Review Article

www.ijrap.net

(ISSN Online:2229–3566, ISSN Print:2277–4343)

EPIGENETIC REPROGRAMMING IN PSORIASIS AND ITS AYURVEDIC INTERPRETATION IN MANDALA KUSHTA: A REVIEW

Vidhya Prabhakaran [1]*, Chhaju Ram Yadav [2]

[1] PhD Scholar, PG Department of Kriya Sharir, National Institute of Ayurveda, Jaipur, Rajasthan, India

[2] Professor, Dean (PhD) and HOD, PG Department of Kriya Sharir, National Institute of Ayurveda, Jaipur, Rajasthan, India

Received on: 22/5/26 Accepted on: 22/7/26

***Corresponding author**
E-mail: vidhya.prabhakaran002@gmail.com

DOI: 10.7897/2277-4343.174149

ABSTRACT

Psoriasis is a chronic immune-mediated inflammatory skin disorder in which genetic susceptibility and environmental factors interact to influence disease onset, progression, and recurrence. Emerging evidence highlights the significant role of epigenetic mechanisms, including DNA methylation, histone modifications, and microRNA dysregulation, in regulating inflammatory gene expression without altering the DNA sequence. These reversible modifications contribute to abnormal keratinocyte proliferation and persistent activation of pro-inflammatory cytokines such as TNF-α and IL-17.This narrative review explores the role of epigenetic factors in psoriasis and correlates them with the Ayurvedic concept of Mandala Kushta. Relevant biomedical literature on epigenetic alterations in psoriasis was reviewed, alongside classical Ayurvedic texts describing the etiopathogenesis, Dosha-Dushya involvement, recurrence, and environmental influences associated with Mandala Kushta. Current evidence indicates that epigenetic alterations in psoriasis are dynamic and influenced by environmental triggers including diet, stress, infections, and toxins. Similarly, Ayurveda describes Mandala Kushta as a chronic and recurrent disorder resulting from Dosha-Dushya Sammurchana involving Kapha, Pitta, Rakta, Twak, and Mamsa, precipitated by Nidana Sevana, Agnimandya, and Ama formation. The relapsing nature of the disease and the influence of dietary, behavioural, and psychological factors show notable conceptual parallels with epigenetic regulation. Furthermore, Ayurvedic interventions such as Shodhana and Rasayana therapies may exert immunomodulatory, antioxidant, and metabolic effects that could potentially influence epigenetic pathways. Integrating epigenetic insights with Ayurvedic understanding of Mandala Kushta offers a promising framework for translational research, identification of epigenetic biomarkers, and development of personalized, integrative approaches for psoriasis management.

Keywords: Ayurveda, Mandala Kushta, Psoriasis, Epigenetic

INTRODUCTION

Psoriasis is an immune-mediated inflammatory disease that is persistent and recurrent. Psoriatic arthritis and cutaneous psoriasis are just two examples of its wide range of clinical manifestations.[1] Psoriasis prevalence varies widely across the globe, with a global prevalence rate of roughly 2-3% of the population and a greater incidence in up to 11% in Scandinavian nations.[2,3] Other forms of psoriasis include plaque, nail, guttate, inverse, and pustular psoriasis; the most prevalent kind is plaque psoriasis, which is characterised by dry, silvery scales covering reddish regions of skin.[4-6] Generalised pustular psoriasis (GPP) is the most severe and extremely uncommon kind.[7] Psoriasis is largely influenced by hereditary factors; the underlying genetic pathways are still unclear.[8] The importance of environmental factors in the etiopathogenesis of psoriasis, as well as their interaction with genetic and immunological components, is shown by research on a population of twins.[9-10] A significant histocompatibility complex is linked to immunological aspects of the pathophysiology of psoriasis. The most closely related alleles for psoriasis susceptibility are HLA-Cw6, HLA-Cw1, HLA-Cw12, HLA-B27, and HLA-DR*07.[11-15] In genetically susceptible patients, environmental factors like substance abuse, food, stress, trauma, and infections can affect the development of psoriasis. These elements may cause psoriasis flare-ups and cause the condition to strike previously healthy people.[16]

Significance of Human Leukocyte Antigen (HLA) and Antigen Presentation in Psoriasis

The interaction between immune cells, primarily T lymphocytes and antigen-presenting cells, and epidermal keratinocytes is the immunological basis of psoriasis. Several cytokines, including TNF-α, IFN-γ, IL-17, IL-23, and IL-12, mediate this relationship. 17-20 Keratinocyte enlargement and a shorter cell cycle are the outcomes of aberrant leukocyte function and an inflammatory response directed at the patient's epidermal cells. Pathological skin lesions are the outcome of this process. The inflammatory cascade may also be exacerbated by keratinocytes' production of cytokines and release of autoantigens. Acute inflammation turns into chronic inflammation when mechanisms that prevent inflammation are downregulated.[21] There is still little evidence of its involvement in the disease's pathogenesis. It appears to be involved in both innate and acquired immunity pathways, though. According to the literature, this involvement mostly shows up as its function in presenting antigens to T lymphocytes and its effect on NK cells.[11] HLA-Cw6 may interact with receptors that activate NK cells in addition to being a natural ligand for the inhibitory receptor KIR2DL1. The pathophysiology of Psoriasis may be significantly influenced by dysregulation of NK cells.[22] HLA-Cw1 is another allele that has a genetic connection to the development of Psoriasis. HLA-Cw1 is more prevalent among Asians than HLA-Cw6, which is present in all ethnic groups. HLA-B27 is a well-known marker of seronegative spondyloarthropathies, and its association with Psoriatic arthritis is widely reported in the scientific literature.[23-24] HLAC*18 may also be associated with psoriasis. HLA-B57 is also strongly

associated with the pathogenesis of psoriasis and is often associated with a severe clinical course of the disease.[15] HLA-DR*07 was found in patients with Psoriatic arthritis and psoriasis involving the nails.[25]

Table 1: Human leukocyte antigen (HLA) alleles associated with psoriasis pathogenesis.

HLA Alleles	Type of Psoriasis	Ethnic Group Association
HLA Cw6	Droplet psoriasis Type I psoriasis[26]	The general population varies from 14.1% to 59.1% [27]; more frequently in Caucasian patients than in the Asian population[26,27]
HLA Cw1	Erythroderma, pustular psoriasis, and psoriatic arthritis[12]	Most common in the Asian population[12]
HLA Cw12	Severe psoriasis [13]	Most common in the Turkish population[13]
HLA B-27	Psoriatic arthritis [23,24]	Diverse in ethnic groups [23,24]

The PubMed and Google Scholar databases were searched for electronic literature. The terms "Psoriasis," "epigenetics," "DNA methylation," "non-coding RNA," "microRNA," "histones," "environmental factors," and their combinations were among the search parameters.

Epigenetic Changes in Psoriasis

Histone Modifications .

Proteins called histones are found in the nucleus of cells and are responsible for packaging DNA, providing chromosomes with structural support, and regulating gene expression.[17] An essential chromatin subunit made up of the histone octamer of H2A, H2B, H3, and H4 is called a nucleosome. 147 base pairs of DNA were encased in proteins.[27,28] Numerous biological processes that impact DNA expression depend heavily on post-translational modifications of histones, including methylation, acetylation, phosphorylation, ubiquitylation, and ADP ribosylation.[29,30] The pathophysiology of psoriasis is caused by several histone changes.

Non-Coding RNA

Non-coding RNA (ncRNA) is implicated in the pathophysiology of autoimmune illnesses, including psoriasis, according to an increasing amount of clinical research. A type of RNA known as non-coding RNAs (NcRNAs) is incapable of translating proteins. Remarkably, only about 2% of RNA is used to encode proteins, while ncRNA makes up over 98% of the human genome.

The Essential Role of microRNAs in Psoriasis

Pathologically changed keratinocytes have been found to produce miR-203 more frequently, which impacts the proliferation and differentiation of these cells by directly influencing several epidermal genes and is thus implicated in the pathophysiology of Psoriasis.[31,32] The first skin-specific miRNA to be discovered, miR-203, controls keratinocyte development in a way that is dependent on protein kinase C.[32]

Table 2: MicroRNA involved in Psoriasis Pathogenesis

microRNA	Level	Potential Effect
miR-21	↑	Suppression of activated T cells' apoptosis, enhanced keratinocyte proliferation
miR-31	↑	Keratinocyte proliferation, leukocyte chemotaxis stimulation, promoting inflammation and proliferation of keratinocytes
miR-155	↑	TNF-α expression upregulation, stimulation of lymphocyte infiltration
miR-203	↑	Regulation of keratinocyte proliferation and differentiation
miR-99a	↓	Inhibition of HaCaT cell proliferation, downregulation of IGFR-1 expression
miR-125b	↓	Keratinocyte hyperproliferation

Mandala Kushta is classified under Mahakushta in classical Ayurvedic texts such as Charaka Samhita and Sushruta Samhita. Acharya Charaka defines the clinical features of Mandal Kushta as Shwetarakta (faint reddish white), Utsannamandalam (raised patches), Sthiram (stable), Snigdham (unctuous), Annyonya Sansaktm (patches joined with each other).[33] These clinical features closely resemble Plaque psoriasis, which presents with well-demarcated erythematous plaques covered by silvery scales and follows a relapsing-remitting course. From an immunological perspective, Psoriasis is now recognized as an immune-mediated inflammatory disease involving dysregulation of T-lymphocytes, dendritic cells, and cytokines such as TNF-α, IL-17, IL-23, and IL-12. This chronic inflammatory cascade leads to keratinocyte hyperproliferation and abnormal differentiation. In Mandal Kushta, the vitiated Dosha is Kapha, and Dushya is Twak, Shonita, Mamsa, and Lasika. The inflammatory erythema (Raga) correlates with Pitta-Rakta Dushti, while scaling, thickening, and chronicity correlate with Kapha dominance and Mamsa Dhatu involvement. Thus, cytokine-mediated inflammation in Psoriasis can be conceptually aligned with Pitta-Rakta Dushti, and keratinocyte hyperproliferation with Kapha-induced excessive tissue growth.

Genetically, Psoriasis shows a strong association with HLA alleles, particularly HLA-Cw6 and HLA-B27, indicating hereditary susceptibility. Ayurveda describes a similar concept through Beejadushti (defective seed/genetic predisposition), where individuals inherit susceptibility that manifests under appropriate Nidana (causative factors). Therefore, HLA-linked genetic susceptibility parallels Beejadushti in Mandala Kushta. The epigenetic dimension of Psoriasis, DNA methylation changes, histone modifications, and altered expression of microRNAs (miR-21, miR-155, miR-203, etc.) demonstrate how environmental factors modulate gene expression without altering DNA sequence. Ayurveda emphasises the role of Ahara (diet), Vihara (lifestyle), Manasika factors (stress), and environmental exposures in triggering Dosha imbalance. This aligns strongly with the epigenetic concept that environmental triggers influence disease expression. Epigenetic modulation can therefore be interpreted as the molecular equivalent of Dosha-Dushya Sammurchana (interaction between vitiated Doshas and susceptible tissues).

Stress, infections, trauma (Koebner phenomenon), substance abuse, and dietary factors are well-known triggers of Psoriasis flares. Similarly, Mandala Kushta is said to be aggravated by Viruddha Ahara (incompatible diet), excessive intake of Guru,

Snigdha, and Abhishyandi foods, day sleep, and suppression of natural urges, all of which disturb Dosha equilibrium and impair Agni. The Ayurvedic concept of Agnimandya (impaired metabolic fire) may correlate with metabolic and immune dysregulation seen in Psoriasis.

At the tissue level, psoriasis demonstrates rapid epidermal turnover (3–5 days instead of 28 days), parakeratosis, and inflammatory infiltration. In Mandala Kushta, the involvement of Twak, Rakta, Mamsa, and Lasika reflects a deeper systemic pathology rather than a superficial skin disease. This systemic nature corresponds with modern understanding that Psoriasis is not merely cutaneous but associated with comorbidities such as Psoriatic arthritis and metabolic syndrome. Thus, psoriasis and Mandala Kushta share striking parallels:

- Chronic, recurrent inflammatory nature
- Genetic/constitutional susceptibility
- Immune dysregulation
- Environmental trigger dependence
- Systemic involvement
- Importance of lifestyle modification

CONCLUSION

The currently available evidence indicates that epigenetic alterations play a pivotal role in the pathophysiology of Psoriasis. However, further research is necessary to determine whether specific epigenetic modifications act as primary drivers of disease onset or arise as secondary consequences of chronic inflammation. In particular, exploring the dynamic interplay among epigenetic regulators, especially the role of circular RNAs functioning as microRNA (miRNA) sponges, represents a promising direction for future investigation. A deeper understanding of psoriasis through the lens of epigenetics also underscores the importance of lifestyle medicine. Since epigenetic mechanisms are highly responsive to environmental and behavioural factors, patient education regarding weight management, balanced nutrition, avoidance of harmful substances, and meticulous skin care becomes essential. These measures may help interrupt the cascade of epigenetic events that promote keratinocyte hyperproliferation, parakeratosis, impaired apoptosis, and susceptibility to secondary infections. Addressing lifestyle components alongside medical therapy may enhance treatment responsiveness and long-term disease control. In conclusion, emerging immunogenetic and epigenetic insights provide a contemporary molecular framework that conceptually aligns with the classical Ayurvedic description of Mandala Kushta as a chronic, Tridoshaja, systemic disorder characterized by Dosha imbalance, Dhatu vitiation, Agnimandya, and Beejadushti. This integrative understanding strengthens the scientific rationale for incorporating Ayurvedic therapeutic principles in the comprehensive management of psoriasis.

REFERENCES

1. Greb JE, Goldminz AM, Elder JT, Lebwohl MG, Gladman DD, Wu JJ, *et al*. Psoriasis. Nat Rev Dis Primers. 2016;2:16082.
2. Sewerin P, Brinks R, Schneider M, Haase I, Vordenbäumen S. Prevalence and incidence of psoriasis and psoriatic arthritis. Ann Rheum Dis. 2019;78:286-287.
3. Modalsli EH, Snekvik I, Åsvold BO, Romundstad PR, Naldi L, Saunes M. Validity of self-reported psoriasis in a general population: the HUNT Study, Norway. J Invest Dermatol. 2016;136:323-325.
4. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. JAMA. 2020;323:1945-1960.
5. Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clin Med (Lond). 2021;21:170-173.
6. Dhabale A, Nagpure S. Types of psoriasis and their effects on the immune system. Cureus. 2022;14:e29536.
7. Yang SF, Lin MH, Chou PC, Hu SK, Shih SY, Yu HS, *et al*. Genetics of generalized pustular psoriasis: current understanding and implications for future therapeutics. Genes (Basel). 2023;14:1297.
8. Trojacka E, Zaleska M, Galus R. Influence of exogenous and endogenous factors on the course of psoriasis. Pol Merkuriusz Lek. 2015;38:169-173.
9. Di Meglio P, Villanova F, Nestle FO. Psoriasis. Cold Spring Harb Perspect Med. 2014;4:a015354.
10. Lønnberg AS, Skov L, Skytthe A, Kyvik KO, Pedersen OB, Thomsen SF. Heritability of psoriasis in a large twin sample. Br J Dermatol. 2013;169:412-416.
11. Owczarek W. The role of HLA-Cw6 in psoriasis and psoriatic arthritis. Reumatologia. 2022;60:303-305.
12. Huang YW, Tsai TF. HLA-Cw1 and psoriasis. Am J Clin Dermatol. 2021;22:339-347.
13. Onsun N, Pirmit S, Ozkaya D, Çelik S, Rezvani A, Cengiz FP, *et al.* The HLA-Cw12 allele is an important susceptibility allele for psoriasis and is associated with resistant psoriasis in the Turkish population. Scientific World Journal. 2019;2019:7848314.
14. Ruiz DG, Azevedo MNLD, Lupi O. HLA-B27 frequency in a group of patients with psoriatic arthritis. An Bras Dermatol. 2012;87:847-850.
15. Cassia FDF, Cardoso JF, Porto LC, Ramos-e-Silva M, Carneiro S. Association of HLA alleles and HLA haplotypes with psoriasis, psoriatic arthritis and disease severity in a miscegenated population. Psoriasis (Auckl). 2021;11:41-51.
16. Roszkiewicz M, Dopytalska K, Szymańska E, Jakimiuk A, Walecka I. Environmental risk factors and epigenetic alterations in psoriasis. Ann Agric Environ Med. 2020;27:335-342.
17. Mateu-Arrom L, Puig L. Genetic and epigenetic mechanisms of psoriasis. Genes (Basel). 2023;14:1619.
18. Grän F, Kerstan A, Serfling E, Goebeler M, Muhammad K. Current developments in the immunology of psoriasis. Yale J Biol Med. 2020;93:97-110.
19. Blauvelt A, Chiricozzi A. The immunologic role of IL-17 in psoriasis and psoriatic arthritis pathogenesis. Clin Rev Allergy Immunol. 2018;55:379-390.
20. Teng MWL, Bowman EP, McElwee JJ, Smyth MJ, Casanova JL, Cooper AM, *et al*. IL-12 and IL-23 cytokines: from discovery to targeted therapies for immune-mediated inflammatory diseases. Nat Med. 2015;21:719-729.
21. Orsmond A, Bereza-Malcolm L, Lynch T, March L, Xue M. Skin barrier dysregulation in psoriasis. Int J Mol Sci. 2021;22:10841.
22. Temel B, Adisen E, Gonen S. HLA-Cw6 status and treatment responses between psoriasis patients. Indian J Dermatol. 2021;66:632-637.
23. Mease PJ, Chakravarty SD, McLean RR, Blachley T, Kawashima T, Lin I, *et al.* Treatment responses in patients with psoriatic arthritis axial disease according to human leukocyte antigen-B27 status: an analysis from the CorEvitas Psoriatic Arthritis/Spondyloarthritis Registry. ACR Open Rheumatol. 2022;4:447-456.
24. Minh VN, Thi VB, Van TC, Ngoc TN, Ngoc AT, Van ED, *et al*. The relationship between HLA-B27, HLA-Cw06, HLA-DR7 and psoriatic arthritis in Vietnamese patients: disease progression and therapeutic burden. Open Access Maced J Med Sci. 2019;7:300-301.

25. Duran-McKinster C, Ortiz-Solis D, Granados J, Tamayo L, Orozco-Covarrubias L, Ruiz-Maldonado R. Juvenile psoriatic arthritis with nail psoriasis in the absence of cutaneous lesions. Int J Dermatol. 2000;39:32-35.
26. Chen L, Tsai TF. HLA-Cw6 and psoriasis. Br J Dermatol. 2018;178:854-862.
27. Ogawa K, Okada Y. The current landscape of psoriasis genetics in 2020. J Dermatol Sci. 2020;99:2-8.
28. Richmond TJ, Davey CA. The structure of DNA in the nucleosome core. Nature. 2003;423:145-150.
29. Tan S, Davey CA. Nucleosome structural studies. Curr Opin Struct Biol. 2011;21:128-136.
30. Zeng C, Tsoi LC, Gudjonsson JE. Dysregulated epigenetic modifications in psoriasis. Exp Dermatol. 2021;30:1156-1166.
31. Sonkoly E, Wei T, Janson PCJ, Sääf A, Lundeberg L, Tengvall-Linder M, *et al*. MicroRNAs: novel regulators involved in the pathogenesis of psoriasis? PLoS One. 2007;2:e610.
32. Sonkoly E, Wei T, Pavez Loriè E, Suzuki H, Kato M, Törmä H, *et al*. Protein kinase C-dependent upregulation of miR-203 induces the differentiation of human keratinocytes. J Invest Dermatol. 2010;130:124-134.
33. Tripathi B, editor. Charaka Samhita of Agnivesha. Reprint ed. Vol. 2. Varanasi: Chaukhamba Prakashan; 2020. Chikitsa Sthana. Chapter 7, Verse 16. p. 304

Cite this article as:

Vidhya Prabhakaran and Chhaju Ram Yadav. Epigenetic reprogramming in psoriasis and its Ayurvedic interpretation in Mandala Kushta: A Review. Int. J. Res. Ayurveda Pharm. 2026;17(4):124-127. doi: http://dx.doi.org/10.7897/2277-4343.174149

Source of support: Nil, Conflict of interest: None Declared

Disclaimer: IJRAP is solely owned by Moksha Publishing House, a non-profit publishing house dedicated to publishing quality research. Every effort has been made to verify the accuracy of the content published in our journal. IJRAP cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of the IJRAP editor or editorial board members.