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Biochem Trends

Newsletter

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Editorial

Overcoming challenges: The pandemic and beyond

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The global pandemic brought about many challenges, not simply physical challenges, but emotional as well as financial. Isolation, quarantine and lockdown came to be household words. Human contact was momentarily a thing of the past, until technology kicked in and people identified ways and means of bridging the gap. Our roles as researchers and educators changed overnight, we encountered new challenges and our abilities were put to the test. It took a few training sessions and several attempts of learning on the job by academic staff in universities to master online teaching involving, learning management systems, online teaching tools (i.e Zoom, Google Meet, Microsoft Teams), online assignments and even online examinations.

However, this did not come without its own set of challenges, especially when teaching large classrooms. Keeping the students interested and focused was a global issue, with overcoming technical challenges such as lack of smart devices and connectivity problems adding to the challenges in low-income countries. While the latter required external aid, keeping the students motivated was solely the responsibility of the teacher, this could not be carried out merely by having attractive slides, the teacher had to ensure student participation using breakout rooms, online polls, discussion boards and activities all the while attempting to overcome the uncomfortable feeling of talking to themselves (when the students would not or could not switch on their videos).

Undergraduate and postgraduate students in Biochemistry and Molecular Biology faced laboratory closure and suspension of laboratory experiments resulting in many stresses. Several tools have been identified to overcome this challenge. **Virtual laboratories** are top on this list.

While virtual laboratories gave students the opportunities to perform experiments at home, they were not able to replace physical experiments entirely and were only beneficial as a tool in an academic setting. This hindrance was somewhat eliminated using **Teaching labs**. In this situation the practical class was conducted onsite by the tutor in the form of a demonstration with the students connecting online. Further details on teaching large classes, conducting teaching labs and online assessment have been outlined in the report of the 1st Virtual Education Symposium themed "The 'New Normal' Biochemistry and Molecular Biology Education" published in the IUBMB newsletter (https://iubmb.org/wp-content/uploads/2021/12/IUBMB-Newsletter-Issue-12.pdf)

The **Biochemistry Authentic Scientific Inquiry Lab (BASIL)** curriculum provided students with an experience where they were able to make connections between techniques that were computational in nature as well as in wet lab-based techniques. This was a module-based curriculum that allowed the student to generate original hypothesis-based on analysis of proteins of unknown function. This curriculum is available at https://basiliuse.blogspot.com/. While we will continue to be innovative in finding new ways to conduct online teaching and laboratory activities, we are now cautiously entering the laboratories.

Most research that required an onsite presence and were abandoned are being revamped, maintaining health guidelines and being socially responsible have now become key factors to consider. The number of researchers in a lab at a given time, the space between two people and spatial dimensions had to be planned meticulously. Prior reading was made available online to prepare research students before they entered the lab giving rise to students who came into the lab better equipped. The laboratory environment may never have been this hygienic and safe with each person entering being masked and gloved and sanitised. Standard operating procedures (SOPs) for sanitizing and rules for wearing proper protective equipment (PPE) have been established.

We may still not have overcome all hurdles, we are still exploring, we are yet to take the bull by the horns. Yet we have come a long way from where we began. Some of the methods we learnt over the past two years were successful in making us better teachers and researchers. We now move forward integrating some of these methods into our post-pandemic curricula worldwide. We also move forward understanding that the world today is a smaller place and that we are all connected in more ways than one.

Newsletter Editorial committee

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Dr. Maduka de Lanerolle Dias
Newsletter, Editor

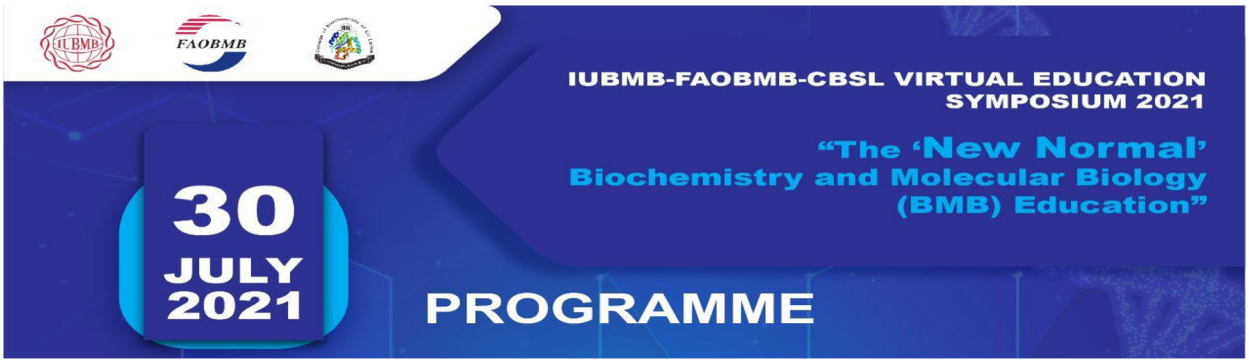
Dr. KDK Peshala Kumari

Prof. Usha Hettiaratchi

Events: 2021

The 3rd CBSL conference,

The 3rd CBSL conference, was held as a hybrid event on the 24th of July 2021. The theme of the conference was "Natural products and microbes for health and sustainability". The line-up included eminent international speakers such as Prof Angelo Azzi (Former President, IUBMB) and Prof Iqbal Choudhary.



The IUBMB-FAOBMB-CBSL Virtual Education Symposium 2021:
The 'New Normal' Biochemistry and Molecular Biology (BMB) Education

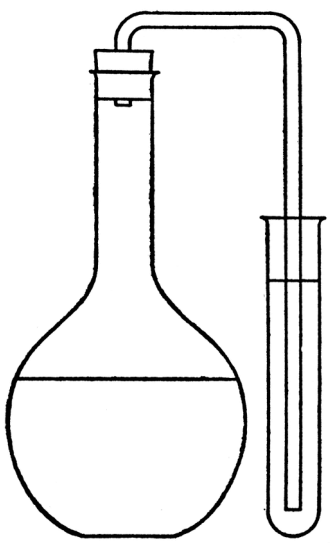
This Virtual Education Symposium was held on the 30th of July 2021. The event provided the participants with a valuable opportunity to explore more creative, innovative and interactive ways of teaching and learning Biochemistry and Molecular Biology, in the 'new normal'. Distinguished educators as well as students from 26 countries participated with the keynote address delivered by Prof. Daniel Dries, Chair of Chemistry and Biochemistry, Juniata College, Pennsylvania, USA. The Presidents of IUBMB and FAOBMB and the Vice Chancellors of Universities of Colombo and Sri Jayewardenepura graced the occasion.

Speakers at the inauguration of the Virtual Education Symposium 2021

Workshop series on natural product research

A series of 10 workshops was conducted under the theme of "Natural Products Research: Modern Drug Discovery using Ethnopharmacology" which was organized by the College of Biochemists of Sri Lanka in collaboration with The Institute for Combinatorial Advanced Research and Education, General Sir John Kotelawala Defense University (KDU- CARE) from June to December 2021.

Renowned scientists in the field contributed as resource persons to enlighten the audience on the pharmacological activities of natural sources, the process of modern drug discovery using herbs, techniques in purification and characterization of bioactive compounds, the procedure of releasing commercial products to the market, *in vivo* studies related to natural product research, ethical considerations of conducting natural product research and the application of nanotechnology in natural product research.



1. Natural resources as sources for drugs
2. Natural resources toward novel drug discovery
3. Separation, Isolating, Chromagraphic and Characterization techniques
4. Commercialization of natural products
5. In vitro Bioassays: anti-cancer, antioxidant and anti-inflammatory activity
6. Toxicity evaluation of natural products
7. Application of nanotechnology for natural product research
8. Ethics related to natural products research

We congratulate the winners of the Oral and Poster presentations

3rd conference of the College of Biochemists of Sri Lanka

The best oral presentation

Development of novel herbal nano-nutraceuticals for diabetes mellitus

Ms. W. N. D. De Silva

Nutraceuticals are a new category of natural molecules that shade the frontier between drugs and food. Molecules used in nutraceuticals not only possess potent biological activities but can also be used as scaffolds for synthetic derivatives, significantly reducing the time and cost of development of new molecules with therapeutic potential. Nutrients, herbals and dietary supplements are major constituents of herbal nutraceuticals which make them instrumental in maintaining health, act against various diseases such as diabetes mellitus and thus promote the quality of life. Nanoencapsulation is an innovative approach that has potential applications in nutraceutical research. The encapsulation of medicinal plants into nano-systems is foreseen as a useful strategy to protect these bioactive compounds from undesirable effects of environmental conditions, thus retaining the structural integrity until the time of consumption or administration. Moreover, this approach may prevent bioactive metabolites from degradation during processing and digestion, thus enhancing subsequent bioactivity and bioavailability, and to promote controlled release as well as targeted delivery. Therefore, the present project is designed to develop, characterise, and evaluate the bioactivities of nanoencapsulated nutraceuticals from Sri Lankan flora.

W. N. D. De Silva

Department of Biochemistry, Faculty of Medicine,

University of Ruhuna, Sri Lanka

The best poster presentation

Phytochemical factories – metabolic differentiation of oil glands

Dr. Samiddhi Senaratne

Plants synthesize phytochemicals that are stored in specialized cells/organs. Species in the genus *Eucalyptus* (Myrtaceae) are rich in phytochemicals such as terpenoids in oil glands. Eucalypts are distributed widely in Australia while a few species are cultivated around the world including in Sri Lanka. Oil glands were initially thought to house exclusively volatile oils. Recent studies have debunked this theory and revealed that they also contain non-volatiles. A major discovery in recent years by our plant physiology research group from the University of Melbourne was the occurrence of two gland types in *E. brevistylis* that differ in their metabolic contents. Two visually distinct gland types, one that is translucent and the other golden-brown, led to the discovery of metabolic differentiation of embedded glands. The study shows that 'sesquiterpene glands', which are translucent-white, contain sesquiterpene alcohols. 'Triketone glands', which are golden-brown, contain β-triketones and sesquiterpene hydrocarbons. 'Triketone glands' seem to develop earlier in ontogeny. The consistent deployment of two metabolically distinct embedded gland types is a rare phenomenon and a novel finding. This proves that plants have mechanisms to maximize the efficiency of phytochemical biosynthesis. Such studies contribute to the development of phytochemicals with importance such as pharmaceuticals and pesticides.

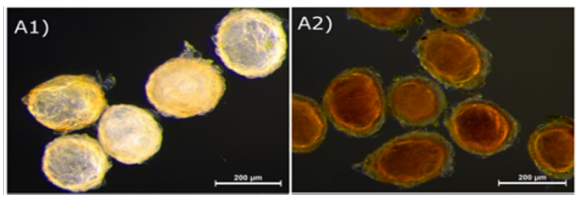


Figure: *Stereomicroscopic images of the two gland types isolated from the leaves of Eucalyptus brevistylis. (A1) translucent-white 'sesquiterpene glands' and (A2) 'triketone glands' in brownish-gold color.*

Dr. Samiddhi Senaratne, earned her B.Sc and M.Sc from the University of Colombo, and received her Ph.D in Plant Physiology at the University of Melbourne Australia, studying the biochemistry of foliar oil glands of *Eucalyptus* species. She has worked extensively on *Eucalyptus* oil gland chemistry and is continuing her research on plant secondary metabolites.

Merit Award - Oral presentation

Increased prevalence of obesity: Who is responsible?

Ms. Gayathri Rathnayake

Obesity has become an epidemic not only in developed countries but also in developing countries. Morbidity and mortality from diabetes mellitus, CVDs and cancers significantly increase with obesity. Obesity is considered as the most common cause of IR and T2DM. Previous studies have demonstrated that 40–80% of the variance in BMI and risk of obesity can be explained by genetic contribution. However, numerous research which have been conducted to identify genes which are responsible for obesity and related metabolic disorders have not been able to describe the development of obesity and metabolic diseases only due to genetics. Further, researchers suggest that obesity and related metabolic disorders are associated with a combination of environmental pollutants (obesogens), gut microbiota and specific nutrients through epigenetic variations. Elevated serum leptin level is present in most obese people and is considered as a state of leptin resistance. Genetic variations of leptin receptor (LEPR) gene including Q223R single nucleotide polymorphism (SNP) is considered as one cause of leptin resistance. Therefore, one of my research interests is focused on association between serum leptin levels with obesity and Q223R polymorphism to fill the current knowledge gap in Sri Lankan context.

Gayathri Rathnayake

Lecturer (Probationary), Department of Medical Laboratory Sciences, Faculty of Health Sciences, The Open University of Sri Lanka, Nawala, Nugegoda.

Merit Award - Poster presentation

In silico identification of a bacterial AlmA-like protein in _Aspergillus flavus_ NRRL 3357

Mr. Priyatharshan Viswanathan

Environmental pollution by petroleum hydrocarbons including crude oil has posed a significant problem in the recent past. Microbial bioremediation processes presents an ecologically and economically sound solution to address this issue. AlmA is a bacterial enzyme which is capable of degrading long-chain alkanes such as those found in crude oil. In fungi however, long chain alkane-degrading enzymes have been poorly described. The objective of this study, was to identify and characterize a fungal long-chain alkane-degrading enzyme, using in-silico methods. Verified AlmA sequence from *Acinetobacter spp.* was obtained from UniProtKB and a PSI-BLAST(20,000 seq) was performed. Highly similar *Aspergillus flavus* NRRL 3357 were obtained and then subjected to 'similar domain search' and 3D model prediction using i-TASSER. The same process was followed with bacterial AlmA 3D modelling. Proteins with similar domains were selected. The two sequences were superimposed in UCSF Chimera which gave an RMSD value of 0.547 angstroms. Validity of the models were further evaluated using ERRAT(87.7895) and verified using 3D(83.02%) and PROCHECK(92.1%). Based on these results it was concluded that the identified *A.flavus* sequence represents an AlmA like monooxygenase which may play a role in long chain alkane degradation.

Priyatharshan Viswanathan *(B.Sc)*

BSc Biotechnology, Microbiology,
Biochemistry(1st Class - Distinction)
University of Mysore - India

MSc Molecular Biology and Biochemistry (Reading)
Faculty of Medicine - Colombo

Merit Award - Poster presentation

Abelmoschus moschatus: A promising nephroprotective agent against Adriamycin-induced nephrotoxicity

Ms. Sachinthi S. Amarasiri

Abelmoschus moschatus Medik. (family; Malvaceae, English name: Musk mallow), commonly known as “Kapukinisssa” is widely being used in the treatment of a variety of diseases in traditional medicine in Sri Lanka. Potential nephroprotective effects of the hexane, ethyl acetate, butanol, and aqueous leaf extracts of *A. moschatus* were evaluated in an animal model of Adriamycin-induced nephrotoxicity. Treatments were carried out for 28 consecutive days as a daily single dose (human equivalent therapeutic dose) of the selected extracts (55 mg/kg, 75 mg/kg, 60 mg/kg, 140 mg/kg) for Adriamycin-induced (5 mg/kg, ip) nephrotoxic rats. The ethical clearance was granted by the Ethical Review Committee, Faculty of Medicine, University of Ruhuna (14.12.2015:3.1). Results revealed a significant attenuation of the features of acute kidney injury induced by Adriamycin, through the results of biochemical, histopathological and immunohistochemical assessments. The nephroprotective effects of the plant were mediated via antioxidant, anti-inflammatory, and anti-apoptotic mechanisms in Adriamycin-induced nephrotoxicity.

Sachinthi S. Amarasiri *(B.Sc. MLS (Hons))*
Lecturer in MLS, Department of Medical Laboratory Science, Faculty of Allied Health Sciences, University of Ruhuna Galle Sri Lanka.

Way forward with Nanomedicine; targeted drug delivery as an innovative treatment strategy against cancers

KDK Peshala Kumari *(PhD)*

Senior Lecturer

Department of Basic Sciences

Faculty of Allied Health Sciences

General Sir John Kotelawala Defence University

Joint Secretary - College of Biochemists of Sri Lanka

During the year 2020, 19.3 million new cancer cases and almost 10 million cancer deaths were reported globally. Hence, cancer has become one of the major global health burdens which expects to reach 28.4 million cases by 2040. A variety of conventional therapeutic modalities applied to treating and managing cancers include surgery, chemotherapy, radiotherapy and radiation-based surgical knives. Apart from that, modern techniques such as anti-angiogenic modalities, hormone-based therapy, dendritic cell-based immunotherapy and stem cell therapies have been introduced recently. However, the success of a particular therapeutic strategy is determined by a number of factors such as the locality of tumor, type of cancer and the stage of progression of cancer. Owing to various limitations, these therapeutic strategies may not be completely successful for all cancer cases. Due to non-specific targeting of tumor cells, conventional as well as most of the modern treating strategies have been less effective in majority of clinical cases. Apart from that a comparatively higher doses of drug should be administered during non-specific targeting in order to reach adequate amount of drug into the malignant cells. Most importantly, non-specific targeting is critical due to the drug entering into adjacent tissues which leads to damage of healthy cells during therapy. Recently, in order to overcome these limitations, efforts have been made to develop novel targeted drug delivery systems applying nanotechnology.

Nanotechnology is manipulation of matter at nanoscale (1 to 100 nanometres) in order to design, characterize, produce and apply structures to produce devices and systems. Due to the extremely small size of nanomaterials, they are presented with exceptional physical and chemical properties.

Application of nanotechnology in health care introduced a new subfield known as nanomedicine. The successful application of nanotechnology in drug delivery paves the path for a revolutionary advancement in therapeutics. Recently, smart drug delivery systems (SDDS) that have been developed using nano-carriers are recognized as an improved treatment approach which turned the conventional drug delivery in to targeted drug delivery. Nano-carrier based SDDS exhibit exceptional properties compared to conventional drug delivery systems. Nano carriers have been successfully improved the water solubility of the anticancer drugs which are poor in bioavailability. Apart from that, it was reported that the drugs are protected from dissolving in the blood circulation which leads to enhance the pharmacological and pharmacokinetic properties of the drugs remarkably.

The nano-drug delivery systems have been designed to deliver anticancer drugs successfully into tumour cells minimizing the entry of drugs in to adjacent healthy tissues. Hence, the drug becomes active only at the targeted cancerous tissues minimizing adverse effects on health tissues. Majority of them are capable of avoiding activation of the host's defense mechanisms while reaching its targeted site of action. The incorporation of anti-cancer drug within a nanocarrier facilitates a sustained release of the drug at the targeted site in a controlled manner. Novel nanosystems have been developed to minimize the loss of volume and the activity of the anticancer drug during circulation in blood prior to reach the targeted site. Thereby application of nano-carriers restricts the drug accumulation in non-targeted organs and improve the therapeutic efficacy of the drug action.

Passive and active targeting strategies have been applied widely to deliver drugs using nano-carriers. In passive targeting of drugs, the nanocarriers enter into tumor cells passively through the mechanism called enhanced permeability and retention effect (EPR), which allows drugs to accumulate in malignant cells in higher concentration than in healthy cells. The cellular phenomenon known as EPR is induced due to structural and biochemical abnormalities developed in malignant cells.

Active targeting is an advanced approach which was developed in order to overcome practical limitations of passive targeting. It is a strategy to functionalize the surface of the nanosystems adding targeting moieties such as antibodies, small ligands and biomarkers which can direct the drug delivery systems towards specific molecular targets in tumour cells.

This approach is much more efficient, because the molecular targets used in this technique are the overexpressed molecules in the malignant cells due to aggravated growth rate of malignant cells. They overexpress certain proteins and nucleic acids such as folate receptors, serum glycoprotein transferrin (transferrin receptor), human epidermal receptor 2 (HER-2), epidermal growth factor receptor (EGFR), membrane proteins, short single-stranded RNA or DNA oligonucleotides, etc. One or more such molecular targets are used to facilitate the selective uptake of drugs specifically into the tumor cells. Once the drug system is directed towards the tumor cells, they are internalized through receptor-mediated endocytosis which leads to accumulation of the particular drug system in elevated concentrations within the tumor cells. As a consequence, the drug delivery system provides a sustainable drug release within the tumor cells over a prolonged period of time.

Recently, a more advanced targeting strategy called stimulus responsive nano-carriers has been developed for controlled delivery of anticancer drugs at the site of tumor using an external trigger. Controlled release of drugs over a period of time through using a non-invasive stimulus ensures the drug delivery to the appropriate environment continuously. The stimuli applying for the purpose might be external or internal and the drug delivery system must be sensitive to the relative stimulus. Ultra-sound, magnetic field, light or radio frequency can be used as external stimuli while pH, temperature and presence of certain enzymes within the tumor cells can be considered as internal stimuli. With the use of such stimuli the anticancer drugs can be released at the targeted tissue with controllable rate throughout a prolonged time period.

A variety of nano-drug delivery systems have been developed recently, including lipid-based, polymer-based, biological-based, carbon-based and metal –based nano-carriers. The choice of the nano-carrier depends on the type and properties of the selected drug and in turn affects the bioavailability, biodistribution, specificity and pharmacokinetics of drug delivery. Apart from that, the stability and the fate of the delivery vehicle depends on several factors such as size, charge, rigidity, surface modifications as well as the solubility of the nanomaterial used. Among different types of nano drug delivery systems, liposomes, micelles, dendritic polymers, and polymer nanoparticles have been widely studied as drug carriers.

Among them liposomes have been discovered as the most biocompatible nano carriers as their chemical structure is similar to the structure of cellular membranes, which make them highly efficient in drug delivery. They are made up of a phospholipids bilayer which enclose an aqueous core. Hence, they are capable of loading both hydrophilic as well as hydrophobic drugs, which make them valuable.

Dendrimers are globular, nanosized (1–100 nm) polymeric macromolecules with a central core and polymeric branches arising from the core. The unique feature of dendrimers is that it consist of repeat chemical units with at least one branch junction and many terminal functional groups. Thereby, dendrimers possess precisely controllable nano-architecture through surface modifications. The nano-architecture of dendrimers can be fine-tuned through decorating with different chemical groups on geometrically symmetrical branches facilitating a wide range of different drug delivery systems suitable to different chemical environments. Apart from that several positive features made dendrimers suitable candidate to develop drug delivery systems including contain an internal molecular cavity and a variety of peripheral functional groups, good fluid mechanic performance, controllable molecular weight, strong adsorption ability and versatility. They have been widely studies as gene delivery vectors.

Micellar nanoparticles are formed by a hydrophobic core and a hydrophilic shell which is synthesized by self-assembly of amphiphilic block copolymers in an aqueous medium. The core acts as a reservoir of the loaded drug and prevent dissolution of the drug, while the shell contribute for the aqueous solubility and steric stability of the nanocarrier. Thereby, micellar based nano delivery systems remarkably enhanced the bioavailability of poor water dissolvable anti-cancer drugs, such as paclitaxel and docetaxel.

Up to date, a variety of novel nano-drug delivery systems have been studied in clinical trials against different cancers which led to release some of them to the market as pharmaceuticals. The first liposomal formulation which obtained approval from US Food and Drug Administration (FDA) was released to the market in 1995. The liposomal system which encapsulated doxorubicin (Doxil), was recommended to treat AIDS-related Kaposi sarcoma. Later in 2005, an albumin-based nano delivery system which encapsulated protein-bound paclitaxel (Abraxane) obtained approval from FAD for the treatment non-small cell lung cancers, breast cancers and pancreatic cancers.

A PEG-PLA polymeric micelle system which contain anticancer drug paclitaxel was approved by the FDA during 2007 for clinical applications A specifically targeted nanocarrier system which composed of ado-trastuzumab emtansine (Kadcyla) obtained FDA approval in 2013 to target human epidermal growth factor receptor 2-positive breast cancers.

Nanocarrier based anti-cancer drug delivery also exhibited potential in overcoming anti-tumour multidrug resistance (MRD), through the action against certain mechanisms of drug resistance. Thereby, nanomedicine has been recognized as a promising technology to overcome the challenging impediments against cancer therapy and will pave the pathway for successful treatment of cancers in near future.

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- ❑ Articles
- ❑ Letters to the editor
- ❑ Research highlights

Please submit to newsletter.cbsl@gmail.com

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Vertical A4 size, 210 x 297mm / 4961 x 7016 pixels

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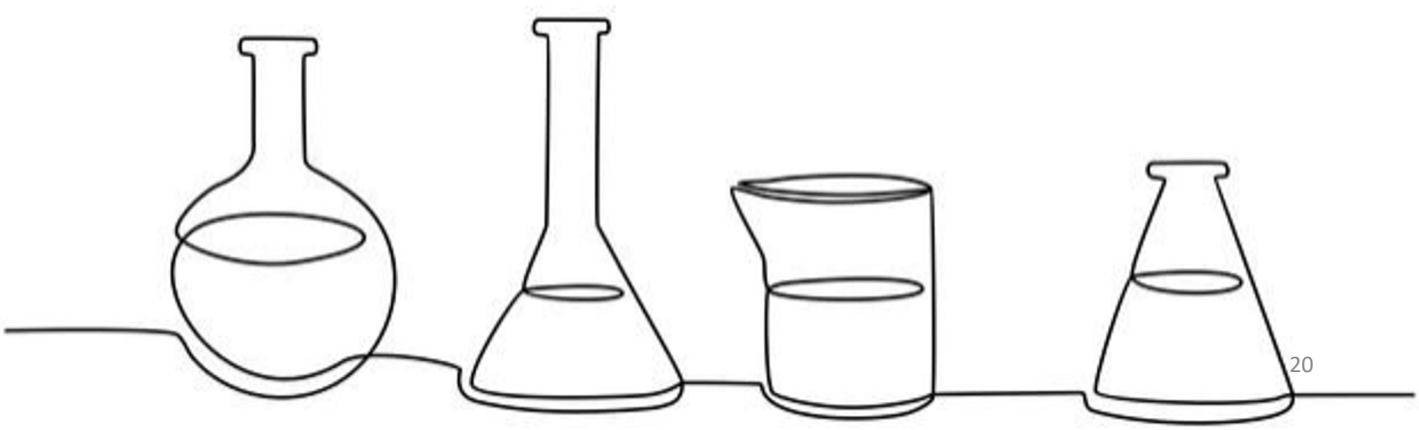
Articles should have a descriptive title, should not exceed 1500 words, including not more than 10 references, and include authors name (s), academic degree (s) and institutions(s), along with a photograph.

Letters to the editor

Letters should have a descriptive title, and should not exceed 500 words, including not more than 10 references. Begin with the salutation " to the Editor" and close with the authors name (s), academic degree (s) and institution (s).

Research Highlights

Short description on Research highlight, with a photograph



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