

Ayurveda and Transdisciplinary Approaches: A Way Forward towards Personalized and Preventive Medicine

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Ayurveda is an age-old medicinal practice gaining global acceptance because of its personalized approaches toward healthcare. The current review focusses on the concepts of Ayurveda and the science behind the traditional knowledge of Ayurveda by combining transdisciplinary approaches, enabling an evidence-based framework. The foremost principle of Ayurveda is to understand tridoshas (Vata, Kapha, Pitta) and Prakriti (inherent nature of individual) to determine the individual's susceptibility to diseases and treatment regimen. In the clinical field, reverse pharmacology can unravel the mechanism of documented Ayurvedic medications, thus facilitating knowledge transfer. Ayurveda positively impacts both phenotypes (Deha Prakriti) and genotypes (Janma Prakriti) through epigenetics by addressing lifestyle behaviour, diet, stress and environmental factors. As a result, the modern biology and Ayurveda will better correlate and understand each other through the Ayurgenomics approach, which outlines the substantial variances in biochemical and genome-wide analysis of differential prakriti phenotype. The protein targets and lead molecule of an ayurvedic drug can be retrieved from traditional knowledge-based information databases involving Ayurinformatics. The impact of Ayurveda's lifestyle and diet principle can be explored through Ayurnutrigenomics, which untangles how Ahara (Diet) and Pathya (diet-dietetics) foster wellness by influencing the phenotype and genetic makeup of an individual with respect to tridoshas. Tridoshas has its own house for the gut flora, underlining the significant association between Prakriti and the microbiome's composition as well as psychobiotics. Incorporating these approaches in Ayurveda could make a paradigm shift between traditional and modern medicine by providing scientific validation to Ayurvedic medicines, thereby aiding health management.

Key words: Tridoshas, prakriti, reverse pharmacology, ayurgenomics, epigenetics, ayurinformatics, ayurnutrigenomics, microbiome

Ayurveda has been practiced and documented as a holistic system of medicine. It has gained increased global acceptance as an alternative and complementary medicine due to its personalized strategy to medicine's predictive, preventative and rehabilitative modules. Ayurvedic medicine's Materia medica provides a vast collection of traditional folklore medicines^[1]. During the Vedic era, traditional ayurvedic medicine was developed and well-described in the oldest literature, like Susruta Samhita and Charaka Samhita. According to Ayurveda, disease emerges from the body due to external influences^[2].

Ayurveda primarily focuses on three Doshas (VPK); Vata (V), Pitta (P) and Kapha (K),

altogether combinedly described as Tridoshas. The Tridoshas work together to preserve an individual's homeostasis throughout their lives, beginning with fertilization and each Dosha has its own set of traits and functions. Vata is responsible for a system's kinetic components (manifestation of shape, cell division, signaling, mobility, waste excretion, cognition), Pitta for its metabolic components (thermo-regulation, energy homeostasis, pigmentation, vision and host vigilance), and Kapha for its structural and stability

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components. Ayurveda concerns inter-individual heterogeneity in predisposition assessment, prognosis and diagnosis, primarily based on the individual's genetic patterns ("Prakriti"). Prakriti is the unique blend of three entities (i.e., Tridoshas). Prakritis are distinct phenotypes characterized by anatomical, psychological, physiological and behavioural factors unaffected by communal, ethnic or geographic factors^[3]. Prakriti is not only hereditarily determined but also impacted by the environment, particularly maternal nutrition and lifestyle, as well as the age of the transmitting parents^[4]. An individual's Prakriti determines susceptibility to disease and response to treatment, so determining their homeostasis is essential in Ayurvedic medicine^[5]. Ayurveda's foremost principle for personalized therapeutics is a hierarchical approach that underpins the doshic components with appropriate adaptations to stabilize these states. Ayurveda recommends medicine and diet based on individual's endophenotype, constitution, and health status during administration. According to Ayurvedic philosophy, an individual is divided into three major groups; causes (hetu), features (linga), and therapeutics (aushadha), collectively known as "Trisutra" for healthy and diseased persons^[6].

Despite recent advances in medicine, there are still significant problems in the clinical field that need to be solved, necessitating additional attention to develop hitherto unknown fields of medicine. Ayurveda provides comprehensive, safe and efficient techniques to treat various ailments^[7]. Ayurveda, more of a living science than a medical science, emphasizes prevention and thorough curing of an illness with a low probability of recurrence. Evidence-based research on Ayurveda can also provide valuable insights as complementary to biomedical sciences in integrative therapy, as it considers nutrition, daily life, exercise and psychological harmony. Ayurvedic pharmacology, centered on natural items, may also provide a successful and well-tolerated method of treating specific ailments^[8]. Some allopathic medications like digitoxin, reserpine, withanolide, taxol, and silymarin were developed from Ayurvedic medicinal plants to treat certain serious illnesses^[9].

Modern medicine employs terminologies like genome, gene expression, epigenetics and metabolomics to define the fundamental root of our

physiology and health in a profoundly reductionist framework. Ayurveda employs a holistic approach that includes concepts like dosha and Prakriti^[10]. Ayurveda uses a blend of internal medicine, herbal medicines and rejuvenation programs in its humoral diagnosis and therapies^[11]. Ayurvedic practitioners emphasize the importance of primary, secondary and tertiary prevention, patient empowerment and self-efficacy as Ayurvedic perspectives in personalized care to healing^[12]. Modern research has validated the effectiveness and safety of Ayurvedic botanical medicines. The ancient medicinal system of Ayurveda has been the subject of many studies worldwide, yielding scientific evidence supporting its activities^[13]. In this Review, we focussed on bridging antique Ayurveda and Modern therapeutic approaches, which could provide insight into scientific validation strategies of traditional medicine to fulfil the needs of evidence-based Ayurvedic medicine towards personalized and preventive healthcare.

PHYTOPHARMACEUTICALS AND AYURVEDA

The Indian government recently proposed amending the Medications and Cosmetics Act and its Rules to define phytopharmaceuticals as botanical-based medications. The schedule requires scientific proof to back up quality, safety and efficacy claims when plant-based compounds are evaluated and marketed as pharmaceuticals. Thus, a new class of drugs will be created analogous to synthetic, chemical pharmaceuticals covered by Schedule Y under the Drugs and Cosmetics Act. This program accelerates pharmaceutical development based on scientific research^[14]. Globalization and industrialization of the Ayurvedic medications needs a standardized and validated criterion for in-use drugs. Besides formulating a new drug, the current Ayurvedic research must focus on Contemporary Ayurveda since there is a great need to explain the principles of Ayurveda in a modern perspective and to answer the rising demand for an evidence-based medicine^[15].

Ayurvedic formulations:

Many sophisticated formulations have been utilized in Ayurveda pharmacology and therapies for centuries. The Traditional Knowledge Digital Library of India has gathered traditional Indian

knowledge, which is publicly accessible through numerous records and authoritative sources^[16]. The principal sources of Ayurvedic medicines are plants, animals and vegetables. Ayurvedic formulations, primarily obtained from plants and their extracts, are known as 'kasthausadhi', which includes aristra, avleha, grafa, churna and taila. 'Rasausadhi' refers to formulations that are primarily composed of metals and minerals, as well as mixtures of minerals and plants; examples include bhasma, lauha, kapibadkva, and rasayana. There are numerous reliable books such as Sarngadhara Samhita, Bhaisajya Ratnavali, Cakradatta, Bharat Bhaisajya Ratnakara, Sahasrayogam and other texts deal with both types of formulations^[17].

India has rich, diverse plant species of which 15 000 to 20 000 are of therapeutic value, but only around 7500 plants are used in the folklore system of medicine^[18]. Numerous multi-ingredient medicines are available in the Ayurvedic formulary and the Ayurvedic classics robustly explain such compositions. To resolve the standardization problem, the Ministry of AYUSH has set up an expert committee for formulations, which brought out Ayurvedic Formulary of India (AFI) and Ayurvedic Pharmacopoeia of India (API). AFI Part I has 444 formulations, AFI Part II has 191 formulations, API Part I has 7 volumes of the monograph, and API Part II contains 3 monograph volumes. India's Ayurvedic formulary and Pharmacopoeia have been extensively investigated to treat a multitude of ailments and thus, have market potential. Ayurveda, along with combinatorial sciences and high-throughput screening, may assist in the construction of structure-activity libraries. Drug companies conduct large-scale pharmacological screenings of herbs to produce medications from Ayurvedic botanicals^[19].

REVERSE PHARMACOLOGY (RP)

RP is a transdisciplinary science that integrates traditional knowledge-based documented clinical and experiential data into leads by interpreting observational studies and further transforming these into drug targets through rigorous preclinical and clinical testing^[20]. A RP approach is used to validate the safety and efficacy of drugs, to produce new drugs from different Natural Chemical Entities (NCEs), and is time-consuming. Experiential knowledge/data, exploratory validation and

appropriate clinical/experimental studies are the stages of RP.

Realms of RP and Ayurvedic Pharmacoeidemiology:

Ayurvedic pharmacoeidemiology involves the study of Ayurvedic medication's acceptance, efficacy, safety complementarities and cost-effectiveness in a vast number of people. It also deals with assessments of Ayurvedic prescriptions, registration of Ayurvedic medicine usage, demographic pharmacodynamics/kinetics and the record of any adverse effects^[21]. Pharmacoeidemiology-based knowledge, recommendations from clinical transcripts and classic literature and hits from database observational medicines as well as single case studies, would all fall into the experiential realm of RP. The experiential domain would gather data from traditional medicine's unusual rationales, ranging from new clinical findings to serendipitous discoveries.

In clinical and paraclinical studies, an experiential study involves monitoring and recording clinical data, and exploratory studies involve human or *in vitro/in vivo* models. The experimental phase is the final stage and provides the premise of efficacy, safety and quality that can match any NCEs. Mechanistic investigations could be considered paraclinical and rather than Ayurvedic statistics, clinical testing designs must consider the Ayurvedic pramanas (knowledge acquisition through investigative processes) including apta (learning), pratyaksha (perception), anumana (inference), upamana (comparison), and yukti (logical reasoning)^[22]. In Ayurvedic drug development, translational research is a two-way strategy that involves bedside to bench and RP to facilitate efficient knowledge transfer^[23]. The first strategy, from bedside to bench, focuses mainly on herbo-epidemiological systematic reviews and Ayurvedic medicinal clinical trials. Several Ayurvedic plants/formulations have been researched and they have provided hits and leads to develop novel drugs. Traditional knowledge and experience databases could offer novel functional leads to lessen the three key barriers i.e., time, money and toxicity. As a result, the traditional discovery path of "lab to utility" becomes "utility to lab"-a truly reversed strategy method^[24].

UNDERSTANDING OF DISEASE ETIOPATHOGENESIS IN AYURVEDA SYSTEMS BIOLOGY

Understanding disease etiopathogenesis at the genetic level provides a tactical edge in identifying targets and overcoming associated hurdles to find ways to reduce and treat/maintain the condition. Kayachikitsa, or Ayurvedic internal medicine, focuses on the etiopathogenesis, diagnosis, and therapy of disorders^[25]. Variations in the genomics of diseased and healthy individuals could be analyzed to identify regions of the genome that vary in frequency and can be related to disease using Genome-Wide Association Studies^[26]. Molecular pharmacology and “Omics” research underline the disease phenotype that could offer potent herbal components against complex disease conditions leading to the discovery of novel therapeutic strategies.

Bioinformatics, functional genomics and microarray (DNA/Protein Chips) are a few technological sectors that have quickly gained a foothold and industries that use the genetic information of humans and other species have evolved as leading manufacturers^[27]. Scientific validation of Ayurvedic therapies could be answered with the recent advancements and dissemination of clinical trials.

AYURGENOMICS

Ayurgenomics is a new field that integrates Ayurveda with genomics aiming to characterize genomic correlations for the Prakriti phenotypes reported in Ayurveda^[28]. Beejabhaga (chromosome), Beejabhagaavayava (Genes), and Beeja (sperm/ovum) are the terms referred to in Ayurvedic genetics^[29]. Gene expression reflects the cellular functions of the biological system, and genetic variations lead to mutations and variations in gene frequencies in an individual's phenotype (DNA)^[30]. Pharmacogenetics is the exploration of the hereditary basis underlying population disparities to drug responsiveness, which could help the scientific basis of understanding the variations in the human genome. Variations in the gene are an important criterion in understanding the adverse effects of drugs and disease conditions. The core principle of Ayurveda emphasized by ‘Charaka’ about 4000 y ago is that “Every patient is unique, and so should be treated as a distinctive entity.”

The Ayurvedic philosophy of treatment focuses on the patient as a whole, taking consideration of individual needs, including the safe use of medication, diets and practices^[13].

Ayurgenomics establishes a significant relationship between traditional and contemporary medicine by offering systematical validation for infusing Ayurveda's practical prophylactic techniques into modern care with an understanding of fundamental concepts^[31-33]. The central idea is based on the ‘dosha–dhatu–mala’ doctrine, which deals with ‘tridoshas^[34]. Prakriti, in genomic terms, is a system that determines a person's susceptibility to certain ailments and aids in disease diagnosis and prognosis and the selection of appropriate therapies. There is speculation that the Prakriti (phenotypic traits) listed in Ayurveda can be associated in molecular terms, leading to the assumption that the Prakriti might be linked to a human being's genotype^[35]. Ayurgenomics uses cutting-edge technology to interpret Ayurvedic principles, paving the way for evidence-based Ayurveda and, as a result, greater global acceptability^[28]. Ayurgenomics elucidates combination therapy according to Prakriti type - a study methodology that goes from bedside to workbench could provide vital information.

P4 medicine (predictive, preventive, personalized, and participatory) is a new discipline in modern medicine that has emerged in the last 10 y and that made a transition to focus on a wellness-centered system instead of disease-focussed^[31-33]. This method is highly integrated with other fields of medicine, such as lifestyle, integrative, personalized, functional and preventive medications. New Ayurgenomics uses big data analytics and machine learning to describe the authenticity of traditional medicinal concepts in context with contemporary science^[36-38]. As an evidence-based system of medicine, contemporary science can assist Ayurveda, and even Ayurvedic science may benefit modern science, notably through its preventative countermeasures, especially in P4 medicine. The scope of Ayurgenomics is primarily focused on its predictive (early diagnosis of genetic susceptibility to disease, notably for understanding various chronic conditions), preventative (concerned with inbreeding disorders) and personalized features^[35].

Ayurgenomics outlines the basis of individual differences and it shares many parallels with

pharmacogenomics, which is intended to be the foundation of personalized healthcare. It would be crucial to comprehend the probable relationship between 'Prakriti' (nature) and the genome. genotype, phenotype, and therapeutic constitution are the three main organized directories that will form a functional characteristic towards prescribed medications. Ayurvedic scriptures contain almost 5800 clinical evidence and symptoms. According to Ayurvedic chronobiological laws, an entire environmental circumstance must be addressed while advising lifestyle and nutritional guidance^[13].

Prakriti has been linked to particular genetic and physiological parameters in several studies. In a study conducted in 2005, 76 people tested for their Prakriti and Human Leucocyte Antigen (HLA) DRB1 kinds. The researchers discovered a link between the HLA phenotype and the Prakriti type, with the K type having a greater allele frequency of HLA DRB1*10 than the P and V types^[39]. Pharmacogenomics was demonstrated with Prakriti types by correlating metabolic variability with CYP2C19 genetic diversity and HLA polymorphisms^[40]. A study in 2015 showed that changes in hypoxia-inducible factors due to differentially expressed EGLN1 gene not only impact the prognosis of the disease condition but also implicated in various ailments^[41-43]. This finding was significant in Kapha Prakriti and may be linked to aspects specified for Prakriti assessment. Another study examined the effects of walking (isotonic exercise) on diabetic patients and found that Vata-Pitta, Pitta-Kapha, and Vata-Kapha types significantly reduced their systolic blood pressure^[44]. Thus, the categorization into Ayurvedic phenotypes reflects the differential regulation of these processes and thus must be tested at the multiorgan genetics level, which would be supported by the enrichment of genes related to critical cellular pathways. Gene network, hub genes, and functional data metrics may then be condensed into latent variables applying dimensionality reduction techniques, which could then be layered with Prakriti information to create objective V, P, and K classifiers using supervised classification methods. Measurements of Anthropometric parameters would be helpful to interpret Ayurvedic phenotype screening since anthropometrics has been linked to physiological and behavioural traits^[45].

TRANSCRIPTIONAL PROFILING AND AYURVEDA SYSTEMS BIOLOGY

The effect of a personalized approach concerning Ayurveda focuses on the fundamental awareness of interindividual variances in baseline health conditions, beginning with their genesis in relation to determinants and contributing variables. Transcriptional profiling of pooled RNA from VPK showed disparities in key cellular mechanisms that overlapped with biochemical mechanisms, revealing the possibility of genetic variations and their cellular expression, as indicated in Ayurveda^[46]. The baseline variations in healthy people identified by Prakriti phenotyping could help to categorize people in the preclinical phase before progressing to intermediate pathophenotypes. Knowing if a person has a main mutation connected to a specific prakriti could be crucial in preclinical prevention because prakriti principles are connected to health management^[5].

An examination of genetic differences in a group of differentially expressed genes revealed a wide range of genetic polymorphisms that varied between the Prakriti types. Interestingly, despite false discovery rate correction, core regulatory genes (FAS, EGLN1, AKT3, FBN2, RAD51) remained significant, and alterations to these genes are anticipated to cause various symptoms and functions^[47]. Integrating prakriti approaches can aid in the identification of key and hub genes that are linked to complex phenotypes and respond to both extrinsic and intrinsic inputs.

Prakriti provides phenotypic frameworks for comprehending human individuality and the stratum of individuals regardless of population tags via P-P linkages. Based on genetic and genomic investigations, EGLN1 could be the best example of a molecular contributing factor to tridosha^[5]. As more genomes are sequenced, and gene functions are discovered, application of old therapeutic wisdom is necessary to the fast-evolving genomic landscapes.

AYURVEDA AND EPIGENETICS

Epigenetics, derived from the Greek word "epigenesis", refers to the impact of genetic events on development. Epigenetics is the study of alterations in gene expression that are perhaps heritable but do not modify the underlying DNA sequence. Epigenetics ultimately has an impact on

how genes are read by the cells. From a Western perspective, Single Nucleotide Polymorphisms (SNPs) and epigenetic aspects capable of influencing drug response are at the forefront of personalized medicine, but Ayurveda involves polyherbal-formulated drug^[48]. Lifestyle behaviour, nutrition and digestion, stress and environmental factors are the four main factors that affect an individual's health. In Ayurveda, Janma Prakriti (genotype) is the key to Deha Prakriti (phenotype), which are considered dynamic^[49]. According to Ayurveda, an individual's health entirely depends on Deha Prakriti (psychosomatic constitution). An unbalanced psychosomatic constitution leads to disease manifestation. The epigenetic mechanism underpins the entire process, and the epigenetic modifications are reversible^[50]. The two strands of DNA separate during DNA expression and the knowledge present in each strand is reproduced, resulting in messenger Ribonucleic Acid (mRNA), transfer RNA (tRNA), which piles up the designated amino acids to make the particular protein, uses the information carried in mRNA. At the cellular level, mRNA, tRNA, and protein contain traits and qualities representing Vata, Pitta, and Kapha. In brief, Vata (information transmission), Pitta (transformation), and Kapha (protein) relate to messenger RNA, tRNA, and protein, respectively (structure)^[51].

Furthermore, a study showed that the gene PGM1 is active in metabolic pathways, including glycolysis and coincides with the pitta phenotype (which is constituted by digestion, metabolism, and energy production), proving the genetic validity of Ayurvedic Prakriti categorization^[52]. Methylated DNA Immunoprecipitation (MeDIP) microarray investigation of DNA methylation across prakriti phenotypes revealed CpG islands and promoters that were uniquely characterised for the VPK Prakritis. It supports the hypothesis that the underlying prakriti categorization has an epigenetic foundation^[53]. Such epigenetic fingerprints relating to individual Prakritis could be significant in comprehending and utilizing the supremacy of Ayurvedic medicine as well as determining its mechanism for providing positive health and well-being outcomes. These findings lay a scientific foundation for comparing holistic medicine to genetic diversity and epigenetic regulation, which underpin differential gene expression and related risk factors. Honey,

saffron and ghee have a long Ayurvedic history and the ability to regulate epigenetics. With more research, dietary chemoprevention employing phytochemicals and other Ayurvedic medicine techniques could relate the gap between epigenetic regulation of molecular modifications and holistic treatment of imbalance and neoplasia^[54].

Epigenetics is the external change of DNA that affects gene expression by turning genes on and off without causing any alterations to the DNA sequence, which results in a phenotypic change without a genotypic change^[51]. Modifying DNA expression involves DNA methylation, chromatin remodelling, histone modification and microRNA (miRNA)^[55]. Ayurveda addresses the root causes of epigenetic alterations, and as a result, it has a positive effect on the expression of both the genotype and the phenotype. Consequently, epigenetics is considered to be a key Ayurvedic process^[56].

AYURINFORMATICS

Bioinformatics is a rapidly expanding field of study that employs computational methods to answer biological questions. With the use of information and networking technology, Ayurveda has to be structured all over the world to fulfil the growing demands of this mobile cyberculture. As a result, Ayurveda necessitates the development of Ayurinformatics to catch up with the modern world. The development of informatics technology that translates sequence data into knowledge relevant to diagnostic and therapeutic purposes could help with the further commercialization of sequence data^[57]. Medical informatics is the study of data acquisition, storage, and its use in healthcare, usually through information technology. There has been an upsurge in demand for Ayurvedic phytopharmaceutical medicines in Western countries^[58] and hence, there is a need to unravel the key targets and their mechanism of action.

Ayur-informatics is a science that applies bioinformatics to Ayurveda medicine to provide traditional Indian medicines, a scientific foundation. It is the use of computer technology in the practice of Ayurvedic medicine, research and healthcare^[59]. Gene prediction, protein structure modeling and prediction, protein folding and stability, macromolecular assembly, data mining and complex biological system modelling are all booming areas

of Ayurinformatics. It is a multidisciplinary field with access to knowledge-based information and digital libraries, electronic medical records, digital imaging systems, telemedicine, clinical decision support^[58], telemonitoring, teliagnostics with teleconsultation, use of digital radios and personal communication services, computer-aided learning in the medical curriculum, emergency communication links networked with medical centres for diagnosis, hospital information system, visualization technology for visualizing the human anatomy^[60]. An intellectual combination of Ayurveda, biology, and information technology is desperately needed.

Many existing-computer-based expert systems are available for Ayurveda practitioners to detect, communicate and interpret data for accurate diagnosis. Some of the decision support and expert system includes AyuSoft (aids in making health-related solutions), Easy AYURVEDA (includes a library of over 500 medicinal plant formulations), Body tune (Computerized Ayurvedic Medicare/ Complementary and Alternative medicine), PRAKES (Preventive and promotional health care advice), PRAKRTI (Ayurvedic services for various functions), PILEX (software deals with diagnosis and treatment of piles), and RASEX (stores the pharmacological and therapeutic properties of rasa drug)^[60].

Ayurinformatics compile different outcomes of data mining, medical informatics, and statistical data to assess Ayurveda databases and offer new research approach options. It is widely believed that the application of data mining-based statistical approaches to Ayurveda research would result in significant advancements in the field. As a result, if the desired outcomes of Ayurvedic clinical procedures are to be demonstrated, the technique should be prepared using information technology and statistical methodologies such as data mining. The research focused on using the k-means algorithm to build Ayurvedic medicinal clusters is supposed to be unsupervised, and could be advancement in Ayurvedic medicine^[61]. Prof. Vaka and Prof. Mukhopadhyay employed an Automated Vocabulary Discovery (text mining technology) to extract texts from the biological databank, which finds a stronger relationship between Ayurvedic texts and assigns them a specific value^[62]. Thus, there is a possibility of a new fascinating relationship between Ayurveda

concepts. These approaches would aid a new era of Ayurinformatics.

AYURNUTRIGENOMICS

Nutrients and bioactive compounds in food have been shown to interact with genes, modulating their expression and as a result, triggering various chronic and diet-related diseases. Nutrigenomics encompasses the impact of genetic diversity on pharmacokinetics and nutrikinetics (effect of nutrients metabolism) and the nutrition's genome-wide study implicated time-dependent responses in transcriptomics, proteomics and metabolomics that represent a biological system's phenotype^[63,64]. The term "nutriome" refers to a person's complete food habits as they interact with their genome or physiome. Even though one's food habit is adverse to a person's genetic constitution, the nutriome may acclimate to that corresponding food habit. An example of nutriome is a carbohydrate-rich diet, but they are prone to diabetes^[65]. Thus, Ayurnutrigenomics has tremendous potential for advancement in nutrigenomics and molecular nutrition research. Nutrigenomics can be a targeted study to check the influence of dietary regimes on genetic makeup, which could alter an individual's phenotype and is expected to contribute significantly to P4 medicine^[66]. One of the newer research disciplines that use nutrigenomics is complementary and alternative medicine, which includes Ayurveda, Siddha, Yoga, Acupuncture, dietary supplements, naturopathy, Unani, etc.,

Ayurnutrigenomics incorporates Ayurgenomics with the inception of Ahara (Diet) and Pathya (planning of diet- dietetics). Ahara, according to Charaka, keeps the Doshas (biological humours) and Dhatus (body components) in balance by fostering health and disease avoidance^[67]. Ayurvedic dietetics primarily balances the biological humours with food energetics and also focusses on Agnibala (enzymatic activity of digestive metabolism), the nature of the foodstuff, the process of food making and environmental surroundings, etc., According to Ayurveda, Ahara refers to distinct food/dietary patterns according to different time schedules, based on age and, most significantly, to suit one's constitution/ Prakriti. It is a comprehensive integration of Ayurvedic nutritional habits concerning an individual's Prakriti, integrating information from genetics, proteomics, and metabolomics to create

a robust evidence-based scientific validation for the maintenance of individualized nutrigenomic dietetics^[68].

Nutrievidence and specific traditional approaches in standard research promote safe and personalized foods and are crucial for promoting Ayurnutrigenomic-inspired foods. Prevention and enhancement of Ayurceuticals to aid healing mechanisms is an essential field of nutrition study for curing diseases^[69]. Ayurnutrigenomic strategies for managing non-healing wounds includes Ahara play an integral part in wound healing. Thus the nutritional supply must have an appropriate amount of calories, proteins, vitamins, and minerals, among other things; in tiny amounts, laghu ahara (light dietetic articles) may be recommended; freshly cooked meals should be consumed; ghee from cows has health benefits; Manda (liquid diet without a solid portion of rice), Peya (liquid diet with some solid portion of rice in it), vilepi (a thick liquid or semisolid diet including a sufficient amount of cooked rice and fewer liquid ingredients) made from old rice and mixed with Goghrita (Cow ghee) and mamsa rasa (Meat Soup), is a healthy wound-healing diet; diets that boost the kapha and vata doshas and have cold qualities should be avoided^[70].

The use of modern approaches integrating Ayurvedic principles of diet correlating with nutritional metabolism research can only help to gain a deeper grasp of Ayurnutrigenomics, and the integration of analytical platforms gives the finest tools for unraveling the consequences of a biological issue on an organism at the integrated metabolic level^[71].

Metabolomics is also an essential module of the systems biology method. It can be used in nutrigenomics to quantify metabolite profiles, behaviour and responses to the body's environment, disease and detrimental variations in a tissue or physiological fluid resulting from food or medication^[72]. Herbal metabolite fingerprints in gene or protein expression patterns are useful in standardizing nutraceuticals, such as those in the "biological fingerprinting" of medicinal plant extracts^[73]. Metabolomics correlates the pharmacological/nutraceutical efficacy of traditional medicines allowing efficient validation^[74]. Focused metabolomic profiling, eg., lipidomics, may be implemented for remedial

nutraceuticals and personalized therapeutic foods in cholesterol-related metabolic disorders/syndromes and inflammatory conditions^[75]. This Ayurveda-inspired impression of personalized nutrition is a revolutionary approach in nutrigenomics which would maintain homeostasis with personalized functional meals and nutraceuticals.

AYURVEDA AND MICROBIOME

The microbiome's complex population of microbes is attributable to advances in DNA sequencing technology and analytics. Recently, more evidence has been linked to the relation of the microbiome to a wide range of diseases^[76-79]. Maintaining health and immunological equilibrium requires a diverse and balanced microbiome^[80,81]. The lung axis contains its own specific microbiome, and crosstalk between the lung and gut microbiomes has been discovered in individuals with gastrointestinal symptoms^[82]. There is a bidirectional flow of information between the gut and the brain. There is also evidence that gut microorganisms can activate immune cells in the gut wall, causing the release of proinflammatory cytokines and, as a result, affecting the blood-brain barrier permeability^[77,83,84].

The father of modern Western medicine, Hippocrates, stated, "All disease begins in the gut." Ayurveda emphasizes good eating and digestion, as well as other elements of lifestyle. Ayurveda is an ancient epigenetic science^[56]. According to Ayurveda, Vata is primarily found in the colon, which houses most gut flora. The Pitta dosha is located in the midgut and is essential for digestion, metabolism, thermoregulation and energy homeostasis. The Kapha dosha is crucial for structural development and maintenance and is principally located in the chest area. Cell cycle genes were upregulated in Vata types, while genes associated with immune pathways were upregulated in Pitta types, and genes associated with immunological signaling pathways were elevated in Kapha types. Each dosha type has its unique brain working cycle^[85,86].

One study disclosed the association between Prakriti and the microbiome's composition. The researchers discovered that VPK Prakriti types have their own microbiome^[87]. The most predominant bacteria belong to the phyla *Bacteroidetes* and *Firmicutes*. There were notable distinctions between the VPK

families in less prevalent bacteria. For example, extreme Pitta people had more butyrate-producing bacteria, which could help them avoid inflammatory disorders. The excessive Kapha women exhibited higher levels of bacteria called *Prevotella copri*, which has been linked to rheumatoid arthritis and insulin resistance in patients^[88]. On the other hand, a probiotic enema provides a virtually rapid path to the colon, which is home to most gut flora. In Ayurveda, enema is known as basti and bastis are a critical aspect of panchakarma, a deep purification and detox treatment regimen that cleanses the body of impurities and promotes health and longevity. Sesame oil, medicinal ghee, buttermilk, lassi, various herbal combinations and in some cases, bone broth, are used as bastis. A better scientific understanding of the mechanisms of bastis positive effects on various health issues can be assessed by investigating how they impact gut flora composition. It would also be beneficial to compare the current use of fecal transplant treatment with all of the various types of basti therapies^[28]. Thus, ancient Ayurveda has its own evidence of correlating Prakriti to the microbiome and diseased.

PSYCHOBOTICS AND AYURVEDA

Psychobiotics is a new scientific discipline that uses probiotics to impact human moods and behaviour^[89]. According to Ayurveda, disturbances in our mental state are frequently associated with Vata imbalance and can be traced back to disorders in the neurological system and the gut. Specific herbs, such as Ashwagandha and Brahmi, are recommended in Ayurveda because they may interact with the microbiome and human mood^[90]. Phyla *Proteobacteria* and *Elusimicrobia* were abundant in the vata Prakriti samples, whereas *Fusobacteria* and *Verrucomicrobia* were abundant in the pitta and kapha Prakriti samples, respectively. Across the three Prakriti types, five statistically significant, differently abundant genera exist, including *Bacteroides*, *Desulfovibrio*, *Parabacteroides*, *Slackia*, and *Succinivibrio*. *Bacteroides* and *Parabacteroides* were prevalent in pitta Prakriti individuals, whereas *Desulfovibrio*, *Slackia*, and *Succinivibrio* were prevalent in vata Prakriti individuals. Bray-Curtis PCoA plot for beta diversity pitta and kapha sample analysis revealed uniformity in the microbiome makeup of the vata prakriti samples. Genera *Enterobacter*, *Mogibacterium*, *Pyramidobacter*,

Rhodococcus, *Scardovia*, *Allobaculum*, *Methylobacterium*, *Propionibacterium*, *Zoogloea*, *Eikenella*, *Cronobacter*, and *Dickeya* were only present in the kapha prakriti individuals. *Enterococcus*, *Moryella*, *Pseudoramibacter*, *Lactococcus*, *Dermabacter*, *Cloacibacterium*, *Chlamydia*, *Flavisolibacter*, *Erysipelothrix*, *Planomicrobium*, *Trichococcus*, *Novosphingobium*, *Hyphomicrobium*, *Anaeroplasma*, *Acinetobacter*, and *Thermus* were only present in the pitta prakriti individuals. Genera *Anaerotruncus*, *Cetobacterium*, *Brachyspira*, *Anaerofustis*, *Robiginitalea*, *Meiothermus*, *Carnobacterium*, *Alloiococcus*, *Pseudobutyrvibrio*, *Sarcina*, *Schwartzia*, *Gallicola*, *Psychrobacter*, and *Desulfococcus* were exclusively present in the vata prakriti individuals^[87,91].

Natural probiotics, such as lassi, have also been used for a long time. Modern microbiome research backs up this theory, indicating that depression and anxiety are connected to dysbiosis and treated with probiotics. Integrative medicine benefits immensely from microbiome research since it allows to comprehend better Ayurveda's old practices in light of modern science^[92].

CONCLUSION

Thus, at the systems level biology, Ayurveda and modern health research could provide a bridge to personalized treatment by considering their impacts in relation to a person's genetic composition (Prakriti). The Ayurvedic approaches focussing on 'omics' disciplines and gut microbiome are of immense significance that may allow to scientifically validate the Ayurvedic medicines and ensures global acceptance. Ayurvedic modalities could be better integrated with existing modern sciences, improving the scope of acceptability and applicability of traditional practices in healthcare management. These translational frameworks could lay the groundwork for evidence-based research and manifest innovative, safer treatments for preventive healthcare in the future.

Conflict of interests:

The authors declare that this article has no conflict of interest.

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