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# The effects of seeds with hot and cold temperaments on serum thyroid hormones, corticosterone and urine vanillylmandelic acid concentrations of healthy rats

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ABSTRACT

*Ethnopharmacological relevance:* Hot and cold temperaments are the basic concepts of Iranian traditional medicine (ITM). Nevertheless, studies on the functional mechanisms of medicinal herbs based on hot and cold temperaments are not very extensive. This study aimed to evaluate the effects of diets containing hot or cold temperament seeds according to ITM on some hormonal and neuromediator parameters with a regulatory role in thermogenesis and energy metabolism in acute (24 hr) and subacute (7-day) experiments that were performed on rats.

*Materials and methods:* Each experiment was performed on 42 male Wistar rats, which were randomly divided into 7 groups. while 1 group received usual diet (controls), 6 other groups were fed with a diet containing 10% seeds, namely, anise, fennel, or ajowan (hot temperament groups) or cucumber, pumpkin, or watermelon (cold temperament groups), respectively. The levels of the rats' serum free thyroxin (FT4), free triiodothyronin (FT3), triiodothyronin (T3), thyroxin (T4), corticosterone and urine vanillylmandelic acid (VMA) were analyzed.

*Results:* After 24 hours, a significant decrease in FT3 was observed in groups that were fed anise or fennel seeds. However, a significant increase in T3 was observed in the ajowan seed-fed group, and no changes in other parameters were observed in this group. On the 7th day, FT4 was significantly increased in fennel seed-fed group; T3 was significantly increased in the anise, fennel, ajowan and watermelon seed-fed groups; corticosterone was significantly increased in the watermelon and pumpkin seed-fed groups; and VMA was significantly increased in the fennel seed-fed group and significantly decreased in the cucumber seed-fed group.

*Conclusion:* Alterations induced by hot and cold temperament seeds in measured hormonal and neuromediator levels that have a regulatory role in thermogenesis and the body's energy metabolism revealed that hot and cold temperament characteristics of studied seeds may most likely be related to their intervention in the body's energy metabolism, in that hot temperament seeds may increase energy metabolism and cold temperament ones may decrease it.



## 1. Introduction

According to Iranian traditional medicine (ITM) manuscripts, four elements of fire, air, water and soil are essential constituents of human and nonhuman beings. Each of these elements has a pair of qualities consisting of warmness or coldness, and wetness or dryness. Fire is warm and dry, air is warm and wet, water is cold and wet, and soil is cold and dry. Temperament (nature or mizaj) as a main concept in ITM means a quality/qualities produced by interaction of opposite qualities of small particles that exist in the mentioned elements. In this concept, each person and even each medicine has its own specific temperament (or temperaments) that falls into one of three categories of simple (hot, cold, wet, and dry), complex (hot-dry, hot-wet, cold-dry, and cold-wet) or moderate (equal quantity of elements) (Ahvazi, 2009).

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Temperament as a basic concept exists in other traditional medical theories as well, including Unani (Greek), Arabic, Roman, Indian, European and Chinese traditional medicines (Shahabi et al., 2008). Based on the ITM's principles, occurrence of an imbalance in the body's temperament leads to the onset of disease condition, and from that point on, treatment is based on restoring the balanced state of the body using medicines with opposite temperament (Avicenna, 2010a).

In ITM, the term "nature" has been used for several meanings and concepts; in one specific concept, it is believed that nature (Qovveh modabbereh) keeps the body healthy and helps cure diseases; in fact, using medicines or foods aids patients' nature to return to its healthy condition (Ibn Hindu, 1990). Traditional physicians considered nature's functions in accordance with natural affairs (Umoor-e-Tabee-ye) (Aghilikhorasani, 2007**).** Natural affairs are principles on which the body's existence and consistency are based and consist of seven factors including elements (Arkan), temperament (Mizaj), humors (Akhlat), organs (Azaa), spirits (Arvah), forces (Quwa), and functions (Af'al) (Arzani, 2013).

Maintenance of a relatively stable internal environment is termed homeostasis (homeo means "the same"; stasis means "to stand or stay"). Physiologists believe that several body systems using specific mechanisms and functions contribute to maintain homeostasis. When any factor (external or internal) starts to move the internal environment away from optimal conditions, the body's systems initiate appropriate counteractions to minimize the change. For example, when working out, there is a production of extra heat that tends to raise the body temperature, and the body responds by sweating (Sherwood, 2010).

Because nature (Qovveh modabbereh) focuses on the integrity of the human body and is featured as a self-controlled system, which is close to the concept of homeostasis, it can be postulated that medicines with hot and cold temperaments contribute to restore the balanced state or homeostasis of the body.

There are few studies that have investigated the ITM theory of hot and cold temperaments affecting homeostasis. A study by Shahabi et al. (2008) showed that hot temperament persons had a more active sympathetic nervous system; a less active parasympathetic nervous system; adrenal corticosteroid and adrenal sympathetic activities; and a higher rate of deviation of the immune system toward T-helper 2 responses in comparison with cold temperament persons. In our previous study, hot temperament seeds decreased food intake and weight gain and increased serum glucose levels with no significant differences in water consumption and urine output compared to cold temperament seeds in healthy rats (Parvinroo et al., 2014).

Mostafavi (2005) believed that hot temperament people have higher basal metabolic rate in comparison to cold temperament people. He also compared properties of hot and cold temperament persons with thyroidal dysfunction symptoms and signs and suggested that cold temperament persons show hypothyroid symptoms such as hypothermia; however, hot temperament people have hyperthyroid symptoms such as hyperthermia. Hypothermia and hyperthermia are related to imbalanced heat production, thermogenesis, and energy homeostasis.

Thyroid hormone is the major regulator of thermogenesis and works synergistically with the sympathetic nervous system (SNS) in homeothermic species (Silva, 2006). T3 is the most metabolically active thyroid hormone (Kelly, 2000) and increases energy metabolism, heat production and thermogenesis (Silva, 1995; Kim, 2008). The SNS and the adrenal medulla are considered to be the two parts of a system, called sympathoadrenal system. Norepinephrine is the main SNS neurotransmitter, and epinephrine is predominantly synthesized in the adrenal medulla. Assessment of sympathoadrenal system activity has usually been based on the measurement of catecholamines in urine and plasma (such as epinephrine and norepinephrine). The SNS has a critical role in mammalian thermogenesis when exposed to cold and dietary intake (Landsberg and Young, 1983). Glucocorticoids also have complex effects on thermogenesis and temperature homeostasis. It is not a primary function of these hormones to increase thermogenesis but rather to coordinate thermogenic responses to substrate or food availability (Silva, 2006). Corticosterone (the major glucocorticoid in rodents) has been shown to be essential for the maintenance of body temperature during cold stress (Maickel et al., 1967). Studies show that corticosterone can lead to impaired energy metabolism in rat liver (Jani et al., 1991) and brain mitochondria (Katyare et al., 2003).

The objectives of this study were to assess the differences between the effects of seeds with hot-dry and cold-wet temperaments on several neuro-hormonal parameters with a regulatory role in thermogenesis and energy metabolism. In this study, the effects of three hot temperament seeds including fennel (*Foeniculum vulgare* Mill.), anise (*Pimpinella anisum* L.), and ajowan (*Trachyspermum ammi* [L.] Sprague) from the family Apiaceae and three cold temperament seeds including watermelon (*Citrullus lanatus* [Thunb.] Matsum. & Nakai), pumpkin (*Cucurbita pepo* L.) and cucumber (*Cucumis sativus* L.) from the family Cucurbitaceae on serum free thyroxin (FT4), free triiodothyronin (FT3), triiodothyronin (T3), thyroxin (T4), corticosterone (the major glucocorticoid in rodents) and urine vanillylmandelic acid (VMA) as the principal end-product of epinephrine and norepinephrine in healthy rats after feeding periods of 24 h (acute study) and 7 days (subacute study) are investigated. Because hot and cold qualities have been considered as principal qualities in ITM manuscripts (Avicenna, 2010a), in this study, we describe the studied seeds' temperaments in two categories of hot and cold. Names and

**Table 1**
Names and traditional uses of seeds with hot and cold temperaments.

| Scientific name | Family | Common name | Traditional name | Traditional uses |
|---|---|---|---|---|
| *Foeniculum vulgare* Mill. | Apiaceae | Fennel | Razianaj | Strengthening eye-sight, increasing milk secretion, lithotrity, diuretic, emmenagogue, carminative, and treating nausea and chronic diarrhea. |
| *Pimpinella anisum* L. | Apiaceae | Anise | Anisun | Cough, dyspnea, increasing milk secretion, lithotrity, diaphoretic, emmenagogue, diuretic, aphrodisiac, carminative, and treating halitosis, hemorrhoid, diarrhea, borborygmus, cold headache and vertigo. |
| *Trachyspermum ammi* (L.) Sprague | Apiaceae | Ajowan | Nankhah | Increasing milk secretion, diaphoretic, diuretic, emmenagogue, carminative and treating paralysis, trembeling, hiccough, vomiting, nausea, severe dyspepsia, kidney and bladder stones, and borborygmus. |
| *Cucurbita pepo* L. | Cucurbitaceae | Pumpkin | Qar | Fattening and treating hemoptysis, cough, fever, bladder and intestinal ulcers,and dysuria. |
| *Citrullus lanatus* (Thunb.) Matsum. & Nakai | Cucurbitaceae | Watermelon | Bettikh hendi | Fattening and treating hemoptysis, cough, fever, bladder and intestinal ulcers, and dysuria. |
| *Cucumis sativus* L. | Cucurbitaceae | Cucumber | Qathad | Diuretic and treating dysuria, spleen and liver tumefaction, and fever. |