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Review Article

PITTA DOSHA AND AYURGENOMICS: FROM CLASSICAL FUNCTIONS TO MOLECULAR EVIDENCE

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ABSTRACT

Ayurveda describes human constitution *(Prakriti)* through three *Doshas-Vata, Pitta* and *Kapha. Pitta,* predominantly associated with *Agni mahabhuta*, is traditionally linked with digestion, metabolism, thermoregulation, vision, complexion and higher mental functions. With the emergence of ayurgenomics, increasing research has explored whether these classical constitutional characteristics correspond to measurable molecular and physiological differences. This narrative review examines the relationship between the classical functions and properties of *Pitta* and contemporary physiological mechanisms, with particular emphasis on molecular evidence linking *Pitta*-dominant *Prakriti* with biological characteristics. Classical Ayurvedic sources from the *Brihatrayi* were considered alongside peer-reviewed studies on genomics, transcriptomics, epigenomics, metabolomics, immunophenotyping, metagenomics and pharmacogenomics published between 2005 and 2026. Available evidence suggests that *Pitta*-dominant individuals may exhibit distinctive metabolic activity, drug-metabolizing capacity, inflammatory responses and epigenetic patterns. Reported findings include associations involving CYP2C19 metabolizer status, PGM1 genotype, *Pitta*-specific SOX11 promoter methylation and the EGLN1-VWF hypoxia-related pathway. These observations indicate potential applications of *Prakriti*-based approaches in stratified medicine, pharmacogenomics and disease-risk assessment. However, the current evidence remains limited by inconsistent replication, variation in *Prakriti* assessment methods and relatively small study populations, with underrepresentation of females and diverse ethnic groups. Further multicentric studies using standardized phenotyping and robust molecular approaches are required to establish the biological validity and clinical relevance of *Pitta Prakriti*.

INTRODUCTION

Individual variation in physiology, disease risk, and drug response remains a challenge in modern medicine, with precision medicine aiming to capture this diversity before illness develops. Ayurveda addressed this centuries ago through *Prakriti*, a constitution-based model defined by the balance of the three *Doshas- Vata, Pitta*, and *Kapha*- which shapes lifelong physical, physiological, and psychological traits, disease susceptibility, and treatment response[1]. Among them, *Pitta*, associated with *Agni* (fire *Mahabhuta*), governs digestion, metabolism, temperature, and perception[2]. In Ayurvedic physiology, Pitta and Agni are closely linked, with possible modern parallels to enzymes and the endocrine system [3].

Ayurgenomics is the field that studies possible links between Ayurvedic constitution and genetic or molecular characteristics. It developed from the idea that *Prakriti* may have a genetic and biological basis [4]. This idea has been explored using several omics approaches, including gene-expression studies, genome-wide SNP analysis, DNA methylation, exome sequencing, metabolomics and metagenomics [1,5].

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This review therefore has two main aims: first, to compare the classical functions and properties of Pitta with modern physiology; and second, to summarize the molecular evidence linking *Pitta* Prakriti with genetic, epigenetic, and other biological features, while also considering its possible clinical uses and limitations. This review followed a structured but narrative search strategy. A search of PubMed, Scopus, Google Scholar, and the AYUSH Research Portal was performed for English-language peer-reviewed studies published between 2005 and 2026. Studies were included if they reported original molecular, genetic, or clinical data on constitution-based phenotyping;

The Classical Concept of *Pitta Dosha*

Functions and properties

The classical functions of *Pitta* described in the *Brihatrayi* include digestion and absorption *(Pachana),* vision *(Darshana),* maintenance of normal complexion *(Varna Prasadana),* intellect *(Medha),* and courage *(Dhairya)*[2]. These functions are traditionally described through seven main properties *(Gunas)*: *Ushna* (hot), *Tikshna* (sharp), *Drava* (liquid), *Sara* (mobile or flowing), *Amla* (sour), *Katu* (pungent), and *Snigdha* (slightly unctuous) [2]. From a functional point of view, *Pitta* is associated with digestion, metabolism, biochemical and enzymatic reactions, heat production, blood formation, vision and higher mental functions.

The five subtypes of *Pitta*

Classical Ayurveda divides *Pitta* into five subtypes, each linked to a different area of function: *Pachaka Pitta* (digestion), *Ranjaka Pitta* (coloration and blood formation), *Sadhaka Pitta* (mentation and emotion), *Alochaka Pitta* (vision) and *Bhrajaka Pitta* (skin and complexion) [6]. *Sadhaka Pitta* is described as being located in the heart and is traditionally related to higher brain functions. In modern terms, these functions have been discussed in relation to rapidly acting neurotransmitters and neuropeptides [6]. This subtype-based description provides a useful framework for comparing classical Pitta concepts with modern physiology.

Modern Physiological Correlates of *Pitta* Functions

The classical functions of *Pitta* can be compared with several modern physiological systems. These comparisons provide a possible bridge between Ayurvedic concepts and contemporary physiology, although the correspondence should be understood as a framework for interpretation rather than as proof of equivalence.

***Pachaka Pitta* and the digestive system:** *Pachaka Pitta*, described as the "cooking" function of *Pitta* in the gastrointestinal tract, can be compared with the coordinated action of digestive enzymes, gastric acid, bile, gastrointestinal hormones and local regulatory signals[2]. The concept of *Jatharagni*, or digestive fire, is linked with this process: classical descriptions present *Agni* as a continuous force that influences digestion and the activity of hormones, enzymes, and coenzymes, with the state of *Agni* affecting health and disease [3].

***Ranjaka Pitta*: Hepatic and hematopoietic functions**

Ranjaka Pitta is traditionally associated with pigmentation of the blood and can therefore be compared with liver and blood-forming functions. In a cross-sectional study of hematological parameters across different constitutions, *Pitta Prakriti* individuals had hemoglobin, packed cell volume, and red blood cell counts that were significantly higher within the normal range than those seen in *Vata* and *Kapha* [7]. Similarly, a landmark whole-genome expression study reported differences in biochemical measures, including liver function and lipid profiles, as well as hematological parameters such as hemoglobin between extreme *Prakriti* groups [1].

Alochaka* and *Bhrajaka Pitta

Vision and skin function are also traditionally linked with *Pitta*. Visual function has been discussed in relation to the endocrine and other regulatory systems associated with *Pitta*[3]. In Ayurvedic pathology, disturbance of *Bhrajaka Pitta* and *Rakta*, which are involved in maintaining normal body colour *(Prakrita Varna),* is described in *Pandu*. The clinical picture of *Pandu* includes pallor and discoloration and has been compared with anemia [8].

***Pitta* and female reproductive physiology**

Recent studies are beginning to expand this field beyond the male-dominated cohorts used in much of the earlier research. In a cross-sectional study of 240 women aged 18 to 30 years who were phenotyped using the CCRAS Ayu Prakriti portal, *Pitta*-dominant women had shorter menstrual cycles, heavier bleeding, and more inflammatory symptoms [9]. These findings may be consistent with the classical descriptions of *Pitta* as hot and sharp, but more research is needed, and female-specific constitutional physiology is still underrepresented in molecular studies.

From *Guna* to Measurable Property: A Hypothesis Framework

The seven *Pitta gunas* can be compared with measurable biological processes, but these links are proposed hypotheses rather than facts. They are best viewed as a framework for future research.

Table 1: Proposed modern correlates of the seven *Pitta gunas* (hypothesis framework) [2]

***Pitta guna* (property)**	**Proposed modern correlate**
Ushna (hot)	Thermogenesis, basal metabolic rate, thyroid hormones and inflammatory or fever responses.
Tikshna (sharp)	Proteolytic enzyme activity, gastric acid.
Drava (liquid)	Body secretions such as secretion and rapid drug metabolism, including the CYP2C19 extensive-metabolizer phenotype as bile, sweat and gastrointestinal or exocrine secretions.
Sara (mobile)	Membrane transport and movement of blood through the microcirculation.
Amla (sour)	Acidic digestive secretions and the bile acid pool.
Katu (pungent)	Inflammatory mediators and TRP-channel-related pungency.
Snigdha (slightly unctuous)	Lipid metabolism and cell-membrane fluidity.

Ayurgenomics: The Molecular Evidence for *Pitta Prakriti*

Molecular evidence for *Pitta Prakriti* now spans transcriptomics, genomics and exome sequencing, HLA immunogenetics, immunophenotyping, epigenomics, pharmacogenomics, metabolomics and metagenomics. The findings at each level are summarized below and in Table 2.

Transcriptome

In the foundational study of constitutionally extreme individuals, genome-wide expression profiling identified *Pitta*-specific overexpression of immune-response genes, consistent with the classical role of Pitta in host surveillance, and later re-analyses placed hub genes such as TLR-4, FAS and HLA-DQB1 among the constitution-differentiated genes[1,10]. More recent transcriptomic work has also reported *Prakriti*-specific differences in cytokine regulatory networks and NFkB signaling [11].

Genome and exome

Genome-wide SNP analysis of extreme-*Prakriti* individuals identified variants that separate the constitutions regardless of ancestry, with PGM1 associated with the *Pitta* phenotype. The study also reported an association between PGM1 (phosphoglucomutase 1) and the *Pitta* phenotype, in line with its earlier description in the *Charaka Samhita* (related to energy production)[5]. This PGM1-*Prakriti* relationship has also been discussed in later reviews of constitutional genetics[12]. In the exome, an independent line of work points to stronger antiviral readiness: the replicated IFIT5 low-expression allele was significantly less frequent in *Pitta* than in *Kapha*, supporting an enhanced innate antiviral response in this constitution [13,14].

HLA Immunogenetics

HLA DRB1 allele distribution varies across *Prakriti* groups [4]. This immunogenetic layer suggests *Pitta* may exhibit stronger innate defense against initial infection while carrying risks of faster deterioration and drug-related liver complications, underscoring the value of *Prakriti*-based screening [15].

Immunophenotype

Leukocyte marker profiling shows higher CD14 expression in *Pitta*, indicating greater inflammatory potential[7,16]. Together with the transcriptomic and exome findings, *Pitta* emerges as the constitution with the most active immune tone.

Epigenetic

DNA-methylation profiling shows that *Pitta Prakriti* carries a distinctive epigenetic landscape related to metabolism and immunity, making it resilient in some contexts but vulnerable to inflammatory and metabolic disorders [17].

Pharmacogenomics

The clearest signal is the fast-metabolizer phenotype: CYP2C19 extensive-metabolizer genotypes were reported in 91% of *Pitta* individuals, with the *1/*3 genotype found only in *Pitta*, matching the classical characterization of *Pitta* as fast-metabolizing[18].

Metabolome

Plasma metabolomics classified constitutions with 97.87% accuracy and showed *Pitta* dominance in energy metabolism, amino-acid turnover, lipid regulation, and androgen biosynthesis [19].

Physiology-genetics: the hypoxia and thrombosis axis

Genetic variation in the hypoxia and thrombosis axis also differentiates the constitutions: the HAPE-risk EGLN1 rs479200 TT genotype was less common in *Pitta*, and the VWF rs1063856 T allele, linked to bleeding susceptibility, was more common in *Pitta* than in *Kapha* [20,21].

Metagenome

6S rRNA profiling identified *Prakriti*-specific gut signature taxa, with a *Pitta* signal in women that

was enriched in butyrate-producing taxa and in xenobiotic-degrading functions, mirroring the host's rapid toxin metabolism [22,23]. A cross-tradition comparison with the Korean Sasang system confirmed the same toxin-metabolizing pattern in the Pitta-equivalent class [24].

Table 2: Summary of multi-omics evidence related to *Pitta Prakriti*

Evidence level	Key finding for *Pitta*	Reference(s)
Transcriptome	Genome-wide expression profiling showed over-expression of immune-response genes in *Pitta*, especially response to biotic stimuli; the pattern matches *Pitta's* classical role in host surveillance. Hub genes linked to complex disease (TLR-4, FAS, HLA-DQB1) were among the constitution-differentiated genes.	1, 10, 11
Genetics (GWAS)	Genome-wide SNP screening of 3,416 individuals identified 52 SNPs that differentiated the *Prakriti* groups independent of ancestry; PGM1 (phosphoglucomutase 1, an energy-metabolism gene) was associated with the *Pitta* phenotype.	5
Genetics (exome)	About 1,181 genes separate the *Prakriti* groups (including IL6R and SLC14A2); the IFIT5 low-expression allele is rare in *Pitta*, suggesting stronger antiviral defense; a SERPINA10 variant differentiates constitutions	13, 14
Genetics (HLA)	HLA DRB1 allele distribution differed by *Prakriti*: DRB102 absent in *Vata*, DRB113 absent in *Kapha*, DRB1*10 more frequent in *Kapha*.	4
Immunophenotype	*Pitta* showed higher CD14 (monocyte marker) expression, indicating greater inflammatory potential; CD25 and CD56 were higher in *Kapha*.	7, 16
Epigenetics	*Pitta* showed the highest gene-body methylation burden (204 regions) in the high-metabolism group; SOX11 promoter methylation was reported as *Pitta*-specific	17
Pharmacogenomics	CYP2C19 extensive-metabolizer genotype reported in 91% of *Pitta*; the *1/*3 genotype was found only in *Pitta*; poor-metabolizer genotype least common in *Pitta*.	18
Metabolomics	*Pitta* plasma showed enhanced degradation of branched-chain amino acids, with androgen, retinoid, estrogen, and toxin metabolism dominant and vitamin D derivatives highest among the constitutions.	19
Physiology-genetics (Hypoxia)	The EGLN1 rs479200 TT genotype, a risk genotype for high-altitude pulmonary edema, was uncommon in *Pitta*; the ancestral rs480902 T allele was more frequent in *Pitta* and correlated positively with altitude globally.	20
Thrombosis axis	The VWF rs1063856 T allele, associated with bleeding susceptibility, was more common in *Pitta* than in *Kapha*, and the EGLN1-VWF interaction differed by constitution.	21
Metagenome (taxonomy)	Gut microbiome 16S profiling of 135 extreme-*Prakriti* individuals identified *Prakriti*-specific signature taxa; *Pitta* women were enriched in butyrate-producing Blautia species and other signature taxa.	22
Metagenome (function)	*Pitta* gut microbiome was enriched in polysaccharide metabolism, xenobiotic degradation, and lysine and branched-chain amino-acid biosynthesis, consistent with strong digestive and detoxifying capacity.	23
Cross-tradition comparison	*Pitta* and its Korean Sasang counterpart (Soyangin) both showed high microbial toxin-metabolizing capacity, including polycyclic aromatic hydrocarbon degradation, confirming the pattern across traditions.	24

Summary of the *Pitta* molecular signature

Taken together, these findings form a coherent picture of *Pitta Prakriti* as the constitution with an activated immune and antiviral gene program, the fastest drug and toxin metabolism of the three constitutions, dominant branched-chain amino acid and androgen metabolism, a distinct epigenetic profile, and gut microbial functions that mirror the metabolic character of the host [1,13,14,17,18,19,23,24]. The convergence is notable because it arises from independent lines of evidence: exome studies point to stronger antiviral readiness in *Pitta*[13,14], while metabolomic and metagenomic studies independently identify toxin and xenobiotic handling as a hallmark of *Pitta* [19,23,24]. One caution is warranted: genus-level microbiome findings differ between studies conducted in the same population, so the functional direction of the microbial evidence is currently more reproducible than the identity of the specific bacterial taxa [25].

Translational and Clinical Implications

Stratified and P4 medicine

Ayurgenomics provides a possible framework for stratified medicine, in which people are grouped according to biologically meaningful characteristics. The TRISUTRA consortium was developed to study *Prakriti* across ethnically and geographically diverse Indian populations with the broader goal of supporting predictive, preventive, personalized, and participatory (P4) medicine [26]. The idea has also been discussed as a way of connecting classical constitutional concepts with modern genomics [27] and as a basis for biomarker discovery and early, actionable intervention in integrative medicine [28]. A recent perspective further suggests that *Prakriti* reflects genetic, environmental, and time-related influences and could support molecular discovery and therapeutic repurposing through the *Anukta Vyadhi* framework [29].

Pharmacogenomics and perioperative medicine

The reported association between *Pitta* and the CYP2C19 extensive-metabolizer genotype suggests that constitutional type may be related to differences in drug metabolism. This could be relevant to drugs that depend on CYP2C19 for activation or clearance, including some proton pump inhibitors and clopidogrel[18]. *Prakriti*-based approaches to drug discovery and development have therefore been proposed as one route toward more personalized care[30]. Beyond drug metabolism, an integrative review has suggested that *Deha* and *Manas Prakriti* may also influence perioperative stress physiology through the hypothalamic-pituitary-adrenal axis, with possible implications for anesthetic dosing, hemodynamic stability and recovery after surgery [31].

Disease-risk stratification

The findings related to hypoxia suggest that *Prakriti* may have value as one factor for studying susceptibility to HAPE and thrombotic outcomes at high altitude [20,21]. In complex diseases, ayurgenomics has also provided proof-of-concept findings in rheumatoid arthritis, where genes related to oxidative stress, including SOD3 and PON1, were identified as possible determinants in the *Pitta* subgroup [32]. In endometriosis, whole-exome analysis reported that *Pitta*-dominant patients had a moderate burden of pathogenic variants compared with the *Vataja* group[33]. In a study of 60 patients receiving chemotherapy and phenotyped using AyuSoft, *Pitta*-dominant patients had relatively few physical symptoms but greater psychological strain and more susceptibility to chemotherapy side effects[34]. Another recent conceptual study proposed a genetic inflammatory index and suggested that *Vata* and *Pitta* constitutions may have a greater pro-inflammatory genetic tendency and more rapid epigenetic age acceleration than *Kapha*. These are emerging findings and need further validation [35].

Infectious disease

The reported relationship between HLA patterns and *Prakriti* has also led to hypotheses about differences in immune responses and possible differences in susceptibility to COVID-19 and disease progression. These ideas still need to be tested in well-designed clinical studies involving people with both higher and lower susceptibility [15].

Limitations and Critical Appraisal

The ayurgenomics literature includes both positive findings and important limitations. A balanced review therefore needs to consider where the evidence is strong, where it is uncertain, and where studies have not reproduced earlier findings.

Limited replication in a clinical setting.

A prospective study of 351 patients with epilepsy who were receiving phenytoin alone found no significant association between *Prakriti* and CYP2C9 or CYP2C19 genotype or phenotype. The authors concluded that *Prakriti* assessment had limited usefulness for individualizing phenytoin therapy [36]. This is an important negative finding and shows that the pharmacogenomic claims cannot yet be applied broadly.

Differences in phenotyping methods.

A systematic critical review identified 64 different *Prakriti* assessment tools published between 1987 and 2024. Only 20 had undergone any form of validation, and only two tools (CCRAS-PAS and ACPI) partly met the review criteria[37]. Without standardized

and validated assessment tools, it is difficult to compare results across studies.

Limitations of study populations

Many omics studies included small samples and predominantly male participants. Even the largest genome-wide study included only a few hundred individuals with extreme constitutions[5]. Female-specific constitutions, mixed or composite *Prakriti* types and replication across different ethnic groups remain insufficiently studied [9,28]. More work is also needed to understand how *Prakriti* itself is determined, how stable it remains over time, and how strongly it is inherited before it can be used as a dependable clinical variable [38].

Future Directions

The next steps in this field follow directly from these limitations:

- Develop and prospectively validate standardized Prakriti assessment tools, including testing their reliability over time and their performance in different populations.
- Conduct larger, multicentric and multi-ethnic studies that include women and people with composite constitutions.
- Measure the genome, epigenome, transcriptome, metabolome, and metagenome together in the same study populations to see whether the proposed *Pitta* pattern remains consistent across different biological levels.
- Test the proposed inflammatory-index hypothesis using epigenetic clocks in *Prakriti*-stratified populations [35].
- Use national genomic resources, including the AYUSH Genomics Consortium and CSIR GENOMET datasets, to support larger discovery and replication studies based on constitutional type [39].

CONCLUSION

Pitta dosha is described in Ayurveda as the principle responsible for transformation, and many of its classical functions can be compared with modern processes involved in metabolism, temperature regulation, blood formation, and neurophysiology. Research in ayurgenomics, including studies of genetics, epigenetics, transcriptomics, metabolomics and immune markers, suggests that *Pitta Prakriti* may be associated with higher metabolic activity, differences in drug metabolism, and specific inflammatory and hypoxia-related genetic patterns. However, these findings should not yet be treated as definitive clinical markers. Their practical value will depend on reliable *Prakriti* assessment, larger and more diverse study populations and prospective pharmacogenomic trial. With stronger evidence and standardized methods, *Pitta Prakriti* may eventually be useful as one factor for studying differences in metabolism, inflammation and response to medicines.

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