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A synthesis of traditions: A comparative and integrative review of diabetes mellitus from Unani and modern medical perspectives

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Abstract

The global burden of diabetes mellitus (DM) continues to escalate, posing a significant public health challenge that underscores the limitations of purely conventional therapeutic models. This review undertakes a comprehensive comparative analysis of diabetes from both the modern biomedical and the Unani medical perspectives. The report traces the historical evolution of the disease from ancient observations to the discovery of insulin and the Unani concepts of *Ziabetes Shakri* and *Sue Mizaj*. It provides a detailed exposition of the modern pathophysiology of diabetic complications, particularly diabetic peripheral neuropathy (DPN), detailing key molecular mechanisms such as the polyol pathway, advanced glycation end-products (AGEs), and oxidative stress. Parallel to this, the Unani medical paradigm is explored, with its foundational principles of *Mizaj* (temperament) and *Quwa* (faculties) presented as a holistic, systems-based model. A critical analysis reveals significant conceptual overlaps, with the Unani concept of *Sue Mizaj Haar* (hot temperament) aligning with modern notions of chronic inflammation and oxidative stress, and *Zouf-e-Kulya* (renal weakness) correlating functionally with modern pathophysiology of glomerular hyperfiltration in diabetic kidney disease. The report also evaluates the pharmacological properties of key Unani formulations, demonstrating that their multi-component nature can modulate multiple biochemical pathways, a characteristic validated by recent clinical studies. This integrative review concludes that Unani medicine is not merely a collection of remedies but a rational, philosophical system that can offer a complementary framework for holistic diabetes management. An integrated approach, combining the mechanistic precision of modern medicine with the systemic and preventive strategies of Unani medicine, holds great promise for developing more effective, patient-centred, and sustainable solutions to the global diabetes crisis.

Keywords: Diabetes mellitus, Ziabetes Shakri, Unani medicine, modern endocrinology, pathophysiology, diabetic peripheral neuropathy, herbal medicine, integrative healthcare

Introduction

The Global Health Crisis of Diabetes and the Promise of Integrative Perspectives

The 21st century has seen diabetes mellitus (DM) evolve into a pandemic of unprecedented scale, making it one of the leading causes of morbidity and mortality worldwide. This global health crisis is driven by a complex interplay of socioeconomic, demographic, environmental, and genetic factors, placing an enormous strain on healthcare systems and economies [1]. The International Diabetes Federation (IDF) reported that in 2021, an estimated 537 million adults aged 20-79 were living with diabetes globally [3]. Projections indicate this number will rise sharply to 643 million by 2030 and to 783 million by 2045 [3]. The burden is particularly severe in low- and middle-income countries, where over 81% of the adult diabetic population resides [4]. This epidemic is inextricably linked to the rapid global shifts toward urbanization, which often entail more sedentary lifestyles, reduced physical activity, and increased consumption of high-calorie foods, all of which contribute to rising rates of overweight and obesity [7].

The human and economic costs of this crisis are staggering. In 2021, diabetes was responsible for an estimated 6.7 million deaths, and its treatment incurred a global health expenditure of nearly 966 billion USD [4]. Beyond these immediate costs, diabetes leads to a wide spectrum of debilitating and life-threatening complications, including blindness, cardiovascular disease, kidney failure, and gangrene of the lower extremities [6]. One of the most prevalent and financially burdensome complications is diabetic peripheral neuropathy

(DPN), which can lead to foot ulcers, gangrene, and potential amputation ^[1]. In some high-income nations, up to 27% of direct medical costs for diabetes are attributable to DPN, highlighting the urgent need for more effective and comprehensive management strategies ^[11]. A significant number of cases remain undiagnosed, with a 2021 IDF report indicating that almost half (44.7%) of adults with diabetes are unaware of their condition ^[4]. This reality points to a crucial deficiency in a reactive, symptom-focused medical model and emphasizes the need for a more proactive, preventative approach. This global context justifies a re-evaluation of all potential therapeutic frameworks, including traditional systems of medicine that focus on holistic health and preventive care.

The limitations and adverse effects associated with conventional anti-hyperglycaemic drugs have prompted a resurgence of interest in traditional and complementary systems of medicine ^[12]. The World Health Organization (WHO) has actively encouraged further investigation into traditional medicinal herbs for the treatment of diabetes ^[13]. Among these systems, Unani medicine, a Greco-Arab system of healing with a history spanning centuries, offers a rich philosophical and therapeutic framework for understanding and managing complex chronic diseases like diabetes. Unani medicine posits a holistic view of the human body, emphasizing the maintenance of a balanced internal state through a unique conceptualization of physiology and pathology. This review is therefore dedicated to a comparative and integrative analysis of diabetes from both modern and Unani medical perspectives. The objective is to delineate the historical understanding, etiological factors, pathophysiological mechanisms, and therapeutic approaches in both systems. By identifying and exploring the conceptual parallels and divergences, this paper aims to demonstrate the potential for an integrated approach that leverages the strengths of both paradigms to address the escalating global health challenge of diabetes mellitus.

2. Historical Evolution of Diabetes: From "Siphoning" to Insulin: The history of diabetes is a testament to the continuous evolution of medical understanding, with ancient physicians on different continents independently describing its key symptoms long before the advent of modern diagnostic tools. This section traces the historical progression of this knowledge, comparing the foundational contributions of Greco-Arab scholars with the key milestones in modern biomedical history.

2.1. Ancient and Greco-Arab Perspectives on Ziaabetes

The earliest known mention of a condition resembling diabetes dates back to 1500 BC in the Eber's Papyrus, an ancient Egyptian medical document that described a symptom of excessive urination (polyuria) ^[1]. Later, the Greek physician Buqrat (Hippocrates, c. 400 BCE) also provided descriptions consistent with diabetes, noting excessive urinary flow accompanied by body wasting ^[1]. However, it was Aretaeus of Cappadocia (c. 81-138 CE) who provided the first comprehensive clinical description and coined the term 'diabetes' ^[1]. Derived from the Greek word 'diabainein,' meaning 'to run through a siphon,' the term vividly captures the condition's primary symptom of excessive urination.¹ Aretaeus famously described the disease as a "melting down of flesh and limbs into urine,"

noting the unquenchable thirst and rapid physical emaciation that characterized the affliction ^[1].

Following Aretaeus, Jalinoos (Galen, c. 131-201 CE) referred to the condition as 'Diarrhoea Urinosa' (diarrhea of urine) or 'dipsakos' (the thirsty disease) and considered it a rare ailment of the kidneys ^[1]. This view persisted for centuries within the Unani and other medical traditions. The Indian physicians Susruta, Charaka, and Vaghbata (c. 5th-6th century CE) made a profound observational discovery by noting that ants and flies were attracted to the urine of affected individuals due to its sweetness ^[1]. They named the disease "Madhumeha," meaning "honey urine," providing a diagnostic criterion that was both simple and effective. This same empirical observation was independently documented by the Persian physician Al-Razi (Rhazes, c. 900 CE), who was the first to use the term 'Ziabetes' and a similar diagnostic method to identify the presence of sugar in urine ^[17].

The pinnacle of the Greco-Arab understanding of diabetes was reached by Ibn Sina (Avicenna, 1025 CE). In his seminal work, *Al-Qanun fi al-Tibb* (The Canon of Medicine), he provided a detailed and nuanced description of the disease, distinguishing between primary and secondary forms ^[1]. Ibn Sina's work expanded the understanding of diabetes beyond the kidneys, noting clinical features such as abnormal appetite, sexual dysfunction, and the critical complication of diabetic gangrene, which is a hallmark of advanced disease ^[1]. This comprehensive approach moved the understanding of diabetes from a localized kidney ailment to a systemic disorder with multi-organ effects, laying the intellectual groundwork for later Unani scholars.

2.2. The Dawn of Modern Endocrinology

The path to the modern understanding of diabetes began with the re-emergence of scientific inquiry in Europe. In 1674, Thomas Willis observed that elevated glucose in the blood preceded its excretion in the urine, giving the disease the name 'pissing evil' ^[1]. Over a century later, in 1766, Mathew Dobson confirmed the presence of sugar in both the urine and the blood of diabetic patients, a crucial step in defining the disease as a metabolic disorder ^[1]. A pivotal moment arrived with Paul Langerhans' discovery in 1869 of the islets of cells within the pancreatic tissue, although their function was not immediately understood ^[1]. The direct link between diabetes and pancreatic malfunction was definitively established in 1889 by Von Mering and Oscar Minkowski, setting the stage for the most significant breakthrough in the disease's history. The discovery and development of insulin by Frederick G. Banting, Charles H. Best, James B. Collip, and John J.R. Macleod in 1921-1922 marked a revolution, transforming diabetes from a rapidly fatal condition into a manageable, albeit chronic, one ^[1].

3. The Modern Medical Paradigm of Diabetes

Modern medicine defines diabetes as a group of metabolic disorders characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both ^[21]. This section provides a detailed overview of the modern medical paradigm, focusing on its epidemiological burden, pathophysiological mechanisms, and current management strategies, particularly for diabetic peripheral neuropathy (DPN).

3.1. Epidemiology, Risk Factors, and Clinical Burden

The global prevalence of diabetes is a stark indicator of its clinical burden. Projections from the IDF indicate a dramatic increase in the number of people living with diabetes, with the total number of adults aged 20-79 expected to reach 783 million by 2045 [3]. This rise is attributed to a combination of an aging global population and a shift in lifestyles toward urban, sedentary behaviours that promote obesity and other metabolic risk factors [7].

Among the multitude of diabetic complications, DPN is one of the most common and serious. It is defined as a peripheral nerve dysfunction in people with diabetes, after the exclusion of other causes [1]. The prevalence of DPN is estimated to be between 6% and 51% in adults with diabetes, depending on factors such as age, disease duration, and glycemic control [24]. For patients with diabetes for more than 10 years, the prevalence can exceed 50% [11]. The clinical manifestations of DPN range from sensory symptoms like numbness, tingling, and paraesthesia ("pins and needles") to motor signs such as minimal distal muscle weakness and a loss of ankle reflex [1]. Pain, often described as cauterizing or electrical, is a common symptom in approximately 20% of DPN patients and is typically worse at night, severely disrupting sleep [1]. The most severe outcome of DPN is a loss of sensation in the feet, which significantly increases the risk of unrecognized foot ulcers, infections, gangrene, and ultimately, amputation [1]. This makes DPN the most common cause of non-traumatic lower-limb amputation in high-income countries, imposing a high financial burden and a reduced quality of life on patients [11].

3.2. Pathophysiology of Diabetic Complications (with a focus on DPN): The pathogenesis of DPN is complex and multifactorial, but chronic hyperglycaemia is widely considered the central initiating factor [1]. Elevated blood glucose levels disrupt cellular metabolism and homeostasis, triggering a cascade of biochemical pathways that lead to progressive nerve injury [1]. The primary molecular mechanisms include:

- **The Polyol Pathway:** Under hyperglycaemic conditions, a minor metabolic route called the polyol pathway is activated. The enzyme aldose reductase converts excess intracellular glucose to sorbitol, consuming the cofactor nicotinamide adenine dinucleotide phosphate (NADPH) in the process [1]. This depletion of NADPH reduces the activity of Na-K ATPase, leading to the accumulation of intra-axonal sodium and myoinositol depletion, which directly impairs nerve conduction velocity and function.¹
- **Advanced Glycation End-Products (AGEs):** In a state of chronic hyperglycaemia, glucose non-enzymatically glycosylates proteins and lipids, forming irreversible compounds known as AGEs [1]. These AGEs accumulate on nerves and in the microvasculature, leading to vascular dysfunction, increased oxidative stress, and the activation of inflammatory pathways. The accumulation of AGEs in mitochondria is particularly damaging, as it impairs energy production and increases the generation of reactive oxygen species (ROS), contributing to a progressively neurotoxic environment [1].
- **Oxidative/Reductive Stress:** The polyol pathway and AGE formation contribute to a state of oxidative stress,

characterized by an imbalance between the production of free radicals and the body's antioxidant defenses.¹ This increased free radical activity directly damages nerve cells, impairs nerve blood flow, and promotes chronic inflammation [1]. Oxidative stress is now recognized as a central mechanism in the pathogenesis of DPN, leading to neuronal apoptosis and nerve dysfunction.¹¹

- **Microvascular Complications:** The nerves, with their high metabolic activity, are highly dependent on a rich blood supply for oxygen and nutrients [26]. The hyperglycaemic state and its downstream effects such as AGE formation and oxidative stress damage the endoneurial vessels that supply peripheral nerves [1]. This damage leads to endothelial swelling, vessel wall thickening, and lumen occlusion, causing nerve ischemia (lack of blood flow) and hypoxia (lack of oxygen), which further contributes to nerve fiber damage [1].

3.3. Diagnosis and Current Management Strategies

The diagnosis of DPN relies on a thorough clinical examination and a battery of objective tests. These include a careful inspection of the feet, assessment of ankle and knee reflexes, and sensory examinations using a 10-g monofilament test to identify patients at high risk of ulceration [1]. Other standard diagnostic tools include the Vibration Perception Threshold (VPT) test and Nerve Conduction Velocity (NCV) tests, which are crucial for characterizing and staging the severity of neuropathy [1].

Current treatment for DPN is primarily focused on symptom management, as there is no approved disease-modifying treatment to halt disease progression other than maintaining glycemic control [1]. The pharmacological approach for pain relief typically involves a stepped-care model. First-line drugs include anti-seizure medicines like pregabalin and gabapentin, and certain antidepressants such as duloxetine, venlafaxine, and tricyclic antidepressants (TCAs) [10]. While these drugs can provide symptomatic relief, their efficacy and tolerability vary, and they are often associated with side effects such as drowsiness, dizziness, dry mouth, and constipation [10]. For severe pain, opioid analgesics and topical agents like high-concentration capsaicin patches may be used [32].

Non-pharmacological management is also a cornerstone of DPN care. Patient education on meticulous foot care, including daily inspections and proper hygiene, is emphasized to prevent foot ulcers and amputations [1]. Other lifestyle interventions include maintaining strict glycaemic control, managing blood pressure, and being physically active [25]. Alternative treatments such as transcutaneous electrical nerve stimulation (TENS) and acupuncture are also used, but their efficacy can vary. This landscape of treatment, with its focus on symptom palliation rather than causal modification, highlights a significant gap in care, creating a demand for new, holistic therapeutic strategies [1].

4. The Unani Medical Paradigm of Diabetes

The Unani system of medicine, or Greco-Arab medicine, is an ancient system of healing built upon a logical and philosophical framework. This paradigm offers a unique lens through which to view diabetes, providing an alternative to the modern biomedical model. The conceptual basis of Unani medicine, its understanding of diabetes, and its therapeutic modalities are detailed in this section.

4.1. Fundamental Principles of Unani Medicine

Unani medicine is founded on a set of seven fundamental principles, collectively known as *Umoor-e-Tabiya*, which describe the structural and functional components of the human body^[1]. These principles are: *Arkan* (elements), *Mizaj* (temperament), *Akhlat* (humors), *Aaza* (organs), *Arwah* (pneuma or vital spirit), *Quwa* (faculties or powers), and *Afal* (functions)^[1]. Of these, *Mizaj*, *Akhlat*, and *Quwa* are central to the Unani understanding of disease.

- **Mizaj (Temperament):** The concept of *Mizaj* is a cornerstone of Unani medicine, representing the qualitative state of the body or its individual organs^[37]. It is a reflection of the balance of the four primary humors (*Akhlat*): *Dam* (blood, hot and moist), *Balgham* (phlegm, cold and moist), *Safra* (yellow bile, hot and dry), and *Sauda* (black bile, cold and dry).³⁹ Health is maintained when these humors are in a state of optimal balance, or homeostasis, both qualitatively and quantitatively^[37]. Disease (*Marz*) is a consequence of a deviation from this state, known as *Su-e-Mizaj* (abnormal temperament)^[1].
- **Quwa (Faculties or Powers):** Each organ is endowed with a specific power, or *Quwa*, that enables it to perform its physiological function^[1]. The *Quwwat-e-Tabiyyah* (natural faculties) are responsible for digestion and metabolism and are divided into four sub-faculties: *Quwwat-e-Jaziba* (the power of absorption), *Quwwat-e-Masika* (the power of retention), *Quwwat-e-Mughayira* (the power of transformation or metabolism), and *Quwwat-e-Dafi'a* (the power of propulsion or excretion)^[41]. This framework provides a rational, systems-based model for understanding organ function, where a disease can be traced to the dysfunction of a specific *Quwa*.

The philosophical roots of Unani medicine are deeply intertwined with ancient Greek thought. The theory of four *Arkan* (elements) earth, water, air, and fire was a foundational concept proposed by philosophers like Aristotle and Hippocrates to explain the origin and continuation of life^[1]. These elements were not viewed as simple matter but as substrates that give rise to the qualities of hot, cold, moist, and dry, which in turn constitute the humors and temperament of the body^[1]. This comprehensive system demonstrates that Unani medicine is not merely a collection of folk remedies but a coherent philosophical and scientific tradition that sought to explain the fundamental mysteries of life and disease within the intellectual context of its time.

4.2. Unani Etiopathogenesis and Classification of Diabetes: In Unani medicine, diabetes is referred to as *Ziabetes* in general, and *Ziabetes Shakri* for diabetes mellitus in particular^[1]. The core Unani theory of diabetes is that it is fundamentally a disease of the kidneys. Unani physicians believed that the primary cause of *Ziabetes Shakri* is a pathological temperament of the kidneys, described as *Sue Mizaj Haar* (hot temperament), combined with a weakness of its retentive power, or *Quwwat-e-Masika*^[1]. This dysfunction causes the kidneys to absorb and expel water and nutrients from the blood almost immediately, without proper metabolic transformation. This is what leads to the cardinal symptoms of excessive thirst and frequent urination^[1]. This functional description, focusing on the

kidneys' inability to retain what it should, is a powerful and elegant explanation for the disease within the Unani framework.

Unani scholars classified diabetes into two main types based on the quality of the urine: *Ziabetes Shakri* (Diabetes Mellitus) is characterized by sweet urine, while *Ziabetes Barid* (Diabetes Insipidus) is distinguished by excessive urination without the presence of sugar^[1]. More advanced classifications, as described by Hakeem Muhammad Hasan Qarshi, categorized the disease based on the primary organ or system involved, including: *Ziabitus mi'wiyya* (intestinal), *Ziabitus kabidi* (hepatic), *Ziabitus kalvi wa masani* (renal/vesicle), *Ziabitus Asabi* (nervine), and *Ziabitus ghudadi wa Banqarasi* (glandular/pancreatic).⁴¹ This classification demonstrates a nuanced understanding of the disease's systemic nature, recognizing that its origins could lie in various organs, including the pancreas, a concept that aligns remarkably well with modern endocrinology.

4.3. Unani Therapeutic Modalities

The therapeutic approach in Unani medicine is guided by the principle of correcting the underlying *Sue Mizaj* (abnormal temperament) and restoring the strength of the affected *Quwa* (faculties)^[1]. The management of *Ziabetes* often involves a comprehensive regimen of dietary modifications, lifestyle changes, and pharmacotherapy (*Ilaj bil Dawa*). For DPN, the goal is to relieve pain (*Taskeen of Pain*) and enhance nerve function using drugs with properties described as *muhallil* (resolvent), *mukhaddir* (anesthetic), and *muqavie aasab* (nervine tonics)^[1].

Unani pharmacotherapy utilizes a wide array of single and compound formulations. Key single drugs with reported anti-diabetic and related beneficial properties include:

- **Gymnema sylvestre (Gurmar):** Known as the "sugar destroyer," this herb has been shown to stimulate insulin secretion and promote the regeneration of pancreatic beta-cells^[13].
- **Nigella sativa (Kalonji):** This herb possesses significant antioxidant and anti-inflammatory properties. A 2025 meta-analysis showed that kalonji supplementation significantly reduced fasting blood sugar, HbA1c, total cholesterol, and LDL cholesterol in people with type 2 diabetes^[45].
- **Momordica charantia (Karela):** Used in many Unani formulations, its active constituents like charantin and polypeptide-p are known to lower blood glucose and improve insulin sensitivity^[13].
- **Eugenia jambolana (Jamun):** This fruit is a common ingredient in many antidiabetic formulations and is known for its hypoglycemic and antioxidant effects^[13].
- **Cinnamomum verum (Darchini):** Its essential oil has been traditionally used for a range of ailments including diabetes and neurological disorders.¹ It possesses antioxidant, antimicrobial, and warming stimulant properties, which are believed to help in managing diabetic complications^[48].

The use of highly potent substances, such as *Aconitum chasmanthum* (*Beesh*), in formulations for nerve-related conditions (*Wajaul asab*) is a notable aspect of Unani pharmacy^[49]. These powerful drugs are often subjected to a process of detoxification or purification (*Tadbeer*) to moderate their potency, enhance their efficacy, and

eliminate harmful effects ^[50]. This sophisticated approach to pharmaceutical preparation is a key distinction of Unani medicine, highlighting a tradition of rational drug use that goes beyond simple herbalism ^[50].

5. Bridging the Paradigms: A Modern-Unani Comparative Analysis

The apparent divide between modern and Unani medicine is largely a matter of language and scale. While one system describes pathology at the molecular level, the other uses a philosophical and qualitative framework. A comparative analysis reveals that these two paradigms are not contradictory but rather complementary, often describing the same fundamental biological phenomena from different conceptual viewpoints.

5.1. Conceptual Correlates: Mapping Unani Pathology to Modern Mechanisms

A direct mapping of Unani etiological concepts to modern pathophysiological mechanisms reveals profound parallels. The Unani concept of *Su-e-Mizaj Haar* (hot temperament), which is believed to cause inflammation and disease, finds a direct molecular correlate in the modern understanding of oxidative stress and chronic inflammation ^[53]. The

biochemical cascade initiated by hyperglycemia including the formation of AGEs and the activation of free radicals creates a state of cellular hyper-reactivity and damage that perfectly fits the Unani description of a "hot" temperament ^[1]. This convergence of concepts suggests that both systems are targeting the same fundamental biological processes, albeit with different terminologies and therapeutic tools. Similarly, the Unani concept of *Zouf-e-Kulya* (renal weakness) and a deficient *Quwwat-e-Masika* (retentive power) of the kidney directly corresponds to the functional pathology of diabetic kidney disease (DKD) ^[1]. Modern research shows that high blood glucose levels lead to glomerular hyperfiltration and increased intraglomerular pressure, which damages the filtering units of the kidney and leads to the excretion of proteins and essential nutrients ^[56]. The Unani description of the kidneys "failing to retain what is essential" is a functional and accurate representation of this physiological dysfunction, demonstrating an understanding of renal pathology that was based on meticulous observation rather than a knowledge of cellular mechanisms.

Table 1 provides a concise summary of these conceptual parallels, serving as a framework for an integrative dialogue between the two systems.

Table 1: Comparative Etiopathogenesis of Diabetes: Unani vs. Modern Concepts

Unani Concept	Key Unani Attributes	Modern Correlate	Key Modern Mechanisms
Su-e-Mizaj Haar	Imbalance of hot humor, leads to inflammation and fever.	Oxidative Stress & Inflammation	Increased free radicals (ROS), AGEs, pro-inflammatory cytokines.
Zouf-e-Kulya	Weakness of kidneys, impaired retentive power (Quwwat-e-Masika).	Renal Dysfunction (DKD)	Glomerular hyperfiltration, increased intraglomerular pressure, altered reabsorption.
Ziabitus Asabi	Aberrant function of the nervous system, leads to pain (Waja).	Diabetic Peripheral Neuropathy	Demyelination, axonal injury, polyol pathway, nerve ischemia.
Tafarruqe Ittesal	Discontinuity in tissues, a primary cause of pain.	Tissue Injury/Degeneration	Nerve fiber loss, foot ulcers, gangrene, and amputation.

5.2. Pharmacological Validation of Unani Herbal Remedies: The therapeutic value of Unani medicine is often rooted in its use of polyherbal formulations, which exhibit multi-targeted pharmacological activities. This approach, in which a single formulation can address multiple aspects of a disease, stands in contrast to the modern model of single-

molecule, single-target drugs. The scientific validation of many Unani herbs provides a strong foundation for an integrated therapeutic strategy.

Table 2 provides a detailed overview of the pharmacological properties of key Unani herbs, highlighting their multi-faceted actions.

Table 2: Pharmacological Actions of Key Unani Antidiabetic Herbs

Unani Name	Modern Botanical Name	Traditional Unani Action	Scientifically Validated Pharmacological Activity
Gurmar	Gymnema sylvestre	Regulates sugar in urine.	Stimulates insulin secretion, regenerates pancreatic beta cells, inhibits glucose absorption, hypoglycemic.
Kalonji	Nigella sativa	Antioxidant, anti-inflammatory.	Reduces fasting blood sugar, HbA1c, total cholesterol; potent antioxidant and anti-inflammatory effects.
Karela	Momordica charantia	Blood purifier, anti-diabetic.	Lowers blood glucose, improves insulin sensitivity, beta-cell regenerative effects.
Darchini	Cinnamomum verum	Warming stimulant, nervous tonic.	Enhances insulin sensitivity, antioxidant, antimicrobial effects.
Jamun	Eugenia jambolana	Reduces blood sugar.	Decreases blood sugar, slows starch-to-sugar conversion, antioxidant activity.
Methi	Trigonella foenum-graecum	Improves digestion, anti-diabetic.	Improves glucose tolerance, slows carbohydrate absorption, anti-inflammatory.

The efficacy of these traditional remedies is not purely anecdotal. The Unani approach of using multiple compounds from a single or compound formulation to restore systemic balance is now supported by a growing understanding of their multi-targeted effects. For instance, the use of *Kalonji* ^[45], with its potent antioxidant and anti-

inflammatory properties, can be seen as a direct intervention against the oxidative stress and chronic inflammation that are central to DPN pathology ^[11]. Similarly, the use of nervine tonics to alleviate pain (*Taskeen of Pain*) ^[1] reflects a traditional understanding of nerve-related conditions. The inclusion of potent, potentially toxic ingredients like *Beesh*

in formulations is a sophisticated pharmaceutical practice, as Unani practitioners employ specific detoxification methods to modulate the drug's properties, a process that merits further investigation to understand its modern chemical and toxicological basis [50].

5.3. Clinical Evidence and the Path Forward for Integration

Recent clinical research provides compelling evidence that Unani formulations are effective and safe in the management of diabetes and its complications. A randomized, single-blind, standard-controlled trial evaluated the efficacy of a Unani formulation comprising *Habbe Beesh* and a local application of *Roughan Darchini* in the management of DPN [1]. The 60-day trial with 60 DPN patients compared the Unani formulation with the modern standard, Methycobalamine, for symptomatic relief [1]. The study found that the Unani test formulation produced a statistically significant improvement within the test group for subjective parameters such as pain, numbness, burning sensation, and paresthesia [1]. While the inter-group comparison for subjective parameters was not significant, the Total Symptom Score (TCSS) showed a statistically significant improvement ($p < 0.005$) for the test group relative to the control [1]. This finding is particularly important as it suggests that the formulation may be more effective at alleviating the overall burden of symptoms, a more holistic measure, than addressing any single symptom in isolation. Furthermore, no side effects or toxicity were observed during the trial, underscoring the potential for these formulations as safe therapeutic options [1].

Another case series on the Unani formulations *Qurse Ziabetes Khas* and *Habb-e-Asab* in DPN patients reported promising results, including a marked reduction in pain intensity and an improved quality of life (WHOQOL-BREF scores) [58]. These clinical studies, designed with modern scientific rigor (e.g., randomization, statistical analysis, use of scoring systems), represent a critical step toward validating traditional therapies in a way that is credible to the wider scientific community. They demonstrate that Unani medicine is not a static system but is actively evolving to meet the standards of modern evidence-based practice, creating a clear pathway for integrating these therapies into contemporary healthcare models.

6. Discussion and Future Directions

This review has established that the seemingly disparate worlds of modern and Unani medicine are, in fact, conceptually linked. Modern medicine, with its reductionist approach, has meticulously detailed the molecular and cellular mechanisms of diabetes, while Unani medicine, through its holistic and philosophical framework, has provided a systems-level understanding of the same disease for centuries. The conceptual parallels between Unani *Sue Mizaj Haar* and modern oxidative stress, and Unani *Zouf-e-Kulya* and modern glomerular hyperfiltration, suggest that both systems are effectively observing and responding to the same underlying pathology.

The pharmacological validation of Unani herbs, with their multi-targeted actions, offers a powerful rationale for their therapeutic efficacy. This "poly-pharmacology" may be more effective at addressing the complex, multifactorial nature of diabetes than single-target drugs, while potentially minimizing adverse side effects. The clinical trials

discussed, though preliminary, demonstrate that Unani formulations can be both safe and effective, and that Unani researchers are adopting the methodological rigor required for high-impact scientific validation.

This synthesis of traditions points toward a clear roadmap for future research and clinical practice. First, there is a critical need for more large-scale, double-blind, randomized controlled trials to rigorously validate the efficacy and safety of Unani formulations for diabetes and its complications. Second, the standardization of Unani polyherbal drugs is essential to ensure consistency and reproducibility across studies, a prerequisite for their acceptance in a global context. Third, future research should focus on elucidating the precise molecular mechanisms of action of these multi-compound formulations. Understanding how a single herbal mixture can modulate multiple pathways (e.g., the polyol pathway, AGEs, inflammation) would not only provide a modern scientific basis for Unani medicine but could also lead to the discovery of novel therapeutic targets and drugs.

7. Conclusion

The global diabetes epidemic is a crisis that demands a shift in perspective, moving beyond the confines of a single medical paradigm. This comparative review has demonstrated that Unani medicine is not an antiquated system but a rational, philosophical framework for holistic health management. Its ancient observations on disease etiology and progression align with modern molecular discoveries, providing a rich source of hypotheses for contemporary research. The therapeutic strategies of Unani medicine, particularly its use of multi-component herbal formulations, offer a promising avenue for developing safe and effective adjunctive or standalone therapies. By embracing an integrated approach that combines the mechanistic precision of modern medicine with the holistic, systems-based wisdom of Unani medicine, the scientific community can create a more comprehensive, patient-centered, and sustainable strategy to combat the global health crisis of diabetes and its devastating complications.

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