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APPLICATION OF AYURGENOMICS IN PERSONALISED SELECTION OF AYURVEDIC HERBS

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ABSTRACT

Genomics is launched in an era of predictive, preventive and personalized medicine & it is hoped that in the near future there would be a paradigm shift in the practice of medicine from a generalized symptomatic approach to an individualized approach based on his or her genetic makeup. In the 21st century, personalized medicine is all about DNA where the single nucleotide polymorphism (SNP) and epigenetic factors influence drug response and form the basis of personalized medicine. But *Ayurveda*, our Ancient system of medicine already has personalized approach towards management of health and disease on the basis of *Prakriti*, which determines inter individual variability in susceptibility to diseases and response to external environment, diet and drugs. Whereas in contemporary medicine, a preventive and curative regime is adopted only after an individual suffers or shows signs of an impending illness and there are no methods to identify healthy individuals who would be differently susceptible to disease. Therefore an integration of *Ayurveda* and genomics called Ayurgenomics, if attempted in a systematic manner could help fill the gap. The present paper is an attempt to apply the principles of *Ayurveda* & Genomics for finding the ways to personalised medicine.

Keywords: Ayurgenomics, *Ayurveda*, Genomics, *Prakriti*, Personalised Medicine.

INTRODUCTION

Ayurveda is a holistic science where there is a personalised approach towards the management of health and disease. According to this system, every individual have their own unique constitution called *Prakriti* which determines the individual variability in susceptibility to various diseases. But in contemporary science, the preventive and curative regime depends upon the symptoms of a disease. It creates a wide gap between these two streams which evolves the sprouts of Ayurgenomics. It is the integration of principles of *Ayurveda* with Genomics. Ayurgenomics term was coined in 2001. Its central concept is oriented in predictive, preventive and personalized medicine. The major hypothesis which is to be proven before the scientific world is *Prakriti* (phenotype) which can be linked with the genotype of a human being.[1]

With the discovery of the double helical structure of DNA and subsequent advancements in the field of molecular biology and genetics, the causes of pathogenesis in many of these diseases have been traced to changes in the DNA from one individual to another. The human genome is composed of 23 chromosome pairs (diploid) where each set (haploid) has 3 billion base pairs of DNA inherited from either of the parents. There are large numbers of variations in the human genome sequence which are called Single Nucleo-

tide Polymorphisms (SNP). Some of these variations are present in large number of individuals and are called as common variations and some are rare. If the variations are present in less than 1% of the population they are mostly classified as mutations. Many rare diseases like haemophilia, beta- thalassaemia etc. are monogenic, caused due to mutations in single genes. Most of the common diseases such as diabetes, asthma, cardiovascular disease and so on are multigenic complex disorders involving many genes. It is generally observed that common diseases are a consequence of cumulative effect of a large number of variations in the genome which independently have small effects that are not sufficient to cause the disease. Further there is a complex interplay of genes and environment involved in most of the diseases. For example, in cardiovascular disease (CVD), various parameters like blood pressure, levels of lipoproteins (HDL and LDL), triglycerides and total cholesterol in the blood along with life style habits such as diet, smoking and lack of exercise, stress etc. have been identified as risk factors in these diseases. Each of these parameters can be modulated by a large number of genes. Thus the combination of variants from different genes and environment could contribute not only to differences in clinical manifestation of disease but also to the variability in age of onset, severity and symptoms of the diseases. Another aspect of the disease is the drug dosage management. Most of these diseases require long term drug administration and there is a high variability in individual response to drug dosage and adverse effects mainly due to variations in the genes responsible for drug transport and drug metabolism within the individual's system. Therefore design of optimum dosage with least side-effects is difficult to establish. Thus an important starting point in understanding the factors responsible for these diseases and how the treatment regime can differ from individual to individual is to study the prototype sequence of a human genome that could be used as a reference for comparison between healthy and affected individuals. With the availability of the complete sequence of the human genome, it is now possible to entertain the thought that not too far in the future, each individual would have a personalized health regime based on his/her genetic make-up. [2,3]

Basic concepts of genetics in *Ayurveda*:

The very concept of genetics mentioned in *Ayurveda* is about the *Beeja* (Sperm/ovum), *Beejabhaga* (Chromosome) and *Beejabhagaavayava* (Genes). The *shukra* (male sperm) and *shonita* (female ovum) can be taken as the basic entity *Beeja*. *Beejabhaga* refers to the part of *Beejaie*, the chromosomes. *Beejabhagavayava* is the most fundamental entity which can be grossly compared to a gene. It is responsible for the expression of a particular trait in an individual. *Prakriti* (innate constitution) is mentioned as the genetically determined relative proportion of *doshas* within the normal range. It is decided right at the time of conception and it remains unchanged throughout the lifespan of an individual. This forms the basic factors which distinguish two individuals both physically and mentally.[4]

In an individual, the *tri-doshas* work in conjunction and maintain homeostasis throughout the lifetime starting from fertilization. Distinct properties and functions have been ascribed to each *dosha*. The kinetic components of a system have been ascribed to *Vata*, the metabolic components to *Pitta* and the structural and stability components to *Kapha*. For instance, *Vata* contributes to manifestation of shape,

cell division, signalling, courage, respiration, movement, excretion of wastes, cognition and also regulates the activities of *Kapha* and *Pitta*. *Kapha* is responsible for growth and maintenance of structure, storage, ability in having sex, proper joints, tolerance, patience, strength, non-greediness and stability. *Pitta* is primarily responsible for metabolism, thermoregulation, energy homeostasis, pigmentation, happiness, vision, and host surveillance. Hence the differences in *Tridoshic* proportions right from the time of fertilization are manifested as different phenotypes that can be with respect to external appearances, body physiology, and response to external environment etc. Thus a continuum of relative proportions of *doshas* results in seven possible constitutional types namely *Vata, Pitta, Kapha, Vata-Pitta, Pitta-Kapha, Vata-Kapha and Vata-Pitta-Kapha*. [5,6]

TABLE 1: Distinguishing features of three contrasting *Prakriti* types *Vata, Pitta & Kapha* and their disease predisposition as described in the original text.

S. no	Features	*Vata*	*Pitta*	*Kapha*
1.	Body frame	Thin	Medium	Broad
2.	Build & musculature	Weakly developed	Moderate	Well developed
3.	Skin	Dry & cracked	Soft, thin, tendency for moles, acne & freckles	Smooth, firm clear complexion
4.	Hair	Dry, thin, prone to brakes	Thin, oily, early greying	Thick, smooth & firm
5.	Weight gain	Recalcitrant	Fluctuating	Tendency to obese
6.	Food & bowel habits	Frequent, variable & irregular	Higher capacity for food & water consumption	Low digestive capacity & stable food habits
7.	Movements & physical activities	Excessive & brisk	Moderate	Less mobile
8.	Tolerance for seasonal weather	Cold intolerant	Heat intolerant	Endurance for both
9.	Disease resistance & healing capacity	poor	Good	Excellent
10.	Metabolism of toxic substances	Moderate	Quick	Poor
11.	communication	Talkative	Sharp, incisive communication with analytical abilities	Less vocal with good communication skills

12.	Initiation capabilities	Quick responsive& enthusiastic	Moderate, upon conviction& understanding	Slow to initiate things
13.	Memory	Quick at grasping, poor retention	Moderate grasping & retention	Slow grasping & good at retention
14.	Ageing	Fast	Moderate	Slow
15.	Disease predisposition/ poor prognosis	Developmental, neurological, dementia, movement of speech disorders, arrhythmia	Ulcer, bleeding disorders, skin diseases	Obesity, diabetes, atherosclerotic conditions

When the relative proportion of *tridosha* in *prakriti* get imbalanced, then abnormalities occur.[7]

Commonly occurring abnormalities due to:

Vitiated *vata*: dystrophy of nails, dermatophytosis, sciatica, cramps in the calf muscle, spasticity of thighs, prolapse of rectum, retraction of eyelids, faintness, giddiness, hiccup, asthenia etc.

Vitiated *pitta:* heating, scorching, burning, broiling, local- fetor (*charamdalan*), sarcothermia(*angavdaran*), bitter taste, faintness etc.

Vitiated *kapha:* anorexia nervosa, torpor(*tandra*), stiffness, loss of strength, increased secretion in throat, erysipelas, lethargy, goitre, obesity, heavy pulse etc.[8]

Researches done in Ayurgenomics:

Various researches were done to find the relationship between phenotype & genotype of a human being:

Research - 1

In order to rule out effect of ethnicity related genetic variation, a study on individuals primarily of Indo-European origin was carried out based on *Prakriti* analysis. In this study, normal healthy individuals belonging to the three extreme and contrasting *Prakriti* groups - *Vata, Pitta, Kapha* were taken. In this study, CYP2C19 gene was followed and the study concluded a strong association between this gene and *Prakriti* phenotype. Correlations were found among biochemical profiles, functional categories of differentially expressed genes and the *Ayurvedic* descriptions between three constitution types. It was observed that the higher levels of markers of metabolic syndrome and chronic inflammation (TG, total cholesterol, LDL, VLDL, High LDL/HDL, low HDL, uric acid, SGPT) in *Kapha* males compared to *Vata* and this was also consistent with over-expression of genes involved in inflammatory response in these individuals. Prothrombin time, indicative of blood coagulation process was observes to be low in *Kapha* males. Further, higher levels of expression of haemoglobin genes in *Pitta* compared to *Vata* and *Kapha* also corroborates with the differences in haemoglobin levels between the *Prakritis* and correlates with the redness of skin as a phenotype in *Pitta* individuals. *Ayurveda* proposes that the proportions of *Doshas* are restrained within allowable limits and disease is a consequence of perturbation from the threshold. 30% of the entire dataset of the genes that were differentially expressed among *Prakriti* groups were reported to be associated with complex and monogenic diseases. Thus *Ayurveda* based method of *Prakriti* classification helped to identify biochemical and expression differences amongst normal healthy individuals.[9] In another study conducted on *Pra-*

kriti, which includes the serotoninergic receptor genes having the functions ascribed to *Kapha dosha* in *Ayurveda* and dopaminergic receptor group of genes having the functions of *Vata dosha* in *Ayurveda*, concluded that dopaminergic receptors shows a more allele frequency in *vata Prakriti* and serotoninergic receptors shows an increased allele frequency in *kapha Prakriti*. [10]

Research - 2

This research was done to prove that the different constitution types are differently predisposed to diseases. In order to test this further, a gene EGLN1 which is a key oxygen sensor that can switch on a subset of genes when required that allows a body to adapt to low oxygen conditions was followed. The gene was found to be differed both with respect to its expression level as well as at genetic level between *Pitta* and *Kapha* constitution types, and the expression differences were co relatable to genetic variations. One of the physiological conditions where oxygen levels are low is at high altitudes to which natives get acclimatized and often un-acclimated suffer from High Altitude Pulmonary oedema (HAPE). High altitude region, according to *Ayurveda* is considered as *Kapha-Vata* predominant region where disorders of a *Kapha-Vata* are more prevalent and *Pitta* was anticipated to have higher adaptive capacity. At the end of the research, it was found that the *Pitta* genotype to be highly represented in natives of high altitude than that of the *Kapha* genotype in those individuals who develop HAPE. Thus from the above research it can be anticipated that individuals who are of the *Pitta Prakriti* or who have the marker linked to the high altitude phenotype may be able to perform better in high altitude conditions. Thus using the Ayurgenomics approach we can identify pathways and genes that differ at the expression level as well as genetic level between contrasting constitution types that are differently predisposed. [11]

Personalized medicine: ultimate goal

The ultimate goal of Ayurgenomics is to attain the personalized medicine. Personalized medicine is the use of diagnostic and screening methods to better manage the individual patient's disease or predisposition towards a disease. The complete gene mapping clubbed with drug response studies forms the basis of personalized medicine and thereby we can attain the goal of right treatment for the right patient at the right time. The major tools to achieve this personalized medicine are Pharmacogenomics, Epigenomics and Ayurgenomics. [12] Pharmacogenomics is the application of genomic technologies to study drug discovery, therapeutic response and pharmacological functions. Epigenetics refers to the study of inheritable changes in gene expression without a change in DNA sequence. The study of these epigenetic factors in the molecular level is a newer perspective which supports the Prakriti genomics. Epigenetic influence includes chemical changes to the DNA and histone proteins modification of an organism.[13] Ayurgenomics is the integration of principles of Ayurveda with Genomics and its main aim is to excavate the genomic counterpart for the various Prakriti phenotype mentioned in Ayurveda.[14]

Personalized selection of medicine in *Ayurveda*: Allopathy mainly emphasise on symptomatic treatment. But *Ayurveda* always emphasises on personalised selection of *Ayurvedic* treatment regimen for a particular patient. 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* (post-

digestive taste), and *Prabhava* (effect), while in modern pharmacology the drug action is attributed to the chemical structure of a molecule. The *rasapanchak* modality is able to deliver treatment as it takes in to 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.[15]

Herbs used according to *rasapanchak* modality in *tridosh vikar:*

Vata vikar: drugs with *madhur, amala, lavan rasa, snigdha guna & ushna virya. . e.g. dashmoola, nirgundi, devdaru, virtaru adigana.*

Pitta vikar: drugs with *madhur, tikta, kashaya rasa & sheeta virya. e.g.* milk, *chandan dvaya, shalaparni, prishniparni, trinapanchmool*

Kapha vikar: katu, tikta, kashaya rasa, tikshna, ruksha guna, ushna virya[16] *e.g. aaragvadhaadi gana, arkaadi gana, valli panchmool, kantak panchmool*

To attain the goal of personalised medicine, one should keep these things in mind: examination of patients (*das vidha rogi pariksha*) & disease (*rog pariksha*) & then *dravya nirdharan*.

Das vidha rogi pariksha:

- ***Prakriti pariksha:*** after examination of *prakriti* of a person, drugs are decided. e.g. to a *vata prakriti purusha*, drugs which aggravates *vata* like herbs having *tikta, kashaya rasa, sheeta & ruksh* property should be avoided. in place of them, *vata shamak or kaphoutpadak* drugs should be used.
- ***Vikriti pariksha:*** to know the pathology of a disease, *dosha, dushya, prakriti desh, kala, bala (rog pariksha)* should also be examined. If all these factors are same & equal, then the disease will be more powerful. If these factors are not same & equal, then the disease will be of low strength. Drugs are decided according to strength of disease.
- ***Sara pariksha:*** *Sara* are of 8 types- *tvak sara, rakta sara, mansa sara, meda sara, asthi sara, majja sara, virya sara, satva sara.* It is done to know the strength, power of a patient. A patient with a heavy body does not mean , he/she has a good immunity & strength. A patient with a weak body does not mean , he/she has a low immunity & weak strength. In fact, exactly opposite happens. Hence *Sara pariksha* is also very necessary in deciding a drug.
- ***Sanghanan pariksha****:* It is done to know the compactness, firmness, power & strength of a body so that a drug can be decided.
- ***Praman pariksha****:* It is also done to know the strength, power of a person.
- ***Satmya pariksha*****:** If a body is *satmya* to all the six *rasas*, then that body is much more powerful, able to face any situation & with long life. If a body is *satmya* to only one *rasa*, then that body is of low power, unable to face difficult situations & with small life. Moderate *satmya purush* are of moderate characterics.
- ***Satva pariksha:*** This *pariksha* is related to mental status of a body. *Satva* are of three types: *pravar, madhyam, avar. Pravar satva* persons are of high intellect & very strong mentally, able to face any situation mild or difficult, don't get annoy if affected by a strong disease. High potency drugs can be given to them. *Madhyam satva purush*, they are also able to handle any situation but with the support of elderly persons. Drugs of medium potency are suitable for them. *Avar satva* persons are mentally very weak & cannot toler-

ate even the mild situations. Weak potency drugs are given to them.

- ***Aahaar pariksha*:** A person's strength & age depends on intake & digestive capacity. If both are good, then the person will be of good strength & can tolerate medicine of any strength.
- ***Vyayam pariksha:*** A person's body power is investigated with the capacity of doing exercises.
- ***Vaya pariksha:*** *Purush vaya* is divided in three parts: ***balavastha***- upto 30 year of age. At this age, body organs are not fully developed. Majority is of *kapha dhatu*, body is weak. *Ushna tikshan dravya* should be avoided at this age & *mridu aushadh* should be given.

Madhyamavastha- Upto 60 years of age. In this age, body is fully developed physically & mentally, body is empowered with fully grown *dhatus. Pitta dhatu* is *pradhan dhatu.* Drugs with any potency mild or strong can be given. ***Vriddhavastha***- after 60 years of age, every organ, mental strength, *dhatus* are degrading at this age. *Vata dosha* is *pradhan dosha.* Powerful drugs are not given in this age. *Mridu & snigdh aushadh* are preferred.[17]

Rog pariksha:

Dosha pariksha*:* Which medicine is to be prescribed to a patient is decided after examination of *doshas* which are getting aggravated in a disease.

***Dushya pariksha*:** While diagnosing a disease, which *dushya* is aggarvated should also be kept in mind. *Rasa, rakta, mansa, meda, asthi, majja, shukra, indriya, snayu, mala* are *dushya*. All carry a different type of treatment regimen.

***Prakriti pariksha*:** This is the basis of personalised medicine in Ayurgenomics. After deciding *prakriti* of a patient, medicine is decided after that.

Desha pariksha: *Jaangala desha*- In these *deshas, pitta* is aggravated normally. Parched lands, excess of sun, poor flora & fauna leads to *rakta & pitta vikar,* but tendency to develop a disease is very low. *Aanup desha- Kapha & vata* are aggravated normally. Rich in water resources, flora & fauna, slow winds & weak sun leads to *kaphaja vikar,* tendency to develop a disease is high. In this way, *desha pariksha* is also very important in deciding a drug. The *desha* terminology is also proved according to ayurgenomics researches, as explained in research-2.

Kala pariksha: Different *doshas* get aggravated in different *kala*. But the concept of *kala & desha* doesn't affect genomic structure of a person. Their effect on every person will be same. But they cause imbalance of *tridosha* for a particular span of time.

Bala pariksha: Investigation of the strength of a disease.

DISCUSSION

'Yagamansam tu yo vidyad desh kalo uppaditam| Purusham purusham vikshaya sa geyo bhishaguttamam'|[18]

A physician who knows correct combination of medicines by examining *desh* (body & habitat), *kala* (time) etc. is the best one.

The main aim of ayurgenomics is to attain the personalised medicine for each & every patient. By considering *dasvidha rogi pariksha & rog pariksha & rasa panchak* of a herb, one can decide a particular herb for a particular patient.

Examples of applications of Ayurgenomics:

Table No. 2: Personalised selection of herbs for *Jwar*:

Herb	*Rasa panchak*	Effect on *dosh*	Useful in *prakriti*	Useful in type of *jvar*
Tinospora cordifolia Willd. (Guduchi) & Trichosanthes dioca Roxb.(Patola)	*Rasa- tikta, Kashaya Guna- guru, snigdh Vipak- madhur Virya- ushna*	Pacifies *Tridosh*	*Tridoshaj*	*Tridoshaj jvar, jirna jvar, visham jvar*
Vernonia cineria Less.(Sahdevi) & Gentian kurro Royle(Trayamana)	*Rasa- tikta, guna- laghu, ruksha, vipaka- katu, virya- ushna*	Pacifies *kapha vata*	*Kaphaj vataj*	*Kapha vataj jvar*
Swertia chirayita Karst.(Kirattikta), Momordia charantia Linn.(Karvellak) & Alstonia scholaris R.Br.(Saptaparna)	*Rasa- tikta, guna- laghu, ruksha, vipak- katu, virya- ushna*	Pacifies *kapha pitta*	*Kaphaj pittaj*	*Kapha pittaj jvar*
Nymphoea stellata Willd.(Utpala)	*Rasa- madhur, Kashaya, tikta, guna- laghu, snigdha, pichchhila, vipak- madhur, virya- sheeta*	Pacifies *vata pitta*	*Vata pittaj*	*Vata pittaj jvar*
Ricinus communis Linn.(Eranda)	*Rasa- madhur, guna- laghu, snigdha, tikshna, vipak- madhur, virya- ushna*	Pacifies *vata*	*Vataj*	*Vataj jwar*
Vitex negundo Linn.(Nirgundi)	*Rasa- katu, tikta, guna- laghu, ruksha, vipak- katu, virya- ushna*	Pacifies *vata*	*Vataj*	*Vataj jwar & visham jwar pratibandhak*
Santalum album Linn.(Chandana)	*Rasa- tikta, madhur, guna- laghu, ruksha, vipak- katu, virya- sheeta*	Pacifies *pitta*	*Pittaj*	*Pittaj jvar*
Piper longum Linn.(Pippali)	*Rasa- katu, guna- laghu, snigdha, tikshna, vipak- madhur, virya- anushna sheeta*	Pacifies *kapha*	*Kaphaj*	*Kaphaj jvar & visham jvar pratibandhak*

Ammomum subalatum Roxb.(Brhidala)	*Rasa- katu, tikta, guna- laghu, ruksha, vipaka- katu, virya- ushna*	Pacifies *kapha*	*Kaphaj*	*Kaphaj jwar*

Table No. 3: Personalised selection of herbs for *Kasa:*

Herbs	*Rasa panchak*	Effect on *dosh*	Useful in *prakriti*	Useful in type of *kasa*
Solanum surattense Burm.f.(Kantkari) & Solanum indicum Linn.(Brihti)	*Rasa- tikta, katu, guna- laghu, ruksha, tikshna, vipak- katu, virya- ushna*	Pacifies *kapha vata*	*Kapha vataj prakriti*	*Kapha vataj kasa*
Sesbania grandiflora Pers. (Agastya)	*Rasa- tikta, guna- laghu, ruksha, vipak- katu, virya- sheeta*	Pacifies *kapha pitta*	*Kapha pittaj*	*Kapha pittaj kasa*
Commiphora mukula Engl.(Guggulu)	*Rasa- tikta, guna- laghu, ruksha, tikshna, vishad, vipak- katu, virya- ushna*	Pacifies *tridosh*	*Tridoshaj prakriti*	*Tridoshaj & Jeerna kasa*
Vitex negundo Linn.(Nirgundi)	*Rasa- katu, tikta, guna- laghu, ruksha, vipak- katu, virya- ushna*	Pacifies *vata*	*Vataj*	*Vatik kasa*, pulmonary oedema
Cassia occidentalis Linn.(Kasamarda)	*Rasa- tikta, madhur, guna- laghu, ruksha, tikshna, vipak- katu, virya- ushna*	*Pitta sarak*	*pittaj*	*Pattik kasa*
Piper longum Linn.(Pippali)	*Rasa- katu, guna- laghu, snigdha, tikshna, vipak- madhur, virya- anushna sheeta*	Pacifies *kapha*	*kaphaj*	*Kaphaj kasa*

From the above examples, it is clearly explained that how on basis of *prakriti*, *dosha* involvement & time, different herbs are used for different individuals. When multiple variables, like *prakriti* not matching *dosha* etc. is seen, then herbs are combined logically to address this multifactorial issue.

CONCLUSION

The concept of personalised medicine is well established in *Ayurveda*. In *Ayurveda*, *tridoshas* are considered as basic parameters. Everything, every matter, every investigation and every examination rotates around *tridoshas*. Even *prakriti* is based on *tridosha*. That's why treatment in *Ayurveda* basically depends on *prakriti* of a patient. Even then, *Ayurveda* doesn't stop on *prakriti*. It also speci-

fies its treatment individual to individual. It not only explains personalised medicine but also dose & duration of the drug which again depends on patient's *agni, satva, bala, roga bala etc*. Therefore we can say that the concept of personalised medicine was well understood from the ancient times. The term Ayurgenomics is coined just to interpret the principles of *Ayurveda* with the latest modern tools and thereby it paves the ways for evidence based *Ayurveda* and thereby a better global acceptance.

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