

“Science means learning to say—I don’t know”: An interview with Dr. Ashok D.B. Vaidya

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ABSTRACT

Dr. Ashok D.B. Vaidya, the stalwart in the fields of Experimental Pharmacology, Clinical Pharmacology, and Reverse Pharmacology turns 75 on Nov, 27, 2011. A former Clinical Research Head of CIBA Geigy Research Centre, his name has been synonymous with the concept of the Golden Triangle for resurgence of Ayurveda and its reinterpretation in modern scientific terms. At a time when most fields are populated by intellectual dwarfs and unethical operators, he stands like a giant—a scientist, a philosopher, and an ardent fighter for ethical values. In this free-wheeling interview with Ravindra R. Pandharinath, he discusses the milestones in his life, his inspirations, and dreams for the confluence of modern science, modern medicine, and Ayurveda as the new health care model for the 21st century

Key words: Dr. Ashok Vaidya, golden triangle, reverse pharmacology

RRP: Please tell us about your childhood. What were your earliest influences?

AV: I was born at Kathi's Jetpur in Saurashtra. We lived in a three storey citadel-like house built by my great grandfather, Arya-Vaidya Mayaram Sundarji. My grandfather was a doctor and my father kept the Ayurvedic tradition alive. So, I inherited the legacy of both modern medicine and Ayurveda. In fact, we ran an Ayurvedic pharmacy, Dhanvantari Aushadhalaya, in our house. Our product *Rambaan Pills*, a formulation developed by my great grandfather for malaria, was a big hit, as it included Ayurvedic ingredients to counter cinchonism, the side effects of quinine. It was this heady mix of the smells

and sights of Ayurvedic plants and formulations that shaped my neuronal pathways. My parents came from diverse but rich family backgrounds that cherished the best of the traditions, modern education, ethical values, and independence of thoughts and action. Several of my relatives were eminent freedom fighters, pioneers in education, poets, writers, administrators, and scientists. Their dedication and achievements have left an indelible mark on my mind. Several guests to our home—dramatists, journalists, musicians and saints—captivated my heart. Some of the most influential of them are: Sri Nathalal Joshi, Sri Makarand Dave, and Kaka Kalelkar. Sri Nathalal Joshi, my spiritual guide, taught me, “Ashok! Let the test tube be your rosary—your path to God!” Makarandmama, my maternal uncle, a saint-poet of Gujarat, discussed with me concepts, such as *Chandrasekhar limit* and the theory of relativity, in my young days. Sri Meghani, whom Gandhiji gave the epithet of *Rashtriya Shayar*, inspired me by his research in folk literature. Sri Kalelkar, an eminent freedom fighter, writer, educationist, and Gandhiji's close associate, reinforced my love for literature (I had read many classics by my matriculation). Sri Kalelkar advised my parents not to put me in a routine school, lest my curiosity and passion for knowledge be diminished. So, in the initial years, my mother taught me at home. I love to learn because I love my mother immensely. Later, I joined the school headed by Dr. Manubhai Vaidya, my uncle, a great educationist; it encouraged free thinking. Later, Virani High School, at Rajkot, helped to shape my personality and communicative skills. Overall, for me,

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childhood was being special, receiving love, creativity, and learning from all.

RRP: What were your earliest ambitions? What attracted you more—medicine, literature, or something else?

AV: I was drawn to both literature and medicine. But, I knew firsthand that poetry was fine, even noble, but that may not help me support my large family. So, I chose medicine at a very young age. I wanted to be fourth in the lineage of Vaidya—Doctors.

RRP: You have been an illustrious alumnus of the Seth GS Medical College and KEM Hospital, Mumbai. What are your memories about your *alma mater*?

AV: I stood first at the Intermediate examination in the erstwhile state Saurashtra. At that time, the first five rank holders from other universities got direct admission to the GS Medical College. That's how I got into it. I soon realized that every moment here was filled with learning with joy. I remember when I was asked about my hobbies in my interview during admission, I had replied, "They are very many, ranging from the holy Gita to Hollywood." Here I participated in games, elocution competitions, won the staff versus students debate, became the General Secretary and learnt a lot about medicine and life from my Gurus. I completed my MBBS and MD from this college and met the loves of my life—Rama and Pharmacology—in this very institute. I was fortunate to have been trained by Professors like P Raghavan, RJ Vakil, UK Sheth, RS Satoskar, BB Gaitonde, NK Bhide, RD Ganatra, SD Store, K Ramamurthy— each one was a stalwart in their fields. My eminent classmates Manu Kothari, Ajit Phadke, Rajni Khokhani, Jayant Doshi, Lalit Shah, Madhu Ingle, Mahendra Sheth, KB Bhagava, Ramesh Shah, and Datta Samant also provided enabling stimuli.

RRP: So, you completed MD in Pharmacology here before moving out for further studies?

AV: No, my MD was in Internal Medicine, I chose Clinical Pharmacology for my Ph.D. later. I had joined Haffkine Institute for a short, but important stint as a Typhoid Officer, wherein I was entrusted with the responsibility of examining patients and collecting their blood samples, from different parts of Mumbai from the Chief Minister's bungalow to Dharavi slums and conducting Widal test and culture. I was also trained in histopathology and microbiology. So, my first research paper discussed results of 300 liver biopsies.^[1] Later, I came back to GS Medical and started the first unit of Clinical Pharmacology with Prof. Sheth. Dr. M.J. Shah offered us five beds in his ward for our research. In 1967,

as Rama too completed her registrarship, we moved on to Yale for our advanced research. I was awarded the Merck International Fellowship.

RRP: How was the transition from GS to Yale? Was it a cultural shock or something that you were looking for and mentally prepared?

AV: I had received the best possible education in India and already had a firm foundation in research with several publications in my name. Clinical Pharmacology was my passion. Yet, my early days at Yale were filled with apprehension and a mild depression. But soon I realized that to be successful at Yale, I had to first unlearn my methods of learning. In India, the education was highly information oriented. Here the first thing I learnt was that *Science means learning to say "I don't know."* I learnt to be comfortable, saying so and to say "I shall find out" and to ask questions to the right people/literature to reduce my ignorance. I learnt that Clinical Pharmacology, like any discipline related to health, cannot be a stand-alone. It must be integrated with real bedside experience of patients and on strong foundations of basic sciences. Hence, I undertook full courses in Biochemistry, Molecular Biology, Nuclear Medicine, and Biomedical Electronics to expand my horizons in Clinical Pharmacology. I'd learnt, through Satoskar that research in Clinical Pharmacology is not mere clinical trials. It begins by thorough washing of the glassware! Besides the laboratory, as a physician in the cardiology clinic, I had to take care of patients with hypertension and disorders involving biogenic amines.

I interacted with some of the most brilliant minds at Yale—Robert Levine (Eminent Human Ethicist), Arnold Eisenfeld (Steroid pharmacologist), Melvin van Woert (L-dopa/5-HTP therapy), Lewis Thomas (later the Director of Sloan Kettering Cancer Research Center), Alvan Feinstein (the Medical Statistics guru), Aaron B. Lerner (the discoverer of melatonin), Paul Greengard (Nobel Laureate), John McLean Morris (the discoverer of the morning-after pill), G van Wagenen (A pioneer in primate reproductive biology), and Pravin Bhatt (Virologist, Laboratory Animal Health).

At Yale, I experienced and learnt to appreciate the freshness of the present. In India, we often clutter the present with the burden of the past. Once when I told Dr Lerner that I came from a medical school where Prof. RJ Vakil showed the antihypertensive effects of *Rauwolfia serpentina*, his response was "What did he do later?" To someone brought up in a culture where resting on the past laurels was a norm, to be told that doing so means "wearing them on the wrong place," came as an enlightenment. My students, at Yale, too contributed to my learning in very many ways. I remember

a student who approached me while I was conducting an experiment and inquired “What are you doing? If it is known, give me a reference; if it is new, show me.” The entire milieu was thus conducive to creativity. I remember vividly the Histamine Club dinners wherein great minds such as Robert Levine enthralled the audience with their knowledge, but did not hesitate to declare their ignorance when they did not know a particular thing. I sometimes miss all this in India. Reading the journals, conducting and supervising research, and interacting with young scientists compensates, it and retains neuroplasticity.

RRP: Can you tell us about any memorable case studies or research work at Yale?

AV: There are several but my favorite is the paper published in *New England Journal of Medicine (NEJM)* wherein we correlated hypothermia in a patient with carcinoid syndrome during treatment with parachlorophenylalanine with depletion of serotonin.^[2] I also remember the patient of Zolinger–Elison Syndrome treated with a histamine synthesis inhibitor, who reported hair growth over his bald head. In his case paper, I had then quoted Caraka, in Sanskrit, who had long back suggested that excess salt intake resulted in hyperacidity, eczema, hypertension, and hair loss. I also showed a strong inhibition of the enzyme histaminases by two alkaloids, berberine and sanguinarine. The latter is the toxic principle of the plant *Argemone mexicana* known to cause epidemic dropsy by adulteration of edible oils.

RRP: As you were really enjoying your research and personal growth at Yale, why did you decide to come back?

AV: Rama and I had decided long back that we would return to India within 3–4 years. Because, the longer you stay, the tougher it is to return. You become used to a milieu which rewards individual performance, while in India, family and other obligations take precedence over the individual. We were clear about our priorities. We wanted to return where we belonged. So, it wasn't a tough decision. I am glad that our daughter Vidita too has returned from Yale to TIFR.

RRP: So, you returned and joined CIBA Research Centre. What about your work there and with Vaidya Antarkar, when was it initiated?

AV: In fact, both - phase I and II trials of new chemical entities of CIBA Research Centre at KEM Hospital and the clinical screening of whole plants/Ayurvedic formulations at Podar Ayurvedic Hospital - occupied me. The drug discovery project was an ambitious mission at CIBA. With eminent scientists, it was a very educative and an exciting period for me. There was a focus on natural

products. It was great pleasure working with Dr. Bal Joshi, an expert phytochemist, who first thought about the clinical unit at Podar Hospital, with Vaidya Antarkar. For synthetic compounds, we had an outstanding team of medicinal chemists, pharmacologists, parasitologists, and toxicologists. More than 20,000 compounds/plant products were studied. Sintamil, Aubril, and Satrogyl emerged as new drugs. Several more were in the pipeline. The impression that the CIBA research has failed is not valid. The endeavor laid the foundation of drug discovery in India. For me, it was a great education in drug discovery. I learnt how and why most drugs are killed on the altar of phase I and II trials. In fact, I look at myself as an undertaker of new chemical drug candidates. CIBA Research Center was ultimately closed down, for reasons best known to the top management at Basel. It was indeed a windfall in the real estate. I still think that it was a great blow to research on Indian medicinal plants. Nevertheless, I continued at CIBA as its Medical Director. I am grateful to some of the outstanding colleagues Dr TG Rajagopalan, Dr MD Nair, Dr S Rajappa, Dr CL Kaul, Dr Joy David, Dr RR Rao, Dr Niranjan Mankodi, Dr Arun Bhatt, and others who participated in the team work. Prof TR Govindachari and Prof RS Grewal were the decision makers to focus the efforts on diseases of the third world.

RRP: Let us now talk about your significant contributions—research in Ayurveda and reverse pharmacology. I still remember your first double-blind placebo-controlled randomized clinical trial (with Vaidya Antarkar) of Arogyavardhini in viral hepatitis. All the tools of modern clinical trial were, for the first time, used for validating the efficacy of an Ayurvedic product. Do you think that the validation of Ayurveda using tools of modern science has now become a trend?

AV: Validation was the first step. That was Revivalism. Now, we are aiming at Renaissance! From validation, we moved on to reverse pharmacology, which is now accepted by CSIR, ICMR, and CCRS (AYUSH), all the apex bodies related to medical research. The clinical trial of Arogyavardhini was followed by further work on *Picrorhiza kurroa* and the active principles, namely, picrosides.^[3] Now, Dr. RA Mashelkar, Dr. Narendra Mehrotra, and I had evolved, at Chitrakoot, a *golden triangle partnership consisting of modern medicine, traditional medicine, and life sciences* as the basis for this renaissance. ICMR has granted an Advanced Centre of Reverse Pharmacology at Kasturba Health Society, where we have already started training in reverse pharmacology. Recently Maharashtra University of Health Sciences has initiated the plan for a fellowship program in Reverse Pharmacology.

RRP: This sounds interesting. But, is the integration of Ayurveda and modern medicine—two systems which are so diverse, one supposedly holistic and the other reductionist, really possible?

AV: For this, our mindsets need to change first. Both so-called reductionist and holistic approaches have their own strengths and limitations and epistemologically, their integration is the most challenging task before us. The process would take decades as evidence has to be marshaled at all levels of biological organization. But, an integrative synthesis can bring out the best in each system and may result in a truly remarkable contribution to the global human health. Let me give an example. *R. serpentina* (Sarpagandha) has been used in Ayurveda for long for the treatment of hypertension, anxiety, neurosis, and snakebites. Then the alkaloid reserpine was isolated from it and used as an antihypertensive. That was a classic example of reductionist science. Dr. Gananath Sen conducted his trials in humans and on dogs. This experiment paved the way for the study, by Arvid Carlsson, of blocking the catecholamine uptake into synaptic vesicles by reserpine. It also led to the development of first animal model for reserpine-induced depression in rats and later to the development of a whole generation of antidepressants. Reserpine use was severely limited due to its ability to cross blood–brain barrier and cause severe depression in some patients. Recently, a quaternary derivative of reserpine has been synthesized, which does not cross blood–brain barrier, and thus may not cause depression. Today, reserpine is dead, but sarpagandha lives; and so the antidepressants.

RRP: So, you think that both the approaches are useful, but what will be their place in the healthcare scenario of the 21st century?

AV: Both approaches are mutually supportive. We need one for economical treatment of our patients and the other for research. Standard extracts of whole plants have been shown to be effective in the treatment of several diseases. They provide an easily available, economical and culturally acceptable way of therapeutics. On the other hand, new molecules derived from the understanding of Ayurveda from the molecular biology perspective would be useful as scaffolds for chemical research, which fuels the 21st century pursuit of knowledge. Recently, with Mukund Chorghade and Bhushan Patwardhan, we have initiated this approach, by an international collaborative R and D program.

RRP: One cannot discuss the 21st century health scenario without considering the Intellectual Property Rights (IPR)? What is your take on this issue? Are you a votary of rewarding the innovation or prefer the greater common good to prevail over profits?

AV: The whole issue of IPR has been often contrived to suit the MNCs of the G-5 nations of the world. I support the notion that intellectual efforts must be rewarded and that innovation must be recognized and encouraged by the society. But under the current patent regime, whose rights are protected? Whether the creators/innovators benefit or the mighty corporations who employ them? The scientists have no say in the matter; they simply surrender their rights to the corporations. I am glad that the concept of cultural rights is finally being accepted. Hence, a part of money originating from patents based on ethnobotanical knowledge base will go the tribals who invented and preserved the basic tradition. I suggest that on similar lines, any innovation coming from an Ayurvedic lead should result in part of patent money going to the activities of AYUSH. In some matters, however, there should be no patent protection, for example, in terminal cancer. Similarly, when 3000 children die every day of malaria, how can you look at it as an opportunity for making money? Remember, several important inventions, such as oral contraceptives that changed the drugs scenario, have not been patented. In India, the creation of the Traditional Knowledge Digital Library (TKDL) has been a commendable effort to stall the IPR on the known uses of Ayurvedic plants.

RRP: Talking of the positive aspects of patents, the trend of patent-filing by CSIR, encouraged by Dr. Mashelkar, is reported to be dwindling. The issue of quality of patents also needs to be addressed. What is your opinion about it?

AV: As a leader of CSIR, Dr. Mashelkar had the challenging task of countering the several ills that affected the Indian research scene. He emphasized the issue of patents and worked like an evangelist to promote the culture of patent filing. However, the enthusiasm seems to be on the wane after his retirement. This bespeaks of noncontinuity in policy in our research councils, with a change in leadership. There is a need to file patents with sizeable market potential, with a quality review by peers. The wealth of knowledge in our traditional systems needs to be explored in a manner that the criteria of novelty, nonobviousness and utility for a patent are fulfilled.

RRP: Which of the domains in the AYUSH would you like to highlight?

AV: The nondrug measures, such as Yoga, naturopathy, traditional diet, and nutritional practices, can become the new foci for research in the era of wellbeing and nutraceuticals. Look at the way Gandhiji practiced and encouraged naturopathy. There is a need of meticulous research and an independent path to pursue what Gandhiji was promoting at that time. His views on unpolished rice, jaggery prepared in iron vessels, whole wheat flour, goat

milk, and honey were much ahead of the times. Take another example. The concept of fasting is important in Hindu, Jain, and Muslim religious traditions, but it has not been studied well with respect to its health benefits, for example, innate immunity. Shivambu—autourine therapy is yet another area awaiting exploration. Its concept is much wider than just drinking one's own urine. It has been shown that urine contains cancer-regressing molecules. Fasting, avoidance of substances with salty, spicy and, sour tastes, more fruits and vegetables in the diet are recommended with Shivambu. Dr. BV Khare had treated several cancer patients using Shivambu kalpa. The role of endogenous keto-aldehydes in spontaneous regression of cancer has been explored.^[4] Advances in life sciences and modern medicine should be gainfully employed for understanding and interpreting Ayurveda and traditional health practices. Some traditional phenomena and concepts novel to modern science may open up new directions for research. With Tillu and Patwardhan, Systems Ayurveda and Systems Biology are being explored with such a vision. Darshan Shankar and group have done remarkable work in their documentation of the local health practices and also in networking at the village levels. But much more work in Ayurvedic Pharmacoepidemiology needs to be done to conduct research in these fields and to propagate the validated practices.^[5]

RRP: Let us go back to “reverse pharmacology”. Can you explain the concept and its role for a renaissance in Ayurveda?

AV: Conventional Pharmacology follows the path of “Experimental–Exploratory–Experiential.” Reverse Pharmacology, thus has two connotations, both from different origins. In the West, it refers to the discovery of a ligand for the drug-like action of a novel human molecule. You come up with a molecule occurring within human body, and you want to find out what its therapeutic action can be. On the other hand, for us, it means discovery of the safety, efficacy, and mechanism of action of a standardized drug whose human effects are known by usage. Therapeutic action of several Ayurvedic preparations have been described for thousands of years; but their exact mechanism cannot be explained in the modern scientific, say molecular biological terms. Doing so is an important goal of reverse pharmacology for us. Anyway, in the above case, “human” comes first! In conventional pharmacology, it comes last (as in case of human trials). Traditionally pharmacologists would attempt to “kill it early,” while we would try to “feel it early”. Thus, it is not just the application of pharmacology to traditional systems; it also means contributing to the development of pharmacology through observations at the bedside. It means a paradigm shift that would help

new drug discovery.^[6] A major national initiative for herbal drug development from Ayurveda New Millennium Indian Technological Leadership Initiative (NMITLI) was undertaken by CSIR from 2002 to 2007. This program has led to interesting hits, leads, and drug-candidates for diabetes, arthritis, and hepatitis.^[7]

RRP: Are you optimistic about the pace of these developments, especially when major stakeholders, such as Ayurvedic manufacturers, international regulators, and the practitioners of Ayurveda and modern medicine, don't seem to have imbibed the spirit of these changes? How do you plan to change this picture?

AV: Let me list in brief what has been achieved in the past three decades—first and foremost, we have succeeded in bringing Ayurveda to global attention. It is no longer folklore, but has been perceived as an organized, scientific health system. Some postcolonial powers are threatened by its emergence with evidence, and hence its recognition is delayed. But, it can't be delayed for long. We have presented to the EU an alternative framework for study of safety and efficacy of Ayurvedic products by emphasizing that Ayurveda is not merely herbal drugs, but a holistic and robust health care system.^[8] Second, both modern science and Ayurveda have opened up and are in a process of rapid change. Third, therapeutic utility of more than a hundred medicinal plants used in Ayurveda has been confirmed through use of established modern scientific techniques. The mechanism of action of several Ayurvedic preparations has been interpreted at the molecular level. Most importantly, it has opened minds, freed them from Macaulayan prejudices and complexes. In fact, I am convinced that the nation has taken on a movement, which would continue for a hundred more years. As I have told you earlier, *We have planted and nurtured a sapling; but that is a sapling of a banyan tree.*^[9] Moreover, we are advocating the concept of Vaidya-scientists who will transform the Ayurvedic research scene in days to come.^[10] It is a long process; but it has surely begun.

RRP: It has indeed been a long and eventful journey, both for the resurging Ayurveda and for you personally. What are your plans for future?

AV: Research has always been my passion and it would continue. On the personal front, I feel the need to spend more time and energy for an inward journey.

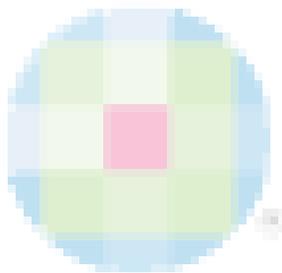
RRP: Congratulations and best wishes for your future. Thank you.

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