

On Building a Golden Triangle between Traditional Medicine, Modern Medicine and Modern Science

Speech delivered by Dr. R. A. Mashelkar, 25 May 2003

1. Ayurveda literally means 'science of life'. It encompasses the total sweep of life sciences and pursues the quest for understanding life in all its ramifications. Ayurveda is one of the earliest systems of health care. It is not a mere compendium of therapeutic recipes. Nor is it the first one to use herbs. These have been used from times immemorial. Instead, it is one of the earliest frame-works, which systematized knowledge. This framework is not only self-consistent but also uses cause and effect arguments to correlate manifestations of sickness, its causes and treatment. When this framework was developed in ancient India, the notion of a molecule did not exist. Nor was the definition of a cell and the role it plays in life processes known. The discovery of DNA and functional genomics was more than three thousand years away. In spite of this, it offered an effective treatment for many disorders, particularly, which have multiple causes. For some degenerative diseases, most Indians consider it to be the treatment of last resort. There is a general belief that when all other treatment fail, Ayurveda may yet succeed; and it often does.
2. 20th Century has revealed some of the greatest insights into our understanding of life at increasingly higher levels of organization – molecular, sub cellular, organelles, cells, tissues, organs, organisms, species and ecosystems –the most remarkable feature of modern medicine is its close integration with the basic sciences – physics, chemistry and biology. For example, we would not have had 'gene therapy' a new frontier of modern medicine, if the structure of DNA was not known, which itself has been possible due to the structural elucidation achieved X-ray diffraction, the contribution of then modern physics advances whereas the connection between modern medicine and modern science was always strong, the connection between modern science and traditional medicine, including Ayurveda has been poor. And so has been there a poor connection between modern medicine and traditional medicine. India can benefit enormously, if it can build a golden triangle between traditional

medicine, modern medicine and modern science. In this lecture, I will make a case for this golden triangle.

3. The fact that such a connection needs to be established has been recognized for a long time. For example, after visiting the Central Institute of Research in Indigenous Systems of Medicine at Jamnagar on 2nd November 1955, Pandit Jawaharlal Nehru had observed – ‘*a fascinating inquiry is going on in this research institute and it may well lead to very fruitful results. The only right approach has to be one of Science, that is, of experiment, trial and error. In whatever type of medicine we may deal with, we cannot profit by its study unless we apply the method of science. Nothing should be taken for granted. Everything should be tested and proved and then it becomes a part of scientific medicine – old and new.*’ Unfortunately this message, which was given almost 50 years ago, has been lost somewhere.
4. The importance of such linkages has been stressed over and over again. Bharatiya Vidya Bhavan had launched in 1977 a project entitled “*Ancient Insights and Modern Discoveries*”, which was a national cooperative endeavour to explore the possibilities of meaningful correlations of ancient ideas and concepts and modern scientific discoveries. Modern scientific discoveries are made without any regard to the clues that flow from our ancient wisdom. Here is a brilliant example.
5. Among scientific journals, *Science* and *Nature* are perhaps the most prestigious. Real breakthroughs find a place in these journals. T.L. Lentz and colleagues reported in 1982 in *Science* that acetylcholine receptors may serve as receptors for rabies virus. In *Sushruta Samhita*, the ancient Indian Classic on the Science of Life, there is a fascinating account of *Datura* as a prophylaxis for rabies. The active principles of *Datura stramonium* are atropine and related alkaloids that predominantly block the muscarine action of acetylcholine, precisely what was discovered by Lentz and others thousands of years later. In view of Lentz’s findings, *Datura* for rabies may represent the first documented example of prophylaxis by receptor blockade. However, the use of *Datura* was found by people centuries ago, who were not trained in modern science. On the other hand, modern scientists had no clue about the

work reported in *Sushruta Samhita*. How do we build the bridges between the two? To understand this, let us first understand the characteristics of modern science and traditional knowledge.

6. Scientific knowledge is supposed to be objective and verifiable knowledge. In essence, the scientific method consists of careful observation of nature and cautious confirmation of all conclusions. Good science excludes all unsubstantiated hypotheses. Observation and experiment are the methods of science. As new observations are added to the total body of scientific knowledge, some of the older observations lose their relevance and become obsolete. This dynamic aspect of science is perhaps its most outstanding attribute.
7. We need to recognize that scientific knowledge generated in formal laboratories is not the only knowledge system. There is knowledge generated in the 'laboratories of life' by people over centuries. India has nurtured and refined systems of knowledge of their own, relating to such diverse domains as geology, ecology, botany, agriculture, physiology and health. We are now seeing the emergence of terms such as 'parallel', 'indigenous' and 'civilizational' knowledge systems. Such knowledge systems are also expressions of other approaches to the acquisition and production of knowledge.
8. Unfortunately, scientists reject traditional knowledge as extraneous. During the colonial period of the world history, which was also the period of phenomenal growth in S&T, science was perceived, projected and accepted as an essential feature of the western civilization. An unfortunate and retrograde corollary of this was that modern scientific knowledge was seen as an adversary of traditional wisdom and traditional knowledge. The two were seen as mutually exclusive. This has been a regrettable syndrome, because it had the effect of belittling the intellect and wisdom of vast fraction of the world's population and the heritage of the whole humankind. We know better today.

9. We need to remind ourselves of a profound statement that Mahatma Gandhi had once made. He said, *'I do not want my house to be walled in on sides and my windows to be stuffed. I want the cultures of all the lands to be blown about my house as freely as possible'*. Gandhiji implied that our mind should be open and uninhibited. It should be open to new ideas and new thinking. There should be no artificial boundaries and walls or borders between different domains of knowledge as well as the practitioners of these knowledge systems.
10. It is only by fusing the ancient wisdom and modern science India can create world class products, because new products cannot compete with products, which have only tradition and empirical observation as the knowledge base. The knowledge to be integrated into the traditional products has to emerge from modern science, especially modern biology and chemistry.
11. What would be the most fundamental change required for breaking the walls and opening the windows that Mahatma Gandhi referred to? I believe it is going to be that of mutual trust, respect and confidence between the practitioners of modern science and the holders of the ancient wisdom. This has to get reflected in several ways, including the choice of research problems. We had Professor Ernst, the Nobel Laureate, give the Science Congress plenary lecture in Pune in January 2000. He described the work on getting a molecular level understanding of the Chinese system of 'acupuncture' by using the latest advanced tools in high-resolution solid state NMR. You can see that the western scientists are scientifically probing the ancient practices of the East! Whereas our own Indian research is invariably focussed on the left over problems of the west. We will need an attitudinal change in reconsidering our choice of problems and also a change in our value system.
12. This realization seems to be dawning on our institutions now. I will begin at home. CSIR happens to be the largest chain of publicly funded industrial R&D institutions in the world. We are a formal system of innovation and we had closed our mind to informal systems of innovation. But we are changing now. I will cite an example to illustrate the point. It concerns our twenty laboratory

networked program on discovery of bioactive molecules for their use as drugs and therapeutics. Our research is based on the clues that we get from our vast plant based traditional medicine systems including Ayurveda. For the first time, CSIR forged relationships with Indian traditional systems of medicine, namely Ayurvedic and Siddha systems. I still remember that when CSIR signed the MOU with *Arya Vaidyashala* in Kottakal, Professor Valiathan, who brought both the partners together, said *'This is a holy place where two rivers are meeting; the river of traditional knowledge and ancient wisdom represented by Arya Vaidyashala and the river of modern knowledge represented by CSIR'*. The only question I asked myself was that why did it take almost fifty years after the prophetic words by Nehru for these two rivers to merge? I believe this is because we did not heed the advice of Gandhiji and we 'walled our houses on all sides and stuffed our windows.' These windows are now opening up.

13. CSIR's programme includes the identification of target therapeutic areas, selection of extracts, discovering of active fractions, molecular description of active fractions, optimization through mixing of fractions from various extracts, understanding the mechanism of action, toxicology studies and clinical trials and discovery of entirely new herbal products which are efficacious, safe and are reasonably consistent in molecular concentrations. Leads on twenty diseases have been obtained. A product called ASMON, which acts on Asthma, and which is a herbal formulation, is replacing synthetic drugs today. An anti-ulcer herbal formulation which is showing to be superior even to the best setting synthetic drugs is going into clinical trials now. There are many leads that a team of around 500 scientists working in a Team India fashion is exploring. I wish such programmes had started 50 years ago!
14. Currently, under CSIR's New Millennium Indian Technology Leadership Initiative (NMITLI) programme, several scientists have been working on establishing pharmaco-epidemiological evidence-base to Ayurvedic medicines, practice and development of standardized herbal formulations. Randomized controlled clinical trails for rheumatoid and osteoarthritis,

hepatoprotectives, diabetes, hypolipemic agents, asthma, Parkinson's disease and many other disorders have reasonably established clinical efficacy. A review of some of the exemplary evidence-based researches and approaches has been also made. It is clear that we must increase our presence internationally through well researched publications related to quality, safety and efficacy of Ayurvedic medicines in international peer-reviewed journals. The Ayurvedic, pharmaceutical and medical scientists must come together to make this possible.

Ayurveda and Intellectual Property Rights

15. There are ways by which modern scientific discoveries are protected through the system of patents. But how do we protect traditional knowledge and products based on it. In particular, the protection of Traditional Medicine (TM) under intellectual property rights (IPRs) raises two types of issues. First, to what extent it is feasible to protect it by using the existing IPR system? Certain aspects of TM may be covered by patents or other IPRs. There have also been many proposals to develop *sui generis* systems of protection. Such proposals are based on the logic that if innovators in the "formal" system of innovation receive a compensation through IPRs, holders of traditional knowledge should be similarly treated.

16. The grant of patents on non-original innovations (particularly those linked to traditional medicines), which are based on what is already a part of the traditional knowledge of the developing world have been causing a great concern to the developing world. It was CSIR that challenged the US patent No. 5,401,5041, which was granted for the wound healing properties of turmeric. This 'second *Haladi Ghati Ladai*', as it has been referred to, has been a pathbreaking fight for the first time, it asserted the rights of the holders of traditional knowledge from India in international fora. In a landmark judgment, the US Patent Office revoked this patent in 1997, after ascertaining that there was no novelty; the findings by innovators having been known in India for centuries.

17. This case was followed by yet another case of revocation (May 2000). The patent granted to W.R. Grace Company and US Department of Agriculture on Neem (EPO patent No. 436257) by European Patent Office was squashed again on the same grounds that its use was known in India. India filed a reexamination request for the patent on Basmati rice lines and grains (US Patent No. 5,663,484) granted by the USPTO, and Ricetec Company from Texas has decided to withdraw the specific claims challenged by India and also some additional claims.
18. There is a problem on the grant of such patents linked to the indigenous knowledge of the developing world that needs to be addressed jointly by the developing and the developed world. We need to understand that there is a distinction between the patents that are granted based on modern research and patents, which can be categorized as traditional knowledge based patents. A recent study by an Indian expert group examined randomly selected 762 US patents, which were granted under A61K35/78 and other IPC classes, having a direct relationship with medicinal plants in terms of their full text. Out of these patents, 374 patents were found to be based on traditional knowledge not that all of them were wrong. The Governments in the third world as well as members of public are rightly concerned about the grant of patents for non-original inventions in the traditional knowledge systems of the developing world. At International level there is significant level of support for opposing the grant of patents on non-original inventions. For example, more than a dozen organizations from around the world got together to oppose the EPO Neem patent and the entire process took five years. Such a process of opposition is, understandably expensive and time consuming.
19. It is through an Indian initiative that a solution has been found to this problem, which has reached an international acceptability now. The Indian Government has taken steps to create a Traditional Knowledge Digital Library (TKDL) on traditional medicinal plants and systems, which will also lead to a Traditional Knowledge Resource Classification (TKRC). Linking this to internationally accepted International Patent Classification (IPC) System will mean building the bridge between the knowledge contained in an old Sanskrit *Shloka* and the

computer screen of a patent examiner in Washington! This will eliminate the problem of the grant of wrong patents, since the Indian rights to that knowledge will be known to the examiner. Hopefully, wrong patents on Turmeric, Neem, etc., will be the things of the past!

20. Eventually the creation of TKDL could serve a bigger purpose in providing and enhancing its innovation capacity. It could integrate widely scattered and distributed references on the traditional knowledge systems in a retrievable form. It could act as a bridge between the traditional and modern knowledge systems. Availability of this knowledge in a retrievable form in many languages will give a major impetus to modern research in the developing world, as it itself can then get involved in innovative research on adding further value to this traditional knowledge; an example being the development of an allopathic medicine based on a traditional plant based therapeutic. Sustained efforts on the modernization of the traditional knowledge systems of the developing world will create higher awareness at national and international level and will establish a scientific approach that will ensure higher acceptability of these systems by practitioners of modern systems and public at large.
21. The community of Indian research workers contributing to this important task of integrating the ancient with the modern, need to always to look for protection of any intellectual property which meets the basis requirements of novelty, usefulness and non obviousness. Can the existing knowledge and products based on them protected? The answer is 'No' what preexists, what is the public domain cannot be protected. Natural products cannot be protected. Further, the preparations that have been used for many many years constitute knowledge in public domain. Therefore, they cannot be patented. However, if new uses are found, a 'use' patent can be obtained.
22. If this is the case, what we can protect? If a non-obvious technique has been employed for fractionation of constituents of a herbal formulations, then an international patent becomes possible. Similarly, if synergism is shown between two fractions, which is very likely in Ayurvedic preparations,

patenting at international level is permitted. All the preparations arising out of Ayurveda should be tested for as many diseases as possible. Anyone that is found effective in diseases that have not been already described in literature can be patented for that particular disease.

Science based products

23. Ayurvedic products can have four different types of uses. Firstly, they are likely to be used for minor ailments like dyspepsia, unpleasant taste, anorexia, biliousness, etc. The second major set of uses is likely to include detoxifiers, rejuvenators, toners, resistance builders and for longevity. Both these sets of preparations are likely to be available over the counter (OTC). The third use will be support therapy, where these therapeutics may be given along with the allopathic preparations. The traditional medicine may even partially replace the allopathic medicines. These will most probably be prescribed by the existing medical practitioners who will be using combo-therapy to take advantage of the synergy between the two sets of preparations, for the overall benefit of the patient. In combo-therapy, use will be made of bioenhancers, detoxifiers, toners and specific therapeutic agents, which accelerate recovery. Similar use may also be made by the hospitals based on existing system. With time this combo-therapy concept may become accepted in India too. The fourth use of the traditional medicines is likely to be the treatment of diseases of the old age for which these systems have already shown a great degree of efficacy. The diseases of the old age which will be of increasing concern to the West include various forms of cancer, AIDS, Osteoporosis, Arthritis, and related diseases, Alzheimer and Parkinson's diseases (to some extent) and Obesity. These diseases are likely to be treated in three ways in future viz., through completely allopathic treatment, through completely traditional methods in special traditional systems based hospitals where both the philosophy and treatment will be traditional and the third and the most likely method will be a combination of both in which quick reduction of diseases intensity will be brought about through allopathic system but the long term treatment, convalesce and building resistance will be achieved by using techniques of the traditional systems of medicine.

24. To create new Ayurvedic products knowledge based on modern biology and chemistry needs to be integrated. This will result in better definition of the existing products; improved understanding of the mechanism of their action, modified composition at molecular level and better understanding of interactions amongst various molecules. Some of the potential knowledge based new products are described below.
25. Traditional preparation based on plant extracts can end up containing hundreds of molecules. Many of them are fillers, whereas some may be even toxic. The remaining may be beneficial. It has been shown quite often that there can be considerable degree of synergy among various molecules of a plant extract. Thus, in such a case, the whole fraction or its sub fraction will be appropriate preparation, particularly if some of the other fractions turn out to be relatively toxic. The advantage of a trim product containing limited number (say around 10) of molecules is that it can be molecularly defined (rather than the HPLC defined products used at present). Further, the interaction of these molecules with other drugs can be investigated and documented much more easily. As the concentration of the active molecules is likely to be high, such products will be fortified in nature. If the mechanism of action of such products can be explained at molecular level, the product will automatically have higher credibility.
26. There are products in Ayurveda which themselves are not efficacious against a particular condition but enhance the efficacy of another drug. Such components are routinely been found by one of the CSIR laboratories that these contain components, which may increase the bioavailability of an Allopathic drug or act as a catalyst for some other biological activity. The new area of research is a clear result of trying to understand Ayurvedic practices through the techniques of modern biology. If any such bioenhancers can be discovered from the practices of traditional systems of medicine of the whole world, for highly toxic drugs used for diseases like various kinds of cancer, AIDS etc. they will bring down the dosages and thereby the toxicity of

the current drugs. New bioenhancers may be discovered based on the possible mechanisms through which these agents may be acting.

27. Though detoxification is practiced in other traditional systems of medicine also, Ayurveda has much more elaborate procedures of detoxification. For most purposes, however, the mild detoxification procedures through the digestive tract and the skin are practiced. These can be practiced even without a prescription, for maintenance of good health. If molecularly defined detoxifiers can be generated along with their mechanisms of action, this mild therapy can become extremely popular with the health conscious people of all regions.
28. With the use of products, which are molecularly defined and mechanistically understood, there is great potential of using fractions from plant extracts not used for therapeutic purposes at present. Such new herbal preparations can significantly increase the number of therapeutic preparations of herbal origin available for the health-care of the world.
29. Apart from the molecularly defined, mechanistically understood non-toxic herbal fractions containing only a few molecules, there are other important preparations, which are rather unique to the current practices of the Indian Systems of Medicine. These are *Bhasmas*, which are made from mixtures of metals (or minerals) and herbs. Most of the time, these are calcined in sealed earthen containers through burning cow dung cakes or in furnaces. The final products are fine powders (about 50 microns in diameter). They use elements like lead, tin, iron arsenic, silver, gold, boron, mercury, sulphur, or compounds like calcium hydroxide, potassium nitrate etc. Nearly ten percent Ayurvedic products are *Bhasmas*, whereas in the case of Siddha, the percentage may exceed fifty. Normally, most of the elements used in these preparations have been classified in standard scientific textbooks as toxic. For example, lead in any concentration is described to be toxic. Not only that, it is known to accumulate in various tissues. However, these are considered to be fast acting healing agents and thus are used quite freely particularly by Siddha practitioners. Apparently, no toxic effects have been reported from them.

However, to make these preparations acceptable internationally, it is necessary not only to show that they are efficacious and non-toxic but also to define their physico-chemical characteristics by accurate scientific measures. As it is, the states in which these elements are present in *Bhasmas* are not clearly known, though the general impression is that they are oxides. Secondly, the role of herbs is also not clear. Is it that the herbs really get pyrolysed and some complex between the pyrolysed herb and the element gets formed, which becomes the active component? Knowledge of the mechanism of their action and the reason for the lack of toxicity (if needed they are non-toxic) can be of great help in making these products acceptable international.

30. Apart from *Bhasmas*, there are special preparations of the Indian system, which are specific. For example, these systems provide toning preparations for various systems of the body like brain, circulation system etc. These should be separated from general rejuvenators and promoted. Similarly, during convalescence, these systems provide special remedies apart from toners. For example, in the case of strokes, these therapies sometime accelerate the recovery significantly.
31. A new concept of Ayurvedic practices – from the practice in Ayurveda of adding *trikatu* (a mixture of black pepper, long pepper and ginger) to many formulations has resulted in notion of a ‘bio-enhancer’, which improves the bio-availability and bio-efficacy of a drug without itself acting as a drug. Piperine has already been shown to be a bio-enhancer for rifampicin during the treatment of tuberculosis. The concept developed by Regional Research Laboratory, Jammu, based on Ayurvedic practices can be easily assimilated by not only allopathic system but also by other traditional systems of medicine. Search for bio-enhancers working in different ways from Ayurvedic preparations needs international attention, research effort and eventual use.
32. How do we get scientists interested in such research? The first need is to expose good scientists to the accumulated wisdom of the ISM. There is no doubt that enormous opportunities of doing focused basic cum applied research exist in this area. For example, the mechanisms of action of *Bhasmas*,

detoxification, mechanisms involved in reversal of aging, bioenhancers, and molecular synergism offer a large number of scientifically challenging and commercially useful issues to work on. Initial interactions between scientists and practitioners of ISM may be difficult because of different operational nomenclatures, but with time communication becomes excellent. For holding discussions and having interactions with ISM practitioners, there is a need for group meetings but also more importantly, there is a need for 'meeting of minds': What is urgently required is the change in attitude of scientists, traditional practitioners and industry on one hand and the special policy initiatives by the Government on the other. Then only can we create the golden triangle of traditional machine, modern machine and modern science.