molecules such as proteins, nucleic acids, cell membranes and their interaction with drug molecules, solvents, and etc. Applications of MD include determining the stability,

conformational changes, proteins folding, drug design, and structure determination. The main idea behind MD is atoms in macromolecules like proteins are not static; they rather are flexible and dynamic. They often do not exist at the lowest energy conformation (known as global minima) and therefore, observe atomic fluctuations. MD simulations determine the paths which atoms move at a given temperature and pressure, which are known as trajectories. A trajectory depends upon the forces generated due to intermolecular interactions. The force experienced by each atom is calculated using the first derivative of the potential energy with respect to the position. If initial positions and velocities of the atoms are known, then one can determine new positions and velocities by integrating the Newton's equation for motion (Eq. 1). Each atom is treated as a point mass.

$$m \frac{d^2 \mathbf{r}_i}{dt^2} = \mathbf{F}_i = - \frac{\partial V(\mathbf{r})}{\partial \mathbf{r}_i} \quad \dots \dots \dots \text{Eq. 1}$$

Potential energy exert due to various interactions is determined by set of mathematical expressions known as force fields, which are expressed by different parameters. The standard force field equation with different interaction terms is described below. [See a standard computational chemistry text book such as Ref[1]

$$V(\mathbf{r}) = \underbrace{\sum_{i,j} \frac{k_b}{2} (r_{ij} - r_{ij}^0)^2 + \sum_{i,j,k} \frac{k_\theta}{2} (\theta_{ijk} - \theta_{ijk}^0)^2 + \sum_{i,j,k,l} \frac{k_\phi}{2} (1 - \cos(\phi_{ijkl} - \phi_{ijkl}^0))^2}_{\text{Bonded terms}} + \underbrace{\sum_{i,j} \sum_{i < j} \left[\epsilon \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \frac{q_i q_j}{r_{ij}} \right]}_{\text{Non-Bonded terms (van der Waals + electrostatics)}}$$

The equation contain various parameters, for instance σ and ϵ in van der Waals term (also known as Lenard Jones potential) describes depth of the energy well and equilibrium bond length respectively. Most of these parameters were obtained experimentally or by ab initio calculations. Generally, one can find those common parameters like for atoms in proteins in the standard force fields such as AMBER and CHARMM. Once the trajectories are determined statistical thermodynamic properties are calculated applying Ergodic hypothesis, which states time average of a trajectory is equal to the ensemble average. MD determines the time averages where as experimental observations correspond to the ensemble averages. Another important consideration in MD is modeling solvent effects. There are two popular solvent models

known as explicit and implicit solvent models. In explicit solvent models, solvent molecules such as water molecules are explicitly included in the simulations, whereas in the implicit solvent model solvent effects are represented by effective dielectric constant. Explicit solvent simulations are computationally more demanding than implicit solvents, since that involves more atoms.

Why large computational power is required to perform MD simulations?

Generally the MD time step is taken as 2 fs (femto seconds, $1 \text{ fs} = 10^{-15} \text{ s}$) which is extremely small. The reason is that the time step should be smaller than the fastest motion of the system, which generally corresponds to the stretching of C-H bonds. However, biological activity occurs on ns (nano seconds) to μs (micro seconds) time scale. In order to see considerable protein folding (small proteins) or certain conformational changers, it must be simulated at least for 1 μs . This corresponds to 500 million time steps. (Larger systems require more time steps to see the activity.) For each step one must calculate forces (as described earlier), find the derivative respect to the distance and numerically integrate in time to find the new positions. There are thousands to billions of atoms in different biomolecules. Each atom interacts with many of the other atoms. As a result, enormous numbers of computations are required to determine the forces, but each computation is rather independent from all other computations. Therefore, performing computation in parallel has a high advantage in MD.

Most MD codes have the capability of running parallel. Increasing number of processors (CPUs) can perform the task much faster. Conventionally, MD codes used to runs on departmental computer (CPU) clusters, but to simulate large systems for considerable time, require large number of nodes in a supercomputer. There are many supercomputer centers around the world, and they have hundreds of thousands of processors running in parallel, connected via high speed optical network. Therefore access require huge amount of funding. Major problem in supercomputers are; they consume huge amount of electrical power and generate lot of heat. Moreover, long MD simulations generate huge amount of data (Tera bytes of data), thus it is a difficult task to move those data from a supercomputer to another site to do analysis.

Why GPUs are useful?

GPUs offer cost effective solution for parallel

computing, particularly in MD simulations. A single GPU can have 1000s of cores which can perform massively parallel computations effectively. As a result GPUs can bring supercomputer like performance to individual desktops. Currently the key manufacturer of state of the art GPUs is NVIDIA. Their early GPUs such as GeForce and Quadro used mainly for gaming, graphics and visualization, but after 2009 they started producing high end graphic cards like Tesla, Fermi, and Kepler which are capable of doing general purpose computing including scientific tasks. NVIDIA created a parallel computing platform known as Compute Unified Device Architecture (CUDA) to access the GPU with high level programming languages such as C/C++ and FORTRAN. OpenCL is another high level program



Figure 1: GeForce GTX Titan GPUs

GTX-Titan, GTX-780, K20, K40 and K80 are some of the popular and powerful GPU accelerators that support MD simulations (particularly in AMBER). The high performing K40 GPU has 12 GB memory and 2880 GPU cores, but much costlier than popular GeForce (GTX) graphic cards.

Computer performance in scientific calculations is measured by floating point operations per second (FLOPS). Scientific computing deals with real numbers and operations involving real numbers such as addition, multiplication, and division. Such a number can be represented as $\text{rep}\{\text{sign}\} \times (\text{Mantissa}) \times 10^{\text{Exponent}}$.

In computing, only limited space in memory is allowed to store a number and it can be specified by the number of bits (binary representation). The most common way of representing a floating point number is either single precision or double precision. The number of bits occupied by each precision model is listed in table 1.

Obviously, the double precision numbers require more memory than single precision, but provide much

accurate representation. Therefore, most computational chemistry codes run on CPUs prefer double precision. However, early GPUs didn't support double precision operations. Even though the later GPUs support double precision operations, speed of operations are much less than single precision. This is one of the limitations of GPUs. To compromise the speed and accuracy, most MD codes use a mixture of single and double precision operations. Nevertheless, MD codes like AMBER claims that the accuracy and precision is comparable to the standard CPU implementation. In default, they use single precision for calculating most of the forces, while use double or fixed precision for accumulation of forces.

Table 1: Bits corresponding to single and double precision representations

Precision representation	Sign	Exponent	Mantissa	Total
Single	1	8	23	32
Double	1	11	52	64

Leading MD packages such as AMBER, CHARMM, GROMACS, NAMD, and LAMMPS, support MD on GPUs. For instant, in AMBER, most commonly used code to run MD is known as PMEMD, and they recently modified this code using CUDA platform to run in GPUs. This code is known as PMEMD.CUDA. GPUs enable many researches to achieve significant speed up in MD simulations. In general speed of MD simulation is measured in terms of number of nano seconds performed per day (ns/day). The speedup of GPUs is measured relative to the performance of the CPU code. There are test calculations known as benchmark calculations to compare the relative speedups. Usually, in MD GPUs provide 4-10 times speedups. Details of the benchmark studies can be found in official website of MD packages. For AMBER you can find benchmark studies from Ref[9].

Another important aspect in MD is visualizing the structures and trajectories. One of the most popular programs for this purpose is Visual Molecular Dynamics (VMD). Unlike MD simulations, visualization of large biomolecules and MD trajectories are memory intensive, particularly for rendering, ray tracing with shadows, and visualizing molecular surfaces. All these operations can be accelerated by GPUs. Moreover, molecular orbitals calculations and their visualization can be performed

much faster with the GPUs than the CPUs.

My research experience with GPUs

Finally I'll take an example from my own research to explain the use of GPUs. In my PhD studies I investigated the effect of ethanol in Toll-Like Receptor (TLR3) protein dimer/double stranded RNA complex (PDB ID: 3CIY) using MD simulations. This is a fairly large and complicated system and total number of atoms including explicit solvent molecules are nearly 400,000. I ran these simulations in an Intel Xeon workstation with 2 GTX-titan GPUs using PMEMD.CUDA and able to get nearly 10 ns/day speed. If I do the same calculation with 8 parallel CPUs I can get a speed only around 3 ns/day. Therefore, GPUs helped me to finish my calculations much faster.

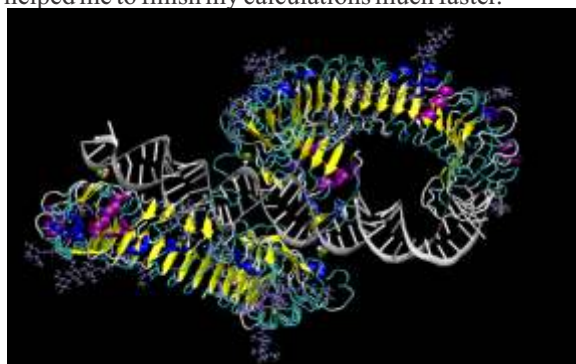


Figure 2: secondary structure representation of TLR3/dsRNA complex. GLYCAM units also shown in ball and stick model.

Future of GPGPU

This article described only GPU applications for MD simulations in computational chemistry. Today GPUs are very much useful for many other disciplines such as geoscience, computational medicine, computational physics, computational biology, etc. The main advantage of GPU is it can perform very much cost effective computations. A GPU workstation can be constructed for few thousand of dollars. This type of workstation / desktop machine with few GPU cards can perform what earlier did using computer cluster or supercomputer. On the other hand, one of the world's fastest supercomputers such as Titan in Oak-Ridge National Laboratory uses parallel CPU-GPUs computation to perform large (petascale) simulations. Finally, I conclude mentioning that future of the GPU computing and computational chemistry will be

brighter than present.

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Health Implications of Maillard Reaction: The Dark Side

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As the saying goes, “You eat with your eyes first”. When you think of bakery products or grilled and roasted meats, the first thing that comes into your mind is the beautiful golden brown color along with the rich flavors associated with it. Baked breads, roasted coffee, biscuits, French fries, and grilled steaks all owe their tempting appearance, aroma, and taste to a complex reaction which was discovered more than 100 years ago. Named after the French chemist L.C. Maillard who first reported the reaction in 1912, Maillard reaction (MR) is considered as one of the most widely practiced chemical reactions in the world. However, MR also has its negative consequences. This article is focused more toward the harmful chemicals that are formed during MR and their effects on health.

Chemistry of Maillard reaction

The MR is an extremely complex reaction which has been known to generate more than 2500 flavor compounds. A few decades after the discovery of MR, an American chemist J.E. Hodge developed a comprehensive reaction scheme for the reaction. MR involves a non-enzymatic interaction between reducing sugar and amino acids, proteins, or peptides, and can be divided into three phases. In the first phase, a reducing sugar undergoes a condensation reaction with a free amino group to form an N-glycosylamine (Figure 1(a)) which rearranges to give an Amadori product if the reducing sugar is an aldose (Figure 1(b)), or a Heyns product if the reducing sugar is a ketose.

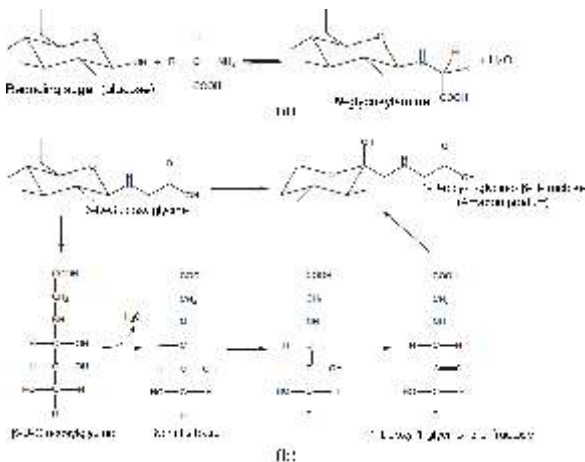


Figure 1 (a) Condensation of a reducing sugar with an amine to form an N-glycosylamine. (b) Amadori

rearrangement.

The second phase involves the subsequent degradation of Amadori or Heyns products via several pH dependant, alternative routes such as enolization, fission reactions, and Strecker degradation. At pH ≤ 7, Amadori or Heyns rearrangement products mostly undergo 1,2-enolization to form furfural or 5-hydroxymethylfurfural (HMF). At pH >7, Amadori compounds degrade via 2,3-enolization, which results in the formation of reductones and several other dicarbonyl fission products including diacetyl, hydroxydiacetyl, and pyruvaldehyde (Figure 2).

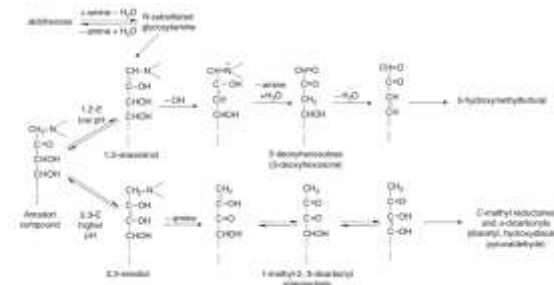


Figure 2. Hodge scheme for Maillard reaction.

These highly reactive dicarbonyl compounds further react with amino acids to form aldehydes and α-aminoketones in a reaction known as Strecker degradation (Figure 3). Alternatively, this reaction also produces pyrazines and nitrogen-containing heterocyclic compounds such as pyrroline and pyrrolidine. Strecker degradation reaction has been suggested as the most common route for aroma compound generation in MR. During the second phase, several other reactions such as cyclisations, dehydrations, retro-aldolisations, rearrangements, and isomerisations also occur, which result in the formation of a range of flavor intermediates and flavor compounds.⁷

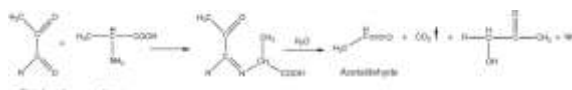


Figure 3. Strecker degradation.

The final stage marks the formation of brown, nitrogenous melanoidin pigments, mainly by polymerization of carbonyl compounds through aldol

condensation. The reaction rates of this diverse array of reactions are strongly governed by temperature, pH, and the type of the reactants (e.g., type of amino acids or proteins, type of sugars). Figure 4 depicts a simplified scheme for the generation of flavor compounds by MR.

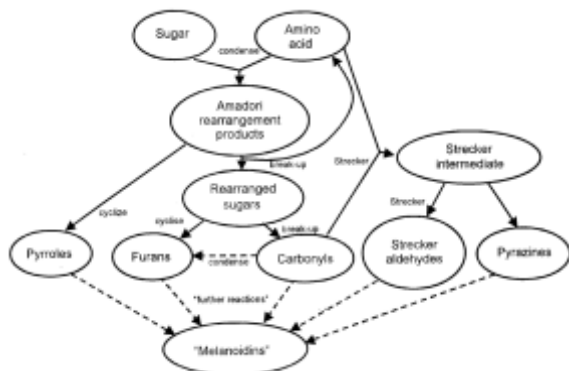


Figure 4. A simplified scheme for the formation of flavour compounds from the Maillard reaction (Adopted from Jousse et al., 2002)

The dark side of Maillard reaction

Although MR is beneficial as a means of improving sensory properties of foods, the reaction also presents negative consequences, mainly due to the loss of nutritive value of proteins and formation of potentially harmful chemicals. The loss of nutritive value has been attributed to the decrease of amino acid digestibility, destruction and/or biological inactivation of essential amino acids (e.g., lysine and tryptophan), and cross-linking of protein molecules.

Formation of toxic compounds

MR has been shown to generate neo-formed contaminants (compounds that are not naturally present in foods, but that may develop during thermal processing) that may result in potential human health risks. Dicarbonyl compounds, heterocyclic compounds and acrylamide are some well-known neo-formed contaminants linked with MR. Chemical structures of some selected potentially toxic Maillard reaction products (MRP) are given in Figure 5.

Dicarbonyl compounds, which are generated by the degradation of Amadori products (Figure 2), play an important role in the formation of heterocyclic aroma compounds during the MR. However, several dicarbonyl compounds such as glyoxal, methylglyoxal, diacetyl, and maltol (Figure 5) found in coffee and baked serial products have been reported for their mutagenicity. Further, mutagenic activity of these compounds has been attributed to their reactivity with puric bases.

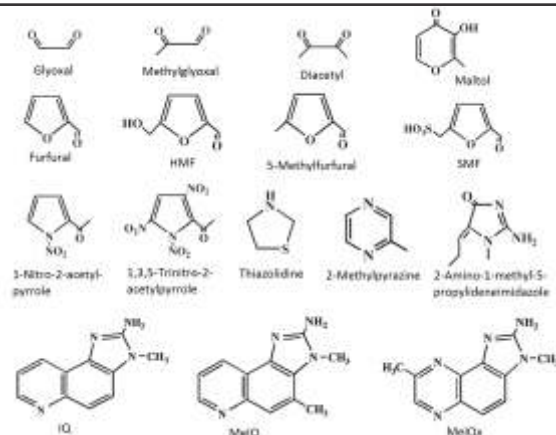


Figure 5. Chemical structures of some mutagenic and carcinogenic Maillard reaction products.

HMF: 5-hydroxymethylfurfural; SMF: Suloxymethyl furfural; IQ: 2-amino-3-methylimidazo[4,5-f]quinoline; MeIQ: 2-amino-3,4-dimethylimidazo[4,5-f]quinoline; MeIQx: 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline

Furfural, HMF, and methyl furfural fall in to the group of furans, which are considered as the most abundant products of the MR. HMF, which is an intermediate in the MR, has received considerable attention recently owing to its potential toxicity and abundance in thermally processed foods. Bread and coffee have been identified as the most important contributors to dietary intake of HMF. A possible pathway for the synthesis of HMF during the MR is given in Figure 6.

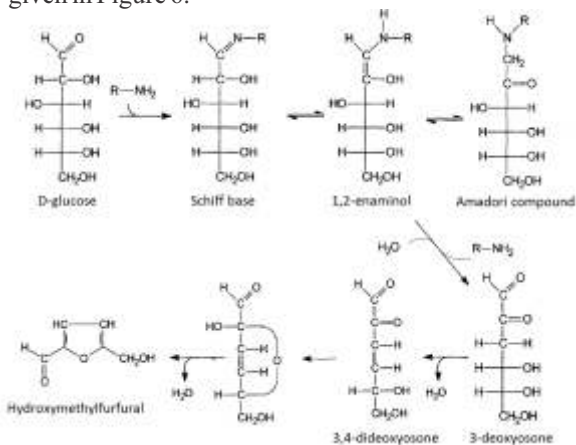


Figure 6. A possible pathway for the synthesis of 5-hydroxymethylfurfural.

In vitro studies with bacterial test systems have demonstrated that furfural, HMF, and 5-methylfurfural are mutagenic compounds possessing DNA breaking activity in the presence of Cu^{2+} . With an estimated acute oral LD50 value of 2.5 g/kg, HMF has proven to be cytotoxic at higher concentrations, causing irritation in

Acrylamide is another important heat-induced contaminant having potential carcinogenic activity. Acrylamide was added to the list of food-borne toxicants following its detection in several heat treated foods such as potato chips and crisps, coffee, and bread by the Swedish National Food Administration in 2002. MR has been identified as one major pathway for acrylamide formation in foods. Asparagine, a major amino acid in potatoes and cereals, has been identified as the main precursor for the formation of acrylamide during the MR. Two major hypothetical pathways for the formation of acrylamide are via the Strecker aldehyde route and glycoconjugation of asparagines. A

Glc + Gly $\rightarrow$ 4-Hydroxy-3(2H)-furanones + Pyrazine cation radical + Many other components

Pyrazine cation radical + Creatinine $\rightarrow$ Imidazoquinoxaline-type mutagens

The diagram illustrates the chemical pathway for the synthesis of Acrylamide. It begins with the reaction of an Amino acid ($Z-CH(NH_2)-COOH$) and a Dicarboxylic compound ($O=C(R_1)-C(=O)R_2$). This reaction, involving the loss of H_2O , forms an intermediate cyclic structure. Subsequent loss of CO_2 leads to a Schiff base intermediate ($Z-CH=N-C(R_1)=C(R_2)-COOH$). This intermediate can follow two main pathways:

- Strecker Pathway:** Reaction with H_2O yields a Strecker aldehyde ($Z-C(=O)-CHO$), which then reacts with NH_3 to form a Strecker amino aldehyde ($H_2N-C(=O)-CH_2-CHO$). This intermediate can cyclize to Acrylamide or undergo further reactions (indicated by a dashed arrow and a question mark).
- Acrolein Pathway:** The Schiff base intermediate can lose $R_1-CO-CO-R_2$ to form Acrolein ($CH_2=CH-CHO$). Acrolein reacts with NH_3 to form Acrylamide ($CH_2=CH-C(=O)NH_2$).

The toxicity of acrylamide is well-documented. Acrylamide has been shown to be neurotoxic, mutagenic, and carcinogenic to rodents as well as humans. Carcinogenicity of acrylamide has been attributed to its ability to form DNA adducts, which results in mutagenesis. Additionally, acrylamide has been shown to cause tumorigenesis in a range of rodent organs including lung, uterus, skin, mammalian gland, and brain. Acrylamide is considered to have no

threshold limit of exposure as it is a genotoxic carcinogen.

Advanced glycation endproducts

The MR is not only restricted to food systems, but also occurs in biological systems. When occurring in the human body, the MR is referred to as Glycation. The term Advanced Glycation Endproducts (AGEs) is used to describe the large group of heterogeneous compounds that originate from MR in human body. Although the term was restricted for MRP produced in the human body at one point, the researchers now use the terms AGEs and MRP interchangeably, irrespective of the site of origination.

Mounting evidence suggest that endogenous AGE generation is associated with various pathological processes leading to the development of chronic diseases such as diabetes, kidney diseases, atherosclerosis, and neurodegenerative diseases. It has been discovered that AGEs, via receptor and non-receptor mediated mechanisms, induce pro-inflammatory activities and generate reactive oxygen species. The relationship between dietary MRP and the risk of chronic diseases has not yet been clearly defined. Many recent research studies provide evidence to support the hypothesis that food-derived AGEs make a substantial contribution to the development of chronic diseases. However, at present, the evidence to support this hypothesis is weak due to flaws of the research studies conducted in the area. More well-designed, clinical longer cohort studies should be conducted in future to establish the relationship between the intake of dietary MRP and chronic disease risk.

Maillard reaction products: are they as bad as they look?

Despite all the negative effects, the fact that Maillard reaction products (MRP) pose a serious health risk to humans still remains controversial since several studies have failed to establish a correlation between MRP and subsequent adverse health effects associated with them. These observations can be explained by the possible beneficial effects of some MRP. While some MRP show cytotoxic, genotoxic, mutagenic, and carcinogenic properties, several others have shown to possess antioxidant, anti-mutagenic, and anti-carcinogenic activity.

Antioxidant activity of MRP was first reported in the early 1950s. Numerous research studies have demonstrated that the crude MRP as well as the high-

molecular weight and low-molecular weight fractions act as antioxidants by scavenging free radicals and reactive oxygen species, chelating metal pro-oxidants, and inhibiting hexanal oxidation and lipid peroxidation reactions. Furthermore, numerous studies have proven that some MRP including melanoidin pigments possess other health-promoting effects such as chemopreventive and antimutagenic properties. It can be assumed that antioxidant and antimutagenic MRP counteract with the toxic MRP, neutralizing their harmful effects to a certain extent.

The Challenge for Food Scientists

Although the discovery of the MR dates back to more than 100 years, the chemistry behind its network of complex reactions is yet to be revealed completely. While some pathways lead to the formation of desirable products in terms of food quality and safety, others result in the formation of toxic compounds. As with many other processes, the key is to find the balance between the reactions that form favorable and unfavorable intermediates and end-products. The greatest challenge for food scientists in future is to characterize the harmful and beneficial MRP and optimize the food processing operations in such a way that the resultant products have the best appearance and flavor profiles with the minimum levels of neo-formed contaminants.

Meanwhile, the wise choice for the consumers would be to control the dietary exposure of potentially harmful MRP by limiting the foods containing such compounds and by altering the cooking methods which produce these toxic chemicals until the safety of such products is assured through science-based risk assessment methods.

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Guest Article 05

Heavy Metal Removal from Wastewater

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'Heavy metals' are chemical elements with a specific gravity that is at least 5 times the specific gravity of water and these are one of the major pollutants containing in wastewater. Agricultural, manufacturing, pharmaceutical, industrial or residential processes can be considered as some major sources of discharging heavy metals into the environment. Continuous monitoring of the effluents is needed as dangerous constituents such as heavy metals can enter the water table and eventually the groundwater flow. These contaminants can then be moved to water supply aquifers down flow and can enter the human body through water. Living organisms require trace amount of some metals but excessive levels can be detrimental to the organism. These metals may enter human body through food, water, air, or by absorption through skin. Though some elements are harmless at normal concentrations, they may be toxic if they are present in higher concentrations. Hazardous heavy metals can easily affect human beings in various ways. Heavy metals become toxic when they are not metabolized by the body and accumulated in the soft tissues. Therefore, treatment of wastewater plays an important role because heavy metal content can be reduced by introduction of proper treatment processes.

Atomic Absorption Spectroscopy (AAS) is usually used for the determination of heavy metals due to its simplicity, sensitivity and specificity. Flame Atomic Absorption Spectroscopy (FAAS) is a common analytical technique used for the qualitative and quantitative determination of an element in a sample. Major advantages of this technique state

inexpensiveness, ease of use, high sample throughput and high precision. Ultimately, this is the most suitable equipment for day-to-day use. Though, AAS technique is widely used, there are a few disadvantages too. Those disadvantages include, problems associated with refractory elements, difficulty of differentiating between oxidation states of an element, and capability of analyzing only the liquid samples.

Adsorption processes are widely used for the removal of heavy metals from wastewater. Adsorption occurs when molecules diffusing in the fluid phase are held for a period of time by forces emanating from the adjacent surface. Adsorption operations are carried out by the addition of an adsorbent into the adsorbate containing solution for a given period of time to allow the adsorbate to be adsorbed. There are three types of adsorption processes; batch adsorption (single stage), multistage cross-current adsorption, multistage counter-current adsorption. All these processes are widely used in industrial settings. Adsorbents can be prepared using a wide range of materials. Current researches are heavily based on low cost adsorbent materials or materials that can be found free of charge. These materials are very useful as they can be replaced cost effectively once the maximum adsorption capacity is reached. One of the major categories of low cost adsorbent material is coconut based products. Coconut shell, husk, coir pith, coconut tree sawdust can be used to prepare activated carbon. Activation process can be mainly divided into two categories; chemical activation and physical activation. In chemical activation, a catalyst is impregnated into a raw material.

The impregnation influences the pyrolysis by maintaining minimum tar formation and volatilization. Chemical activation is used for wood-based carbons industrially and generally carried out within the temperature range 400-800 °C. Physical activation process is also called as partial gasification. This is achieved by the direct reaction of carbonized char with a gaseous or vapor state activant. In both these processes, the porosity is developed by removing amorphous (or tarry) carbons which are present in the interstitial positions in a disorganized manner. Porosity is responsible for the retention of contaminants in adsorbent materials and also, the adsorption capacity increases with increasing surface area.

Other important categories of adsorbents are adsorbents derived from agricultural by-products, industrial solid wastes and polysaccharide based materials. Silk cotton hull, peat moss, sago industry waste, waste bio gas slurry, banana pith, orange peel, fruit stones (olive, apricot, peach), almond shells, rice hulls, maize cob, red mud containing porous zeolite and tea waste are some of the materials which can be used as raw materials to prepare adsorbents. Anaerobically digested sewage sludge with the additive coconut husk can be used as a good adsorbent material for the removal of pollutants and this provides a disposal solution for the sewage sludge which is an increasing problem nowadays. Materials containing high amount of carbon is well known to be used as precursors for activated carbon. Carbonaceous waste generating from petroleum refineries can be used as precursors for active carbon. Waste car tires can also be used to produce activated carbon as it has high carbon content. These materials are capable of removing not only heavy metals but also some other substituents such as cations, anions, textile dyes, organic compounds and dissolved gases which are present in waste water.

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Retrosynthesis

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“A problem solving technique for transforming the structure of a target molecule to a sequence of progressively simpler structures along a pathway which ultimately leads to simple or commercially available starting materials for a chemical synthesis”
(E.J. Corey)

Introduction

The preparation of a desired organic compound from readily available starting materials is called organic synthesis. With complex molecular architectures multistep synthesis is needed. Organic synthesis is often very similar to a game of chess. In chess series of logically planned moves are required. Similarly in a synthetic problem, series of systematically planned chemical transformations are required to make the target molecule.

The process of deconstructing the desired organic molecule into readily or commercially available starting material via planned bond disconnections with strategic prioritization is referred as retrosynthesis. This is the exact reverse of chemical synthesis. The symbol is used along with the curved line drawn through the bond is being breaking to show the retrosynthesis process.

Robert Robinson first introduced this idea as imaginary breaking of bonds to break down the target molecule during his seminal work with tropine synthesis in 1917 (Figure 1).

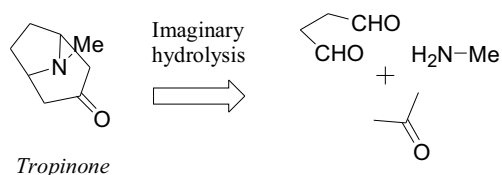


Figure 1. Robinson's analysis

In 1960s, undoubtedly the most decorative synthetic chemist in the history of organic synthesis, Prof. E.J Corey at Harvard University developed the concept of retrosynthesis. The systematic synthetic planning via logical disconnections in complex molecular synthesis was soon recognized by the scientific community and Corey was awarded with Nobel Prize in Chemistry 1990.

Useful retrosynthetic terminologies

FGI - (Functional group interconversion)

Synthone - Generalized fragment produced by the disconnection

Synthetic equivalent- A reagent carrying out the function of synthone.

Target molecule - The molecule we wish to prepare.

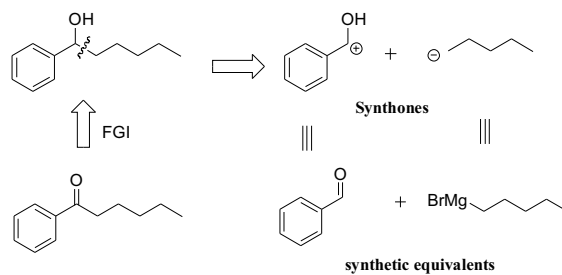


Figure 2.

General guidelines

[1]. Must be logical

Retrosynthesis is a reverse of a synthetic reaction. Therefore disconnection must be logical to have a viable chemical reaction. **Figure 3** (A) shows a bad disconnection where 1,3-dibromobenzene is produced as synthone. The forward reaction is not possible in this fashion unless organometallic chemistry is applied. Following the better disconnection strategy (B), the forward reaction can be easily achieved using the nucleophilicity of the phenate ion.

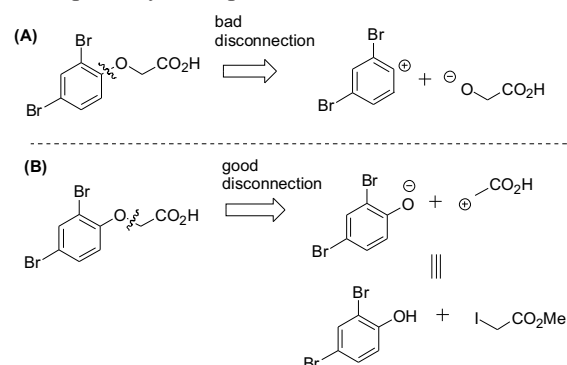


Figure 3

[2]. Simplify the Target

As shown in **Figure 4**, substituted rings can be simplified by strategically disconnecting the side chains.

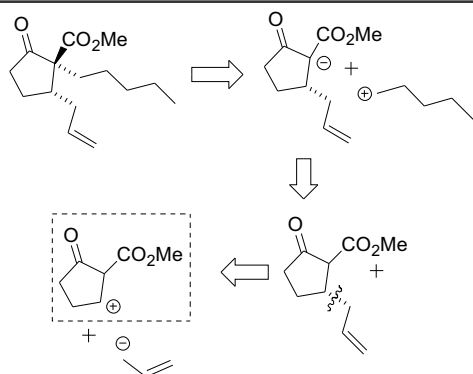


Figure 4

[3] Strategic bond disconnections

(a) Heteroatom disconnections

Esters and amides are often easier to make therefore disconnection of those bonds would be a good strategy.

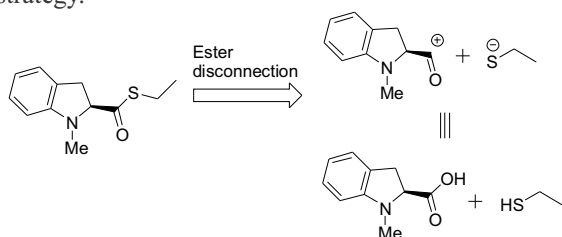


Figure 5

(b) Branch point disconnection

In acyclic systems, branch point disconnection gives a straight chain which is usually commercially available or can be obtained easily.

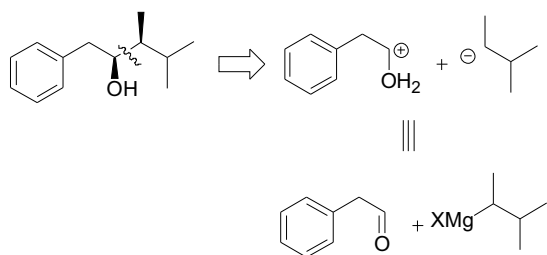


Figure 6

(c) Linked ring disconnection

When two rings are connected with a single bond, strategic ring junction disconnection will simplify the target.

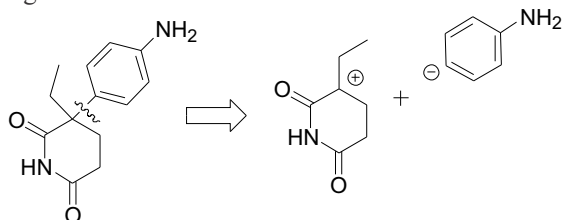


Figure 7

(d). Disconnection of ring systems

Bond disconnection should not result even larger rings.

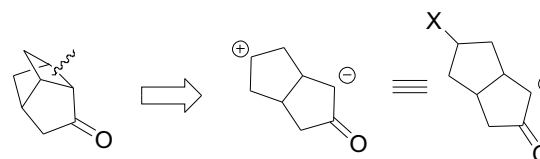


Figure 8

[4] Use known reliable reactions via recognizing the pattern

Identification of moieties within the target which are associated with reliable chemistry is known as pattern recognition.

(a) α,β -unsaturated carbonyl pattern via Aldol reaction

α,β -unsaturated carbonyl pattern is a common structural motifs finds in many complex organic molecules. As shown in the figure 3, α,β -unsaturated carbonyl pattern could be easily formed using the aldol reaction.

Retrosynthetic analysis

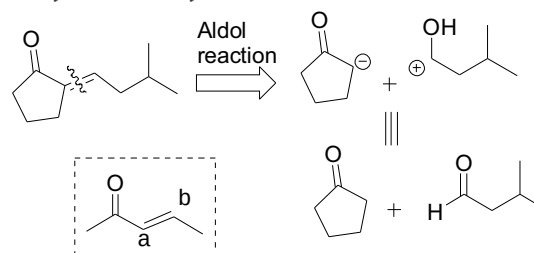


Figure 9.

(b) Diels-Alder (D-A) pattern

The Diels-Alder reaction region selectively forms two C-C bonds in one step. The disconnection of six membered rings to reveal diene and dienophile is often straight forward using *retro*-Diels-Alder strategy as shown in figure 5.

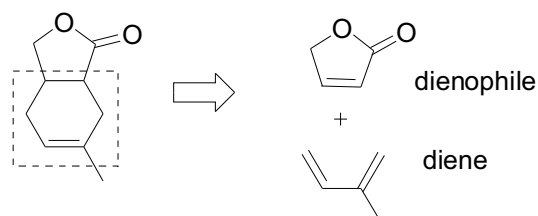


Figure 10.

[5] Start with the protecting groups

Protecting group manipulation plays a key role in organic synthesis. Therefore most probable final step of a synthesis is unmasking the protecting groups which have been used during the synthesis.

Strategically putting back those protecting groups should be considered during the retrosynthetic analysis as shown in Figure 11.

Retrosynthesis

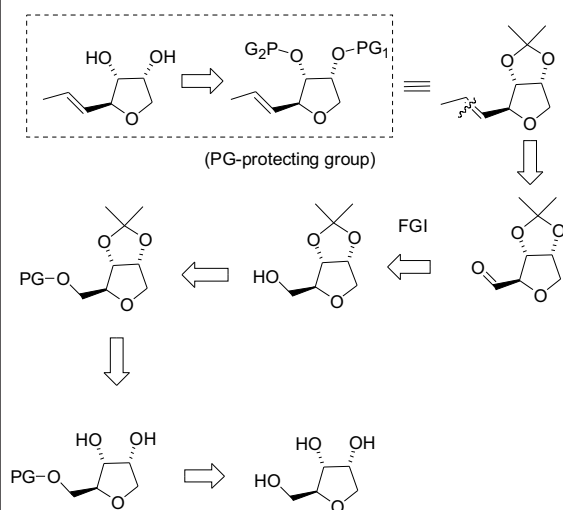


Figure 11.

[Activity: Design a chemical synthesis pathway based on retrosynthetic analysis shown in Figure 11.]

[6] Try to spot the common chirons like amino acids embedded in the target molecule as shown in the dotted circle in Figure 12.

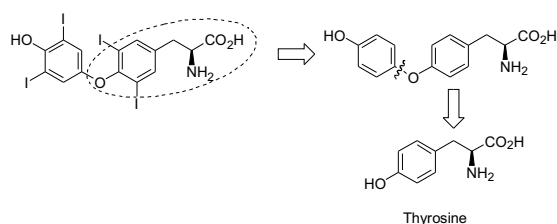


Figure 12

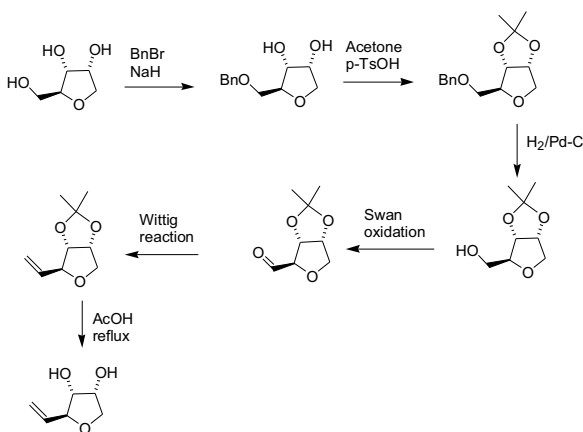
[7] Make it short as possible

“Get the most done in the fewest steps and in the highest yield” (R.E. Ireland)

References

1. Robinson, R. *J. Chem. Soc.*, **1917**, 111, 762
2. Corey, E. J. Nobel Lecture, 1990.

Solution



Certificate Courses at CCS

with hands-on experience

We are happy to announce that CCS is offering following certificate courses

Course	No. of credits	Starting date	Day and Time	Early bird fee (before 10 th Oct)	Regular fee (From 11 th Oct)
Cosmetic Science	2	08/11/2015	Sunday 4.15-6.15 pm	Rs. 6000	Rs. 7500
Food Chemistry & Technology	3	08/11/2015	Sunday 12.50-4 pm	Rs. 7500	Rs. 9000
Nanotechnology	2	06/11/2015	Friday 4-6 pm	Rs. 6000	Rs. 7500
Atomic Spectroscopic Methods and Analysis	2	02/11/2015	Monday 4-6 pm	Rs. 6000	Rs. 7500
Green Chemistry & Sustainable Technology	1	04/11/2015	Wednesday 4-6 pm	Rs. 4500	Rs. 6000

The classes for above courses are held for 8-15 weeks depend on the number of credits. Application forms can be obtained from CCS office, 341/22, Adamantane house, Welikada, Rajagiriya or can be downloaded at <http://www.ichemc.edu.lk/>. Please contact 011 4015230, 011 2861653, 011 2861231 or email Dr Lamabadusuriya at manuja_uoc@hotmail.com for any inquiries.

45th Annual Sessions of the Institute of Chemistry Ceylon 2016

Theme:

Ethics and responsibilities of professional Chemists for the National Development

Date: June, 2016

CALL FOR ABSTRACTS AND EXTENDED ABSTRACTS

Last Date for receiving abstracts and extended abstracts is 31st January 2016

AWARDS 2016

The following awards will be presented at the Annual Sessions 2016 of the Institute of Chemistry Ceylon.

- **Dr. C L de Silva Gold Medal Award**

Awarded for an outstanding research contribution in any branch of Chemical Sciences and/ or the use of such research for National Development during the last five (5) years in Sri Lanka. Credit will be given for the utilization of local raw materials, and where the contribution has already resulted in (i) a publication in a Citation Indexed Journal or (ii) Registering a Patent or (iii) where the contribution has already resulted in a positive impact in the development and innovation in the industry.

- **INSTITUTE OF CHEMISTRY SILVER MEDALS**

Devanathan Memorial Award

Awarded for an exceptional research contribution of an original nature in the field of Physical Chemistry and or related areas, such as Physical-Inorganic, Physical-Organic and Biophysical chemistry.

Chandrasena Memorial Award

Awarded for an exceptional research contribution of an original nature in the field of Organic Chemistry and/ or related areas such as Biochemistry, Pharmacognosy, Molecular Biology and Bioactivity studies.

Ramakrishna Memorial Award

Awarded for an exceptional research contribution of an original nature in the field of Inorganic and/ or Analytical Chemistry and/or related areas such as Bio-inorganic Chemistry or Bio-analytical Chemistry.

- **INSTITUTE OF CHEMISTRY BRONZE MEDALS**

Kandiah Memorial Awards

Awarded for the best research contribution in Chemistry carried out by a postgraduate student registered for a postgraduate degree by either course work or/ and research at a Higher Educational Institute in Sri Lanka and for work carried out in Sri Lanka, with the exception of special analysis that cannot be done in the country. Such results should be less than 20% of the findings from the work. Sandwich programs carried out partially abroad do not qualify for the award.

Kandiah Award for Basic Chemistry

For research predominately in basic Chemistry (Organic, Inorganic, Physical, and Analytical).

Kandiah Award for Applied Chemistry

For research in Chemistry related areas such as polymer, food, biochemistry, biotechnology, where interdisciplinary research is involved and provided that chemistry has a central role and comprises at least 50% of the content.

Kandiah Memorial Graduateship Award

For the best piece of research in the Chemical Sciences carried out by a Graduate Chemist of the College of Chemical Sciences/ Institute Chemistry Ceylon registered with a Higher Education Institute for a Post Graduate Degree.

- **Professor M. U. S. Sultanbawa Award for Research in Chemistry**

Awarded for the best research paper presented at the Annual Sessions of the Institute of Chemistry Ceylon, for work carried out and completed in Sri Lanka.

Closing date for receiving applications/ nominations for the above awards: **29th February 2016**

Further information could be obtained from the Registrar, Institute of Chemistry Ceylon or www.ichemc.edu.lk

PUBLICATIONS OF THE INSTITUTE OF CHEMISTRY CEYLON

Monograph	Title	Author	Price
01	Textile Fibers	Mr T Rajasekeram	Rs.50/-
02	Principles of Food Preservation	Prof U Samarajeewa	Rs.75/-
03	Biotechnology	Prof C P D W Mathew	Rs.75/-
04	Recombinant DNA Technology	Prof J Welihinda	Rs.75/-
05	*Natural Toxins in Foodstuffs	Prof E R Jansz & Ms A S Perera	Rs.50/-
06	Fat Soluble Vitamins	Prof E R Jansz & Ms S Malavidana	Rs.50/-
07	Nucleic Acid and Protein Synthesis	Prof J Welihinda	Rs.75/-
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09	Corrosion of Materials	Dr A M M Amirudeen	Rs.75/-
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11	*Environmental Organic Chemistry	Prof S Sotheeswaran	Rs.150/- (US \$3)
12	Enzyme Kinetics and Catalysis	Prof (Mrs) S A Deraniyagala	Rs.100/-
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14	Organotransition Metal Catalysts	Prof S P Deraniyagala & Prof M D P De Costa	Rs.75/-
15	Some Important Aspects of Polymer Characterization	Prof L Karunanayake	Rs.75/-
16	*Hard & Soft Acids & Bases	Prof (Mrs) Janitha A Liyanage	Rs.65/-
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02	Zinc Metalloproteins	Prof (Ms) R D Wijesekera	Rs. 175/-
03	Conformational Analysis and Reactivity of Organic Molecules	Prof S Sotheeswaran & Dr. (Ms) H I C de Silva	Rs. 175/-

General Publications

- ★ **Chemist & The Environment** (Rs.300/-)
- ★ **Infrastructure Support Services for Industrial Development** (Rs.200/-)
- ★ **Chemical Industries in Sri Lanka – Part II** (Members: Rs. 200/-, Non-members: Rs.275/-)
- ★ **Proceedings of the Workshop on the Technological aspects of the Production & Processing of Essential oils in Sri Lanka** (Rs.100/-)
- ★ **Proceedings of the Training Seminar on Towards a Cleaner Industrial Environment in the New Millennium** (Rs.150/-)
- ★ **A-Level Chemistry Facts, Patterns & Principles by Dr. Seetha I Rodrigo** (Rs.1500/-)
- ★ **Proceedings of the Prof R S Ramakrishna Memorial Training Seminar on Modern Analytical Methods** (Rs.200/-)
- ★ **Historical Accounts of the Educational Activities (1972 - 2004)** (Rs.350/-)
- ★ **Proceedings of the Training Seminar cum Workshop on Sampling, Statistics and Standardization in Chemical Analysis and Environmental Management** (Rs.150/-)
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- ★ **Industry & Environment** (Rs. 200/-)
- ★ **Herbal Medicine Phytopharmaceuticals and Other Natural Products: Trends and Advances** (Rs. 500/-)
- ★ **Chemistry in Sri Lanka** (Rs. 150/-)





RSC NEWS

THE ROYAL SOCIETY OF CHEMISTRY SRI LANKA SECTION

1. Membership

According to the records sent to us from the parent body, a breakdown of the membership is as follows:-

Category

Number

CChem, FRSC	11
FRSC	04
CChem, MRSC	12
MRSC	22
AMRSC	12
Affiliate /Under Graduate.	04
Total Membership as at July 2015	65

2. Committee of Management

The following were elected to the Committee at the 54th Annual General Meeting held in July 2015.

Hony. Chairman - Prof. Sudantha Liyanage
(till 25.08.2015)
Mr. R M G B Rajanayake
(from 25.08.2015)

Hony. Secretary - Mr. W K Samarakoon

Hony. Treasurer - Mr. I M S Herath

Committee Members -

Prof. Sudantha Liyanage (from 25.08.2015)
Prof W S Fernando Dr Poshitha Premaratna
Dr Piyal Ariyananda Dr M P Deeyamulla
Dr N Sirimuthu Mr Sulith Liyanage
Mr S Perasiriyan

Co opted Members

Dr Rajitha Hanarasinghe
Mr W A P Silva

3 Activities

3.1 Contributions to Activities of the Institute of Chemistry Ceylon

- (a) Full page advertisement of "Chemistry in Sri Lanka".
- (b) Contribution for the Interschool Chemistry Quiz
- (c) Award for the Best Performance at the Graduate ship Examination in Chemistry Levels 3/4 Theory Examination

3.2 All - Island Inter School Chemistry Essay Competition.

3.3 Inter University Chemistry Essay Competition

3.4 Book donation programme

3.5 A/L Teacher training workshop

3.6 Advanced Level Chemistry Seminar

3.7 Industrial Visit for B.Sc Special degree students, M.Sc students and RSC Members

3.8 Collaboration with SLAAS E-2 workshop and seminars

3.9 Supporting Chemical Societies of Universities in Sri Lanka

4. Web Site

The members are reminded of the web site of our Section, the address of which is as follows:-
www.rsc.org/Membership/Networking/International/sections/SriLanka/index.asp.

Mr W K Samarakoon
Hony Secretary

Theme Seminar

"The Role of Chemistry in Food Safety and Food Security"



Mr. E G Somapala



Dr. W M W Weerakoon



Prof. Upali Samarajeewa



Prof. T R Ariyaratne



Dr. Noble Jayasuriya



Prof. H D Gunawardhana



section of participants

Annual Dinner & Induction of New President, Mr. K R Dayananda



Prof. Siromi Samarasinghe,
Chief Guest



Mr. K R Dayananda was ceremonially inducted as the new President by presenting him the President's Medal.



section of participants



section of participants



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