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Epigenetic Mechanisms in Traditional Medicine Systems: A Comprehensive Literature Review

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Abstract:

This literature review takes a closer look at the fascinating intersection of epigenetics and traditional medicine systems, particularly Siddha, Ayurveda, and the use of herbal remedies. It explores how bioactive compounds found in these ancient healing practices interact with epigenetic mechanisms, ultimately influencing health outcomes. We focus on three

key epigenetic processes: DNA methylation, histone modifications, and microRNA regulation. These processes play crucial roles in mediating the therapeutic effects of traditional remedies. By examining the current scientific evidence, we aim to demonstrate how these age-old approaches can effectively modulate epigenetic pathways, offering potential strategies for preventing and treating a variety of diseases. This insight could lead to new and innovative medical interventions in modern healthcare. The findings of this review highlight the promise of traditional medicine systems as valuable sources of epigenetic therapies. However, we must also consider the challenges of translating these ancient practices into standardized treatments that are clinically effective. Key areas for future research include standardizing herbal preparations, enhancing the bioavailability of active compounds, and conducting rigorous clinical trials. Despite these hurdles, we believe that merging traditional medicinal knowledge with contemporary understandings of epigenetics could usher in significant advancements in personalized medicine. This integration holds the potential for more targeted, effective, and individualized treatment strategies that blend the wisdom of ancient practices with the insights of modern science.
Key words: Epigenetics, Traditional Medicine, Siddha, Ayurveda, Herbal Medicine, DNA Methylation, Histone Modifications, MicroRNA Regulation,

Introduction

Epigenetics is a fascinating field that explores heritable changes in gene expression that don't involve alterations to the DNA sequence itself. This area of study has become increasingly important as it connects traditional medicine systems with the latest advancements in molecular biology. Scientists refer to the resulting complex of biochemical modifications as the "epigenome," which plays a crucial role in determining how and when our genes are expressed (Feinberg, 2018). Interestingly, traditional medicine systems like Ayurveda and Siddha have long recognized the significant impact that lifestyle, diet, and environment have on our health. These age-old principles align remarkably well with what we're learning today about epigenetic regulation (Kanherkar et al., 2017). The merging of ancient healing traditions with the latest advancements in epigenetic science opens up exciting new pathways for treating chronic diseases. As modern research continues to validate these traditional practices through scientific inquiry, it's becoming increasingly important to understand the epigenetic mechanisms that underpin these therapies. This understanding is vital for integrating these approaches into today's healthcare systems (Hardy & Tollefsbol, 2011). This review seeks to bring together current evidence on how traditional medicine systems, especially Ayurveda, Siddha, and herbal medicine—affect epigenetic mechanisms to enhance health and address various ailments. By exploring the molecular pathways through which these time-honored methods influence gene expression, we can gain valuable insights into their therapeutic potential and any limitations they may have.

Epigenetic Mechanisms: An Overview

Epigenetic regulation encompasses a variety of interconnected mechanisms that manage gene expression without changing the DNA sequence itself. The three main epigenetic mechanisms at play are DNA methylation, histone modifications, and non-coding RNA-mediated regulation.

DNA Methylation

DNA methylation refers to the addition of methyl groups to cytosine residues in DNA, which often leads to the repression of genes. This process is facilitated by enzymes known as DNA methyltransferases (DNMTs), which are essential for numerous cellular functions (Portela & Esteller, 2010). Changes in DNA methylation patterns have been linked to a range of diseases, including cancer, cardiovascular issues, and neurodegenerative disorders.

Histone Modifications

Histones are the proteins that help package DNA into a compact structure called chromatin. When histones undergo modifications—such as acetylation, methylation, phosphorylation, or ubiquitination—they can change the architecture and accessibility of chromatin, ultimately influencing gene expression (Berger, 2007). The levels of acetylation are

regulated by enzymes known as histone acetyltransferases (HATs) and histone deacetylases (HDACs), while various methyltransferases and demethylases manage the states of methylation.

Non-coding RNA Regulation

MicroRNAs (miRNAs) are small non-coding RNAs that play a crucial role in regulating gene expression after the transcription process. They work by binding to specific messenger RNAs (mRNAs), leading to either their degradation or the suppression of their translation. These tiny but powerful molecules are involved in many physiological and pathological processes, making them key targets for new therapeutic strategies (Sun et al., 2008).

Epigenetics: How Your Environment Can Influence Your Genetics

Epigenetic changes can respond rapidly to a wide range of environmental factors, including our diet, lifestyle choices, stress levels, and exposure to toxins. This remarkable ability of epigenetics to adapt means we're deeply connected to our surroundings. It opens up exciting possibilities for targeted interventions, and we're already witnessing this in traditional medicine practices. As one insightful study notes, "Each individual carries their health in their own hands. Their actions make a direct and very personal impact on their health through the mechanism of epigenetics" (Ayurveda and Epigenetics - PMC, 2020).

Ayurveda and Epigenetics: Bridging Ancient Wisdom with Modern Science

Ayurveda, the ancient healthcare system practiced in India for thousands of years, predates our understanding of genetics by a long shot. It's fascinating how closely its principles align with what we're learning today in the field of epigenetics. This traditional system emphasizes personalized care, adapting recommendations to suit each person's unique constitution, known as Prakriti. Such tailored approaches can have a powerful influence on gene expression.

Understanding Prakriti and Its Connection to Genetics

In Ayurveda, individuals are classified according to their Prakriti, which is a psychophysiological constitution established at the moment of conception. There are two types of Prakriti in Ayurveda: Janma (birth) Prakriti, which corresponds to one's genotype, and Deha (body) Prakriti, which reflects the phenotype (Ayurveda and Epigenetics - PMC, 2020). Recent studies suggest that different Prakriti types may exhibit varying gene expression patterns, adding an intriguing layer of scientific validation to this ancient classification system.

Epigenetic Changes Induced by Ayurvedic Lifestyle Factors

Ayurveda identifies four key determinants of health and disease: lifestyle and behavior, diet and digestion, stress, and environmental factors. These elements align closely with known epigenetic modifiers:

Dinacharya and Ritucharya (Daily and Seasonal Routines): Following daily routines that sync with natural cycles can optimize the biochemical processes that influence gene expression.

Ahara (Diet): Ayurveda views food as an essential epigenetic factor that helps regulate gene expression. Ayurvedic dietary principles are designed to promote health. Research in nutritional epigenetics supports this, revealing that "individual nutrients and bioactive food components, or the total diet, can change DNA methylation and subsequently alter gene expression" (Ayurveda and Epigenetics: Unlocking Your Genetic Potential, 2025).

Stress Management: Techniques such as meditation and mindfulness in Ayurveda have been shown to epigenetically influence gene expression related to cortisol, which, in turn, affects mental health.

Detox (Panchakarma): This set of Ayurvedic detoxification therapies initiates cell repair mechanisms and may help correct abnormal patterns of gene expression.

By embracing these lifestyle components, Ayurveda offers a nuanced perspective on health maintenance, highlighting how environmental influences can impact gene expressional concept that modern epigenetic research has only recently begun to validate.

Incorporating Gene Regulation into Siddha Medicine

A through Rs. Siddha medicine, a traditional indigenous Indian medical system largely practiced in South India, has shown a potential impact on epigenetic mechanisms. New molecular pathways of Siddha formulations in respect to gene expression are currently being revealed in recent studies.

Siddha Formulations and Its Epigenetic Pathways

Diverse Siddha medicines studied for their epigenetic effects include Pancha Pashana Chendhuram, Chithiramoola Kuligai, Nandhi Mezhugu, Maha Vallathy Leghiyam, Pooranachandirodayam, Vallarai Nei, Karanthai Legium, Narasimha Leghiyam, Rasa Parpam and Thambira Chendhuram (Subathra et al., 2024). These complex formulations encompass a wide array of bioactive compounds that exert effects on various epigenetic pathways concurrently.

There is some research evidence that proves the influence of Siddha medicines on the gene expression. The studies at in vitro, and clinical level suggest that Siddha medicines may have a substantial influence on critical epigenetic pathways, such as microRNA (miRNA)expression, DNA methylation, and histone modifications (Subathra et al., 2024). Such effects probably play a role in the ability of these medicines to be useful for the treatment of a few conditions, especially chronic diseases.The recruitment of ac-H3 and ac-H4 in the promoter region of TopoIIβ gene is increased by tetramethylpyrazine, a compound commonly used in traditional medicine. It facilitates elevated TopoII β expression via epigenetic regulation and promotes SH-SY5Y cell neuronal differentiation (Epigenetic effects of herbal medicine, 2023).

Molecular Insight of Epigenetic Mechanism in Herbal Medicine

The efficacy of herbal medicine is more and more associated with the modulation of epigenetic mechanisms. Many bioactive compounds derived from plants have been found to affect DNA methylation, histone modifications and non-coding RNA regulation.

Oral Bioavailability of Herbal Compounds

Several herbal compounds can modulate the DNA methylation patterns, often through the inhibition of DNMTs:

Curcumin: This polyphenol of Curcuma longa (turmeric) blocks DNMTs leading to "demethylation and subsequent reactivation of tumor suppressor genes in cancer cells" (Link et al., 2013). "The Review of the Literature: Epigenetics and Herbal Medicine: "Curcumin treatment was found to "inhibit DNA methyltransferases" leading to demethylation which "contributed to the reactivation of tumor suppressor genes."

EGCG (epigallocatechin-3-gallate): This polyphenol from green tea “inhibits DNMT activity and induces the demethylation of tumor suppressor genes, including p16 and RASFF1A, in cancer cells” (Fang et al., 2003). EGCG has shown significant impacts on prostate cancer cells through modulating DNA methylation patterns (Role of Flavonoids as Epigenetic Modulators, 2021).

Resveratrol: Sourced from grapes and red wine, resveratrol was found to “inhibit DNMT activity and induce the demethylation of the BRCA1 gene, a tumor suppressor gene, in breast cancer cells” (Literature Review: Epigenetics and Herbal Medicine).

Histone Modification of Herbal Medications

Herbal compounds also show significant impacts on histone modifications:

Curcumin: Studies show that curcumin "inhibits histone deacetylase (HDAC) activity, leading to increased histone acetylation and upregulation of tumor suppressor genes" (Balasubramanyam et al. 2004).

EGCG: The catechins from green tea showed that these can "inhibit HDAC activity and induce histone acetylation resulting in upregulation of genes implicated in cell cycle arrest and apoptosis in cancer cells" (Thakur et al., 2012). EGCG induces "an accumulation of acetylated histone H3 in global cellular chromatin leading to epigenetically reactivation of p21/waf1 and Bax in prostate cancer cells that ultimately causes cell cycle arrest and apoptosis" (Role of Flavonoids as Epigenetic Modulators, 2021).

Resveratrol: Has been shown to activate the histone deacetylase SIRT1 and therefore promote the deacetylation of histones and regulation of gene expression (Boily et al, 2009)

Herbal Intervention in Regulation of microRNA

Herbal medicines greatly impact microRNA expression profiles, thereby influencing downstream cellular pathways as follows:

Curcumin: One study finds that curcumin "regulates the expression of a variety of miRNAs including miR-21, miR-34a, and miR-200," in cancer cells (Sun et al., 2008). These miRNA changes can be correlated with "the inhibition of…cell proliferation, invasion, and metastasis" (Literature Review: Epigenetics and Herbal Medicine).

EGCG: Green tea catechins 'upregulate the expression of tumor suppressive miR-NAs, such as miR-16 and miR-let-7 but downregulate oncogenic miRs, such as miR-21, in cancer cells,' according to one study (Tsang & Kwok, 2010).

Resveratrol: "It has been known that resveratrol modulates the expression of a number of miRNAs (Tili et al., 2010), including miR-34a, miR-122 and miR-335, in various disease models. "These miRNA alterations have been shown to be involved in an array of cellular processes including regulation of apoptosis, metabolism, and metastasis." (Literature Review: Epigenetics and Herbal Medicine)

Therapeutic Potential and Clinical Applications

Regardless, the epigenetic effects of traditional medicines have great therapeutic promise in several diseases, especially those that have an epigenetic component.

Cancer Prevention and Treatment.

Traditional medicines with epigenetic activity may be especially valuable in cancer treatment:

Inhibition Of Cancer Progression During Carcinogenesis: Herbal compounds EGCG and resveratrol may inhibit cancer progression by sustaining proper patterns of DNA methylation and histone modifications.

Potential therapeutic: Our findings describe a novel mechanism through which these compounds may help combat the progression of the disease: They can reverse altered epigenetic modifications in cancer cells (Epigenetic effects of herbal medicine, 2023).

Synergistic Mechanisms: For example, traditional medicines can be synergistic with conventional cancer therapies, as they may target different epigenetic mechanisms that are not targeted by standard of care.

Neurodegenerative Disorders

This suggests that epigenetic dysregulation plays a role in many neurological diseases, and therefore, traditional medicines that have epigenetic effects may prove to be valuable:

Berbamine hydrochloride (BBMH): A TCM compound with anti-Alzheimer's effect concerning the improvement of microglia and macrophages related functions in mouse brain tissue and regulation of calcium homeostasis in brain tissue (Editorial: Natural compounds regulating epigenetics, 2023)

Dopaminergic: Tetramethylpyrazine supplies nutrients for the dopaminergic pathway and activates the AMPK mTOR pathway.

Diseases Inflammatory & Immune System

Traditional medicines have anti-inflammatory effects partly via epigenetic mechanism:

Allergic Conditions: Changes in epigenetics determine the development and functioning of different immune cells, and any dysregulation is associated with allergic conditions and autoimmune diseases. Traditional herbal molecules can help reverse these epigenetic signatures.

Asthma: "Raising HDAC levels in the lungs of patients with severe, steroid-refractory asthma may provide a means of reducing airway hyperresponsiveness and reestablishing steroid sensitivity" (Making HDACs p you to be HR (HDP …). Therapeutic potential of HDAC-modulating dietary and herbal compounds.

Implications and Future Directions

While there is a lot of promising evidence, understanding and applying the epigenetic effects of traditional medicines has many challenges.

Quality Control for Standardization

Most notable are the challenges presented through the "variability in phytochemical composition" and the "lack of standardized preparations" which create difficulties for consistent epigenetic effects (Literature Review: Epigenetics and Herbal Medicine). "Standardization of herbal extracts, dosage standardization, bioavailability, and inter-individual differences in epigenetic responses" must all be addressed in future research.

Specificity and Off-Target Effects

Existing epigenetic therapies, even those of natural origin, are often "not very specific, which translate into off-target effects" (Epigenetics, Epigenomics, and Personalized Medicine, 2024). Vague CMs heightens toxicity danger and limit drug efficacy, most especially in cancer wherein recognizing regular from malignant cells is essential.

Clinical Translation

There are challenges that need to be addressed in translating laboratory findings to clinical application:

Bioavailability: Several herbal compounds, like curcumin, get poorly absorbed, so their efficiency without complex formulations is limited.

Epigenetic Changes are Reversible: Since the epigenome is dynamic and reversible, this is both a challenge and a therapeutic advantage: correcting loss of function (over-methylation/capping) effects may not be permanent.

Individual Differences: Responses to epigenetic therapies can vary widely from person to person, requiring tailored approaches.

Future Research Directions

Conductive to the development of traditional medicine and epigenetics, future research should focus on:

Integration of omics: Integrating epigenomics data with other omic approaches (genomics, transcriptomics, proteomics and metabolomics) to explore how traditional medicines alter disease pathways.

Improving Delivery Systems: Designing more effective delivery systems like nanoparticles or more specific delivery vectors that can enhance bioavailability and facilitate targeted delivery

Whereas longitudinal studies aiming at monitoring individuals' exposure to classical medicines and environmental factors in order to prove causal links with epigenetic reprogramming.

Integrating Traditional Medicine with Modern Science: Exploring the possibility of incorporating traditional medicine concepts, such as Ayurvedic Prakriti classification, alongside epigenetic profiling for personalized medicine.

Conclusion

This presents an important step forward in understanding how traditional medicine systems are associated with epigenetic mechanisms contributing to their therapeutic effects. Ayurveda, Siddha and herbal medicine seem to modulate DNA methylation, histone modification and micro-RNA expression, leading to reversal of disease-like dysregulated epigenetic landscape.

The convergence between ancient wisdom and modern science provides exciting new opportunities to develop innovative approaches for treating chronic diseases such as cancer, metabolic diseases, inflammation and neurodegenerative diseases. Research in epigenetics and traditional medicine is still evolving, but it has the potential to change disease prevention and treatment and offer more practical and effective healthcare solutions for each of us.

Epigenetics took a rare detour back to ancient medicine and, for a change, they became one and the same. Further exploration of the epigenetic mechanisms at the heart of traditional therapies represents a means of bridging cultural and scientific divides; such cross-cultural collaboration and understanding lays the groundwork for improving the health of the individual patient, as well as global health overall.

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- rmation of self-help groups to generate sustainable income, can support survivor-led interventions and long-term rehabilitation and reparations.

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