



Review Article

Prakriti-based medicine: A step towards personalized medicine

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Abstract

The concept of personalized medicine has been around for as long as people have been practicing medicine. From *Charaka* to Hippocrates, all have practiced the personalized approach for treating a disease. In the 21st century, personalized medicine is all about DNA. Whereas the single nucleotide polymorphism (SNP) and epigenetic factors influence drug response and form the basis of personalized medicine, the *tridosha* theory forms the basis of *Prakriti*-based medicine. It is well established by now that western allopathic medicine is excellent in handling acute medical crises, whereas *Ayurveda* has successfully demonstrated an ability to manage chronic disorders that Western medicine has been unable to cure. With effective integration of 'omics' *Prakriti*-based medicine can play a vital role in this changing scenario of global health wisdom as *Ayurveda* offers its modalities by way of *ahara* (diet), *vihara* (lifestyle), and *aushadhi* (medication), which are the three pillars of *prakriti*-based medicine making it a holistic science. *Prakriti*-based medicine and other traditional medicine systems have the potential to offer remedies to the challenging health issues like adverse drug reactions, drug withdrawals, and economic disparities among few. An integrative global approach could do wonders to health sciences benefiting a broad spectrum of patients.

Key words: Ayurgenomics, epigenetics, pharmacogenomics, personalized medicine, pharmacogenetics, single nucleotide polymorphism

Introduction

"It's far more important to know what person has the disease than what disease the person has"

–Hippocrates

Medicine today targets therapy to broadest patient population i.e. "ONE DRUG FITS ALL" approach, but the importance of personalized medicine has long been understood in medical profession.^[1] Personalized medicine (individualized medicine) is defined as medical care for each patient's unique condition and has its roots in understanding of diseases that date back to 1500 B.C. *Ayurveda*, the traditional system of Indian medicine, traditional Chinese medicine and Korean medicine, all have well defined systems of constitutional types used in prescribing medicine bearing resemblance to personalized medicine.^[2] Father of western medicine, Hippocrates was also known to advocate personalized medicine. He evaluated factors like person's constitution, age and

physique in decision making when prescribing drugs.^[3] Upon the discovery and elucidation of the molecular basis of hereditary diseases beginning in the early 20th century, modern version of an ancient tradition is being revived. In the 21st century, personalized medicine is all about DNA.

Single nucleotide polymorphism and personalized medicine

The recent completion of the human genome sequence has shifted research efforts in genomics towards function of human genome, its regulation, and how sequence variation contributes to disease and varied response to therapy. Each of us carry genome inherited from our parents and the inherited differences in DNA sequence contribute to phenotypic variation influencing an individual's anthropometric characteristics, risk of diseases and response to environment.^[4] The recognition of these inter-individual differentiations that brings variation in drug response is an essential step towards personalized medicine viz "Right treatment for the right patient at the right time."

According to Modern Science, humans are 99.9% identical. The genetic variation due to single nucleotide polymorphism (SNP) is the most common between different human beings. The phenotypic differences arise due to SNP and it contributes 0.1% of

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the differences. There are 3 billion nitrogen bases and 30,000 genes in human chromosomes. Fifty percent of the human genome has repetitive sequence and 1.42 million SNPs are distributed throughout human genome, an estimated 1 SNP per 1000 base pair (bp).^[5] The complete mapping of these genetic polymorphisms that influence drug response forms the basis of personalized medicine and these differences could be helpful in the understanding of adverse drug reactions (ADRs)^[6] [Figure 1]. Efforts are being directed towards identifying SNPs in genome wide analysis that predispose humans to common chronic diseases such as obesity, cardiovascular disorders, diabetes, and to identify successful markers.

Ayurveda: A step towards personalized medicine

“Every individual is different from another and hence should be considered as a different entity. As many variations are there in the universe, all are seen in human beings”.

Charaka Samhita

Ayurveda is a natural health care system that originated in India more than 5000 years ago. It emphasizes the treatment of disease in highly individualized manner as it believes that every individual is unique having different constitution. *Ayurveda* classifies all individuals into different ‘*Prakriti*’ types based on the theory of *tridosha* and each type has varying degree of predisposition to different diseases. This is independent of racial, ethnic, or geographical considerations and may provide appropriate means of classifying phenotypes to be considered collectively for genotyping. Similarly it classifies the drugs according to the *rasapanchaka* (ayurvedic pharmacology), which states that the drug action is ascribed to certain attributes present in the drug namely *Rasa* (taste), *Guna* (property), *Virya* (potency), *Vipaka* (postdigestive taste), and *Prabhava* (effect), while in modern pharmacology the drug action is attributed to the chemical structure of a molecule.^[7] The *rasapanchak* modality is able to deliver treatment as it takes into consideration the *prakriti* of the person as well as the pharmacodynamics and pharmacokinetic properties of a drug unlike a modern treatment that elicits varied response from person to person having same drug for the same disease.

If personalized medicine is to be realized a systematic classification of human population is necessary but modern medicine classifies human population based on ethnicity. Geographic patterns of genetic variation shows that inter-individual variation in drug

response is common.^[8] This gap could be effectively filled by *Ayurveda* and its vision as ayurvedic classification is independent of racial, ethnic, or geographical considerations and may provide appropriate means of classifying phenotypes to be considered collectively for genotyping. What is required is a connection of phenotypic features (*prakriti*) with genotype as personalized medicine aims to design drugs with maximum efficiency and safety for a particular disorder. Ayurvedic system of medicine and other traditional systems of medicine have a personalized approach in treating a patient with centuries of practice, rightly called experiential science.^[9] Their intervention and assistance in personalized treatment has now become a necessity.

Tools to achieve personalized medicine: Epigenomics, pharmacogenomics, and ayurgenomics

Apart from inherited genetic variations (most commonly SNPs), variation in drug response is influenced by changes in gene function that occur without a change in the nuclear DNA sequence. The study of such changes is done under an emerging field of Epigenetics, which is drawing attention of scientists across the globe. The major underlying mechanisms of such changes are RNA inactivation, histone modifications and DNA methylation. Unlike DNA mutations, epigenetic variations are potentially reversible. Therefore, one of the long term goals of epigenomics is to map the DNA methylation patterns in various diseases to find out epigenetic markers of common chronic diseases, variation in drug response, and simplify the path to personalized therapy. The future of epigenomics therapy holds tremendous potential for not only individualized health care but also for population-wide disease screening and prevention strategies.^[10,11]

Pharmacogenetics is the study of inter-individual variations in DNA sequence related to pharmacokinetics and pharmacodynamics. Genetic variation in drug targets can have a profound effect on drug efficacy by exhibiting polymorphic variations in genes that encode the functions of transporters, metabolizing enzymes, receptors and other proteins. This explains individual difference for many therapeutic agents with over 25 examples already identified.^[12-14] Pharmacogenomics is the application of genomic technologies to study drug discovery, therapeutic response and pharmacological functions with the aid of genomic technologies such as Polymerase chain reaction (PCR), Restriction Fragment Length Polymorphism (RFLP), DNA microarray and bioinformatics to find out genetic basis of interindividual and interracial variation in drug response.^[1] Pharmacogenomics is the foundation to personalized healthcare. Table 1 shows the current areas and ongoing projects in achieving the herculean task of personalized therapy.

Ayurgenomics is the integration of the principles of *Ayurveda* with genomics. The primary challenge of Ayurgenomics is to establish the correlation between DNA and ‘*Prakriti*’. The basis of individual variations in *Ayurveda* indicates that individuals with *Pitta Prakriti* are fast metabolizers while those of *Kapha Prakriti* are slow metabolizers. Different *prakriti* may have different drug metabolism rates associated with drug metabolizing enzyme (DME) polymorphism as well. A correlation between CYP2C19 enzymes involved in metabolism of a number of drugs genotypes and *prakriti* has been studied.^[15-17] Therefore Ayurgenomics seems to bear similarities with pharmacogenetics and has the potential

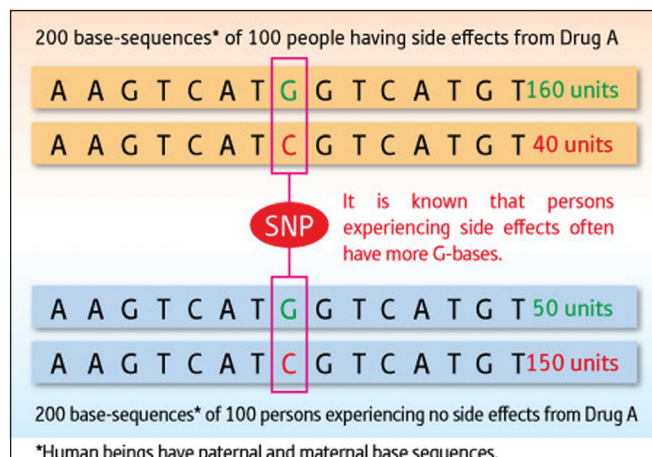


Figure 1: The relationship between snps and side effects of drugs

to be a platform to achieve personalized drug therapy. The understanding of “SNP science” lead to the concept of personalized medicine which goes parallel with the concept of “*Prakriti* based medicine (Ayurgenomics).”

Potentials of *prakriti* based medicine

The promotion of health and prevention of diseases are stressed by both *Prakriti* based medicine and personalized medicine. Fields of genomics, proteomics, metabolomics, and now epigenomics (‘omics’ technology of system biology) study the contribution of genes, proteins, metabolic pathways and non-genetic factors to human physiology and variations in pathways that has vital role in disease susceptibility of an individual. It is here that Ayurgenomics can play its role in explaining how current drugs can be used more effectively by targeting them on patients of particular *Prakriti*. Table 2 highlights the research work carried out in this direction. With effective integration of ‘omics’ *Prakriti*-based medicine can play a vital role in this changing scenario of global health wisdom as *Ayurveda* offers its modalities by way of *ahara* (diet), *vihara* (lifestyle) and *aushadhi* (medication), which are the three pillars of *prakriti*-based medicine. The potentials of *prakriti*-based medicine lie in:

1. Promotion of health and quality of life and thereby longevity.
2. Prevention of disease.
3. Understanding patient needs and risk factors for various chronic conditions.
4. Personalizing health care by monitoring *ahara*, *vihara*, and *aushadhi* on individual basis.
5. Disease management.
6. Reduction in morbidity and mortality.
7. Provision of new approaches for diagnosis and drug development.
8. Reducing the trial and error approach of health care system.
9. Minimizing adverse drug reactions.

10. Making healthcare affordable for people of various economic strata.
11. To utilize appropriate technologies for development of single and polyherbal products to make it globally acceptable.
12. To promote integrated research by AYUSH with modern medicine/modern science institutions and Indian systems of Medicine.

Prakriti-based medicine and personalized medicine: An answer to adverse drug reactions

‘If the misery of poor be caused not by the laws of nature but by our institutions great is our sin’.

Charles Darwin

“It takes 50 years to get a wrong idea out of Medicine, and 100 years a right one into Medicine.”

John Hughlings Jackson

Disparity in healthcare system particularly related to affordability issues specifically in developing countries needs immediate attention. Similarly ADRs rank as the fourth leading cause of death, ahead of pneumonia, diabetes and traffic accidents, and only about half of patients treated with conventional drugs adequately respond to pharmacotherapy.^[18,19] Of the 1233 new drugs marketed between 1975 and 1999, only 13 were approved for treating tropical diseases affecting developing countries.^[20] On comparing the 60-80% of health expenditures that patients in low income countries have to cover themselves with the 30-35% of health expenditures covered by individuals in high income countries, the extent of disparities in accessing health care become strikingly evident. India currently has the world’s second-largest population with a significant economic disparity and a high rate of infectious and chronic diseases. These are some of the grave issues of healthcare system. The Indian genome variation (IGV) consortium 2005, initiated the single largest study to find out the genetic landscape of IGV related to disease and drug response.^[21-23] The database obtained from

Table 1: Progress in personalized medicine

Journal and issue/project	Title	Author/Director of project
AAPS PharmSci. 2000; 2 (1):	Pharmacogenomics: The promise of personalized medicine.	Mancinelli L, Cronin M, Sadee W
Clinical cancer research, 2008 14; 7988	Advances in breast cancer: Pathways to personalized medicine	Olufunmilayo I. Olopade, Tatyana A. Grushko, Rita Nanda, and Dezheng Huo
Journal of genetics, 2008 87, 3-20	Genetic landscape of the people of India: A canvas for disease gene exploration.	Indian Genome Variation Consortium 2008
Database, Vol. 2010, Article ID baq022, doi:10.1093/database/baq022	IGVBrowser-a genomic variation resource from diverse Indian populations	Ankita Narang, Rishi Das Roy, Amit Chaurasia, Arijit Mukhopadhyay, Mitali Mukerji, Indian Genome Variation Consortium 3 and Debasis Dash
On going projects of the genome centre of the Japanese foundation for cancer research	Prediction of adverse effect by single nucleotide polymorphism analysis	Tetsuo Noda
On going projects of the genome centre of the Japanese foundation for cancer research	Characterization of individual cancer by gene expression profile	Tetsuo Noda
On going projects of the genome centre of the Japanese foundation for cancer research	Developments and application of bioinformatical methods for cancer research and construction of integrated cancer databases for cancer research	Tetsuo Noda

Table 2: Progress in ayurgenomics

Journal and issue/institute	Title	Author/Principle investigator
Evidence Based Complementary Alternative Medicine 2005, 2(4): 465-473	<i>Ayurveda</i> and traditional Chinese medicine: A comparative overview.	Bhushan Patwardhan, Dnyaneshwar Warude, P. Pushpangadan and Narendra Bhatt
The Journal of Alternative and Complementary Medicine 2007, 13(9):1011-1020	Utilization of <i>Ayurveda</i> in health care: An approach for prevention, health promotion, and treatment of disease. Part 1— <i>Ayurveda</i> , the science of life.	Hari Sharma, H.M. Chandola, Gurdip Singh, Gopal Basisht
The Journal of Alternative and Complementary Medicine 2008, 14(5):571-576	Ayurvedic genomics: Establishing a genetic basis for mind-body typologies.	Bhushan Patwardhan, Gerard Bodeker
Available online: www.ayurvednews.com/archives/September 19, 2008	Ayurgenomics: CSIR study establishes links between <i>Ayurveda</i> and modern science for predictive and personalized medicine.	Vikas Sharma
Journal of Translational Medicine 2008, 6(48)	Whole genome expression and biochemical correlates of extreme constitutional types defined in <i>Ayurveda</i> .	Bhavana Prasher, Sapna Negi, Shilpi Aggarwal, Amit K Mandal, Tav P Sethi, Shailaja R Deshmukh, Sudha G. Purohit, Shantanu Sengupta, Sangeeta Khanna, Farhan Mohammad, Gaurav Garg, Samir K Brahmachari, Indian Genome Variation consortium and Mitali Mukerji
Available online: http://ecam.oxfordjournals.org , 2009, 1-6 Downloaded from http://ecam.oxfordjournals.org by on October 10, 2010	Traditional medicine to modern pharmacogenomics: <i>Ayurveda Prakriti</i> Type and CYP2C19 gene polymorphism associated with the metabolic variability.	Yogita Ghodke, Kalpana Joshi and Bhushan Patwardhan
Available online: http://ecam.oxfordjournals.org , 2010, 1-5	Traditional medicine to modern pharmacogenomics: <i>Ayurveda Prakriti</i> type and CYP2C19 gene polymorphism associated with the metabolic variability.	Yogita Ghodke, Kalpana Joshi and Bhushan Patwardhan
Journal of Clinical and Diagnostic Research. 2010,4:3003-3005	Adaptogenic potential of herbal Immunomodulators as new therapeutic approach to combat swine influenza A/ H1N1 crisis.	S. Singh, M. Gupta, and S. Gautam
Holy family hospital, Okhla Road, New Delhi-25	Genetic susceptibility to rheumatoid arthritis using A novel combination of <i>Prakriti</i> based case control selection and molecular analysis tools	Dr. Bheema Bhatt
Sri Ramchandra medical college and research institute, (Deemed University)	Pre-clinical studies of a polyherbal and a herbomineral formulation in the management of urolithiasis- A comparative study.	Dr. A. Hannah Rachel Vasanthi
West Bengal school of natural product studies, Jadavpur University,	Evaluation of safety profile of herbs used in <i>Ayurveda</i> with CYP-450 enzymes inhibition method	Dr. Pulok Kumar Mukherjee
Central council for research in <i>Ayurveda</i> and <i>Siddha</i>	Golden triangle partnership	Department of Ayush, Ministry of Health and Family Welfare, Government of India

the study will be helpful in reducing bottlenecks in personalized approach towards common, chronic, and complex diseases both in reference to the Indian and global context.

Populations throughout Africa, Asia, and Latin America use traditional medicine (TM) to help meet their primary healthcare needs^[24] as shown in Figure 2. TM is not only accessible and

affordable, but more relied upon and an integral part to everyday life and well being among various populations of the world. Organizations working on issues related to traditional medicine are given in Table 3. Various new research activities have been already initiated by Central Council for Research in *Ayurveda* and *Siddha* (CCRAS), Department of Ayush, Ministry of Health and Family Welfare, and Government

Table 3: Organizations working on traditional medicine issues

Nongovernmental organizations (NGOs) Worldwide, many NGOs are working in the field of traditional medicine. Just a few examples are given here

Cochrane collaboration: <http://www.cochrane.org/cochrane/general.htm>

Ford foundation: <http://www.fordfound.org/>

PRO.ME.TRA: <http://www.prometra.org/>

World wide gund for nature: <http://www.panda.org/>

World conservation union: <http://www.iucn.org/>

Global professional associations

Liga medicorum homeopathica internationalis

(International homeopathic medical league): <http://www.lmhi.net/>

World federation of chiropractic: <http://www.wfc.org>

World self-medication industry: <http://www.wsmi.org/>

Specific initiatives also exist

Global initiative for traditional systems of health: <http://users.ox.ac.uk/~gree0179/>

Research initiative on traditional anti-malarial methods: http://mim.nih.gov/english/partnerships/ritam_application.pdf

Source: World Health Organization, Geneva, May 2002, WHO Policy Perspectives on Medicines — Traditional Medicine-Growing Needs and Potential

of India (<http://www.ccras.nic.in/>) in the direction of drug discovery, drug standardization, treatment for acute and tropical diseases and supportive therapy to chronic diseases like cancer, HIV, schizophrenia, psoriasis among many others.

Conclusion

It is well established by now that western allopathic medicine is excellent in handling acute medical crises, whereas *Ayurveda* has successfully demonstrated an ability to manage chronic disorders that Western medicine has been unable to. *Ayurveda* and other traditional health practices can form the basis for a new, improved approach to public health, including health promotion, and affordable primary care functions, especially for communicable and chronic diseases. *Ayurveda's* holistic approach and its emphasis on prevention have the potential to improve the health status of the world's population. Since the sequencing of human genome, scientists are striving for the goal of personalized medicine. Several factors influence a patients' response to drugs viz. heredity, age, lifestyle and environment. A systematic integration along with an interdisciplinary approach forming the "Golden Triangle of *Ayurveda*", modern science and modern Medicine can pave the path to Personalized Medicine and offer remedies to the challenging health issues^[25] [Figure 3]. *Ayurveda* not only offers personalized treatment but personalized nutrition and personalized lifestyle by way of both drug and non drug modalities suited to an individual's *prakriti* making it a holistic science. These attributes of *Ayurveda* can play a major role in disease prevention and promotion of health towards longevity with a better quality of life, which forms the basis of personalized medicine.

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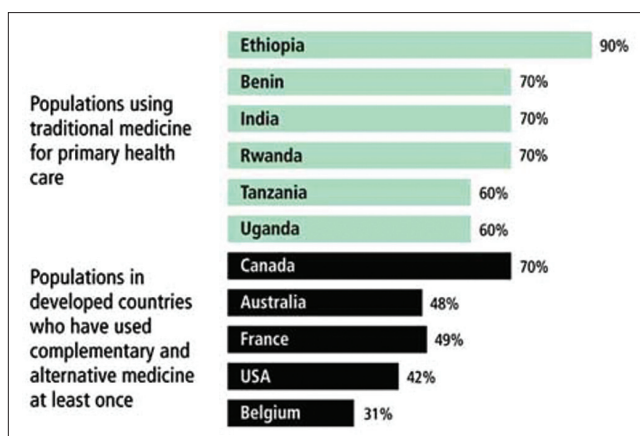


Figure 2: Popularity of traditional medicines (tm) and complementary alternative medicines

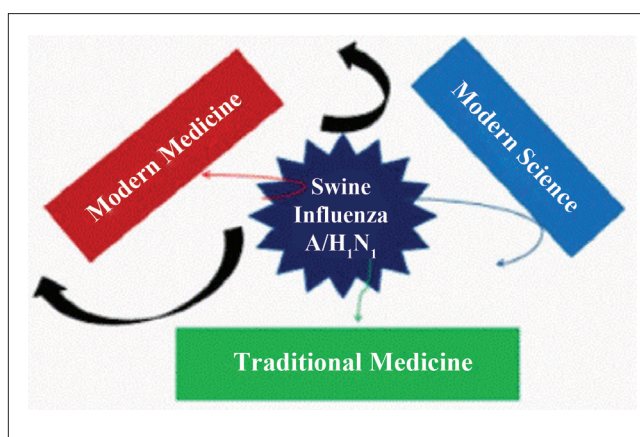


Figure 3: The golden triangle of traditional medicine, modern science and modern medicine

use 'Golden triangle diagram in the article. The authors are also grateful to Dr. B. Ravishankar and Dr. H.M. Chandola for their encouragement & support, and Dr. Yogesh Deole for his constructive inputs.

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हिन्दी सारांश

मनोदैहिक प्रकृति पर आधारित उपचार- व्यक्तिपरक चिकित्सा की ओर एक कदम

बिजया चटर्जी, जिगीशा पंचोली

जब से चिकित्सा का अभ्यास शुरू हुआ व्यक्तिगत चिकित्सा की अवधारणा भी उसी समय से अस्तित्व में रही है। व्याधि निवारणार्थ व्यक्तिगत चिकित्सा का विचार चरक से लेकर हिप्पोक्रेटस तक के चिकित्सकों ने किया है। २१वीं शताब्दी में व्यक्तिगत चिकित्सा पद्धति डी.एन.ए. पर आधारित है। आधुनिक विज्ञान में औषध की प्रतिक्रिया को एकीय नाभिकीय बहुरूपता (SNP) तथा आनुवंशिक कारक प्रभावित करते हैं, उसी प्रकार त्रिदोष सिद्धान्त प्रकृति पर आधारित चिकित्सा का आधार है। यह प्रमाणित सत्य है कि उग्र व्याधियों के शमन में पाश्चात्य चिकित्सा उत्कृष्ट है जब किचिरकालिक व्याधियों के शमन में आयुर्वेद सफलता पूर्वक प्रयुक्त है जो कि पाश्चात्य चिकित्सा द्वारा असाध्य हैं। आहार, विहार और औषध जो प्रकृति पर आधारित आयुर्वेद चिकित्सा के आधार स्तम्भ हैं यदि इनका "ओमिक्स" के साथ प्रभावी एकीकरण कर दिया जाए तो आज के स्वास्थ्य के बदलते वैश्विक परिदृश्य में आयुर्वेद एक महत्वपूर्ण भूमिका निभा सकता है तथा उसे एक सम्पूर्ण चिकित्सा पद्धति का दर्जा दिया जा सकता है। प्रकृति पर आधारित चिकित्सा तथा अन्य पारम्परिक चिकित्सा पद्धतियों में इतनी क्षमता है कि वे आज के चुनौतीपूर्ण स्वास्थ्य के मुद्दे जैसे प्रतिकूल औषध प्रतिक्रिया, आर्थिक असमानतायें इत्यादि से निपटने में सक्षम हैं। एकीकृत वैश्विक दृष्टिकोण का स्वास्थ्य विज्ञान में प्रयोग कर व्यापक रूप से रोगियों को लाभ पहुंचाया जा सकता है।

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