REPORT OF THE ICMR STRATEGIC THRUST SYMPOSIUM ON TRANSLATIONAL RESEARCH AND REVERSE PHARMACOLOGY

The past three decades have witnessed a resurgence of Ayurveda in India. The process was initiated with the application of Reverse Pharmacology (RP) to Ayurveda, which was followed by an integrative synthesis (of medical science and Ayurveda) that can bring out the best in each system and may result in a truly remarkable contribution to global human health.[3,4] It culminated in the evolution of the concept of a golden triangle partnership consisting of modern medicine, traditional medicine, and life sciences at Chitrakoot in 2003, which was later on adopted by the relevant research councils and departments, Government of India. While this process is being hailed as the ‘renaissance of Ayurveda’,[2] the ontological challenges in collaborative research involving Ayurveda and modern sciences are also being debated.[3,4] As multi-level efforts are being made to translate the concept into research and later into clinical practice, several new challenges are also emerging. This symposium was specifically planned to address these challenges and opportunities for translational research involving Traditional Medicine (TM) in general and Ayurveda in particular.

Inaugural session
Dr. Rama Vaidya, the organizing secretary and the Dean, Medical and Research Centre, Kasturba Health Society (MRC-KHS) elaborated on the model of trans-discipline bridge involving Ayurveda (with its basis of DravyaGuna); modern medical science based on pharmacology and life sciences, with inputs from epidemiology and biostatistics. Such an approach would provide a platform for a team with triple competence for Integrative Medicine (IM). This would lead to Translational research (TR) having observational therapeutics and Ayurvedic epidemiology as its cornerstones. Dr. V. M. Katoch, Director General, ICMR and secretary, Department of Health Research (DHR), Government of India expressed his deep concern about ground realities not very favorable to the aforesaid approach. However, he refused to accept replicas of USA and Europe as our models in health care. ‘Preserve heritage, sustain it, make it modern and make it useful’ was his mantra. While Dr. Mrudula Phadke, Ex-VC of Maharashtra University of Health Sciences, Nashik (MUHS) suggested several alternatives for introducing Ayurveda in the medical curriculum. Dr. Narendra Bhatt, an eminent Ayurvedic consultant and researcher cited several interesting clinical examples of translational research opportunities from Ayurvedic fundamentals. He emphasized that epistemologically Ayurvedic mind works in a different manner. Hence, several seemingly unrelated disorders could be traced to a common mechanism and treated for that. He stressed that joint disorders could be differentiated into 97 subtypes by Ayurveda. Shri Dhirubhai Mehta, the president of KHS elaborated the efforts at Sevagram to reach health care delivery ‘Unto this last’. Dr. Ashok DB Vaidya, Research Director KHS and the moving spirit behind the symposium, while giving a rapid account of the attacks on Ayurveda in the past few decades, alleged that an organized lobby is making sustained efforts to discredit Ayurveda. He gave several examples of path-breaking research in Ayurveda that have gone unnoticed for decades, e.g., anticancer activity of neem[9] and of plants having potential to become global drugs, e.g., Mucunapruriens for Parkinson’s disease and cognition, Withania somnifera as a radio-sensitizer/immune enhancer.

Session 1: An overview of health research in traditional medicine
It began with a talk by Dr. Darshan Shankar, Ex Director, Foundation for Revitalisation of Local Health Traditions (FRLHT), a pioneer researcher/specialist in local health traditions and practices. He asserted that medical pluralism is the future of health care and India, like China, can play a leadership role in it. He underlined the need for emergence of new disciplines like Ayur-Nutrition and Ayur-Genomics, and new bioassays and in-vitro in-vivo Correlation (IVIC) models to facilitate this process. Dr. TanujaNesari, the Dean, Tilak Ayurveda Mahavidyalaya, discussed various approaches to strengthen the practice of TM (e.g., application of laboratory methods) and also ways in which TM can be used to define and treat diseases (e.g., use of Manjistha against platelet aggregation or describing pathogenesis of cancer from Ayurvedic viewpoint). Dr. Ashwinikumar Raut, Director Clinical Research, KHS-MRC outlined a pragmatic curriculum and pedagogy, envisaged at MUHS, to develop a trans-discipline fellowship program of RP and integrative healthcare research for scientists with a background in Medicine/Ayurveda/Pharmacy/Life Sciences.

Session 2: Leads from natural products and life sciences
The discussion in this session revolved around lifestyle...
diseases like hypertension, metabolic syndrome, obesity, and diabetes. Dr. Namrita Pathak, Vaidya Scientist and Research Associate at KHS-MRC, outlined a novel 7-step approach comprising of 'Aabar, Vyavahar, Sleep and Yoga Nidra, Ayurvedic and other interventions, Pragya, Anandam, Yoga and meditation' to address these diseases and presented encouraging results of a 'Steps to Swasthya' a weekly clinic run at KHS-MRC. Dr. Supriya Bhalerao, Senior Research Officer, Dept Clinical Pharmacology, TNMC-BYL Nair Hospital while exploring the experimental–exploratory phases of RP, outlined the steps to develop Ayurvedic Epidemiology. Dr. Jayesh Sheth, Director, FRIGE, Ahmedabad presented a study demonstrating that the DNA damage caused by hyperglycemic stress can be reverted by a blend of traditional herbal compounds and nutritional modification. Dr. Renuka Munshi, Associate Prof and In charge Dept Clinical Pharmacology, TNMC-BYL Nair Hospital opined that although a number of Ayurvedic/TM approaches have the potential to treat/prevent these diseases, there was a dearth of well-documented, controlled clinical studies to validate these claims. She also described studies involving three plants and two plant based formulations in management of diabetes using different in-vitro and in-vivo experimental models, clinical efficacy, and safety. The discussion in this session touched several areas such as the effect of a pregnant woman’s diet on the health of the second or third generation and the potential of the vast, unexplored database related to Ayurvedic epidemiology.

Session 3: New domains of Ayurvidya for health sciences

The session was full of highly stimulating presentations involving the use of sophisticated technologies to understand and validate TM. It began with a presentation by Dr. Jayant Bellare, Dept of Chemical Engineering, IIT, Bombay that demonstrated for the first time that the presence of nanoparticles and unconventional chemistry was responsible for biological activity of Ayurvedic Bhasmas and Homeopathic tinctures. In the latter, nanostructures and aggregates of starting materials were found to be present in extremely dilute tinctures (10^400 parts) thus validating the molecular basis of Homeopathic medicine. Dr. Mihir Joshi, HOD, Crystal growth laboratory, Dept of Physics, Saurashtra University dwelt on an equally novel concept of biocrystals having role in diseases like urolithiasis, arthropathies, gall stones, and cataract. He discussed the in vitro gel technique to grow biocrystals and the effect of various herbal extracts to inhibit or dissolve these biocrystals. Dr. Vidita Vaidya, Associate Professor, Dept of Biological Sciences, TIFR elucidated the role of curcumin in adult neurogenesis. She suggested that the dose of turmeric/curcumin, the age of the animal, route of administration, and the duration of treatment were important in determining the outcome of these studies. Under optimized conditions, curcumin was shown to have neuroplasticity with cognitive improvement in aged animals. Dr. Kalpana Joshi, Prof and Director, Symbiosis International University, Pune informed the audience of the advances in development of AyuGenomics along with the role of AyuSoft software (developed at C-DAC) to determine the Prakriti of an individual. This work of Dr. Bhushan Patwardhan and Dr. Joshi has led to papers appearing in Proceedings of the National Academy of Sciences (PNAS) and other high impact journals. Dr. Girish Tillu, the young Vaidya Scientist and Assistant Prof, Symbiosis International University discussed application of the systems approach to bridge the gap between data rich biology and concept rich Ayurveda. He presented the concepts and logic of Ayurveda at four levels in a poster on 'Systems Ayurveda'.

The first level refers to the Purusha and Loka, the second one to body, mind and its function, the third one with disease stage and process and the last stage with the eight branches of Ayurveda and itschikitsa. On a different track, Dr. B. Dinesh Kumar, senior scientist from National Institute of Nutrition, Hyderabad showed the significance of preclinical safety and efficacy studies for clinical protocol as rodent and nonrodent toxicology together accounts for 79% of human toxicology. ‘Everything is toxic, it’s a matter of dose’, and ‘Examine everything, including urine and stools of animals’ was his advice.

Session 4: Hits, leads and candidate drugs from Ayurvedic plants

The tone of the session was set by Dr. Chhaya Godse, Assistant Director, Biochemical pharmacology, MRC-KHS through an overview of antimalarial drug discovery and development using RP approach. She also provided Ayurvedic perspective about targets of malaria and relevant treatment modality, apart from highlighting the potential of plants like Neem, Saptaparni, Kirat, Parijat, and formulations like Ayush-64 for further exploration. A detailed review of Ayurvedic texts and modern preclinical studies related to different pharmacological actions of Tinospora cordifolia was provided by Dr. Padmaja Marathe, Dept of Pharmacology, GS Medical College, Mumbai. Several unknown facets of the most studied turmeric were explained by Dr. Jayashree Joshi, Deputy Research Director, MRC-KHS, (e.g., there are 4767 pubmed cited papers on curcumin alone, 258 of them on its pharmacokinetics). Citing its less reported effects on platelet aggregation, oral submucosal fibrosis, neuronal regeneration, and Cervical Low Grade Squamous Intraepithelial Lesions (LSIL), she made an appeal to declare turmeric as our National Spice along the same lines as the Taj Mahal and the peacock. The story of the failure of the RP of a potent time-tested drug Guggulu, narrated by Dr. Ashwinikumar Raut, (with insightful inputs
by Dr. Ashok Vaidya) uncovered a simple, yet neglected fact that the success of RP depends upon integration of not only TM and modern medicine, but also of biological science and pharmacy. It uncovered avenues for further research, for example, bioavailability and pharmacokinetic studies, design, and development of novel dosage forms such as granule-filled sachets and inhalations for better solubility and patient compliance. This thread was carried further by DB Anantha Narayana, Hon Chairman, Herbal pharmacopoeia Committee, Ministry of health and family Welfare, Government of India, in his plea for preformulation R and D for integrative phytopharmaceuticals. He underscored the significance of physico-chemical properties of the drug and dosage forms (e.g., crystalline structure, hygroscopicity, bulk density, and drug-excipient interaction) and of scrupulously following the methods described in standard texts.

Session 5: Valedictory
This session consisted of presentations and discussion that drew inferences from earlier deliberations resulting in specific action-oriented programs, suggestions for translational research in its varied dimensions or for networking across all stake-holders. Dr. Rama Vaidya implored for pragmatic infrastructure for research and emergency care facility in Ayurvedic colleges and for R and D networking among TM, modern medicine and life sciences. For the latter, she emphasized adequate resources and efforts are essential for the training of Vaidya Scientists and Physician scientists from conventional system of medicine interested in TM. Dr. K. R. Kohli, Director, Ayurveda, Government of Maharashtra described his efforts, both as a researcher and a policy planner to promote translational program for noncommunicable diseases vis-à-vis TM. Dr. Abhay Chowdhary, Director, Haffkin Institute reviewed in detail the current initiatives and activities related to communicable diseases from XII 5-year plan perspective and stressed the importance of nationally consistent surveillance systems and for considering animal and human health together in view of reemergence of communicable diseases through animal contact/products. Alex Hankey, a theoretical physicist and conducting ongoing research in Ayurveda gave an example of translational research by demonstrating the common sense of the vata-pitta-kapha biorhythm of diurnal changes in humans, tracing its origins to the nematode physiology. He remarked that Western ‘trained’ minds imbued with linear thinking find it difficult to understand complex, cyclic, and multi-level changes caused by plant medicines. He showed how use of ‘Complexity Biology’ could result in translation across disciplines, cultures, and health systems.

The valedictory address was delivered by Dr. K. Satyanarayana, coordinator, Dept of Health Research, Government of India on National goals for health: A pathway for affordability and accountability. He lamented the state of ‘much talk, no action’ related to the government response on TM. He was most concerned about the lack of awareness about drug development in the government leadership. His recommendations included evolving networks of all stake holders, including industry, and refocusing on communicable diseases. The session came up with several concrete suggestions/resolutions including the following:

- To request Government of Maharashtra to spend at least 5% of its health budget on AYUSH.
- List at least five standard Ayurvedic preparations for each national priority health problem.
- To prepare a status report as to the prevailing situation for integrative Ayurveda with suggestions for a change.

Apart from the high quality presentations from leading researchers and thought-provoking discussions in each session, the symposium was remarkable in several new trends. For example:

- Inclusion of Pharmaceutics in the integrative health care set up. The importance of design and development of dosage form in the RP path was underlined by examples of Tinospora cordifolia and guggul.
- Growing use of sophisticated instruments for characterization and analysis of TM (electron microscopy and TEM imaging for Bhasma) and of innovative conceptual tools for understanding its principles (SystemsBiology).
- Increasing use of TM frameworks to understand the cause of disease or ways to treat or prevent it.
- Enthusiastic participation by a team of young Vaidya scientists, well-versed in the tools of modern science and technology.
- By any account, it was no ordinary symposium. In words of Dr. Darshan Shankar, it was a visionary trail like Ayurvedic Statistics, Ayugenomics, and Vaidya Scientists. The scientific rigor and the intensity of the discussions were remarkable. But the most remarkable component was its spirit. It is rare to witness a scientific gathering, driven by a common passion; to be its part was indeed a rare privilege!

Precedings
A novel way of enticing the participants was actualized in the publication of the ‘PRECEDINGS’ that was brought out and released at the inaugural session. The term, a neologism, was given clarity by the Sanskrit term PRAK KATHAN. This initiative was much appreciated because abstracts whet the appetite but do not provide satiety. And sometimes proceedings after a symposium are either too delayed or may not materialize. One is sure that this pattern of the ‘PRECEDINGS’, much more than abstracts and
less than full papers, would be adopted for other symposia/conferences too.

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