

*Medal Lecture***Need for Integration of Ayurveda with Modern Biology and Medicine[#]**SUBHASH C LAKHOTIA* *Cytogenetics Laboratory, Department of Zoology, Banaras Hindu University, Varanasi 221 005, India*

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Mankind's concern for health since the beginning of civilization led each community to develop its own health/medical care system. Ayurveda, the oldest and a well-documented Indian health-care system, is being practiced for several thousand years. It is expected that the system would have had an evidence-based origin. However, in the current perspective and practices, it is largely experience-based system with myths, fallacies and inappropriate commercial practices having made inroads in its otherwise integrative health-care practices and philosophies. Historically, the so-called 'modern medicine' practices and formulations had their origins in traditional health-care systems, especially the Indian and Chinese. However, the traditional and the modern medicine systems today are competitive and mutually exclusive. The Ayurvedic Biology initiative aims to re-understand Ayurveda in light of the remarkable developments in all disciplines of natural sciences, including biology and understanding of human body and its systems, so that not only the claimed effectiveness of the various formulations and practices is rationally assessed but also the physiological, cellular and molecular bases of their actions get revealed. Recent experimental studies on Ayurveda indeed illustrate the advantages of Ayurvedic Biology approach. More such studies would generate the much needed evidence-based practices, and also provide simple quality-control systems for Ayurvedic formulations. This can be expected to finally lead to emergence of integrative health-care practices, incorporating the best of traditional and modern health-care systems and procedures.

Keywords: Ayurvedic Biology; Amalaki Rasayana; Rasa-Sindoor; Neurodegeneration

Introduction

It is indeed a great honour to be delivering the *INSA Aryabhatta Medal 2018* lecture during the Anniversary General Meeting of INSA held at the Physical Research Laboratory, Ahmedabad. Keeping in view the multi-disciplinary audience, I find it appropriate to talk about Ayurvedic Biology, which is one of my current research interests and which I believe would be of a wider interest and relevance.

Studies in *Ayurvedic Biology*, initiated and catalyzed by Professors M S Valiathan and R Chidambaram in early years of the current millennium, aim to re-understand Ayurvedic formulations and practices in the context of contemporary knowledge in biology and other sciences (Lakhotia, 2016; Valiathan, 2006a, b, 2016). Ayurveda as a formal health-care system seems to have started in India

several thousand years ago with the compilations by *Carak* and *Susruta* being its foundation pillars (Sharma, 1994, 1999; Valiathan, 2006a, 2016). This knowledge base, available mostly through handwritten manuscripts, has been transmitted and expanded during the interim period by many scholars. In view of the antiquity and absence of documentation, we do not know the bases on which the detailed procedures and specifications were formulated by the scholars in ancient times. These may perhaps be never known.

Since its formulation several thousand years ago, Ayurveda, like the many other traditional health-care systems across the globe (Lakhotia, 2015b), has been followed and practiced without a break. Most of the medicines used in 'modern medicine' were initially derived from the knowledge base of traditional health-care systems including Ayurveda (Valiathan, 2016).

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However, while the modern medicine has been and continues to be driven by vigorous research and development, the field of Ayurveda has hardly anything to claim as new developments beyond the traditional literature. The practice of Ayurveda, during its long history, has 'faithfully' followed the ancient texts without any serious attempts to understand or to validate the principles and philosophies enunciated in the classical treatise of Ayurveda as available now. This has unfortunately led to a situation where this "classical" knowledge system is often not considered "classy".

Poor State of Understanding of Principles of Ayurveda

An urgent need for establishing Ayurveda on sound-footing has been felt for a long time. This was emphasized more than 100 years ago in 1916 by Kaviraj Gananath Sen in his address on the occasion of the foundation stone-laying ceremony of the Banaras Hindu University at Varanasi (Shah, 2017). Kaviraj Sen stated "Whatever may have been the past glory of Ayurveda, it would be self-deception on our part to think that we still sit on a high pedestal. The fact is unfortunately just the other way. The number of Ayurvedic physicians in India is legion but soundly educated exponents of the ancient system are not yet numerous. Besides this, there is yet a good deal of conservatism which is contrary to the liberal spirit of Ayurveda and which must be overcome." He continued "In other words, we must establish them on the sound-footing of actual observations and experiments according the methods of the West, we must make good the losses we have already sustained."

Mahatma Gandhi, despite being the most ardent follower of 'Swadeshi' and naturopathy, was also critical of the prevailing state of Ayurveda. While inaugurating the Ashtanga Ayurveda Vidyalaya, Calcutta, on May 6, 1925 he spoke "I have hitherto confined my remarks to medicine and surgery in general, but when I come to the Ayurvedic and the Unani system, I am filled with greater doubts. There was a time when I used to swear by the Ayurvedic medicine and used to commend it to all my friends, who went in for Western medicine, to go to these Ayurvedic physicians. But I feel sorry to have to own to you that I was undeceived and I found that

our Ayurvedic and Unani physician lack sanity. They lack the humility. Instead of that I found in them an arrogance that they knew everything, that there was no disease which they could not cure" (Publications Division, Govt. of India, 1999, The Collected Works of Mahatma Gandhi, vol. 31, p. 282, <http://www.gandhiashramsevagram.org/gandhi-literature/mahatma-gandhi-collected-works-volume-31.pdf>). Nearly two decades later (May 26, 1946), Gandhi was asked, "Why do you go to the doctors for examination and diagnosis and not to the vaidyas?" The answer, reflecting his mis-trust of Ayurvedic practitioners because they did not undertake any research, was "The vaidyas do not possess the knowledge of the human body as the doctors do. The basis of diagnosis in Ayurveda is the theory of tridosha. They have not got to the bottom even of that. The doctors are ever carrying on research and making new discoveries. One either goes forward or backward. Nothing remains static in the world. Those who become static, become lifeless." (Publications Division, Govt. of India, 1999, The Collected Works of Mahatma Gandhi, vol. 91, p. 43 <http://www.gandhiashramsevagram.org/gandhi-literature/mahatma-gandhi-collected-works-volume-91.pdf>). Continuing his concern for the absence of research by Ayurvedic practitioners and their excuse that the government was not providing appropriate institutional support, he wrote in *Harijan* on August 4, 1946: "I am unable to subscribe to the condemnation of the State for not providing institutions for research. I have always blamed the Vaid's apathy in the matter of real research. The top ones are busy making money. The others are too ignorant to do so or are easily satisfied with what they find in the orthodox Ayurvedic books. I am sorry for this view. I come to it, in spite of my great regard for the Ayurvedic system and the Unani which are suited to the soil." (Publications Division, Govt. of India, 1999, The Collected Works of Mahatma Gandhi, vol. 91, p. 415, <http://www.gandhiashramsevagram.org/gandhi-literature/mahatma-gandhi-collected-works-volume-91.pdf>).

Such strong views expressed in the past by very knowledgeable persons unfortunately appear to be substantially reflective of the reality even today. Intellectuals in India are largely partitioned in 2 groups – i) believers in western philosophies and approaches, and ii) the "pro-Indian faithful" who remain

unquestioning followers of the ancient wisdom! Consequently, like many other things, Ayurveda has also suffered since it is negated by those trained in “modern Science and Medicine” but faithfully followed by Ayurvedic practitioners and common man without any serious attempt to validate and understand its age-old principles and practices in light of contemporary knowledge. Both attitudes need change.

Need for Serious, Unbiased and Integrated Research in Ayurveda: the Ayurvedic Biology Initiative

In view of the above and as has been noted earlier (Lakhotia, 2013a, 2015a, b; Lakhotia, 2016; Valiathan, 2006a, b, 2016), it is clear that Ayurveda, and for that matter all traditional health-care systems, need detailed and extensive unbiased studies with highest rigor so that the rich traditional wisdom can be enriched further by transforming it from experience-based to evidence-based system as well. We need to rediscover and understand the principles of Ayurveda in the context of contemporary knowledge using an unbiased approach. *Ayurvedic Biology* promotes such an approach (Lakhotia, 2016; Valiathan, 2006a, b, 2016). We need in-depth and unbiased studies of the ancient texts in synergy with scientific experimental studies. This requires participation of learned and open minded practitioners of Ayurveda, linguists with a good understanding of Sanskrit and other languages in which classical texts exist, experimental scientists and medical doctors with expertise in fields like plant taxonomy, plant physiology, human physiology, cell and molecular biology, chemistry, material sciences, modern medicine etc. These systematic and in-depth studies need to be directed to understand i) the mechanisms of biological actions of the large variety of the standard Ayurvedic formulations (*Rasayanas*, *Bhasmas*, *Asavas*, etc.), ii) understanding of the chemical, physical and material science perspectives underlying the elaborate procedures employed in preparation of various formulations, iii) biochemical bases of actions of the various “*Anupana*”, iv) bases of various “*Dosaprakritis*” in terms of modern physiology, immunology, metabolomics, microbiomics, genomics and epigenomics, v) physiological and immunological effects of the diverse “*Pancakarma*” procedures, vi) role of epigenetics in these procedures and in the response of the subject to a given therapy and life-style, etc. Equally important is to define precise identity

of various herbs and their parts and the seasonal and geographic effects on their efficacies as described in traditional Ayurvedic literature and to standardize the preparatory procedures.

New insights from Ayurvedic Biological Studies

Several Ayurvedic Biology studies, that have been undertaken or are in progress, have already established the advantages of unbiased experimental approaches to fulfil the above objectives. In addition, such studies may also unravel novel therapeutic strategies. Our studies on *Amalaki Rasayana* (a herbal *Rasayana* primarily based on the Indian Gooseberry or Amla fruit) and *Rasa-Sindoor* (a *Bhasma* preparation based on mercury and sulphur) in *Drosophila* model suggested that the broad effects of these formulations on flies were in general similar to those described in classical Ayurvedic practices (Dwivedi *et al.*, 2012). Interestingly, both these formulations were found to enhance levels of different hnRNPs (heterogeneous nuclear RNA-binding proteins), which are involved in transcriptional and post-transcriptional regulation of gene expression, and of CBP300, a histone acetyl transferase required for modifying chromatin for elevated gene expression (Dwivedi *et al.*, 2012). Interestingly, it was also found that both these formulations suppressed induced but not developmental apoptosis (Dwivedi *et al.*, 2015) and *Amalaki Rasayana*, but not *Rasa-Sindoor*, enhanced tolerance of flies to oxidative stress, which may contribute to the increased life span by *Amalaki Rasayana* therapy (Dwivedi and Lakhotia, 2016). In other studies, *Amalaki Rasayana* was found to improve the DNA-repair activity in aged rats (Swain *et al.*, 2012) and to improve the telomerase activity in human blood cells (Guruprasad *et al.*, 2017). *Amalaki Rasayana* was also found to improve myocardial energetics, muscle contractile function and exercise tolerance capacity in rats (Kumar *et al.*, 2017). Together, these effects are expected to promote ‘healthy aging’ and longer life-span, the major usages prescribed for *Amalaki Rasayana* in classic Ayurvedic texts (Sharma, 1994).

In agreement with earlier reports that enhanced levels of hnRNPs and/or CBP suppress neurodegeneration seen in diseases like Huntington’s and several Spino-Cerebellar Ataxias (Caccamo *et al.*, 2010; Sofola *et al.*, 2007) and our earlier finding

(Dwivedi *et al.*, 2012) that *Amalaki Rasayana* and *Rasa-Sindoor* feeding enhanced the levels hnRNPs and CBP in *Drosophila* tissues, we found that these formulations substantially suppressed the Huntington's and Alzheimer's disease associated neurodegeneration in fly models, with the mercury-based *Rasa-Sindoor* being much more effective (Dwivedi *et al.*, 2013). Encouraged by these results in fly models, similar studies were extended to mouse models of Alzheimer's and very significantly, both these formulations suppressed Alzheimer's symptoms in the mouse models (Saba *et al.*, 2017; Tiwari *et al.*, 2017). Furthermore, unpublished studies in the laboratory of Prof. S. Ganesh at IIT, Kanpur, show that seizures and other neurological symptoms displayed by mouse models of Lafora disease are remarkably suppressed by either of these two Ayurvedic formulations (S. Ganesh, personal communication). Ongoing studies in my laboratory show that transcripts of a large number of genes become significantly elevated or reduced in the affected tissues in fly models of Huntington-like neurodegeneration; interestingly, most of these transcripts are restored to near-normal levels when *Amalaki Rasayana* or *Rasa-Sindoor* is administered to the affected larvae (Yashvant Patel and S. C. Lakhotia, unpublished). Thus our systematic and unbiased experimental studies have unravelled novel and potentially effective therapeutic applications of these Ayurvedic formulations in different neurodegenerative disorders (Lakhotia, 2013b, 2017). Since neurodegenerative disorders are becoming increasingly common and as yet without safe and satisfactory therapies, these findings in fly and mammalian models raise great hopes that these Ayurvedic formulations may indeed turn out to be very effective (Lakhotia, 2013b, 2017). These leads now need to be taken up by practitioners of Ayurveda for evaluation of therapeutic potential of *Amalaki Rasayana* or *Rasa-Sindoor* in human patients.

A common apprehension about Ayurvedic formulations, especially for those based on metals is their potential toxicity. We did not find any toxic effects of *Amalaki Rasayana* or of the mercury and sulphur based *Rasa-Sindoor* in any of our studies in fly or the mouse model. A study on the zebra fish also did not find any adverse effect or toxicity of *Rasa-Sindoor* on its behavior (Biswas *et al.*, 2018). Advanced physico-chemical studies have also shown the *Rasa-Sindoor* particles to be in nanoscale size

after the classically recommended processing, and which cannot be metabolized in the body to any toxic form of mercury (Mukhi *et al.*, 2017; Ramanan *et al.*, 2015). Thus the claimed fear of toxicity of heavy metals in traditional Ayurvedic formulations seems to be unfounded but may occur due to poor quality-control measures and/or when the elaborate preparatory steps are not properly followed.

A recent study on effects of administration of *Guduchi* and *Madhuyashti* to *Drosophila* revealed complex responses of traits like reproductive output, life-span and stress responses, which indicates the need for a holistic analyses of Ayurvedic *Rasayanas* on a broad spectrum of life-history traits (Singh *et al.*, 2018; Singh and Tapadia, 2019).

The *Tridosha* concept of Ayurveda, based on certain defined bodily dispositions of a person, is used to provide personalized therapeutic regimes since each person is believed to have a specific *Prakriti* depending upon the relative proportions of the three *Dosas*, viz., *Vata*, *Pitta* and *Kapha* (Patwardhan *et al.*, 2015; Rastogi and Chiappelli, 2017; Sharma, 1994). Several recent studies have attempted to find biochemical, physiological, genomic and/or epigenetic correlates that may underlie the specific *Dosa-Prakriti* of an individual. A study using biochemical, hematological and genome wide expression parameters of individuals displaying the three most contrasting constitutional types showed striking differences in their liver function tests, lipid profiles, and haemoglobin levels; likewise a correlation was also found between the *Prakriti* types and expression of core biological processes like transport, regulation of cyclin dependent protein kinase activity, immune response and regulation of blood coagulation (Prasher *et al.*, 2008; Sethi *et al.*, 2011). Another study that examined differential methylation of promoter and untranslated regions of genes also claimed correlation of methylation patterns of certain genes with the *Prakriti* types (Rotti *et al.*, 2015). Another study (Govindaraj *et al.*, 2015) suggested that the *Prakriti* classification of Ayurveda may indeed have a genetic basis. These encouraging findings, however, need to be followed at a much larger scale involving Ayurvedic practitioners and those well conversant with physiological, biochemical, genomic and epigenetic studies so that the validity of the *Prakriti* types can be rationally ascertained and appropriate diagnostic

assays established to identify the *Prakriti* type of an individual with experimental rigour.

Integration of ‘Traditional’ and ‘Modern’ Health-Care Systems

Every “Old” thing may not be “Gold”, and even gold needs periodic cleaning! Science and technology and the health-care systems in India were obviously well developed in ancient times. However, those principles and practices cannot and should not be accepted as such just because of their antiquity. Neither should they be thrown out because of their antiquity. In order to take advantage of the wisdom underlying the science and technology in ancient literature, we must dispassionately examine them in light of the current understanding of principles and processes of Natural Sciences *so that we know not only what, but also why and how?*

I should point out that, encouraged by the traditional health-care systems, innumerable studies have been carried out during the past several decades to identify their ‘active compounds’ and exploit them for developing novel target-specific drugs. Although there has been notable success in some cases, such ‘reductionist’ approach has, in general, severe limitations as borne out by the ‘side-effects’ manifest with most of the so-called ‘target-specific’ drugs. In this context, it appears desirable to follow the ‘holistic’ and ‘systems’ view inherent in Ayurveda and systematically examine the numerous *Rasayanas*, *Bhasmas* and *Asavas* described in classical literature for their modes of actions and effectiveness in specific health-conditions.

Following the upsurge in popularity of Ayurveda in recent times, quality control has become a major concern not only for the various *Rasayanas* and other Ayurvedic formulations but also for the other Ayurvedic processes and practices like *Pancakarma* and various massages. Since most of the Ayurvedic formulations are complex mixes of various herbal and/or mineral components, their quality control through physico-chemical parameters may not be feasible,

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except in a few simpler formulations (Shengule *et al.*, 2019). Appropriate biological quality control parameters using model organisms need to be defined. At the same time, the tendency of industry and practitioners to designate any so-called ‘herbal’ preparation as ‘Ayurvedic’ needs to be curbed. The prevailing mutual mistrust between practitioners of traditional and modern health-care systems has to be resolved. The Ayurvedic and other traditional health-care system practitioners need to come out of their shells, and be exposed to and trained in contemporary principles of biology, especially genetics and genomics, cell and molecular biology, developmental biology, physiology etc. At the same time, practitioners of contemporary science and medicine need to appreciate the systems organization of living body and the holistic philosophy inherent in Ayurveda. Such combined efforts only would help in separating myths and facts that are inherently present in any age-old tradition and knowledge base. An integration of the contemporary diagnostic procedures with the holistic principles of Ayurvedic and other traditional health-care systems would go a long way in ensuring ‘health for all’ objectives of any society (Katoch, 2018; Lakhota, 2015a; Patwardhan, 2014; Patwardhan *et al.*, 2015; Ramaswamy, 2018; Rastogi, 2015; Shankar, 2018). *There is a strong need to correlate different languages and philosophies to find and understand the commonalities.*

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