

Effect of Spearmint (*Mentha spicata* Labiatae) Teas on Androgen Levels in Women with Hirsutism

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Mentha spicata Labiatae, known as spearmint and *Mentha piperita* Labiatae, known as peppermint can be used for various kinds of illnesses in herbal medicine and flavoring in industry. *M. spicata* Labiatae grows on the Anamas plateau of Yenişarbademli town of Isparta, located in southwest part of Turkey. In this town, clinicians thought that consumption of tea steeped with *M. spicata* or *M. piperita* caused a diminished libido. Because antiandrogenic effects of spearmint and peppermint were found previously in rats, it was decided to observe the effect of this herbal tea on the androgen levels in hirsute women.

Twenty-one female hirsute patients, 12 with polycystic ovary syndrome and 9 with idiopathic hirsutism were included to the study. They were took a cup of herbal tea which was steeped with *M. spicata* for 5 days twice a day in the follicular phase of their menstrual cycles. After treatment with spearmint teas, there was a significant decrease in free testosterone and increase in luteinizing hormone, follicle-stimulating hormone and estradiol. There were no significant decreases in total testosterone or dehydroepiandrosterone sulphate levels. Spearmint can be an alternative to antiandrogenic treatment for mild hirsutism. Further studies are needed to test the reliability of these results and the availability of spearmint as a drug for hirsutism. Copyright © 2007 John Wiley & Sons, Ltd.

Keywords: *Mentha spicata*; androgens; hirsutism; women.

INTRODUCTION

Mentha, a member of the Labiatae family, originates from Eastern Asia and there are two major forms, *Mentha piperita* Labiatae (peppermint) and *Mentha spicata* Labiatae (spearmint). The historical use of mentha is not different from its use in modern herbal medicine. *Mentha* can be used for common cold, cough, sinusitis, fever, bronchitis, nausea, vomiting, indigestion, intestinal colic and loss of appetite (Starburck, 2001).

Spearmint is a common constituent of the Indian and Eastern Asia diet. It is used with spices to give the food a special flavor and fragrance. It is also used for flavoring chewing gums, toothpaste, confectionery and pharmaceutical preparations (Saleem *et al.*, 2000). Spearmint essential oil is a common constituent in hygiene and cosmetic products, and substantial amounts are used in the food and beverage industries (Spirling and Daniels, 2001). In countries of the Middle East and Africa, the dry or fresh leaves of spearmint are added during the brewing of tea, where it provides a pleasant aroma and refreshing taste. The ancient Romans believed that the smell of mint 'stirred the mind and the taste to a greedy

desire of meat' (Fabre, 2003), a historical perspective that is interesting in the light of the present-day understanding of the mutagens formed during the cooking of meat (Sugimura *et al.*, 2004). There was an investigation that confirmed that spearmint had significant inhibitory effects against the cooked meat heterocyclic amine mutagen both *in vitro* and *in vivo* (Yu *et al.*, 2004).

M. spicata Labiatae is 30–100 cm long and has a strong odor. It has smooth or gray haired leaves. Its flowers are pale blue and collected at the edges of the branches as a long and narrow spike. *M. spicata* contains about 0.21–2.1% volatile oil, 29–74% carvone, 4–24% limonene and 3–18% cineole. Carvone is the most important constituents of *M. spicata*. It likes humidity and dark places. *M. spicata* grows on the Anamas plateau of Yenişarbademli town of Isparta, located in southwest part of Turkey, this plateau is rainy and 1800–2400 m above sea level (Akdogan *et al.*, 2004; Baser, 1993).

Clinicians have investigated whether the men who live in Yenişarbademli town have been admitted to the hospitals with the complaints of diminished libido. They thought that daily consumption of four cups of tea steeped with *M. spicata* or *M. piperita* caused diminished libido.

Previously the effects of *M. piperita* and *M. spicata* herbal teas on testicular function were investigated in an experimental rat model and found that testosterone levels were decreased (Akdogan *et al.*, 2004b). Because the antiandrogenic effects of spearmint were found, it was decided to observe the effect of this herbal tea on the androgen levels in hirsute women.

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Contract/grant sponsor: FOFOI-IMSS; contract/grant number: 2002/097.

Hirsutism is defined medically as excessive terminal hair that appears in a male pattern in women (Rosenfield, 2005). About 5% of women of reproductive age in the general population are hirsute, as indicated by a score of 8 or more on the Ferriman–Gallwey scale, which quantitates the extent of hair growth in the most androgen sensitive sites (Rosenfield, 2005). Hirsutism results from an interaction between the androgen level and the sensitivity of the hair follicle to androgen.

This is the first ever study to test the antiandrogenic activity of spearmint in women with hirsutism.

MATERIALS AND METHOD

Patients. Twenty-one female patients who were admitted to the endocrinology outpatient clinic complaining of hirsutism were included in the study. The mean ages of the patients were 22.2 ± 6.2 (18–40) years old. The degrees of the hirsutism of the patients were scored with the modified Ferriman-Gallwey scoring by the same physician. The scores of patients were in the range 8–23 (maximum score: 36). Twelve of the hirsute patients were diagnosed as having polycystic ovary syndrome (PCOS) and other nine were diagnosed as idiopathic hirsutism. Prior to enrollment in the study, all subjects provided written informed consent. They were took a cup of (250 mL) herbal tea which was steeped with *M. Spicata* (% 20 g/L) twice a day for 5 days during the follicular phase of their menstrual cycle.

Preparations of herbal teas. The herbal teas were made by pouring 250 mL (a cup of) boiling water over 1 heaped U.S. teaspoon (5 g) of the dried leaves and steeping for 5 to 10 min. All teas were prepared daily.

Biochemical examinations. Fasting blood samples were taken from all patients for evaluating the biochemical and hormonal status in the follicular phases of menstrual cycles. The blood samples (10 mL) were collected into K₃EDTA tubes from each of the patients after a 12 h overnight fast. The blood was separated by centrifugation at 3000 rpm for 10 min after standing

at room temperature for 15 min. The total testosterone (TT), luteinizing hormone (LH), follicle-stimulating hormone (FSH), dehydroepiandrosterone sulphate (DHEAS) and estradiol (E₂) levels were determined from plasma by using the Architect® System Chemiluminescent Microparticle Immunoassay (CMIA) method. The free testosterone (FT) levels were determined by Biosource Radio Immune Assay (RIA) method. Biochemical parameters including fasting plasma glucose (FPG), AST, ALT, total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol were determined using commercial kits. After 5 days all the biochemical and hormonal analysis were repeated.

Statistical analysis. The Statistical Package of Social Sciences version, 'SPSS 9.05 for Windows' statistical software was used for statistical analysis. The data are presented as the mean \pm SEM. Statistical significance was tested by dependent paired-*t* test. A probability value of less than 0.05 ($p < 0.05$) was considered as statistically significant.

RESULTS

After 5 days of the treatment with spearmint teas, there was a significant decrease in FT (from 5.49 ± 2.94 to 3.92 ± 2.80 pg/mL $p < 0.05$), and a significant increase in LH (from 6.34 ± 4.53 to 8.04 ± 5.14 mIU/mL $p < 0.05$), FSH (from 4.56 ± 1.49 to 5.36 ± 1.84 mIU/mL $p < 0.05$) and E₂ (from 46.50 ± 29.01 to 63.43 ± 47.57 pg/mL $p < 0.05$). There were no significant decreases in TT and DHEA-S levels (Table 1). In the biochemical parameters there was a significant decrease only in triglyceride (from 95.90 ± 42.29 to 86.42 ± 39.10 mg/dL $p < 0.05$) levels (Table 2).

DISCUSSION

Mentha tea is generally considered as a safe drink for regular consumption (Wichtl, 1994). Spearmint has been in use for centuries by country doctors for curing many

Table 1. Pre- and post-treatment TT, FT, LH, FSH, E₂ and DHEA-SO₄

	TT (ng/mL)	FT (pg/mL)	LH (mIU/mL)	FSH (mIU/mL)	E ₂ (pg/mL)	DHEA-S (μg/L)
Pre-treatment ($n = 21$)	0.75 ± 0.40	5.49 ± 2.94	6.34 ± 4.53	4.56 ± 1.49	46.50 ± 29.01	189.41 ± 92.73
Post-treatment ($n = 21$)	0.67 ± 0.35	3.92 ± 2.80^a	8.04 ± 5.14^a	5.36 ± 1.84^a	63.43 ± 47.57^a	192.60 ± 88.02

^a $p < 0.05$.

TT, total testosterone; FT, free testosterone; LH, Luteinizing hormone; FSH, follicle-stimulating hormone; E₂, estradiol; DHEAS, dehydroepiandrosterone.

Table 2. Pre- and post-treatment FPG, AST, ALT, TC, TG, HDL and LDL

	FPG (mg/dL)	AST (U/L)	ALT (U/L)	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (m/dL)
Pre-treatment ($n = 21$)	94.57 ± 12.68	17.14 ± 5.69	15.47 ± 6.91	173.23 ± 25.82	95.90 ± 42.29	49.04 ± 15.16	105.98 ± 19.13
Post-treatment ($n = 21$)	91.47 ± 11.16	17.61 ± 7.15	15.61 ± 7.42	170.42 ± 31.63	$86.42 \pm 39.10^*$	48.80 ± 14.44	101.00 ± 21.98

^a $p < 0.05$.

FPG, fasting plasma glucose; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TC, total cholesterol; TG, triglyceride; HDL, high density lipoprotein; LDL, low density lipoprotein.

diseases; three or four cups daily between meals can relieve gastrointestinal complaints. This herb is considered stimulant, carminative and antispasmodic (Bhattacharjee, 1998). It has been found to possess antidote properties for poisons. It has been reported as a remedy for inflammation, fevers, bronchitis, infantile troubles, vomiting in pregnancy and hysteria (Kapoor, 1990; Saleem *et al.*, 2000).

In spite of its useful features, it has also some toxic and adverse effects. Contact allergy to the leaves of *Mentha spicata* has been reported, and cases of contact cheilitis from its essential oil, as toothpaste flavoring, have been described. The main allergens appear to be carvone and limonene (Bonamonte *et al.*, 2001; Paulsen *et al.*, 1993; Skrebova *et al.*, 1998). Spearmint and peppermint tea can cause iron deficiency anemia. Impaired non-heme iron absorption is the major cause of iron deficiency, and potent inhibitors of absorption are phytic acid or the polyphenol compounds found in many plants (Charlton and Bothwell, 1983). Polyphenol compounds are widely present in the human diet as components of fruits, vegetables and spices; they are especially high in tea, coffee, red wine, cocoa and other herbal teas (Hurrell *et al.*, 1999).

Previously, it was found that hepatotoxicity and nephrotoxicity occurred after the administration of *M. piperita* and *M. spicata* in rats and the damage seemed to be dose dependent (Akdogan *et al.*, 2003; Akdogan *et al.*, 2004a). Also, the adverse effects of *M. piperita* and *M. spicata* herbal teas on male reproductive functions were investigated in an experimental rat model (Akdogan *et al.*, 2004b). It was found that the consumption of *M. piperita* and *M. spicata* tea decreased plasma testosterone and increased plasma LH and FSH levels and affected spermatogenic activity in rats. Histological examinations also revealed extensive degenerative changes in the germinal epithelium and spermatogenesis arrest in the testicular biopsies in relation to the dose. Despite the beneficial effects of *M. piperita* and *M. spicata* in digestion, people should also be aware of their adverse effects when not used in the recommended fashion or at the recommended dose. The exact factor in the mentha that causes these effects is not known (Akdogan *et al.*, 2004b).

Before planning this study, it was observed that some male patients who live in Yenişarbademli town were admitted to hospitals with complaints of diminished libido after daily consumption of four cups of tea steeped with *M. spicata* or *M. piperita*. Therefore this study investigated the effect of spearmint tea on the androgen level in female patients with hirsutism and a significant decrease in FT levels was found.

It was hypothesized that treatment with some drugs and herbal medicines could result in decrements in endogenous steroid hormones such as testosterone known to be metabolized at least partly by hepatic microsomal enzymes, cytochrome P450 (CYP) 3A4.5. It is recognized that synthetic medications known to induce CYP3A4 activity such as carbamazepine have been found to alter the blood concentrations of a number of steroid sex hormones (Rattya *et al.*, 2001; Stoffel-Wagner *et al.*, 1998). Accordingly, spearmint, a potential inducer of CYP3A4 (Dresser *et al.*, 2002), might also produce similar changes in the concentrations of endogenous androgenic steroid hormones. A significant decrease in FT levels was found after the consumption of spearmint tea. This result may be due to induction of CYP3A4 or a direct effect of spearmint on the synthesis of androgenic hormones.

In the blood, about 2% of testosterone is free and 44% is bound to SHBG. The level of SHBG is increased by estrogens and decreased by normal testosterone administration (Griffin, 2003). In this study it was found that after spearmint tea consumption, there was a significant decrease in FT levels, without decreases in TT levels, perhaps due to an increase in SHBG levels.

The patients took spearmint teas in the follicular phase of their menstrual cycles. In the menstrual cycle FSH, LH and E2 levels increased progressively from menstrual phase to ovulation. In this study, the increase of these hormones levels after the post-treatment period could be due to physiological changes of the menstrual cycle.

A significant decrease in triglyceride levels was found after the consumption of spearmint tea in hirsute women. Women with endogenous hyperandrogenism often have high triglyceride levels associated with insulin resistance and obesity. Partial androgen suppression or the pure antiandrogen treatment with flutamide in PCOS results in no change in insulin resistance or lipoprotein levels, indicating that lipoprotein abnormalities are due to insulin resistance and not to the androgen levels (Vrbikova *et al.*, 2004; Wild *et al.*, 1992). However, another report demonstrated that treatment with flutamide may improve the lipid profile and that this effect may be due to a direct inhibition of androgenic actions (Diamanti-Kandarakis *et al.*, 1998).

Therapy for hirsutism should be directed toward abnormal androgen levels. Hormonal therapies act by either suppressing androgen production such as oral contraceptives or blocking the action of androgens such as spironolactone (Rosenfield, 2005). Spearmint can be an alternative to antiandrogenic treatment for mild hirsutism. However, further studies are needed for testing the reliability and availability of spearmint as a drug for hirsutism.

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