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Review JOAYUSH

Epigenetic Modifications in Health, Disease, and Precision Therapeutics (from Genome to Epigenome)

Dharmendra Mishra*

Abstract

Introduction: *Epigenetic alterations play a crucial role in regulating gene expression in both normal physiological and disease states. These reversible modifications – such as DNA methylation, histone acetylation, phosphorylation, ubiquitination, and chromatin remodelling – are increasingly implicated in complex diseases including cancer and neurodegenerative disorders. Despite advances in standard therapeutic approaches, patient responses remain variable, largely due to genetic heterogeneity and epigenetic dysregulation. This highlights the need for incorporating epigenetic understanding into personalized medicine. Parallel to modern biology, Ayurveda, an ancient Indian system of medicine, emphasizes lifestyle, diet, behaviour, and environmental factors – key drivers of epigenetic modulation – suggesting a conceptual convergence between the two systems.* ***Materials and Methods:*** *This review synthesizes contemporary scientific literature on epigenetic mechanisms and their relevance to disease and personalized medicine, alongside classical Ayurveda concepts such as Deha Prakriti (phenotype) and Janma Prakriti (genotype). Conceptual correlations are drawn between known epigenetic regulators and Ayurveda determinants of health, including diet, digestion, stress, lifestyle, and environmental influences. Current developments in epigenetic diagnostics and therapeutics are also examined to assess their potential integration with personalized and traditional medical approaches.* ***Results and Discussion:*** *Evidence indicates that epigenetic variations provide insights into cellular states and developmental histories that cannot be fully explained by genetic information alone. Unlike the static genome, epigenetic patterns are dynamic and reversible, making them attractive therapeutic targets. Although several epigenetic drugs are approved for clinical use, their lack of specificity limits efficacy and safety. Ayurveda's holistic interventions may influence gene expression indirectly by modulating epigenetic factors, thereby affecting phenotypic outcomes without altering DNA sequence. Understanding epigenetics as a mechanistic bridge offers a scientific basis for Ayurveda principles and supports the integration of traditional knowledge with modern personalized medicine. The development of locus-specific epigenetic modifiers, combined with epigenetic biomarkers, is critical for advancing precision therapies.* ***Conclusion:*** *Epigenetics represents a promising and unifying framework for personalized medicine by linking genetic potential with environmental and lifestyle influences. Ayurveda inherently addresses key epigenetic modulators, suggesting that epigenetic regulation may be a fundamental mechanism underlying its therapeutic effects. Integrating epigenetic diagnostics, targeted therapeutics, and Ayurveda modalities holds significant potential for achieving truly personalized, precise, and holistic healthcare. Further interdisciplinary research is essential to strengthen this correlation and translate it into clinical practice.*

***Author for Correspondence**
Dharmendra Mishra
E-mail: drdmishrania@gmail.com

Assistant Professor, Department of Sharir Rachana, Institute of Teaching and Research in Ayurveda (ITRA), Institute of National Importance (INI), Ministry of AYUSH, Govt. of India, Jamnagar, Gujarat, India

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INTRODUCTION

The completion of the Human Genome Project marked a pivotal milestone in understanding the

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genetic basis of human health and disease. However, it soon became evident that genomic information alone could not adequately explain phenotypic diversity, disease susceptibility, or differential therapeutic responses among individuals [1]. This gap led to the emergence of epigenetics, defined as heritable and reversible modifications in gene expression that occur without changes in the DNA sequence itself [2]. These modifications regulate when, where, and to what extent genes are expressed, thereby shaping cellular identity and function across the lifespan [3].

Epigenetic mechanisms – primarily DNA methylation, histone modifications, nucleosome positioning, and non-coding RNA regulation – are now recognized as central regulators of development, aging, and disease pathogenesis [4]. Unlike genetic mutations, epigenetic changes are dynamic and responsive to environmental stimuli such as nutrition, stress, toxins, physical activity, and psychosocial factors [5]. Consequently, epigenetics has emerged as a crucial interface between the genome and the environment, providing a mechanistic explanation for gene–environment interactions [3, 6].

In parallel, precision medicine [7] seeks to tailor healthcare interventions based on individual variability in genes, environment, and lifestyle. While genomics has significantly contributed to this paradigm, variability in treatment outcomes persists [8], underscoring the need to integrate epigenetic insights. Notably, several epigenetic alterations are reversible, making them attractive therapeutic targets [9].

Interestingly, long before the advent of molecular biology, Ayurveda, the traditional system of medicine originating in India, emphasized individualized health management based on constitution (*Prakriti*), diet, behaviour, environment, and mental state [10]. These determinants closely align with known epigenetic modulators. The conceptual overlap suggests that epigenetic regulation may provide a scientific foundation for understanding Ayurveda's personalized and holistic approach.

This review explores the molecular basis of epigenetic regulation, its role in disease and therapeutics, and its relevance to precision medicine, while drawing integrative correlations with Ayurveda principles to propose a translational framework bridging traditional wisdom and modern biomedical science.

MATERIALS AND METHODS

A narrative integrative review methodology was adopted. Scientific literature was surveyed from peer-reviewed journals indexed in PubMed, Scopus, and Web of Science, focusing on epigenetic mechanisms, disease associations, epigenetic therapeutics, and biomarkers. Keywords included *epigenetics, DNA methylation, histone modification, chromatin remodelling, precision medicine,* and *epigenetic drugs*.

Classical Ayurveda concepts were derived from authoritative texts, such as *Charaka Samhita* [11], *Sushruta Samhita* [12], and *Ashtanga Hridaya* [13], along with contemporary scholarly interpretations. Conceptual correlations were established between epigenetic regulators and Ayurvedic determinants of health, including *Deha Prakriti, Agni* (digestive/metabolic capacity), *Ahara* (diet), *Vihara* (lifestyle), *Manas* (mental state), and *Desha–Kala* (environment and time) [14].

The review emphasizes translational relevance, synthesizing molecular evidence with systems-level traditional insights rather than attempting direct molecular equivalence.

EPIGENETIC MECHANISMS: MOLECULAR OVERVIEW

DNA Methylation (Figure 1)

DNA methylation involves the addition of a methyl group to cytosine residues, primarily at CpG dinucleotides, mediated by DNA methyltransferases (DNMTs) [15]. This modification generally suppresses gene transcription by altering chromatin structure or inhibiting transcription factor binding [16]. Aberrant methylation patterns – global hypo methylation or promoter-specific hyper methylation – are hallmark features of cancer and other chronic diseases [17, 18].

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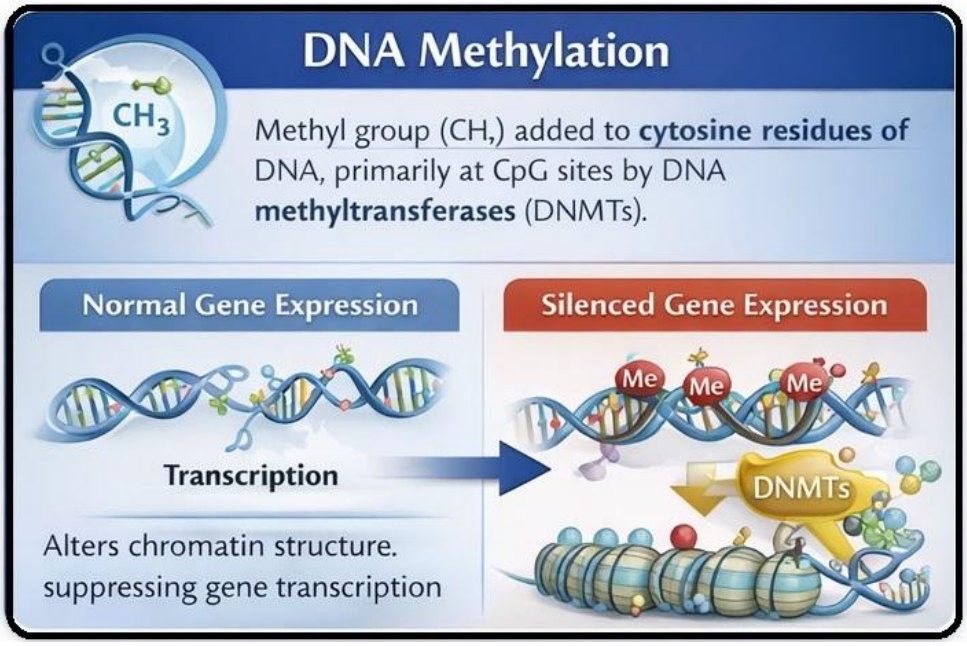


Figure 1. DNA Methylation

Histone Modifications (Figure 2)

Histone proteins undergo post-translational modifications, such as acetylation, methylation, phosphorylation, and ubiquitination, which collectively form the "histone code." These modifications regulate chromatin accessibility and transcriptional activity. For example, histone acetylation is typically associated with transcriptional activation, whereas certain methylation marks may repress or activate gene expression depending on their location [19, 20].

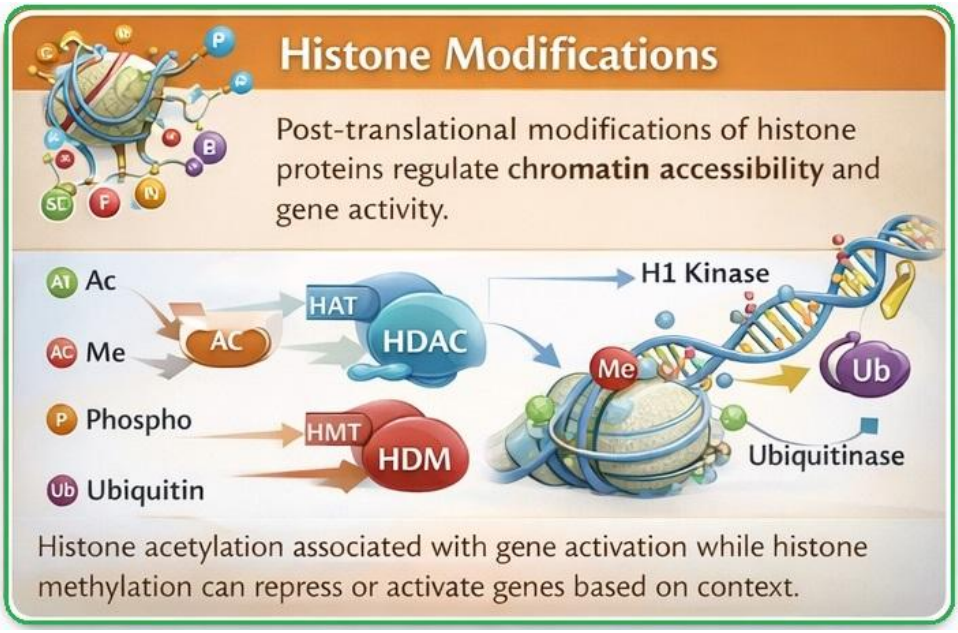


Figure 2. Histone Modifications

Chromatin Remodelling (Figure 3)

ATP-dependent chromatin remodelling complexes reposition or eject nucleosomes, thereby regulating access to DNA [21]. These processes are essential for DNA replication, repair, and transcription and are tightly coordinated with histone modifications [22].

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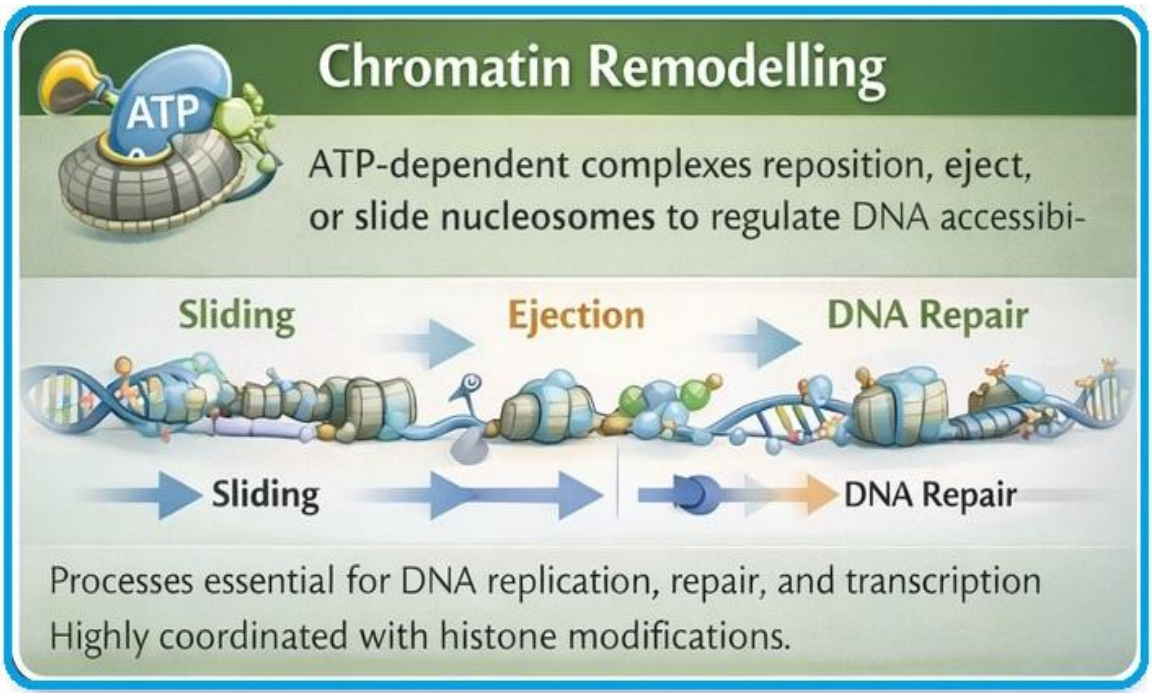


Figure 3. Chromatin Remodelling

Non-Coding RNAs

MicroRNAs and long non-coding RNAs modulate gene expression post-transcriptionally and epigenetically by interacting with chromatin-modifying complexes [23], further adding complexity to epigenetic regulation [24].

EPIGENETICS IN HEALTH AND DISEASE

Epigenetic regulation is essential for normal embryonic development, cellular differentiation, and tissue homeostasis. However, dysregulation of epigenetic mechanisms contributes to a wide range of diseases [25].

Cancer

Cancer is fundamentally an epigenetic disease as much as it is a genetic one. Tumour cells exhibit widespread epigenetic reprogramming, including silencing of tumour suppressor genes through promoter hyper methylation and activation of oncogenes via chromatin remodelling. These changes often precede detectable genetic mutations [26].

Neurodegenerative Disorders

In disorders, such as Alzheimer's and Parkinson's disease, epigenetic alterations affect neuronal plasticity, synaptic function, and neuroinflammation [27]. Environmental exposures and aging-related epigenetic drift significantly influence disease onset and progression [28, 29].

Metabolic and Cardiovascular Diseases

Lifestyle-associated diseases, including diabetes and cardiovascular disorders, are strongly influenced by epigenetic modifications induced by diet, physical activity, stress, and intrauterine environment, supporting the concept of developmental origins of health and disease [30].

EPIGENETICS AND PRECISION THERAPEUTICS

The reversibility of epigenetic modifications makes them promising targets for therapeutic intervention [31]. Several epigenetic drugs, such as DNMT inhibitors and histone deacetylase inhibitors, are approved for clinical use, particularly in oncology. However, these agents often lack locus specificity, leading to off-target effects and limited clinical efficacy [32].

Emerging strategies focus on:

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- Locus-specific epigenetic editing [33].
- Epigenetic biomarkers for disease prediction and treatment response
- Combination therapies integrating epigenetic agents with conventional drugs [34].

Epigenetic profiling enables stratification of patients beyond genetic mutations, thereby refining therapeutic precision.

CONCEPTUAL INTEGRATION WITH AYURVEDA

Ayurveda classifies individuals based on *Prakriti,* a stable constitutional phenotype determined at conception (*Janma Prakriti*) and modulated throughout life by environmental and lifestyle factors. This aligns conceptually with the distinction between genotype and epigenotype. Ayurveda inherently targets epigenetic regulation at a systems level. Therapeutic interventions, such as dietary regulation, detoxification procedures, meditation, and lifestyle modification, may influence gene expression indirectly through epigenetic mechanisms without altering DNA sequence.

Ayurveda stress on:

- *Ahara* (diet) → nutrient-dependent epigenetic modulation.
- *Vihara* (lifestyle and behaviour) → stress-responsive epigenetic pathways.
- *Manas* (mental health) → neuroendocrine–epigenetic interactions.
- *Desha* and *Kala* (environment and time) → environmental epigenomics.

DISCUSSION

- *Ahara*/*Diet-Dependent Epigenetic Modulation:* The capacity of dietary factors has been noticed to regulate gene expression through reversible mechanisms, such as DNA methylation, histone modification, and non-coding RNAs, without altering the genomic sequence. Modern nutritional epigenetics demonstrates that nutrients, phytochemicals, fatty acids, and overall dietary patterns influence metabolic, inflammatory, neurocognitive, and aging pathways. These findings conceptually parallel Ayurveda principles, where *Ahara* is a primary determinant of *Prakriti*, health, and disease susceptibility. Ayurveda literature emphasizes personalized diet, maternal nutrition *(Garbhini Ahara)*, and life-course dietary practices as modulators of phenotype and transgenerational health, aligning closely with emerging epigenomic evidence linking diet, development, and chronic disease risk [35–42].
- *Vihara*/*Lifestyle and Behaviour Responsive Epigenetic Pathways:* It shows how daily activities, such as physical activity, sleep, stress management, mental behaviour, and social habits, influence gene expression through reversible epigenetic mechanisms. Modern research demonstrates that lifestyle factors regulate DNA methylation, histone modifications, and microRNA expression, thereby modulating inflammation, metabolic health, cardiovascular risk, neuroplasticity, and biological aging. Parallel to this, Ayurveda emphasizes *Vihara, Dinacharya, Ritucharya, Sadvritta,* and mental discipline as determinants of health and disease prevention. Emerging Ayurveda–epigenetic literature conceptualizes these behavioural practices as modulators of phenotype and disease susceptibility across the lifespan and even generations, providing a coherent bridge between traditional lifestyle prescriptions and contemporary epigenomic evidence supporting personalized preventive healthcare [37, 39, 40, 42–46].
- *Manas*/*Mental-Health-Related Neuroendocrine Epigenetic:* Interactions pronounce how psychological states and stressors influence brain function through coordinated hormonal and epigenetic mechanisms. Modern research shows that mental stress, nutrition, and early-life experiences modulate the hypothalamic–pituitary–adrenal (HPA) axis and neuropeptides, such as corticotropin-releasing hormone and neuropeptide-Y, leading to epigenetic changes including DNA methylation and histone modifications in stress-responsive genes. These alterations affect emotional regulation, cognition, and vulnerability to psychiatric disorders across the lifespan. Environmental and psychosocial stressors further shape epigenetic programming of neuroendocrine pathways, providing a mechanistic link between mental health, endocrine signalling, and long-term behavioural and disease outcomes [47–49].

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- *Desha and Kala/Environment and Time Based Environmental Epigenomics:* It highlights how spatial context and temporal exposures regulate gene expression through reversible epigenetic mechanisms. Contemporary research shows that environmental factors – such as air pollution, climate stressors, nutrition, chemical exposures, and psychosocial conditions – induce DNA methylation changes, histone modifications, and non-coding RNA regulation. These effects are strongly time-dependent, with critical windows of susceptibility during prenatal development, early childhood, adolescence, and aging. Accumulated exposures across the life course influence epigenetic aging trajectories and disease susceptibility, while certain environmentally induced epigenetic marks may persist across generations. Climate variability and long-term environmental stress further modulate adaptive epigenetic responses, linking ecosystem changes with human health outcomes. Thus, environmental context (*Desha*) and biological timing (*Kala*) jointly shape epigenomic plasticity, providing a mechanistic framework for understanding how the exposure integrates space and time to influence development, adaptation, and chronic disease risk [50–54].

Epigenetics provides a mechanistic framework that bridges molecular biology with holistic medical systems. While genomics defines biological potential, epigenetics determines its functional realization. Ayurveda's personalized approach, cantered on modifiable lifestyle and environmental factors, resonates strongly with epigenetic principles [55].

However, translating these conceptual correlations into clinical practice requires rigorous interdisciplinary research. Integrating epigenetic biomarkers with Ayurveda phenotyping could enhance predictive, preventive, and personalized healthcare. The challenge lies in developing standardized methodologies and validating outcomes through translational studies.

CONCLUSION

Epigenetics represents a unifying paradigm in modern medicine by linking genetic information with environmental and lifestyle influences. The dynamic and reversible nature of epigenetic modifications offers unprecedented opportunities for precision therapeutics. Ayurveda, through its emphasis on individualized lifestyle and holistic regulation, inherently addresses key epigenetic modulators.

Integrating epigenetic diagnostics, targeted therapies, and Ayurveda-based interventions holds significant promise for achieving truly personalized and holistic healthcare. Future interdisciplinary research is essential to strengthen this integration and translate conceptual convergence into evidence-based clinical practice.

Limitations of the Review

This review is primarily conceptual and integrative. Direct molecular validation of Ayurveda interventions through epigenetic endpoints remains limited and warrants systematic experimental and clinical investigation.

Conflict of Interest

Author declares that there is no conflict of interest related to this work. No financial, institutional, personal, or professional relationships with any individual, organization, or association influenced the conception, conduct, or reporting of this review.

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