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New Year Edition, 2021

Editorial board

Editorial…

"Co-WIN 2.0 app" is now the buzz word as India is starting 4th Phase of COVID vaccination from 1st April 2021, in which citizens above 45 years of age will be vaccinated as per Government Guidelines. In addition to that Govt. also communicated those private hospitals that are empaneled under the AB-PMJAY, CGHS or the State's Health Insurance schemes would also be COVID19 Vaccination Centre (CVC) along with the Government health facilities. Government facilities will provide vaccines free of charges while private facilities may charge for vaccination which must not exceed Rs. 250 per dose. Now apart from Health care providers and Front line workers above 45 will get COVID vaccination from Government and selected private health facilities following prescribed procedure.

Presently two COVID-19 vaccines are available in India which have been approved by CDSCO after the Subject Expert Committee (SEC) of Central Drugs Standard Control Organization made recommendations in respect of Accelerated Approval of Covid vaccines developed by M/S. Serum Institute of India (SII) and M/S. Bharat Biotech International Limited. SII has developed the COVID vaccine with a brand name Covishield with a tie up with Oxford-Astra Zeneca and Bharat Biotech has developed the COVID vaccine Covaxin with a technical tie up with Indian Council of Medical Research (ICMR). The vaccine developed by SII in collaboration Oxford-Astra Zeneca has already been approved by several countries and is in use since last few months, but Covaxin has been developed indigenously by M/S. Bharat Biotech International Limited jointly with Indian Council of Medical Research (ICMR). Both the vaccines are easy to store at 2-8 degrees centigrade for its stability, whereas the vaccine developed by Pfizer BioNTech requires to be stored at -70 degree centigrade which needs huge cold chain infrastructure.

Dr. Subhash C. Mandal, Ph.D. -Editor

From Secretary's desk

Dear Friends,

A warm welcome to the new year, I hope the first newsletter of 2021 will speed up your planned activities.

Many congratulations to the editorial team for their contributions to release this newsletter regularly even during this tough time. On behalf of the newsletter team, I appreciate the efforts of article contributors, without whom publication of our newsletter would not be possible.

Our newsletter is a group effort and rely on contributions from all SFE-members for the content. So, let's contribute to our own newsletter. We want to know what projects you're working on. What's new with you and your organization. Let's make it a successful mode of exchanging scientific knowledge in the field of ethnopharmacology. I personally thank the members of the executive and editorial board of the newsletter, coordinators for the local chapters and all SFE-India members for their contributions to the society and the webinar series.

I look forward to the year 2021 and hope to meet and seeing you all face to face again.

Prof. Pulok K. Mukherjee, FWAST, FRSC, FNASc
Secretary, SFE - India

Webinar extracts

Polypharmacology of botanicals as key to breast cancer prevention

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Breast cancer is the most frequently diagnosed cancer occurring in women in Germany with almost 72.000 cases diagnosed in 2013 and an expected increase to 77.000 cases in 2020. It is unquestionable that estrogens play a pivotal role in the development of breast cancer, as about 70 % of all breast cancers cases are estrogen dependent, with four major mechanisms contributing to estrogen-dependent mammary gland carcinogenesis and breast cancer growth. These are the hormonal, the chemical, the inflammatory, and the epigenetic pathway[1]. Consequently, inhibition of any of these pathways may result in breast cancer prevention. So far, we focused on the hormonal pathway, which plays a key role in tumor promotion by estrogenic compounds through an estrogen receptor-α (ERα) dependent mechanism. While conventional therapies focus on the inhibition of synthesis of the ligand E2 or on inhibition of its function on the ERα by receptor antagonists, we hypothesize that the polypharmacological nature of botanical extracts may functionally inhibit ERα by simultaneously activating additional/alternative pathways, which in turn functionally inhibit ERα mediated effects. Those pathways comprise the ERβ signaling and the arylhydrocarbon receptor (AhR) signaling pathway. The examples provided here suggest that activation of the ERβ- [2] or the AhR-signalling [3] pathways by non-toxic, plant-derived agonists may represent a preventive strategy for hormone dependent mammary gland tumors.

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Development and Delivery a Right Antisense Drug: A Therapeutic Approach for the Treatment of Genetic Disorder Diseases

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Antisense oligonucleotides (AON) are known to inhibit gene expression by blocking translation of mRNA. Recently, antisense-based therapy has brought a new hope in fighting against a variety of genetic disorder diseases and has been introduced into the market for the treatment of Duchenne muscular dystrophy (DMD). Duchenne Muscular Dystrophy (DMD) is a genetic disorder disease caused by mutations in the dystrophin gene. Antisense drug is able to correct the mutations in DMD and restore truncated yet functional dystrophins. In 2016 FDA approved the morpholino-based drug “Eteplirsen” for the treatment of DMD. Though another 2'-O-Methyl thioRNA-based lead candidate ‘Drisapersen’ has completed Phase III trials, however, it has been rejected by FDA because of toxicity which limits dosing and efficacy. Both these drugs have poor cell permeability, hence in order to reduce the dose and improve the efficacy, a non-toxic delivery vehicle is required.

In this presentation, we report the synthesis of Internal Guanidinium Transporter called “IGT” using a Hg-free method for scale up and N-terminal modification of IGT with a suitable hydrophobic or lipophilic group to improve the cell permeability, endosomal escape, and mitochondrial localization and reduce toxicity in the MTT assay. For the delivery of antisense morpholino oligonucleotides, IGT-Morpholino conjugate was synthesized to target NANOG in cells, a transcription factor required for cancer stem cell proliferation and embryonic development and is involved in many cancers. Our data shows IGT-PMO-facilitated NANOG inhibition in cultured cells. IGT-PMO can inhibit no tail gene in vivo zebrafish model. Similarly, IGT conjugated thioRNA-based AON has been delivered against exon skipping genes of DMD patient to express right dystrophin RNA. Toxicity and immunogenicity tests have been completed which encouraged us to go for clinical trial.

In summary, a novel internally guanidinium linked nonpeptidic cellular transporter (IGT) has been developed which is synthetically accessible, readily tuned for optimal efficacy, and safe. Cellular internalization of IGT and delivery of antisense morpholinos in vitro and in vivo zebrafish model and antisense effect have been studied. Similarly, IGT conjugated thioRNA-based AON has been delivered against exon skipping genes of DMD patient and could be useful for the development of AON-based therapy for DMD patients.

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Quality Estimation of Agro Produces by Electronic Means

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Measurement of quality of agro-produces is a big challenge. By quality we mean the aroma, appearance, shape, size, taste, hardness etc. All the parameters measurement and quantification in terms of numerical index is an immense challenge. Expert sensory panel evaluation concentrates on the impact and characterization of the complex mixtures as perceived by the human senses. It is expensive to maintain skilled sensory panels and the number of replicate samples which can be evaluated at any time is limited by the onset of human fatigue. Conventional instrumental analytical techniques are also complex, expensive and time-consuming task which requires a well-equipped analytical laboratory and skilled-staff. As a result, there is a need for approaches using alternative techniques such as electronic nose, electronic vision and electronic tongue, which can complement these existing methods. We also perceived that Electronic perception technology can be a solution to address above problems where human perception mechanism is modeled in an electronic machine through training and soft computing algorithms.

We have extensively worked with electronic nose technology for quality estimation of tea, aromatic rice, jasmine, concrete, electronic vision for chilli - turmeric, tea, pulses, rice and electronic tongue for tea. An electronic nose (e-nose) is a device that identifies the specific components of an odor and analyzes its chemical makeup to identify it. An electronic nose consists of a mechanism for chemical detection, such as an array of electronic sensors, and a mechanism for pattern recognition, such as a neural network. Electronic noses were originally used for quality control applications in the food, beverage and cosmetics industries. Current applications include detection of odors specific to diseases for medical diagnosis, and detection of pollutants and gas leaks for environmental protection.

Electronic vision (e-vision) is a vision based technology for assaying the colour and dimensional quality parameters using electronic means. This technology stands on two major objects, one is Image Capturing Devices like camera, scanner etc. and another is Quality Analysis Software. The basic principle of operation is to determine the quality of different agricultural commodities based on its visual appearance or properties. In present scenario, this technology is used in different domains like quality analysis of Staple Crops like Rice, Wheat, different pulses, fruits & vegetables.

The electronic tongue (e-tongue) is an instrument that measures and compares tastes. Taste of food and beverage are composed of thousands of substances. Taste Sensor System can approximate and translate molecule information into visual taste information. Visual taste information becomes easily understandable and communicable when simplified and quantified. Quantified taste allows for Mathematical Optimization. Electronic tongue or taste sensors is an instrument, trained for screening the taste attributes of formulations in a rapid timeframe, when used in addition with human taste assessment data. Sufficient aqueous solubility of test compounds is necessary for application of the electronic tongue.

ENOVISION

E-Tongue

AMMAR

Resham darshan

Handheld e-Nose

Origanum dictamnus: a plant from ancient Greece till modern times. Analysis of its chemical content and evaluation of its relaxing effect on rabbit intestine

Prof. Anastasia Karioti

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Origanum dictamnus L. (Lamiaceae) is a Greek species endemic of the island of Crete, nowadays cultivated in other parts of Greece as well. In 2014 the Community Herbal Monograph was issued [1] giving new opportunities to the development and sustainable cultivation of this important medicinal plant. *O. dictamnus* herb and its aqueous preparations are listed in the category of Traditional Use Herbal Medicinal Products of the EMA for the treatment of several conditions, such as wound healing of skin inflammations and bruises, mild gastrointestinal disorders and relief of cough associated with cold. Despite its importance as a medicinal herb, the first systematic analysis of the non-volatile constituents was reported recently by the work of Chatzopoulou et al., [2] which revealed a variety of phenolic compounds. Continuing this work extended studies on the chemical content of aerial parts, roots and herbal teas of cultivated *O. dictamnus* were undertaken.

Targeted isolations guided by HPLC-PDA-ESIMS and NMR analyzes enabled us to create an in-house chemical library, but also revealed the presence of new constituents reported for the first time. Up to now more than 60 constituents have been identified, among them seven new natural products belonging to the classes of flavonoids, jasmonates and monoterpene derivatives.

Preliminary experiments with dittany infusions on rabbit intestine confirmed the ethnopharmacological use of the herbal drug in mild gastrointestinal disorders, as they produced a dose-dependent relaxing effect both in the jejunum and colon. At the threshold concentrations of 0.1 mg/ml for the colon and 0.3 mg/ml for the jejunum, dittany produced a slight decrease in both the phasic contractions and the basal tone, while at higher concentrations it caused a significant decrease in the tone and a considerable inhibition in the amplitude and frequency of the phasic contractions.

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dentification, pharmacological re-assessment, and conservation of medicinal plants used traditionally for the treatment of snakebite in India

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India has vast potential and rich diversity of snake fauna, of which only 242 species have been identified including 57 venomous or harmful species. Snakebite is a global problem, especially in the tropical countries like Indian subcontinent. Every year over 300,000 incidences of snakebite occur in India of which about 20,000 people die; therefore, treatment of snakebite deserve immediate medical attention. The most effective and accepted therapy for snakebite patients is immediate administration of specific or polyvalent antivenom following envenomation. Unfortunately, this therapy carries an associated risk of anaphylaxis and serum reactions.

Further, due to geographical variation in snake venom composition, antivenom raised against the venom of a snake from a particular geographical origin may not be able to neutralize or prevent local effects of envenomation by snakes from other geographical locations. Therefore, in addition to administration of antivenom, there should be alternative method(s) for the treatment for the snakebite patients. India has vast flora of medicinal plants. Many countries rely on these medicinal plants for the health and well being of its population, but the market demand has led to an increased pressure on the natural resources that lend to the production of some of these plants.

The most serious proximate threats when extracting medicinal plants generally are habitat loss, habitat degradation, and over harvesting. Numerous plant species are used as folk medicine to treat venomous snakebite all over the world, India included. Various plant extract have been reported to neutralize the toxic effects of snake venom. For example, aqueous extract from the *Casearia sylvestris* a typical Brazilian plant have been reported to inhibit the enzymatic and biological activity of PLA_2 enzymes as well as protease activity of *Bothrops* venom. Methanolic root extract of *Vitex negundo* and *Emblica officinalis* have been found to neutralize the lethal effect of *V. russellii* and *N. kaouthia* both *in vivo* and *in vitro* condition. We also reported the inhibition of toxic PLA_2 from *Naja kaouthia* venom by Indian medicinal plants. In ancient Indian books, there are many plants recommended for using in snakebite therapy. Many of these are used by snake charmers, traditional healers as well as local people of India, but without any scientific validation. Therefore, this type of treatment remains questionable and needs thorough scientific investigation. Proper taxonomic identification of medicinal plants used for the treatment of snakebite, their pharmacological reassessment against snakebite, and conservation of these plants medicinal plants are extremely important for finding an alternative therapy against snakebite. Nevertheless, results of these studies will also lead to conservation of biodiversity and rich cultural diversity of the region. For achieving this goal, Medicinal plant conservation strategies need to be well understood and planned for based on an understanding of indigenous knowledge and practices.

Honey: A gift of nature and its multifaceted actions towards the betterment of human health and life style

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According to the history of traditional knowledge-based health beneficial medications, natural products has been reported to be consumed by humans since antiquity and they has proven reports of safe and economical dietary options to treat or prevent several diseases and complications. They can even be used as complementary treatments to provide more comprehensive prevention or management against several diseases for which cures are either difficult, costly or even not available. Honey is a natural product with health-beneficial effects due to its potent antioxidant and anti-inflammatory properties. Honey is a sweet viscous fluid stored in wax-form structures called “honeycombs” after being harvested by honeybees from plants as floral nectar. It is produced through regurgitation, enzymatic activity, and water evaporation within beehives. Honey is composed of at least 181 substances, mainly carbohydrates like fructose (38%) and glucose (31%).

It also contains enzymes, amino acids, vitamins, proteins and polyphenols. The complex composition of honey actually makes it a double-edged sword in terms of its activity and efficacy. The good side of honey is that its major components has potential health beneficial effects. For example, one of the major functions that has been extensively reported for honey is its strong antioxidant activity. The antioxidant property of honey is attributed to its high content of polyphenol, mainly comprising of flavonoids (like quercetin, luteolin, kaempferol, apigenin, chrysin, galangin), phenolic acids, antioxidant enzymes (like glucose oxidase and catalase), ascorbic acid, and carotenoids.

The polyphenols in honey are responsible for various health beneficial effects mainly through suppressing ROS formation by inhibition of enzymes or chelating trace elements involved in free radical generation. On the other hand, the negative side of honey is high variability in its composition based on source, season, type of bees and a number of other factors. Therefore, there is need of balancing these two aspects and that is possible only through proper scientific validation of this natural product in terms of its composition-activity analysis. This will lead to the best possible utilization of this gift of nature. In addition, scientific adoption of “bee keeping” has the potential of changing the life style of rural population. Taken together, popularization of this natural product will not only impart health beneficial affects but also a revenue generating opportunity for a country like India, where various agro-climatic zones are conducive for its cultivation over and above its natural collection sources.

From in-silico to Bedside: Herbal Medicine for the Treatment of COVID-19 and its After effects in Lungs & CNS

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COVID-19 pandemic has emerged as an exceptionally, frightful contagious disease with substantial morbidity and mortality affecting more than 200 countries across the world. There have been over 20 million confirmed cases and 0.7 million deaths by August 2020. SARS-CoV-2 binds to Angiotensin-Converting Enzyme 2 (ACE2), a site that is also involved in the pathology of leading causes of mortality in the world, including cardiovascular, respiratory, and GI dysfunction. ACE2 is a mystery to the medical scientists as it regulates the renin-angiotensin system (RAS), which in turn, has an influence on the cardiovascular system, including the vital organs, kidney, heart, brain, lungs, and vasculature. The main molecular link of these morbidities and COVID-19 prognosis appeared to be ACE2 and Open Reading Frame protein (ORF8).

Unfortunately, there has been no remarkable breakthrough in the management of this disease to date, and the patient is given a treatment based on his observable and diagnosable symptoms. Although several attempts have been made in the research and development of the diagnostics, therapeutics, and vaccines for this COVID-19, there exists no chemotherapeutic agent, so far which is effective in COVID-19. To combat this deadly COVID-19, repositioning of many conventional drugs like chloroquine, hydroxychloroquine, but the clinical drug response is not very encouraging, and their toxicity remains an inevitable issue causing severe adverse effects. Major pathophysiological and molecular derangements that have drawn the attention of scientists for the discovery of the medicine that can be used for the treatment of COVID-19 include prevention of binding of the virus with ACE2 receptors leading to viral multiplication, immunostimulation, inflammation, and cytokine surge.

While studying various phytochemicals from plants reported in *Ayurveda* using molecular docking studies we found *Solanum nigrum* L. (family - Solanaceae) to be one of the most effective in herbal medicine for COVID-19. The results were correlated with published pharmacological studies in vitro studies and then the formulation was registered and taken to the clinical study in patients with COVID-19. Preliminary results provide that the formulation is effective as compared to Standard Care of treatment. The final results are still awaited. It is expected to bring down the not only the mortality in patients drastically but also be effective in prevention of Post Covid complications in lungs and CNS.

Important publications

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GENOME SEQUENCES

Coding-Complete Genome Sequences of NITMA1086 and NITMA1139, Two SARS-CoV-2 Isolates from Belagavi District, Karnataka State, India, Harboring the D614G Mutation

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Ishwar Singh and Umashankar Vetrivel contributed equally to this work. Author order was determined both alphabetically and in order of increasing seniority.

ABSTRACT We announce the coding-complete genome sequences of two isolates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from two coronavirus disease 2019 (COVID-19)-positive samples (RNA isolated from nasopharyngeal swabs) from Belagavi District, Karnataka State, India. Mutational analysis revealed the presence of the D614G substitution in both the isolates.

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