



Exploring Parallels: Dry Dystemperament in Persian Medicine and Its Similarities with the Concept of Dietary Advanced Glycation End Products

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Abstract

Advanced Glycation End Products (AGEs), productions of non-enzymatic reactions between lipids, amino acids, carbohydrates, and DNA molecules glycation, contribute to the enhancement of oxidative stress and age-associated inflammation leading to chronic disease susceptibility. This study aims to provide a hypothetical interpretation of the relationship between Persian Medicine (PM) dietary recommendations and the process of inflammation-related aging through the consumption of AGEs. We comprehensively summarized recent evidence and PM textbooks using related keywords. Consumption of AGE-rich diets is associated with a high level of circulating AGEs, leading to oxidative stress and inflammatory conditions such as metabolic syndrome. Although foods are the primary source of AGEs in the body, cooking methods can play a role in AGE production: high temperature, longer duration of cooking, cooking surfaces, and lower moisture can increase AGE production, especially during cooking animal-derived foods. This concept has some similarities to the PM doctrine that states that many chronic diseases, such as atherosclerosis, cardiovascular disease, diabetes, and cancers develop from dry dystemperament. Foods with dry temperament, such as low-fiber foods undergoing low-moisture high-heat food processing, can lead to dry dystemperament. Hence, PM recommendations may help design better research studies to understand the dietary triggers of chronic inflammation

Keywords: Dietary advanced glycation end products; Persian medicine; Oxidative stress; Metabolic syndrome; Chronic disease

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Introduction

Advanced glycation end products (AGEs) are productions of non-enzymatic reactions between lipids, amino acids, carbohydrates, and DNA molecules glycation, contribute to the enhancement of oxidative stress and age-associated inflammation, so-called inflamm-aging [1, 2]. Epidemiological and experimental studies show that AGEs play a significant role in inflammation-associated aging through several mechanisms, such as oxidative stress, protein cross-linking, enhancing inflammatory processes, and senescence [3]. Consumption of a diet high in AGEs significantly increases their levels in plasma and tissues, contributing to the development of various conditions such as renal disease, clinical symptoms of uremia, and atherosclerosis. In contrast, dietary restriction of AGEs has been shown to prevent the onset of atherosclerosis, renal dysfunction, and both type 1 and type 2 diabetes. Moreover, it enhances insulin sensitivity and supports improved wound healing [4]. Recent studies have demonstrated an inverse relationship between levels of soluble receptors for AGEs (sRAGE) and biomarkers of atherosclerosis and metabolic syndrome, suggesting a protective role of sRAGE against these conditions [2]. Additionally, limited research indicates that higher dietary intake of AGEs is associated with elevated serum AGE concentrations, which in turn increase the risk of metabolic syndrome, diabetes, and related complications by promoting obesity, chronic inflammation, oxidative stress, insulin resistance, and endothelial dysfunction [5]. Two general mechanisms explain the biological effects of AGEs: (1) they alter the structure and, therefore, the function of proteins by crosslinking them (for instance, collagen fiber glycation in the vessel walls and skin alters the proteins' characteristics and their holding tissues). (2) AGEs increase the secretion of pro-inflammatory cytokines and oxidative stress by activating different cells through receptor and non-receptor mechanisms [6]. Endogenous formation of advanced glycation end products occurs through two main pathways: (1) the reaction between a reducing sugar and an amino group on an amino acid forms a Schiff base, which then undergoes rearrangement to form Amadori products. These intermediates subsequently generate AGEs through oxidative degradation. (2) AGEs can also form through the direct interaction of reactive carbonyl compounds with proteins, particularly targeting lysine and arginine residues [7]. However, the primary source of AGEs is exogenous. Exogenous AGEs are mainly derived from foods, particularly those cooked using high-temperature methods. The Maillard reaction contributes significantly to AGE formation by producing Amadori products during cooking techniques such as grilling, frying, or baking [8]. With modern lifestyles and shifts in societal norms

and dietary habits, the increased consumption of processed foods—often prepared at high temperatures—has emerged as a key contributor to the rising burden of AGE-related health issues [9]. As a result, there is growing interest in low-AGE diets, which has drawn the attention of physicians, patients, and even healthy individuals toward traditional dietary patterns and recommendations [10].

Traditional Persian Medicine (PM) is a temperament-based medical system that emphasizes personalized dietary and lifestyle recommendations tailored to an individual's unique constitution [11]. PM texts classify foods based on qualities such as wetness or dryness and describe specific characteristics and effects associated with each category. In this study, we aimed to offer a hypothetical interpretation of the potential relationship between PM dietary recommendations, particularly those addressing dry temperament, and the formation of AGEs, as understood in recent biomedical research.

Materials and Methods

This study presents a brief hypothetical comparative review of the concept of AGEs in conventional medicine and dry temperament in PM. To access relevant published literature, a targeted search was conducted across English and Persian language publications in databases including PubMed, Web of Science, Scopus, Google Scholar, and SID. No time restrictions were applied. Keywords used included “AGEs”, “advanced glycation end products”, “diet”, “food”, “cooking method”, “Persian medicine”, “dry temperament”, and “dry dystemperament”, along with their synonyms and Persian equivalents. To explore the PM perspective on this issue, key PM reference texts such as *Canon of Medicine*, *Zakhireh Kharazmshahi*, *Al-Shamel*, *Exir Azam*, *Makhzan-al-Adviah*, and *Kholase-al-Hikma* were reviewed. The literature and textual search continued until a sufficiently clear explanation of the concept was achieved.

Results

Dietary AGEs in conventional medicine

Exogenous AGEs are primarily formed through the non-enzymatic Maillard reaction during food processing [1]. Around 10% of dietary AGEs are absorbed from the intestinal tract into the bloodstream [6]. The majority of dietary AGEs; however, bypass intestinal absorption and reach the colon, where they may influence gut microbiota metabolism and modify gut integrity, leading to an overall pro-inflammatory impact [12]. These findings underscore the importance of the role of diet in inflammation and gut health, and modulating chronic and systemic inflammatory conditions [1,6].

The Western diet, characterized by high intake of ultra-processed foods, refined carbohydrates, and protein and fat-rich, low-fiber foods, is associated with increased inflammation in the body. Conversely, the Mediterranean diet, emphasizing fruits and vegetables, has been linked to a reduction in systemic inflammation [6]. Certain foods, particularly fats and meats, contribute to higher levels of dietary AGEs, and reducing the intake of butter, margarine, and beef can decrease exogenous AGEs; while foods like low-fat milk, lamb, fruits, vegetables, natural juice, honey, and chicken have lower AGE contents [1]. The Mediterranean diet, recognized for its health-promoting components, is associated with a lower risk of chronic diseases and physical impairments, particularly in the elderly. The study conducted by Goudarzi et al. investigated the impact of an AGE-restricted diet on individuals with metabolic syndrome. After an 8-week intervention, participants on the low-AGE diet exhibited significant decreases in mean serum levels of carboxymethyl-lysine, fasting blood glucose (FBG), homeostatic model assessment for insulin resistance (HOMA-IR), tumor necrosis factor (TNF)- α , and malondialdehyde (MDA) compared to the regular AGE diet group [5]. Studies showed that incorporating a low-AGE diet alongside a low-calorie diet effectively mitigates insulin resistance and central obesity by suppressing oxidative stress and inflammation [13]. In contrast to animal-derived foods that are rich in protein and fat and produce high amounts of dietary AGEs, diets rich in carbohydrates such as fruits, vegetables, dairy, and whole grains, contain lower amounts of AGEs [5].

The level of AGEs in foods is also influenced by the method of food processing and cooking. In the carbohydrate group, higher antioxidants, vitamins, and water content reduce the formation of new AGEs. However, crackers, chips, and cookies processed in a dry-heat setting within this category exhibited the highest level of dietary AGEs [14]. Milk-related products processed in a high moisture index setting, like yogurt and pudding, contained relatively low AGEs. Nevertheless, when combined with hot cocoa, these products showed substantially higher amounts of AGEs, emphasizing the significant role of additives in AGE formation [15].

In Uribarri's study, considering the standard serving sizes, the highest level of AGEs was related to the meat group; however, lamb contained lower dietary AGEs compared to other meats. On the other hand, cooking low-AGE meats (lean red meats and poultry) and animal-derived foods (cheese) under dry heat conditions leads to the production of higher dietary AGEs [4]. This condition is like the process of pasteurization or curing and aging processes, in which food is held at ambient room temperatures for a long time.

In a same food category, preparing food using higher temperature and lower water (such as frying, broiling, grilling, and roasting) is associated with higher dietary AGEs in comparison to same foods cooked at lower temperatures with more water (such as boiling, poaching, stewing, and steaming) [16]. Although high temperature plays a significant role in AGE production, the occurrence of glycation-oxidation reactions in the long term increases the accumulation of dietary AGEs, even at cool temperatures, at a slower rate but over time [16]. Recently, there has been a growing interest in therapeutic diets for losing weight or controlling diabetes and cardiovascular disease through high-protein, low-carb diets, but it is noteworthy that, based on the cooking method, such diets may considerably elevate dietary AGEs and consequently contribute to more health complications in the long term [17].

Dry temperament in Persian medicine

In PM, health and disease are defined in terms of the body's equilibrium, known as "temperament." Illness arises when this natural balance is disturbed, a condition referred to as "dys temperament." PM classifies temperament into nine types: hot, cold, dry, wet, hot-dry, hot-wet, cold-dry, cold-wet, and balanced. Dietary and lifestyle recommendations in PM are tailored to each individual based on their specific temperament state [11]. Various factors—such as seasonal changes, occupational activities, geographical environment, and the natural aging process—can influence an individual's temperament over the course of their life. According to PM, infancy is characterized by a relatively hot-wet temperament. As a person develops from childhood to adolescence, there is a gradual decrease in wetness and a slight increase in heat, leading to a predominantly dry-hot temperament by middle age. With advancing age, the reduction in moisture continues and dryness becomes more pronounced, resulting in a dry-cold temperament in old age [18].

When the body's temperament deviates from its balanced state—referred to as *dys temperament*—various symptoms and disorders can manifest. One common form, *dry dys temperament*, which corresponds to excess black bile humor in PM, presents with a range of clinical manifestations across different organ systems. These may include neurological symptoms such as mental stress, sleep disturbances, persistent headaches, and seizures, gastrointestinal complaints such as stomach pain and hemorrhoids, and urogenital issues including premenstrual syndrome and infertility. In more severe cases, dry dys temperament may even contribute to the development of chronic conditions including cancer, depression, diabetes, atherosclerosis, and cardiovascular disorders [11,19].

Among the various lifestyle and environmental factors influencing temperament, diet plays a particular-

ly significant role. In PM, foods are classified based on their temperamental qualities (also known as nature)—hot, cold, dry, and wet—with each property graded on a scale from 1 to 4. For example, cucumber is considered cold and wet, both in grade 2; while pepper is hot (grade 3–4) and dry (grade 3) [20]. Dietary recommendations are personalized according to an individual's temperament. Those with a balanced temperament are advised to avoid foods with extreme temperamental qualities. In contrast, individuals with dystemperament are generally advised to avoid foods that share the same temperamental qualities as their imbalance. For instance, a person with dry dystemperament should avoid foods with dry qualities and instead increase intake of foods with moist temperaments to help restore balance [21].

Foods with a dry temperament, according to PM include: very cold water, sour or salty foods, extremely hot or dry spices and additives, coffee, lentils, cabbage, eggplant, mango, certain types of fish, aged and processed foods, beef jerky, red meat (especially beef), potatoes, cured sausages, canned foods, sauces, sodas, smoked meats, dried meat slices and products with preservatives [22].

Interestingly, many of the foods considered to have a dry temperament in PM correspond to foods shown in today's studies to be high in AGEs. Foods that are processed, salted, preserved, or not fresh are known to have high AGE levels [9]. In PM, these same characteristics are understood to contribute to the dry nature of such foods [18]. PM teaches that when food loses its natural moisture—especially when it is not fresh—it becomes drier and should be avoided to prevent or treat dry dystemperament and the chronic conditions associated with it [21].

Table 1 presents a comparison between foods recommended or avoided in dry dystemperament and their respective AGE levels, based on the Uribarri study [4]. Generally, foods recommended for dry dystemperament are low in AGEs. For example, fresh fruits and vegetables, which provide moisture and help correct dryness in the body, are encouraged. In contrast, animal-derived foods—particularly red meats—are advised to be limited or avoided. While meats in general are discouraged in dry dystemperament, PM texts specifically identify beef as the most harmful in cold-dry conditions; whereas lamb is considered a better alternative [21]. This aligns with findings from Uribarri's study, which showed lamb to have the lowest AGE content among various meats [4].

An often-overlooked aspect in modern nutrition science is the impact of cooking methods on the quality and nature of food. According to PM texts, the method of cooking plays a crucial role in determining a food's temperament. In fact, the temperament of a food can significantly shift depending on how it is prepared.

Table 1. Comparing the food temperament and the amount of AGEs

Foods to be avoided in dry dystemperament [21]	AGE kU/serving [5]
Chicken	1089
Fig (dried)	799
Lamb	1096
Beef	1384
Red kidney bean	116
Sesame	1084
Olive	502
Eggplant	116
Foods to be consumed in dry dystemperament [21]	AGE kU/serving [5]
Spinach (Soufflé)	598
Pumpkin	556
Fish (Salmon)	974
Plums	50
Apple (baked)	45
Cucumber	31
Cantaloupe	20
Rice	9
Milk	12
Soup (chicken)	3

Certain cooking methods—such as frying, broiling, and grilling—are known to shift the temperament of foods toward dryness and are therefore discouraged, particularly when the goal is to prevent or manage dry dystemperament [21].

Traditionally, water-based cooking methods, such as boiling, steaming, or slow-cooking in the form of stews and soups, were the predominant styles of food preparation in Iranian cuisine. These techniques were thought to preserve or even increase the moisture content and balance of foods. However, with the growing influence of Western cooking practices, high-heat methods such as frying and grilling have become more widespread, replacing these moisture-preserving techniques in many cultures [23].

Interestingly, when we examine today's scientific literature on cooking and AGE formation, we find that the same methods criticized in PM—frying, grilling, and broiling—are associated with the highest levels of AGE production. These high-temperature, low-moisture methods accelerate the Maillard reaction, which contributes to AGE formation. Conversely, cooking methods that involve higher moisture and lower temperatures, such as boiling or steaming, are associated with lower AGE levels [4, 21].

Table 2 compares the effects of various cooking methods on a single ingredient, demonstrating that methods considered "drying" in PM correspond with those that produce higher AGEs in scientific studies. This alignment supports the PM recommendation to avoid low-moisture, high-temperature cooking methods in

order to reduce dietary dryness and limit AGE intake. For example, frankfurter beef—a type of processed beef containing additives—has been shown to contain a higher amount of AGEs compared to unprocessed beef, even when both are prepared using the same cooking method, such as boiling [4]. This observation is consistent with the perspective of PM, which holds that processed foods, particularly those containing additives, tend to shift further toward dryness in temperament [21].

Discussion

The importance of cooking methods in today's diet is often underestimated. However, in PM, significant emphasis is placed on how cooking techniques affect the temperament of food. The cooking process can alter the food's inherent properties: water-based methods tend to shift food toward a wet temperament; while dry preparation methods or those involving high heat can push food toward dryness [21]. As a result, PM recommends avoiding cooking methods such as frying, grilling, and toasting, as they are believed to cause dryness in the body. On the other hand, water-based methods—such as stewing, poaching, steaming, and boiling—are advised for individuals with dry dys temperament [20]. These recommendations are consistent with the findings of Uribarri's study on AGE production, which highlights how different cooking methods

impact AGE levels in food [4].

With the rise of chronic diseases such as diabetes, cardiovascular disease, and kidney disease—conditions often associated with aging—health experts now advocate for the inclusion of foods with higher moisture content, particularly through water-based cooking methods like stews and soups, especially in the diets of the elderly [23]. This approach also aligns with PM principles, supporting the prevention of dry dys temperament through food preparation methods that help maintain moisture and balance. Moreover, new evidence regarding AGE content further reinforces this preventive strategy [24].

A key aspect of the PM diet for preventing dry dys temperament is avoiding salted, dried, and aged foods, such as salted meat, bacon, sausage, salted fish, aged cheeses, and canned foods [18]. According to Uribarri's study, such processed foods, due to their high additive content, can drastically increase AGE levels [4]. An example of what occurs during dry imbalance in the body is the formation of atherosclerotic plaques, which can be understood from both modern medical and PM perspectives. In Avicenna's *Canon of Medicine*, calcified plaques in the arteries are attributed to the accumulation of abnormal black bile, a condition linked to dry dys temperament. Under normal conditions, black bile plays a role similar to that of minerals like calcium in bones. However, when in excess, it

Table 2. Relationship between AGE content of foods prepared using different cooking methods and their associated temperament in Persian medicine

Raw material	Cooking method	AGE kU/serving [4]	Effect on food temperament based on PM
Beef	Broiled in 230° C, within 5 minutes	10,143	Shift towards dry
	Pan fried in olive oil	9,052	Shift towards dry
	Stir fried in canola oil within 15 min	8,570	Shift towards dry
	Frankfurter beef (sausage) Boiled in 100° C	6,736	Shift towards dry
	water within 7 min		
	Roasted	5,464	Shift towards dry
	Stewed	2,199	Shift towards wet
Chicken	Boiled after 10 minutes marinated with lemon juice	1,384	Shift towards wet
	Roasted then barbequed	16,668	Shift towards dry
	Roasted	10,034	Shift towards dry
	Fried in olive oil within 8 minutes	6,651	Shift towards dry
	Pan fried within 13 minutes	4,875	Shift towards dry
	Stir fried in canola oil within 7 minutes	3,726	Shift towards dry
	Potted (cooked in liquid) with onion and water	2,996	Shift towards wet
Potato	Potted within 1 hour	1,351	Shift towards wet
	Boiled with lemon	861	Shift towards wet
	French fries	1,522	Shift towards dry
	Roasted within 45 minutes with 5 milliliters oil/serving	218	Shift towards dry
Egg	Boiled within 25 minutes	17	Shift towards wet
	Fried	1,237	Shift towards dry
	Pan with low heat in corn oil within 12 minutes	67	Shift towards dry
	Scrambled in pan with low heat in olive oil within 2 minutes	29	Mild shift towards dry
	Poached below simmer within 5 minutes	27	Shift towards wet

can deposit in inappropriate areas, such as the arteries, contributing to the rigidity and reduced elasticity of blood vessels. This process leads to the development of atherosclerosis [11, 25].

On the other hand, based on the current studies, accumulation of AGEs in the body plays a pivotal role in the development of atherosclerotic lesions. Research has shown a causal link between the AGE-RAGE-NF-kappa B axis in atherogenesis, suggesting that targeting various sites of AGE production could disrupt this cycle [26].

Studies recommend a low-AGE diet to prevent chronic inflammatory conditions. This approach includes three main strategies: (1) modifying cooking techniques to reduce AGE intake, such as lowering cooking temperatures, increasing moisture, and using specific pH levels and cooking surfaces; (2) increasing the consumption of polyphenol- and antioxidant-rich foods, particularly fresh fruits and vegetables; and (3) incorporating healthy food additives, such as herbs and spices, that have anti-glycation effects [5, 6]. While not exclusively plant-based, the low-AGE diet emphasizes fruits, vegetables, and healthier cooking methods, especially for animal-derived foods.

In PM, dry dystemperament is believed to be a contributing factor in the development of various chronic conditions. Accordingly, dietary recommendations are centered around avoiding both foods and cooking methods that aggravate this imbalance. Foods in PM are categorized based on their temperamental qualities—hot, cold, dry, and wet—with the goal of restoring balance through appropriate dietary choices. For individuals with dry dystemperament, increasing the intake of foods with a wet temperament is advised, with most fruits and vegetables falling into this category.

Moreover, water-based, low-heat cooking methods—such as boiling, steaming, and stewing—are considered beneficial, as they help shift the temperament of food toward wetness. In contrast, high-heat, dry methods like frying, grilling, and baking are thought to increase the dryness of food and should be avoided in such cases. In addition, aged or preserved foods—including old cheeses and salted, dried, or smoked meats—are classified as having a dry temperament and are discouraged in individuals with dry dystemperament [22].

Limitations

This study presents a hypothetical, comparative brief review of recent scientific evidence and PM texts, aiming to explore potential parallels between the conventional medical concept of AGEs and the PM theory of dry temperament. However, it does not establish a definitive or causal relationship between these two frameworks. One notable limitation was that the foods

traditionally recommended in PM for managing dry dystemperament did not always align with the specific items analyzed for AGE content in recent biomedical studies. This mismatch limited the number of directly comparable data points.

For future interventional research, it is recommended to select specific foods from PM sources based on their traditional indications and subject them to laboratory analysis to quantify their AGE content under standardized conditions. Additionally, inconsistency in the methodologies used to assess AGE levels in foods presents another challenge. For instance, one study may describe beef as “boiled at 100°C for 7 minutes,” while lamb may be reported as “boiled for 1 hour with lemon juice.” Such methodological heterogeneity underscores the need for standardized cooking protocols and food categorization in AGE-related research.

Although this study aimed to highlight potential associations between PM concepts and modern biomedical findings, the proposed connections remain speculative and require further empirical investigation to be validated.

Conclusion

High dietary intake of AGEs has been consistently linked to elevated circulating AGE levels, contributing to various adverse health conditions. Persian Medicine recommendations align closely with recent findings on AGEs, particularly in the context of mitigation of the dry dystemperament and its associated health problems. The notable parallels between foods high in AGE content and those associated with dry temperament in PM raise the hypothesis that these two frameworks may reflect similar underlying mechanisms in some respects. Although this connection remains speculative and requires further empirical validation, the extensive body of knowledge in PM—including dietary recommendations, lifestyle modifications, and descriptions of physical and psychological changes related to dry dystemperament—may offer valuable insights for generating new hypotheses in AGE research.

The alignment between PM's traditional dietary guidance and recent findings on AGE-related health impacts presents a promising direction for future studies. This could ultimately contribute to more comprehensive and culturally informed dietary strategies for the prevention and management of chronic inflammatory diseases.

Conflict of Interests

None.

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None.

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