RESEARCH PAPER

Growth Regulation, Hyperplasia and Neoplasia in the Context of Kushtha Roga: An Ayurvedic–Biomedical Conceptual Review

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ABSTRACT

Background Cutaneous tissue homeostasis depends on a highly regulated balance between cellular proliferation, differentiation, migration and apoptosis. Disruption of this balance may result in pathological hyperplasia, while persistent dysregulation accompanied by genetic and epigenetic alterations may contribute to occurrence of neoplasia. Keratinocyte proliferation is regulated by multiple growth factors, cytokines, intracellular signalling pathways and cell-cycle checkpoints.

In Ayurveda, Kushtha Roga represents a broad group of skin disorders involving Tridosha and multiple Dushya, particularly Tvak, Rakta, Mamsa and Lasika/Ambu. The classical concept of Dosha-Dushya Sammurchana provides a multi-factorial model of disease development.

Objective To critically examine the contemporary mechanisms of cutaneous growth regulation, hyperplasia and neoplasia and explore their conceptual relationship with the Ayurvedic pathogenesis of Kushtha Roga.

Materials and Methods A narrative conceptual review was undertaken using classical Ayurvedic literature and contemporary biomedical literature concerning Kushtha, epidermal homeostasis, keratinocyte proliferation, growth-factor signalling, cell-cycle regulation, apoptosis, chronic inflammation and cutaneous neoplasia. The review distinguishes established biomedical mechanisms from proposed Ayurvedic–biomedical correlations.

Results Epidermal homeostasis is regulated by interacting growth-promoting and growth-inhibitory pathways. EGF, FGF, IGF and related signalling systems promote keratinocyte proliferation Dysregulation of these systems may result in excessive epidermal proliferation. Chronic inflammation can further modify the cutaneous microenvironment and contribute to abnormal proliferation and, under specific circumstances, carcinogenesis.

Classical Ayurvedic descriptions of Kushtha identify Tridosha together with Tvak, Rakta, Mamsa and Lasika/Ambu as important components of its pathogenesis. This multi-factorial model can be considered a conceptual framework for investigating interactions among systemic regulation, tissue susceptibility, inflammation and local tissue responses. However, Dosha and Dushya cannot currently be equated with specific molecular pathways.

Conclusion Kushtha Roga should not be regarded as synonymous with hyperplasia, premalignancy or neoplasia. Nevertheless, the Ayurvedic concept of Dosha-Dushya interaction provides a potentially useful hypothesis-generating framework for investigating disturbed tissue homeostasis.

Keywords: Ayurveda; Kushtha; tissue homeostasis; keratinocyte; proliferation; hyperplasia; neoplasia; inflammation; Dosha; Dushya; cell cycle.

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INTRODUCTION

The skin is a continuously renewing organ in which cellular proliferation and differentiation must remain precisely coordinated to maintain epidermal integrity. Keratinocytes respond to growth factors, cytokines, extracellular-matrix signals and neighbouring cells to regulate proliferation, differentiation and repair.

Growth regulation is therefore not controlled by a single pathway. Epidermal growth factor receptor (EGFR), fibroblast growth factor, insulin-like growth factor and related signalling systems stimulate keratinocyte

proliferation, whereas transforming growth factor-β and other inhibitory pathways restrain excessive growth.

When proliferation exceeds normal requirements but remains dependent on regulatory stimuli, an increase in cell number may manifest as hyperplasia. Pathological epidermal hyperplasia is observed in several chronic inflammatory skin diseases and is associated with altered growth-factor responses and abnormal keratinocyte differentiation.

Neoplasia represents a qualitatively different biological process. Tumour cells may acquire sustained proliferative signalling, resistance to growth inhibition and cell death, genomic instability and altered interactions with the tissue microenvironment. Chronic inflammation may contribute to these processes in susceptible tissues, including skin.

The concept of Dosha-Dushya Sammurchana is therefore of interest from a systems-biology perspective. It describes the interaction between pathological factors and susceptible tissues rather than attributing disease to a single local lesion. The important scientific question is not whether Dosha is equivalent to a particular cytokine or signalling molecule. Rather, it is whether Ayurvedic disease phenotyping can identify clinically meaningful biological patterns that can be objectively investigated.

2. AIM

To evaluate the relationship between contemporary concepts of tissue growth regulation, hyperplasia and neoplasia and the Ayurvedic pathophysiological framework of Kushtha Roga.

3. OBJECTIVES

1. To review mechanisms regulating normal cutaneous cellular proliferation.
2. To describe the biological basis of pathological hyperplasia.
3. To summarize mechanisms contributing to neoplastic transformation.
4. To review the classical pathogenesis of Kushtha Roga.
5. To examine the concept of Dosha-Dushya interaction in relation to tissue homeostasis.
6. To identify potential biological markers for testing Ayurvedic hypotheses.
7. To propose a scientifically testable Ayurvedic–biomedical research model.

4. METHODOLOGY

4.1 Review design

This article is a **narrative conceptual review**.

The purpose was to integrate two knowledge domains: Ayurvedic pathophysiology of Kushtha and contemporary biology of cutaneous growth regulation.

The review does not attempt quantitative synthesis or meta-analysis.

4.2 Literature domains

Literature was considered under the following domains:

- Kushtha and Ayurvedic Samprapti
- Dosha-Dushya interaction
- epidermal homeostasis
- keratinocyte proliferation
- growth factors
- EGFR signalling
- IGF signalling
- cell-cycle regulation
- apoptosis
- chronic inflammation
- skin carcinogenesis

5. NORMAL CUTANEOUS GROWTH REGULATION

5.1 Epidermal homeostasis

The epidermis continuously replaces cells lost from its surface. Keratinocyte stem and progenitor cells maintain this process through a balance between self-renewal, proliferation and differentiation.

The basic relationship may be represented as:

Stem-cell renewal
↓
Keratinocyte proliferation
↓
Differentiation
↓
Migration toward the surface
↓
Terminal differentiation and desquamation
↓
Maintenance of tissue homeostasis

This process requires continuous feedback between proliferative and inhibitory signals.

5.2 Growth-promoting pathways

Important regulators of keratinocyte proliferation include:

- EGF/EGFR
- FGF
- IGF
- hepatocyte growth factor
- cytokines and chemokines.

EGF- and FGF-family members, together with IGF and hepatocyte growth factor, have important roles in keratinocyte proliferation, while TGF-β and other signals provide inhibitory control.

The EGFR system is particularly relevant because it participates in epidermal homeostasis, stem-cell regulation and cellular responses to injury.

5.3 Growth-inhibitory mechanisms

Normal proliferation must be terminated once tissue requirements are met.

Important regulatory mechanisms include:

- TGF-β signalling
- CDK inhibitors
- p53-associated responses
- RB/E2F regulation
- differentiation signals
- apoptosis
- cellular senescence.

The RB/E2F system is particularly important for regulating cell-cycle progression in epidermal cells. Abnormal activation of E2F and disruption of RB-associated control are implicated in carcinogenesis.

6. HYPERPLASIA

Hyperplasia is defined as an increase in the number of cells in a tissue.

It is important to distinguish:

Hyperplasia ≠ neoplasia

Hyperplasia may represent an adaptive response to:

- hormonal stimulation
- tissue injury
- chronic inflammation
- growth-factor stimulation.

In pathological epidermal hyperplasia, keratinocytes may demonstrate increased proliferation, altered differentiation and abnormal responses to growth signals.

A simplified mechanism is:

Persistent stimulus
↓
Growth-factor/cytokine signalling
↓
Cell-cycle activation
↓
Increased keratinocyte proliferation
↓
Increased epidermal thickness
↓
Hyperplasia

Importantly, hyperplasia alone does not establish malignancy.

7. NEOPLASIA AND LOSS OF GROWTH CONTROL

Neoplasia involves abnormal cellular proliferation accompanied by biological alterations that allow cells to escape normal tissue regulation.

The development of cancer may involve:

- sustained proliferative signalling
- evasion of growth suppressors
- resistance to apoptosis
- genomic instability
- altered metabolism
- immune evasion
- tumour-promoting inflammation
- invasion and metastasis.

Therefore, neoplastic transformation requires considerably more than simple cellular proliferation.

Conceptual distinction

Feature	Normal growth	Hyperplasia	Neoplasia
Cell number	Regulated	Increased	Abnormally increased
Growth stimulus	Controlled	Often persistent	May become autonomous
Differentiation	Maintained	Usually retained	May become abnormal
Cell-cycle control	Intact	Activated	Frequently disrupted
Genetic alteration	Not required	Not required	Frequently important
Apoptosis	Balanced	May remain functional	Frequently impaired
Malignancy	Absent	Not implied	May be present

8. AYURVEDIC CONCEPT OF KUSHTHA

Kushtha is described in Ayurveda as a broad group of disorders affecting the skin.

In Charaka's description, Kushtha involves the three Dosha and four principal Dushya:

Vata + Pitta + Kapha

with

Tvak + Rakta + Mamsa + Lasika/Ambu.

The disease is therefore presented as a multi-factorial process rather than as a purely superficial skin lesion.

Table 1. Classical components of Kushtha Samprapti

Component	Classical significance
Vata	movement-related Dosha
Pitta	metabolic component
Kapha	stabilizing component
Tvak	Skin
Rakta	Blood/tissue component
Mamsa	Tissue component
Lasika/Ambu	Fluid-related component

The relevance of this model to modern biology lies primarily in its **multi-component nature**, not in presumed molecular equivalence.

9. DOSHA-DUSHYA SAMMURCHANA AND TISSUE SUSCEPTIBILITY

The Ayurvedic disease process may be conceptually represented as:

Nidana
↓
Dosha Prakopa
↓
Dushya Vaigunya
↓
Dosha-Dushya Sammurchana

↓

Sthana Samshraya

↓

Clinical manifestation

From a modern research perspective, this can generate the following question:

Does a specific Ayurvedic disease phenotype correspond to a measurable biological state of tissue inflammation, altered proliferation or tissue remodelling

10. PROPOSED RELATIONSHIP BETWEEN KUSHTHA AND HYPERPLASIA

A hypothesis-generating pathway may be formulated:

Nidana

↓

Dosha imbalance

↓

Dushya susceptibility

↓

Chronic/local tissue disturbance

↓

Inflammatory signalling

↓

Growth-factor activation

↓

Altered keratinocyte proliferation/differentiation

↓

Tissue remodelling

↓

Possible hyperplastic phenotype

This hypothesis can be tested through histopathological examination and proliferation markers.

11. AGE AS A MODIFIER OF GROWTH REGULATION

Age may influence the relationship between tissue injury, regeneration and abnormal growth.

With ageing, changes occur in:

- stem-cell function
- DNA repair
- immune surveillance
- cellular senescence
- tissue regeneration
- inflammatory signalling.

Therefore, age could act as a **biological modifier** rather than a direct cause.

Age → altered growth-regulatory capacity → altered proliferation/apoptosis → altered tissue homeostasis → susceptibility to hyperplasia/neoplastic change

Age-related factor	Biological change	Possible relevance to Kushtha research
Young age	Higher regenerative/proliferative capacity	Faster tissue turnover and repair
Middle age	Gradual alteration of growth-factor and immune signalling	Changes in inflammatory and proliferative balance
Older age	Cellular senescence, reduced repair, altered apoptosis and immune regulation	Greater possibility of persistent tissue dysregulation
Chronic inflammation	Persistent cytokine/growth-factor signalling	May maintain abnormal proliferation in susceptible tissue
Accumulated molecular damage	DNA/epigenetic alterations increase with age	May facilitate neoplastic transformation when other risk factors exist

Ayurvedic interpretation

This becomes particularly interesting when viewed through age-related Dosha predominance:

Bālya → Madhya Avasthā → Vṛddhāvasthā

Traditionally, Kapha predominates in childhood, Pitta in adulthood and Vāta in old age. This can be used as a conceptual framework, but it should not be stated that Kapha/Pitta/Vāta directly correspond to specific molecular pathways.

A potentially publishable hypothesis is:

"Age-related changes in tissue homeostasis may modify the expression of Dosha–Dushya interactions in Kushtha Roga and may influence the balance between cellular proliferation, differentiation, apoptosis and repair."

"Age as a modifier of growth regulation and tissue homeostasis in Kushtha Roga."

This gives you a much stronger research model:

Age → Dosha predominance/age-related physiological changes → tissue susceptibility → inflammatory signalling → growth-regulatory pathways → proliferation/apoptosis balance

12. PRIMARY RESEARCH QUESTION

Are specific Ayurvedic Samprapti patterns in Kushtha Roga associated with measurable alterations in cutaneous inflammatory and proliferative biomarkers?

Secondary research questions

1. Does Dosha predominance correlate with inflammatory markers?
2. Does chronicity correlate with Ki-67 expression?
3. Does histological epidermal hyperplasia correlate with particular Samprapti patterns?
4. Are p53/RB-related abnormalities associated with severe or persistent disease?
5. Does clinical improvement correspond to changes in inflammatory or proliferative biomarkers?

13. CONCEPTUAL MODEL

Figure 1. Proposed Ayurvedic–Biomedical Growth Homeostasis Model

Nidana

↓

Dosha Prakopa

↓

Dushya Vaigunya
↓
Dosha-Dushya Sammurchana
↓
Tvak–Rakta–Mamsa–Lasika involvement
↓
Altered tissue environment
↓
Inflammatory signalling
↓
Growth-factor signalling
↓
Cell-cycle regulation
↙ ↘
Proliferation Apoptosis
↘ ↙
Tissue homeostasis

If regulatory balance is maintained:
→ Repair / normal remodelling
If proliferative signalling persists:
→ Hyperplasia

If additional genetic/epigenetic abnormalities occur:
→ Potential neoplastic transformation

14. DISCUSSION

The principal finding of this conceptual review is that both Ayurveda and contemporary biology describe disease as the consequence of interactions among multiple factors, although their explanatory languages and levels of analysis differ.

Contemporary dermatology recognizes that epidermal proliferation is controlled through a network of growth factors, cytokines, receptor-mediated signalling and cell-cycle regulators. The EGFR and IGF systems are particularly relevant to epidermal proliferation, while the E2F/RB pathway provides an important cell-cycle regulatory mechanism. Chronic inflammation can disturb this equilibrium. Inflammatory mediators may stimulate proliferation, alter differentiation and influence cellular survival. Persistent inflammatory microenvironments can also contribute to carcinogenesis under particular circumstances. .

15. IMPLICATIONS FOR AYURVEDIC RESEARCH

This framework may help shift research from purely descriptive correlations toward measurable hypotheses.

The proposed research sequence is:

Classical concept
↓
Operational Ayurvedic phenotype
↓
Objective clinical measurement
↓
Histopathology
↓
Molecular biomarker
↓
Statistical association
↓
Independent validation

This approach can potentially provide a scientifically rigorous pathway for investigating traditional concepts without reducing them prematurely to molecular equivalents.

remain hypotheses and require prospective validation.

16. FUTURE RESEARCH DIRECTIONS

Future research should proceed in a staged manner.

Phase I – Standardization

Develop reproducible criteria for Ayurvedic phenotyping of Kushtha.

Phase II – Histopathological correlation

Determine whether specific phenotypes demonstrate characteristic patterns of:

- hyperplasia
- inflammation
- differentiation
- tissue remodelling.

Phase III – Longitudinal research

Determine whether biomarker changes correspond to:

- disease activity
- treatment response
- recurrence.

Phase IV – Translational research

Explore whether specific Ayurvedic interventions modify validated biological pathways.

Only after such evidence is generated should claims regarding modulation of growth-regulatory mechanisms be considered.

17. CONCLUSION

Cutaneous tissue homeostasis depends upon a complex interaction between proliferation, differentiation, apoptosis, growth-factor signalling, immune regulation and the tissue microenvironment. Dysregulation of these mechanisms may result in pathological hyperplasia and, when accompanied by additional genetic and cellular abnormalities, contribute to neoplasia.

Kushtha Roga, as described in Ayurveda, represents a multi-factorial disorder involving Tridosha and multiple Dushya, particularly Tvak, Rakta, Mamsa and Lasika/Ambu. This framework offers a potentially useful systems-level perspective for investigating tissue susceptibility and pathological interaction.

The present review proposes that Dosha-Dushya Sammurchana may be explored as a hypothesis-generating framework for studying inflammation, cellular proliferation, differentiation and apoptosis in Kushtha.

However, no direct equivalence between Dosha and molecular pathways can currently be established, and Kushtha should not be regarded as synonymous with hyperplasia, premalignancy or neoplasia.

The most appropriate future research strategy is therefore to combine Ayurvedic phenotyping with histopathology and molecular biomarkers. Such studies may establish whether specific Ayurvedic Samprapti patterns correspond to

reproducible biological phenotypes and may provide a scientifically rigorous bridge between Ayurvedic dermatology and contemporary molecular medicine.

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