

Humanin Biomarker and Its Conceptual Relationship with Diabetes Mellitus (*Prameha*): An Integrative Review

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Abstract- Diabetes Mellitus (DM), a global metabolic disorder, is characterized by impaired glucose regulation, insulin resistance, and progressive tissue damage. In Ayurveda, this condition is described as *Prameha*, a group of disorders arising from *dosha* imbalance, *dhatu* vitiation (*dhatu dushti*) and weakened digestive/metabolic fire (*agni*). Modern biomedical research has identified Humanin, a mitochondria-derived peptide, as a novel biomarker with significant implications for metabolic health. Humanin exerts cytoprotective effects through anti-apoptotic, anti-inflammatory, and antioxidative mechanisms, while enhancing insulin sensitivity and glucose homeostasis. These functions conceptually align with Ayurvedic principles of maintaining equilibrium among *doshas* and preserving tissue integrity. This integrative review synthesizes contemporary molecular insights on Humanin with classical Ayurvedic frameworks. Humanin's role in preventing cellular apoptosis parallels Ayurvedic emphasis on protecting *dhatu*s from depletion. Its regulation of insulin signalling and lipid metabolism corresponds to Ayurvedic understanding of *kapha* and *meda dhatu* imbalances. Furthermore, its antioxidative and anti-inflammatory actions mirror Ayurvedic strategies to mitigate *pitta* aggravation and oxidative stress. By mapping these biological functions to traditional concepts, Humanin emerges as a molecular correlate of Ayurvedic protective mechanisms. The review also highlights Humanin's potential as a biomarker for early detection, disease progression monitoring, and therapeutic targeting in DM. Compared to conventional markers such as HbA1c and fasting glucose, Humanin offers unique insights into mitochondrial health and systemic resilience. Its therapeutic promise lies in Humanin analogy and peptide-based interventions, which may complement Ayurvedic approaches involving diet, lifestyle, and herbal formulations. In conclusion, Humanin represents a bridge between modern molecular biology and Ayurveda, offering a holistic perspective on diabetes

pathophysiology. Recognizing its conceptual relationship with *Prameha* underscores the importance of integrative medicine in advancing personalized care. Future research should focus on validating Humanin's biomarker potential through clinical trials and exploring synergistic therapies that combine peptide science with Ayurvedic wisdom.

Keywords: Diabetes Mellitus, Humanin, Mitochondria-derived peptide, *Prameha*

I. INTRODUCTION

Diabetes Mellitus (DM) represents one of the most significant health challenges of the 21st century, with an estimated 780 million adults projected to be affected by 2045^[1]. Characterized by chronic hyperglycaemia resulting from impaired insulin secretion, insulin resistance, or both, DM leads to progressive organ damage, notably affecting the kidneys, heart, eyes, and nerves ^[2]. The pathophysiology of DM extends beyond glucose dysregulation to involve mitochondrial dysfunction, oxidative stress, chronic inflammation, and cellular apoptosis, which contribute to long-term complications ^[3]. Ayurveda conceptualizes DM under the umbrella of *Prameha*, a systemic metabolic disorder primarily associated with derangement of *kapha dosha*, vitiation of *meda dhatu*, and weakened *agni* ^[4]. *Prameha* involves sequential involvement of multiple *dhatu*s (*meda*, *rakta*, *mamsa*, *majja*, and *ojas*), leading to progressive tissue depletion (*dhatu kshaya*) if left untreated ^[5]. Ayurvedic management emphasizes early intervention to restore *dosha* balance, enhance *agni*, eliminate *ama* (toxins), and protect tissues.

Recent advancements in molecular biology have identified Humanin, a mitochondria-derived peptide, as a promising biomarker and potential therapeutic target in DM. Humanin exhibits cytoprotective, anti-apoptotic, anti-inflammatory, and antioxidative effects, enhances insulin sensitivity, preserves pancreatic β -cell function, and supports glucose and lipid homeostasis [6], [7]. These properties conceptually align with Ayurvedic principles of *dhatu* protection and maintenance of systemic balance (*dosha samya*). This review aims to integrate contemporary biomedical evidence on Humanin with Ayurvedic principles of *Prameha*, highlighting its role as a molecular bridge, a predictive biomarker, and a potential therapeutic target. Comparative insights with conventional biomarkers and integrative therapeutic strategies are also discussed.

II. METHODS

This integrative review employed a narrative synthesis approach. Biomedical literature focusing on Humanin, mitochondrial dysfunction, insulin resistance, and DM were comprehensively analysed. Classical Ayurvedic texts such as *Charaka Samhita* and *Madhava Nidana* were consulted for *Prameha* pathophysiology, *dosha* imbalance, and *dhatu* vitiation.

Key areas of focus included:

1. Mapping Humanin biology to Ayurvedic concepts (*dhatu* protection, *dosha* equilibrium, *agni* preservation).
2. Comparative analysis with conventional biomarkers (HbA1c, fasting glucose, insulin resistance indices).
3. Evaluation of integrative therapeutic strategies combining Humanin-based interventions with Ayurvedic treatments.

Pathophysiology of Diabetes Mellitus

Biomedical Perspective

DM, particularly Type 2 Diabetes Mellitus (T2DM), involves a complex interplay between insulin resistance, β -cell dysfunction, lipid dysregulation, oxidative stress, and chronic inflammation. Mitochondria play a central role in energy production, insulin secretion, and reactive oxygen species (ROS)

regulation. Impaired mitochondrial function leads to reduced ATP generation, excessive ROS, activation of inflammatory pathways, and progressive β -cell apoptosis. Conventional biomarkers such as fasting plasma glucose, HbA1c, and oral glucose tolerance tests primarily reflect glycaemic status but provide limited information regarding mitochondrial health, cellular resilience, or early metabolic dysregulation.

Ayurvedic Perspective

Prameha arises due to *kapha* aggravation, *meda dhatu* vitiation, *agni* impairment, and *ama* accumulation. [8] Lifestyle factors such as overnutrition, sedentary behaviour, irregular sleep, and stress contribute to disease onset. Pathogenesis involves progressive *dhatu* involvement: initially *meda dhatu*, followed by *rakta*, *mamsa*, *majja*, and *ojas*, ultimately leading to *dhatu kshaya* and systemic deterioration. [9] Ayurvedic management focuses on restoring *dosha* balance, enhancing *agni*, eliminating *kapha* and *meda* excess, and protecting *dhatu*s through *Shodhana* (purification therapies), *Shamana* (palliative interventions), and *Rasayana* (rejuvenation) therapies. [10]

Humanin: Molecular Biology and Functions

Humanin is a 24-amino-acid peptide encoded within the mitochondrial 16S rRNA region, expressed in pancreas, liver, skeletal muscle, and brain. [11] Its major functions include:

1. Anti-apoptotic effects: Interaction with Bax and other pro-apoptotic proteins prevents β -cell death.
2. Anti-inflammatory actions: Suppresses pro-inflammatory cytokines such as TNF- α and IL-6.
3. Antioxidative activity: Reduces ROS production, protecting mitochondria and tissues from oxidative damage.
4. Insulin sensitization: Enhances glucose uptake via ERK1/2 and PI3K-Akt pathways.
5. Lipid metabolism regulation: Maintains *meda dhatu* homeostasis, reducing ectopic fat deposition.

Reduced Humanin levels are reported in obesity, insulin resistance, and T2DM, indicating its potential as an early biomarker for metabolic dysfunction.

Integrative Correlation: Humanin and *Prameha*
Humanin's molecular actions conceptually parallel Ayurvedic principles:

- *Dhatu Rakshana* (Tissue protection): Anti-apoptotic effects mean *dhatu* protection.
- *Dosha Samya* (*Dosha* balance): Regulation of insulin and lipid metabolism corresponds to *kapha* and *meda* balance.

- *Agni* preservation and *ama* reduction: Antioxidative and anti-inflammatory actions mitigate oxidative stress and tissue toxins.

Thus, Humanin serves as a molecular correlate of Ayurvedic protective mechanisms, linking modern science and traditional wisdom.

Comparison with Conventional Biomarkers

Feature	Conventional Biomarkers (HbA1c, Fasting Glucose)	Humanin
Glycaemic control	Yes	Partial
Mitochondrial function	No	Yes
Oxidative stress indicator	No	Yes
Early metabolic dysfunction	Limited	Yes
Predictive for tissue protection	No	Yes

Humanin complements conventional markers by reflecting cellular resilience, mitochondrial function, and tissue protection, offering advantages in early detection and personalized care.

Monitoring Humanin levels alongside conventional biomarkers and Ayurvedic assessments may enhance early detection, personalized therapy, and complication prevention.

Therapeutic Implications

Humanin-based interventions:

- Humanin analogs: Synthetic peptides improving insulin sensitivity and β -cell survival.
- Peptide therapies: Reduce oxidative stress and inflammation, enhance metabolic homeostasis.

Integration with Ayurvedic therapies:

- *Shodhana: Virechana* and *Basti* eliminate excess *kapha* and *meda*.
- *Shamana*: Diet, lifestyle, and herbal interventions restore *dosha* balance.
- *Rasayana*: Promotes tissue rejuvenation and systemic resilience.

III. CONCLUSION

Humanin represents a molecular bridge between modern molecular biology and Ayurveda. Its cytoprotective, anti-inflammatory, antioxidative, and insulin-sensitizing properties align with *dhatu* protection, *dosha* balance, and *agni* preservation. Comparative analysis shows Humanin's superiority over conventional biomarkers in detecting early metabolic dysfunction. Integrating Humanin-targeted therapies with Ayurvedic interventions provides a personalized, preventive, and holistic approach for managing DM. Future research should focus on validating Humanin's clinical utility and exploring integrative therapeutic strategies.

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