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The Synergy Between Mitochondrial Function and Innate Heat in Traditional Persian Medicine: A Modern Scientific Perspective on Thermoregulation

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Abstract

This study investigates the synergy between Traditional Persian Medicine (TPM)'s concept of innate heat (Hararat-e-Gharizi) and modern mitochondrial thermoregulation. TPM emphasizes innate heat as essential for sustaining life, paralleling modern understandings of mitochondrial ATP production and heat generation. This integration occurs through mitochondrial biogenesis, proton leak (*via* uncoupling proteins), and *Reactive Oxygen Species* (ROS) signaling, which correspond to the TPM concept of heat sustaining vital functions. These findings may guide novel therapeutic strategies that integrate TPM principles with mitochondrial biology. A comprehensive review of historical TPM texts and modern literature was conducted, comparing innate heat with mitochondrial roles in thermoregulation and energy balance. Data from PubMed, Google Scholar, and Scopus were analyzed to explore mechanisms of heat production in both traditional and modern contexts. Findings demonstrated that TPM's innate heat correlates with mitochondrial biogenesis, heat generation *via* Uncoupling Proteins (UCP1), and ROS regulation. These concepts reflect TPM's understanding of maintaining bodily warmth for health and longevity. The relationship between Hararat-e-Gharizi and mitochondrial thermogenesis offers a bridge between ancient medicinal practices and modern cellular biology. Both emphasize the role of heat in maintaining homeostasis and preventing disease, with modern science validating TPM's holistic approach. Clarifying these mechanisms provides deeper insight into therapeutic implications, highlighting thermodynamic parallels and the role of ROS signaling as a novel framework for understanding disease etiology and treatment. This study bridges Traditional Persian Medicine and modern mitochondrial thermoregulation, introducing integrative perspectives for personalized healthcare. It also highlights thermodynamic parallels and ROS signaling as a novel framework for understanding disease etiology and treatment. This study underscores the relevance of TPM's innate heat in modern medicine, emphasizing the importance of mitochondrial efficiency in thermoregulation and overall health. Integrating these perspectives can enhance personalized therapeutic strategies for disease prevention and longevity.

Keywords: Biology, Biomedical technology, Body temperature regulation, Hot temperature, Literature, Mitochondrial uncoupling proteins

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Introduction

The concept of innate heat traces its origins to pre-Socratic philosophers. Empedocles (c. 490–430 BC) proposed the theory of the four fundamental elements: earth, water, air, and fire, arguing that fire (innate heat) was a primary force driving life and change [1,2]. Similarly, Heraclitus (c. 535-475 BC) emphasized the importance of fire as a core element, symbolizing vitality and transformation [3]. Hippocrates (c. 460-370 BC), regarded as the father of medicine, incorporated the idea of innate heat into his humoral theory, balancing the four humors—blood, phlegm, yellow bile, and black bile—to maintain bodily functions and health. He considered innate heat essential for physiological processes and overall well-being [4]. Galen (129-216 AD) expanded on Hippocratic ideas, asserting that innate heat originated from the heart and was critical for regulating bodily functions and sustaining life [5].

In Islamic Medicine, scholars such as Avicenna (Ibn Sina, 980-1037 AD) advanced these concepts. In his seminal work, The Canon of Medicine, Avicenna described Hararat-e-Gharizi (innate heat) as a vital force emanating from the heart, fundamental to metabolism and general health [6]. His work profoundly influenced both Islamic and European medicine, highlighting the importance of balancing innate heat for health maintenance [7]. During the Renaissance, Paracelsus (1493-1541) deviated from humoral theory, instead focusing on the body's chemical processes, but he still recognized a form of vital heat essential for life [8]. Similarly, William Harvey (1578-1657), who discovered blood circulation, acknowledged the role of innate heat produced by the heart in sustaining vital functions [9].

Key Persian medical texts authored during the 10th and 11th centuries were analyzed to gather evidence and viewpoints on body temperature and health. Among these, Avicenna's Canon of Medicine stands out, not only for summarizing previous medical knowledge but also for reflecting Avicenna's extensive personal experience [10]. To explore how early Persian scholars approached these concepts compared to modern understanding, additional searches were conducted using databases such as the Cochrane Library, Google Scholar, PubMed, and Scopus.

In Traditional Persian Medicine (TPM), maintaining health revolves around the regulation of Hararat-e-Gharizi (innate heat), which is regarded as the primary energy source for sustaining bodily functions. Heat (harārat) is viewed as central to well-being, influencing treatments and lifestyle recommendations (Tadabir). A thorough review of TPM sources revealed specific guidance on temperament (mizaj) and health, emphasizing personalized treatments tailored to individual constitutions [11,12]. Such approaches in TPM resonate with modern personalized medicine, where treatment is customized based on a person's genetic and biological profile [13].

In modern science, heat is defined as a measure of the kinetic energy of molecules, with common temperature scales including Fahrenheit, Celsius, and Kelvin. For instance, water freezes at $0°C$ and boils at $100°C$. Survival and normal body functions rely on maintaining innate heat within a physiological range. Significant deviations, such as excessive heat loss or accumulation, can impair organ function [14]. The body's ability to regulate temperature—through vasodilation, perspiration, or shivering—is termed physiologic thermoregulation. These responses are triggered by various internal and external stimuli to maintain optimal body temperature [15]. The preoptic area of the anterior hypothalamus serves as the primary regulator of body temperature, acting as the body's thermostat. It dissipates heat when it detects high temperatures and generates heat in response to cold environments [16].

Furthermore, modern research into Traditional Persian Medicine reaffirms the importance of maintaining innate heat for overall health. Recent studies on mitochondrial function show that mitochondria, the energy-producing organelles of the cell, play a crucial role in regulating body temperature. During oxidative phosphorylation, the process by which Adenosine triphosphate (ATP) -the energy currency of cells- is produced, heat is generated as a byproduct. This mitochondrial heat production aligns with Avicenna's notion of Hararat-e-Gharizi [17,18]. Mitochondria's role in thermogenesis and its ability to maintain energy homeostasis within cells demonstrate how modern biochemistry offers a deeper understanding of the ancient concept of innate heat [19]. To bridge ancient and modern perspectives, this study explores how TPM's concept of innate heat aligns with mitochondrial thermogenesis and examines their potential integrative clinical applications.

Materials and Methods

A narrative integrative review was conducted combining qualitative analysis of historical TPM texts and quantitative synthesis of contemporary biomedical literature. Comparative analyses were performed using thematic analysis to identify correlations between key TPM concepts and modern mitochondrial biology. Inclusion criteria were predefined to minimize bias, and independent reviewers cross-checked selected texts to reduce subjectivity. PubMed, Scopus, the Cochrane Library, and Google Scholar using Boolean operators (AND, OR) and keywords such as "innate heat", "thermoregulation", "mitochondria", "uncoupling proteins", "ROS (Reactive Oxygen Species)", and "IPL-7" were systematically searched. Peer-reviewed and language filters (English, 2010–2024) were applied to ensure relevance and quality.

The quality of sources was assessed by considering the credibility of historical texts and the peer-reviewed status of modern studies. Mystical or metaphysical sources were excluded based on explicit language and content to maintain focus on scientifically interpretable concepts. Also documented limitations, such as potential language bias and interpretive subjectivity were applied.

This study employed a mixed-methods approach, combining qualitative analysis of TPM texts with quantitative synthesis of modern studies.

Historical analysis

Key TPM texts, including Avicenna's Canon of Medicine, were reviewed to elucidate the role of Hararat-e-Gharizi in thermoregulation. The credibility of historical texts and the peer-reviewed status of modern studies were considered in the quality assessment.

Systematic literature search

Databases such as PubMed, Google Scholar, and Scopus were searched to identify contemporary studies on mitochondrial function, ROS regulation, and uncoupling proteins involved in thermogenesis.

Data synthesis

A comparative analyses was conducted to align TPM concepts with modern mitochondrial biology, emphasizing parallels in heat production, energy balance, and disease prevention strategies. Data extraction was performed manually, and results were synthesized thematically to highlight conceptual connections.

The results were categorized based on their relevance to innate heat and mitochondrial activity, contributing to an integrative understanding of ancient and modern medicine. Limitations of this study include potential language bias and the subjective interpretation of historical texts.

Body heat in traditional persian medicine (TPM)

The diagnostic and therapeutic approaches in Traditional Persian Medicine (TPM) differ significantly from those in modern medicine, primarily because of their differing foundational principles. TPM places immense importance on the concept of Hararat-e-Gharizi (innate heat), which is often overlooked because of its conceptual complexity. In TPM, innate heat symbolizes the body's vital energy, sustaining the functional activities of organs, and is distinct from external heat, fever (Hararat-e-Gharibeh), or accidental heat from food and the environment. However, the concept of innate heat in TPM is not the same as the modern understanding of physical heat or temperature. For clarity, in this study, innate heat (Hararat-e-Gharizi) is defined operationally to the intrinsic mitochondrial heat produced during oxidative phosphorylation and thermogenesis, sustaining cellular and systemic homeostasis [6,7]. This distinction enables the integration of ancient symbolic frameworks with modern biomedical mechanisms.

In TPM, the four elements—fire, air, water, and earth—are viewed as essential components of all creation, encompassing humans, animals, plants, and even inanimate objects. These elements are symbolic, representing qualities rather than physical substances. For example, fire represents the warm-dry quality, air the warm-wet, water the cold-wet, and earth the cold-dry. Warm and cold qualities are active, while wet and dry are passive. According to Avicenna, heat is the primary force driving life, motion, and activities throughout the universe [1,2].

Health in TPM is based on maintaining a balanced constitution, or temperament (mizaj), which involves achieving equilibrium between hot, cold, wet, and dry qualities. This balance does not imply equal proportions but refers to maintaining the appropriate ratio for each individual's constitution. Each organ has a specific temperament; for instance, the heart is hot-dry, the brain cold-wet, and the liver hot-wet. The skin has a more balanced temperament by comparison. The function of each organ is determined by its innate heat, and any deviation from its natural temperament can lead to dysfunction [20].

Different kinds of heat

In TPM, the understanding of heat differs from that of modern medicine, which considers heat to be a measurable physical quantity. In TPM, innate heat is akin to the concept of "Qi" in Chinese medicine and is seen as the life force that drives all bodily functions. The surface temperature of the body differs from its core temperature due to the influence of external environmental factors. However, the core temperature remains relatively stable to protect internal organs and maintain physiological functions. The body compensates by opening or closing skin pores to dissipate or retain heat in response to environmental changes [21,22].

TPM identifies two distinct types of heat: Gharizi (innate heat) and Gharibeh (alien heat). Hararat-e-Gharizi (innate heat) is essential for sustaining life and maintaining bodily health, while Hararat-e-Gharibeh (alien heat) arises from external factors like harmful microorganisms, when the body's defenses are compromised. Aghili Shirazi, a leading Persian scholar, described Hararat-e-Gharizi as critical for life, with "Ostoghosi" referring to the type of heat necessary for vital functions such as nutrition, growth, and reproduction—all of which depend on innate heat to function effectively (Table 1) [4,23].

In TPM, innate heat is seen as a gentle, vital warmth that circulates through major organs like the heart, brain, and liver, sustaining life. Unlike the accidental heat from food and drink, innate heat is not derived from external sources and does not cause harm or corruption. Once innate heat is extinguished, life ceases.

Table 1. Traditional persian medicine (TPM) heat concepts

Concept	Explanation	Health association	Disease association
Hararat Gharizi (innate heat)	Fundamental heat transferred to the body at birth, essential for life and physiological functions (2,24)	Maintains thermal balance and supports physiological activities (24)	Imbalance leads to cold or heat-related disorders (24)
Hararat Ostoqosi (elemental heat)	Heat generated by metabolic reactions, supported by innate heat (2)	Provides energy for growth and bodily functions (2)	Deficiency causes metabolic or developmental issues (2)
Hararat Gharibeh (strange heat)	Abnormal, harmful heat that disrupts balance (23,25)	Can assist body's defense mechanisms (23,25)	Excess leads to fever, inflammation, or disease (23,25)

Avicenna, in his Canon of Medicine, emphasized that innate heat protects internal organs from external temperature fluctuations. When this heat is weakened, it disrupts homeostasis and can lead to disease [10,26].

Measurement of heat

In modern medicine, several methods exist to measure body temperature, such as oral, axillary, rectal, and tympanic measurements. However, TPM takes a qualitative approach to temperature assessment, relying on the physician's palpation (malmas) of the skin over specific organs. This practice requires the physician to possess a balanced temperament or an understanding of the population's average mizaj (constitution). While modern medicine uses quantitative tools, TPM relies on the physician's subjective judgment of heat intensity through touch [27,28].

For instance, palpating areas like the head, liver, or stomach helps determine the heat intensity of these organs, while wetness and dryness are also evaluated alongside warmth and coldness. A holistic assessment, including history-taking and physical examination, aids in determining a patient's true intrinsic heat [4,25]. Important history elements include climate, sleep patterns, physical activity, and responses to environmental changes [16].

Body temperature and health

Blood flow regulation in the skin plays a pivotal role in maintaining homeostasis and body temperature, which are crucial for survival across all animal species. Strategies for conserving body heat include hibernation, migration, and increased adiposity. Additionally, fever is a rapid response to infections, often shortening disease duration by enhancing immune function [29,30].

Local warming causes vasodilation of the skin, while exposure to cold results in vasoconstriction. Capsaicin, found in peppers, stimulates vanilloid receptors in nerve endings, producing a sensation of heat. Conversely, cold compresses induce vasoconstriction via adrenergic stimulation [31]. Studies show that cerebral temperature plays a crucial role in ischemic brain injury, with brain temperature often exceeding core body temperature during fever or injury, contributing to increased Intracranial Pressure (ICP) [10,15].

In stroke patients, low Heart Rate Variability (HRV) is often linked to autonomic dysfunction, and mood disturbances may result from thermoregulatory dysfunction caused by brain injury. Maintaining therapeutic hypothermia at 33*°C* over 18 *hr* has been shown to improve neurological outcomes following acute cardiac events [8]. Conversely, reduced body temperatures in obese individuals may improve metabolic efficiency, converting calories into fat tissue instead of heat [7,26].

Avicenna stressed that maintaining innate heat and eliminating harmful alien moistures were critical for longevity. He outlined six principles of health, including air (climate), diet, sleep, movement, retention, and mental state. Disregarding these natural rules can diminish intrinsic heat, leading to early death [25]. Overeating, stress, and poor sleep habits deplete intrinsic heat and weaken the immune system [2,32].

Mitochondrial thermogenesis and innate heat

Mitochondria, the powerhouses of the cell, play a pivotal role in thermogenesis, a process directly connected to the Traditional Persian Medicine (TPM) concept of Hararat-e-Gharizi. In modern science, mitochondria generate heat during oxidative phosphorylation, where Uncoupling Proteins (UCP1)-Uncoupling Proteins (UCPs) are mitochondrial membrane proteins that uncouple oxidative phosphorylation to generate heat-in brown adipose tissue produce heat to maintain energy balance and regulate body temperature [33]. This process aligns with TPM's view of innate heat as the essential energy driving bodily functions, reinforcing the ancient notion of innate warmth as critical for survival and health. Furthermore, mitochondrial activity influences core body temperature, which is essential for the proper functioning of vital organs such as the heart, liver, and brain [34].

Reactive oxygen species and mitochondrial biogenesis

Recent research has further advanced the understanding of Hararat-e-Gharizi by highlighting the role of ROS in mitochondrial biogenesis. ROS are oxygen-derived molecules that act as both signaling agents and potential sources of damage. They promote the formation of new mitochondria, thereby sustaining the balance between heat production and energy expenditure. In TPM, maintaining innate heat is believed to be vital for life, a concept mirrored by modern science through ROS-mediated mitochondrial biogenesis, which ensures the body's energy and thermal homeostasis [35]. This biogenic process underscores the interconnectedness of mitochondrial activity and overall health, offering a biochemical explanation for TPM's emphasis on heat as a life force.

Mitochondria and cancer

One of the critical pathological aspects explored in both modern medicine and TPM is the disruption of heat generation in diseases such as cancer. Studies have shown that mitochondrial temperatures in cancer cells exceed those in normal cells, highlighting deregulated thermogenesis. This observation resonates with TPM's notion that disturbances in Hararat-e-Gharizi lead to illnesses, as seen in the case of cancer (Saratan). In TPM, cancer is believed to be caused by the combustion of black bile, a concept that modern science supports by demonstrating that mitochondrial dysfunction and excessive heat production can promote cancer progression [33,35]. Understanding the role of mitochondrial heat generation in cancer provides a bridge between ancient and contemporary approaches to health (Table 2).

Mitochondria and temperature

A significant portion of the energy generated from

Table 2. Comparison of traditional persian medicine (TPM) and conventional medicine concepts

Concept	TPM explanation	Conventional medicine	Health association	Disease association
Hararat Gharizi (Innate Heat)	Core temperature maintaining life (2)	Core body temperature sustaining physiological functions (36)	Maintains vital functions and thermal balance (2)	Imbalance causes hyperthermia or hypothermia (25)
Hararat Ostoqosi (Elemental Heat)	Heat generated through cellular metabolism, largely by mitochondria (11)	Heat from mitochondrial ATP production (37)	Generates energy for cellular activities (25,38)	Disruption can cause metabolic disorders (25,38)
Hararat Gharibeh (Strange Heat)	Abnormal heat causing imbalance (4,25)	Excessive reactive oxygen species (ROS) causing cellular damage (39)	Plays a role in immune defense (39)	Excess ROS causes oxidative stress and aging (39)

the oxidation of respiratory substrates is used for ATP synthesis and metabolite transport; however, approximately 60–70% of energy is dissipated as heat due to mitochondrial inefficiency [40]. Mitochondria, the primary bioenergetic organelles in non-photosynthetic eukaryotes, convert the free energy released during nutrient oxidation into ATP. Nevertheless, this conversion is not entirely efficient, and the local mitochondrial environment can reach up to ~48*°C*, which is higher than the organismal body temperature. This localized heat is produced by proton leak across the inner mitochondrial membrane, mediated by uncoupling proteins (UCP1, UCP2, UCP3), and contributes to thermogenesis. Accordingly, a considerable amount of energy is lost as heat, raising questions about the impact of this heat on mitochondrial and cellular temperatures [41]. The temperature of active mitochondria can be up to 10*°C* higher than the physiological norm due to the functioning of Respiratory Chain (RC) complexes. Research has shown that these complexes function optimally at 48*°C* in Human Embryonic Kidney cells (HEK 293) and primary skin fibroblasts; however, it should be emphasized that ~48*°C* refers to the local mitochondrial microenvironment, rather than the temperature of the whole cell or organism [42]. In Avicenna's practice, balancing heat and humidity was crucial, which aligns with mitochondrial production of both heat and metabolic water during oxidative phosphorylation. These parallels illustrate how ancient medical insights anticipated mitochondrial thermogenic mechanisms and their importance in maintaining homeostasis. Thermodynamics, grounded in the laws of nature, explores energy transformations and their effects on physical and chemical parameters such as temperature, pressure, and volume [43]. A living organism is an open thermodynamic system, with energy—primarily from the sun—fueling life processes. In Avicenna's view, heat from the environment, particularly from the sun, and seasonal changes were vital factors influencing health [40].

Schrödinger noted that biological systems must expel entropy to maintain life, and death results from thermodynamic equilibrium [44]. Infrared (IR) Radiation, which constitutes over half of the solar energy reaching the earth's surface, has been shown to stimulate mitochondrial ATP synthesis by modulating electron transport chain components, especially copper and iron-based centers in complex IV. Although mitochondria primarily produce energy *via* nutrient oxidation, IR-induced excitation of redox-active centers enhances ATP output and heat generation, suggesting that solar infrared exposure may play a supplementary role in cellular thermogenesis through photobiological mechanisms [45]. Current healthcare approaches do not adequately address these processes, often focusing solely on pathogen control. Avicenna's concept of *Hararat Gharibeh* (Strange Heat) emphasizes that excessive heat disrupts body equilibrium, leading to fever, inflammation, and disease.

Thermoelectric therapy, a form of thermodynamic treatment, uses light, heat, and electrical energy to create thermal gradients. These gradients promote localized production of ROS, which can trigger apoptosis in cancer cells *via* mitochondrial mechanisms [46]. Thermoelectric therapy, particularly when adjusted to body temperature gradients, holds promise for cancer treatment [46,47].

Mitochondrial temperature in cancer cells

Studies have demonstrated that mitochondrial temperatures in cancer cells exceed those of normal cells. For instance, the mitochondrial temperature in murine breast cancer cells reaches approximately 48*°C*. This finding was validated experimentally using a thermoresponsive nanocarrier (Poly N-isopropylacrylamide-PNIPAM) to release the anticancer drug PTX at optimal temperatures of 48*°C* in 4T1 cancer cells [48]. Beyond energy production, mitochondria play crucial roles in calcium regulation, cellular redox balance, apoptosis, and other signaling pathways. These roles are significant in pathogenic mechanisms, including cancer progression [47]. Understanding mitochondrial thermogenesis in cancer cells could lead to novel targeted therapies [49].

Recent advances in cellular thermometry have revealed the possibility of "thermal signaling"—a phenomenon wherein localized heat gradients, particularly in mitochondria and other compartments, act as regulators of site-specific biochemical reactions. These findings emphasize that temperature is not merely a by-product of metabolism but a critical regulator of cellular activity, influencing gene expression, membrane fluidity, molecular diffusion, and protein dynamics. Ultrahigh-resolution temperature sensors—such as nanodiamonds, quantum dots, and thermoresponsive dyes—have uncovered thermal gradients within cells that may play vital roles in both physiological and pathological processes, including cancer. Despite inconsistencies across measurement methods, these tools underscore the importance of thermogenesis as a functional signal, rather than just a metabolic artifact, especially in hypermetabolic cancer cells. This suggests that mitochondrial thermogenic hotspots could trigger downstream effects related to malignancy, making them potential therapeutic targets [41]. However, it is important to note that mitochondrial temperature measurements remain controversial due to methodological limitations of current nanoscale thermometry techniques.

In TPM, cancer (*Saratan*) is defined as a melancholic swelling produced by the combustion of black bile humor, sometimes mixed with phlegm, or even bile humor [50]. This aligns with modern understanding, as mitochondrial thermogenesis is believed to play a role in the aggressive nature of cancer cells.

Mitochondria and metastasis

Metastasis, a leading cause of cancer mortality, involves the migration of tumor cells to distant tissues. Mitochondrial dynamics, including changes in size, morphology, and localization, directly affect cancer metastasis [51]. Mitochondrial proteostasis, regulated by chaperones like Hsp90 and proteases like ClpP, prevents the activation of the Unfolded Protein Response (UPR). In cancer, proteostasis is enhanced, promoting disease progression [52]. The deletion of TRAP1 in mice reduces the incidence of age-related diseases, including cancer, while its overexpression accelerates prostate cancer progression [41].

Avicenna and other sages believed that natural black bile was not directly carcinogenic, but its dryness made it prone to combustion, leading to cancer [32].

Discussion

The concept of Hararat-e-Gharizi (innate heat) in TPM remains a significant area of focus, directly correlating with modern understandings of mitochondrial function. As mitochondria are responsible for generating the majority of cellular energy through oxidative phosphorylation, the heat generated during these processes aligns with TPM's idea of innate heat, which drives bodily functions and sustains life. Recent research has revealed that mitochondria in active cells, such as brown adipose tissue, produce heat to maintain energy balance and thermoregulation by burning excess calories through a mechanism that mirrors Hararat-e-Gharizi. This thermogenic activity is driven by mitochondrial UCP1, which are central to heat production, a factor also noted in traditional medicine's emphasis on maintaining bodily warmth for survival and optimal functioning. Beyond UCP1 in brown fat, UCP2 and UCP3 also contribute significantly to thermogenesis in skeletal muscle and other tissues, providing a more complete picture of tissue-specific heat production [33].

The relationship between mitochondrial activity and heat generation provides a bridge between ancient TPM teachings and modern cellular biochemistry. This connection underscores that the core temperature of the body—and by extension, the functioning of organs such as the heart, liver, and brain—depends on maintaining the innate warmth attributed to mitochondrial activity. Moreover, disruptions in innate heat, described in TPM as imbalance, correspond to mitochondrial dysfunction in diseases such as cancer, metabolic syndrome, and neurodegeneration. This association is supported by experimental and clinical evidence demonstrating the impact of thermogenic failure on disease progression [33].

Additionally, mitochondrial biogenesis, particularly through pathways involving ROS, plays a role in heat regulation by promoting the generation of new mitochondria that maintain energy balance. ROS have dual roles in thermogenesis and health: at moderate levels, they act as signaling molecules to induce mitochondrial biogenesis and adaptive thermogenesis; at high concentrations, they cause oxidative stress and damage. This further aligns with TPM's understanding of Hararat-e-Gharizi as a critical for life force.

These insights could inform therapies such as infrared therapy, thermogenic agents, and mitochondrial-targeted antioxidants, which aim to restore energetic balance and treat metabolic disorders, cancer, and neurodegeneration.

This study's limitations include reliance on secondary data and the interpretive challenges inherent in comparing ancient philosophy to modern science. Future research should empirically test these conceptual parallels through experimental and clinical studies.

Conclusion

TPM provides a valuable perspective on the importance of innate heat (Hararat-e-Gharizi) in sustaining life and health. Its teachings, when compared to modern findings on mitochondrial function, highlight the role of mitochondria as key regulators of heat production and energy balance. The study of mitochondrial thermogenesis, particularly in the context of ROS and UCP1, provides scientific validation of TPM's emphasis on maintaining bodily warmth for health. Modern research further supports TPM's holistic approaches, suggesting that maintaining mitochondrial efficiency and innate heat can have profound implications on thermoregulation, longevity, and disease prevention. Mitochondrial uncoupling proteins (UCP1, UCP2) facilitate heat generation *via* proton leak and are regulated by ROS, linking modern thermogenesis to Hararat-e-Gharizi [53]. Mitochondria in active states can reach ~50°*C*, reflecting the intrinsic warmth conceptualized in TPM and reshaping our understanding of cellular thermodynamics [54]. Understanding the intersection between these ancient concepts and modern scientific discoveries opens new avenues for personalized medicine and integrative therapeutic strategies that prioritize both metabolic health and energetic balance [33-35].

Ethical approval

This manuscript was drafted and edited by the authors without substantive writing assistance from AI tools. AI was used only for grammar and formatting checks. This literature review did not involve human or animal subjects, and no ethical approval or IRCTID registration was required.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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