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The effect of a single dose of the Thermo Speed Extreme (Olimp) thermogenic supplement on circulatory functions and body temperatures at rest in male and female subjects

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Abstract

Background: The purpose of the study was to examine the impact of a single dose of the Thermo Speed Extreme (TSE) supplement on circulatory functions at rest and body temperatures in men and women. Material and methods: Twenty-five (male and female) subjects volunteered to participate in this study. Prior to the experiment, the anthropometric characteristics, internal and skin temperatures, the heart rate and blood pressure were measured. Then, the subjects took a single dose of the TSE or placebo (PLA) supplement in a double-blind, randomised, cross-over design. Following the supplement consumption, the same physiological parameters were registered in a seated position for 6 h. Results: Statistical analysis revealed significant effects of supplement × time × sex interactions on the cardiovascular system functions. There was no significant influence of TSE on internal temperature. There was a significant effect of gender on skin temperatures and significant correlations between changes in skin temperatures and Δ SBP after TSE consumption in females. Conclusions: The single dose of TSE has an effect on the circulatory and thermoregulatory systems, although the strength of this effect is sex depended. This can be expected to be due to the sex-dependent differences in skin vessels reactivity to components present in the product.

Keywords

thermogenic supplement, gender, body temperatures, circulatory functions

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The effect of a single dose of the Thermo **Speed Extreme (Olimp) thermogenic** supplement on circulatory functions and body temperatures at rest in male and female subjects

Authors' Contribution:

- A Study Design
- **B** Data Collection
- C Statistical Analysis
- **D** Data Interpretation
- E Manuscript Preparation
- F Literature Search
- **G** Funds Collection
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abstract

Background:

The purpose of the study was to examine the impact of a single dose of the Thermo Speed Extreme (TSE) supplement on circulatory functions at rest and body temperatures in men and women.

Material and methods:

Twenty-five (male and female) subjects volunteered to participate in this study. Prior to the experiment, the anthropometric characteristics, internal and skin temperatures, the heart rate and blood pressure were measured. Then, the subjects took a single dose of the TSE or placebo (PLA) supplement in a double-blind, randomised, cross-over design. Following the supplement consumption, the same physiological parameters were registered in a seated position for 6 h.

Results:

Statistical analysis revealed significant effects of supplement x time x sex interactions on the cardiovascular system functions. There was no significant influence of TSE on internal temperature. There was a significant effect of gender on skin temperatures and significant correlations between changes in skin temperatures and Δ SBP after TSE consumption in females.

Conclusions:

The single dose of TSE has an effect on the circulatory and thermoregulatory systems, although the strength of this effect is sex depended. This can be expected to be due to the sex-dependent differences in skin vessels reactivity to components present in the product.

Kev words:

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INTRODUCTION

The use of dietary supplements with a high proportion of bioactive substances with a thermogenic effect has increased in recent years in various social groups, which is probably due to a desire for rapid reduction in body fat and weight [1]. Thermogenics are substances that increase the metabolic rate (by approx. 4-5%), accelerate the metabolism of fats (by approx. 10-16%) and are conducive to weight reduction [2]. The effect of thermogenic substances is based on increasing the activity of the sympathetic nervous system. The more popular substances that meet the criteria of thermogenic agents (i.e. increase the rate of metabolic processes shortly after administration [3], the amount of generated heat and, under certain conditions, body temperature [4, 5]) include: caffeine, synephrine, ephedrine, green tea, garcinia cambogia, yohimbine, yerba maté and capsaicin [6, 7]. Many of these substances have been investigated to determine their quantitative and qualitative effects on metabolism, but some of them have been withdrawn due to adverse reactions triggering excessive stimulation of the cardiovascular function [8-11] associated with increased blood pressure, heart rate and other effects connected with strong stimulation of adrenergic receptors (AR) [12, 13].

Commercial supplement Thermo Speed Extreme (Olimp company) is a combination of, among others, L-tyrosine, green tea extract (catechin), bitter orange extract (synephrine), caffeine, guarana extract and black pepper (piperine). All these components of the "Thermo speed" supplement are known as plant additives inducing thermogenesis in vivo [14]. The mechanism of their activity utilises the enhanced activity of the sympathetic nervous system (SNS) by increasing the production and release of noradrenaline and prolonged stimulation of adrenergic receptors [15, 16]. Therefore, these substances show similarity to the activity of sympathomimetic drugs, AR-receptor agonists [16], and their thermogenic effect may be stronger when they are taken together [1].

Significant differences were found in pharmacodynamics, pharmacokinetics and interactions between different pharmacological substances in women and men [17, 18]. In addition, women are characterised by lower activity of sympathetic nerves and weaker transduction of sympathetic signalling and its involvement in regulating the tension of the blood vessel muscularis than men [19]. Vascular reactivity is similar in two phases of a normal menstrual cycle in Caucasian women [20]. Men show greater reactivity of blood vessels to noradrenaline than women do, perhaps due to the lack of protective effects involving oestrogen and increased adrenergic activity [18, 20, 21].

The results of previous studies conducted on men and women concerning the assessment of the thermogenic effects accompanying the consumption of various bioactive plant substances are insufficient. Researchers have used different preparations, their different doses and combinations of bioactive agents, and they have assessed changes in the metabolic rate, the use of fats and changes in the cardiovascular function. Less frequently, changes in body temperature have been analysed in these studies [22, 23]. Therefore, it seems reasonable to determine the effectiveness of a single dose of the TSE supplement on hemodynamic and body temperature characteristics in men and women, especially as women are most likely to use thermogenic dietary supplements in order to reduce their weight and body fat content.

In view of the above, the purpose of the present study was to determine the circulatory reaction and the temperature characteristics of the body after administration of

a single dose of TSE and to investigate whether there are gender differences in the body's responses to the administered supplement, as manifested by changes in the above functions.

MATERIAL AND METHODS

SUBJECTS

The study involved a randomised group of healthy, non-smoking students (13 women, 12 men) aged 20–27 years. The inclusion criteria were as follows: a daily intake of caffeine < 150 mg, consumption of a mixed diet for 3 days prior to the experiment, regularity of the menstrual cycle, the follicular phase of the cycle (i.e. 1st-9th day of the cycle) (in females). The test exclusion criterion was being diagnosed with metabolic diseases and cardiovascular dysfunctions. The somatic characteristics of the studied males and females are shown in Table 1. Statistical analysis of the examined characteristics showed that both groups were significantly different in body weight, basal metabolic rate (BMR), fat free mass (FFM) and body surface area (BSA).

The study protocol was approved by the Bioethics Commission at the Jerzy Kukuczka Academy of Physical Education in Katowice (No 4/2013).

Table 1. Subjects' characteristics

| Variables | Females | Males |
|--------------------------------|------------|-----------|
| Age | 23 ±1.6 | 23 ± 1 |
| Body mass (BM) [kg] * | 54 ±7.5 | 80 ±5.5 |
| Body height [cm] | 165.5 ±4.5 | 181 ±4 |
| BMI [kg/m/m²] | 20 ±2 | 24 ±1.5 |
| BMR [kcal] * | 1321 ±91 | 2093 ±124 |
| BMR/BM [kcal/kg] | 24.4 | 26.1 |
| Fat mass [kg] | 10.5 ±5.5 | 9 ±3 |
| Fat free mass [kg] * | 43 ±2.5 | 71 ±4 |
| Total body water (TBW) [kg] | 31.75 ±2 | 52 ±3 |
| Body surface area (BSA) [m²] * | 1.58 m | 2.02 m |
| BSA / BM [cm²/kg] | 292.5 | 252.5 |

Values are shown as mean ±standard deviation:

STUDY ORGANISATION AND METHODOLOGY

The experiment was conducted in a double-blind design. A single dose administration of the Thermo-Speed Extreme dietary supplement (Olimp company) (TSE) or placebo (PLA) was used in the study. All subjects participated in both stages of the study. The experiment was conducted after the last meal and 48 h after the last intense physical activity. Prior to the study, body weight and composition were assessed with electrical bioimpedance analysis (Body-Stat 1500, U.K.). The subjects received a commercial thermogenic substance in doses recommended by the manufacturer, i.e. depending on the subjects' sex, 2 capsules for women and 3 capsules for men, or an analogous dose of placebo (filled with microcrystalline cellulose). The detailed composition of the applied preparation (quoting the manufacturer) is shown in the table below (Table 2).

^{*} statistically significant differences between the groups of male and female subjects

Table 2. Detailed composition of the applied preparation (quoting the manufacturer)

| Nutrition information | 1 capsule | 2 capsules |
|--|-----------|------------|
| Thermo factors | 1040 mg | 2079 mg |
| Green tea extract EGCG | 250 mg | 500 mg |
| (55 %) including EGCG epigallocatechin gallate | 137.5 mg | 275 mg |
| Bitter orange extract (p-synephrine) | 167 mg | 334 mg |
| | 10 mg | 20 mg |
| Guarana extract (50%) including caffeine | 40 mg | 80 mg |
| | 20 mg | 40 mg |
| Caffeine | 80 mg | 160 mg |
| Black pepper extract – piperine (95%), including 95% piperine | 2.5 mg | 5 mg |
| | 2.4 mg | 4.8 mg |
| Tyrosine | 500 mg | 1000 mg |

The amounts of consumed bioactive substances in a single dose of the TSE supplement were similar in males and females and were as follows: EGCG 5.1 mg/kg bw; synephrine 0.3 mg/kg bw; caffeine 2.9–3.0 mg/kg bw. The amounts of consumed synephrine in relation to caffeine remained in the proportion of 1:10 and of EGCG to caffeine 275:200.

Prior to consumption, the subjects remained at rest for about 15 minutes, and then their blood pressure (SBP/DBP), heart rate (HR), internal temperature (Ti) and skin temperature (Tsk) were measured before taking the supplement. Then the subjects took the supplement (TSE or PLA) and continued to remain at rest, during which measurements of the above-mentioned variables were continued – in the first hour after taking the preparation at 15-min intervals until the 1st hour, then at 1.5 h, and then from the 2nd to the 6th hour of the experiment, every hour (Fig. 1).

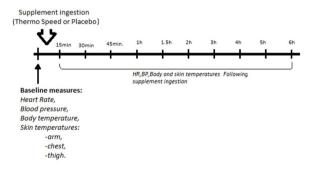


Fig. 1. Overview of the testing sessions

During the experiment, the subjects were asked about their well-being. They did not report changes in their well-being (subjective feelings) after taking the tested preparations. During the experiment, the subjects remained at rest (they were reading books, talking) and did not consume any food or drink except water. The study lasted 6 hours and was conducted in an airconditioned room: ambient temperature $26 \pm 2^{\circ}$ C, relative air humidity 56%, natural air convection.

Blood pressure was recorded with blood pressure measuring instruments (Tensoval Compact by HARTMANN, Germany); the heart rate was measured with a palpability method; the body's internal temperature was assessed (the temperature of the auditory canal isolated from the influences of external factors, Microlife MT50 electronic thermometer), and local skin temperatures were measured at three locations (chest, thigh, arm) with a telethermometer (Raytek RSC ST25XXEU) – on the arm in its anterior part (half the length of the biceps brachii), on the thigh in half of the quadriceps length and on the chest in half of the distance between the anterior axillary line and the nipple.

STATISTICAL ANALYSIS

The obtained results were statistically analysed with a use of the Statistica 12 PL software. The Shapiro-Wilk test was used to check the normality of distribution of the tested variables. To compare anthropometric features between men and women, the t-test was applied for independent variables. In addition, a three-factor analysis of variance (ANOVA) with repeated measurements (supplement (2) \times sex (2) \times time of measurement) was applied. The homogeneity of variances in the analysed groups was verified by the Levene test. If the repeated ANOVA measurements were statistically significant, the Bonfferoni post-hoc test was applied. Moreover, Pearson's correlation coefficients describing relationships between hemodynamic changes and changes in body surface temperatures were calculated. Differences at the level of p < 0.05 were assumed as statistically significant.

RESULTS

Statistical analysis showed that none of the tested variables was significantly altered by the type of the consumed dietary supplement, while sex statistically significantly differentiated the heart rate values (F = 8.48; p = 0.007) recorded during the experiment (Fig. 2). All the examined variables were characterised by statistically significant changes during the experiment. There was a statistically significant interaction of the effect of sex (2) × time of measurement on the SBP values (F = 1.92; p = 0.042) (Fig. 3), DBP (Fig. 4), Ti (F = 3.85; p = 0.000) and local skin temperatures on the chest and the arm, and an interaction of 3 effects of the supplement (2) × sex (2) × time of measurement on the examined SBP values (F = 1.92; p = 0.042) and DBP (F = 3.24; p = 0.000).

The *heart rate* values did not remain constant during the experiment, but no significant differences were found in the heart rate changes depending on the type of the consumed supplement or the subject's sex. The highest HR gain (by about 6 bpm) was reported in the men's group in the 30th minute after taking TSE and in the 45th minute (by about 4 bpm) in the group of women (Fig. 2b).

SBP and DBP ranges fluctuated during the experiment. The volume of SBP and DBP significantly changed during the experiment: SBP (F = 2.81; p = 0.003), DBP (F = 2.93; p = 0.002). The SBP change (the difference between the value at rest and the given measurement point) was strongly shaped (p = 0.03) by the interaction between all the tested factors (supplement x sex x time of measurement). The DBP changes significantly depended on the interaction between the supplement (2) × the subjects' sex (2) (F = 5.63; p = 0.025). A significant reduction in SBP (-7.8 mmHg) was reported in the women's group 1.5 h after consuming the TSE supplement. In the male group, a weaker lowering of SBP (-4 mmHg) and DBP (-9 mmHg) was observed 1 h after consumption of TSE followed by a significant increase in SBP at 1.5 h (Fig. 4b).

Internal temperature changed during the experiment (F = 5.01; p = 0.000), and the nature of its changes over time was significantly dependent on the type of the consumed supplement (F = 3.85; p = 0.000).

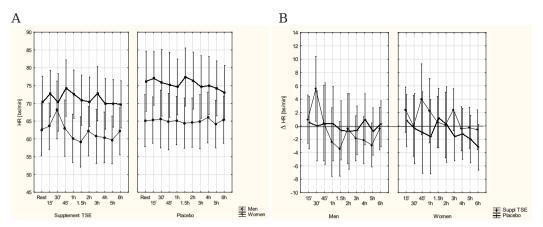


Fig. 2. Changes in the HR and heart rate increases relative to values at rest [Δ HR] in males and females during 6 hours after consumption of a single dose of TSE or placebo

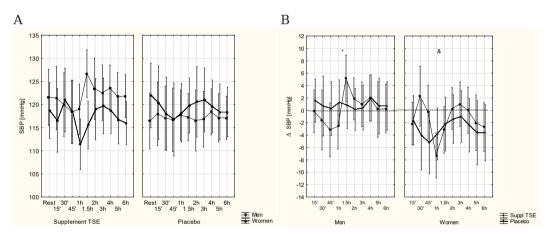


Fig. 3. Changes in systolic blood pressure [SBP] and systolic blood pressure increases relative to values at rest [Δ SBP] in males and females during 6 hours after consumption of a single dose of TSE or placebo

[&] statistically significant differences between the values at rest and at the point of measurement in females

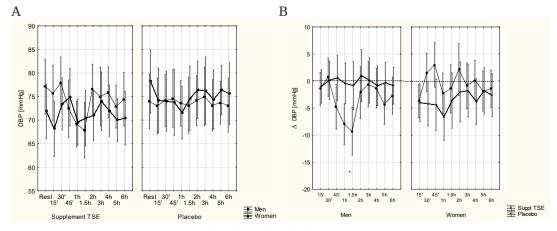


Fig. 4. Changes in diastolic blood pressure [DBP] and diastolic blood pressure increases relative to values at rest [Δ DBP] in males and females during 6 hours after consumption of a single dose of TSE or placebo

^{*} statistically significant differences between the values at rest and at the point of measurement in males;

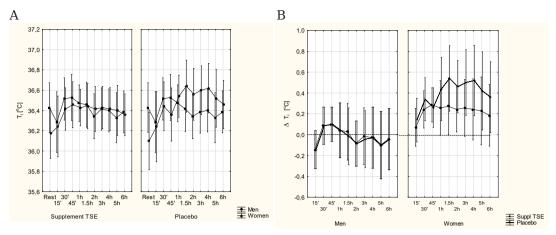


Fig. 5. Changes in internal temperature $[T_i]$ and internal temperature increases relative to values at rest $[\Delta T_i]$ in males and females during 6 hours after consumption of a single dose of TSE or placebo

There was a statistically significant interaction of the effect of sex (2) × time of measurement on the volume of the internal temperature increments during the experiment (F = 2.31; p = 0.017) (Fig. 5b). In the group of females, the $T_{\rm i}$ increase was lower after taking the TSE supplement in comparison to placebo supplementation.

Statistical analysis of *local skin temperatures* and their changes during the experiment showed that the skin temperatures had different values depending on the place of measurement. The skin temperature measured on the chest surface did not differ in a statistically significant way between men and women, nor after consumption of TSE or PLA. It did change over the duration of the experiment, and the nature of these changes was significantly dependent on the subjects' sex (F = 2.04; p = 0.03). After administration of the TSE supplement in the group of females, a significant increase in the skin temperature on the chest surface was reported after the 30th minute (approx. $+1.0^{\circ}$ C), which remained until the end of the experiment (Fig. 6). In the male group, only a temporary increase in Tsk on the chest surface was reported in the 45^{th} minute after administration of the TSE supplement.

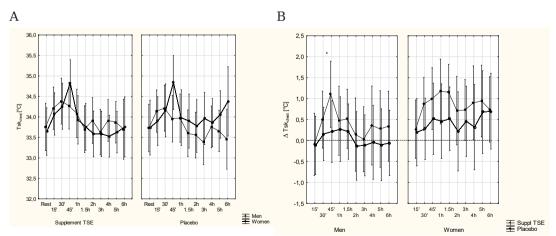


Fig. 6. Changes in the skin temperature on the chest surface [Tsk $_{chest}$] and increase in this temperature relative to values at [Δ Tsk $_{chest}$] in males and females during 6 hours after consumption of a single dose of TSE or placebo

Local skin temperatures measured on the thigh and on the arm were statistically significantly dependent on the subjects' sex (Tsk_{thigh}: F = 3.43; p = 0.001), (Tsk_{arm}: F = 2.26; p = 0.02). Local temperatures changed throughout the experiment, and changes in the temperature of the arm during the experiment showed significant correlations with the subjects' sex (F = 3.08, p = 0.001) (Fig. 7).

After administration of both TSE and PLA in the group of tested women, an increase in Tsk_{arm} was reported in the 45^{th} minute after taking the supplement (+ 1.0° C). In the group of males, a significantly milder increase in Tsk_{arm} (+ 0.5° C) was observed after taking the TSE or PLA supplements (Fig. 7b).

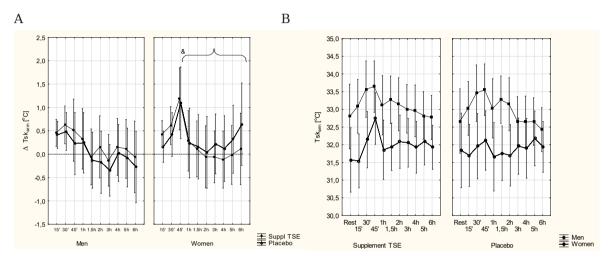


Fig. 7. Changes in the skin temperature on the surface of the arm [Tsk $_{arm}$] and the increase of this temperature relative to values at rest [Δ Tsk $_{arm}$] in males and females during 6 hours after consumption of a single dose of TSE or placebo

 $^{^{\&}amp;}$ statistically significant differences between the values at rest and at the point of measurement in females.

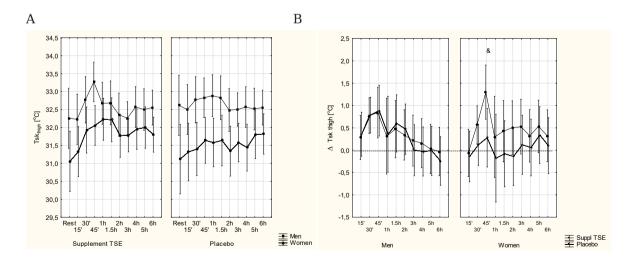


Fig. 8. Figure 8. Changes in the skin temperature on the thigh surface [Tsk $_{thigh}$] and the increase of this temperature relative to values at rest [Δ Tsk $_{thigh}$] in males and females during 6 hours after consumption of a single dose of TSE or placebo

^{*} statistically significant differences between the values at rest and at the point of measurement in males;

 $^{^{\}mbox{\tiny \'e}}$ statistically significant differences in comparison to place bo

In the studied group of females, a significant increase in Tsk measured on the thigh surface (+1.3°C) in comparison to values at rest was observed in the 45th minute after TSE administration (Fig. 7b).

Table 3. The strength of correlations between hemodynamic changes and changes in local body surface temperature in males and females after a single dose of TSE and placebo

| | Δ SBP [mmHg] | | Δ DBP [| Δ DBP [mmHg] | | Δ HR [bs/min] | | |
|--|--------------|---------|---------|--------------|---------|---------------|--|--|
| | TSE | PLA | TSE | PLA | TSE | PLA | | |
| MEN | | | | | | | | |
| $\Delta \operatorname{Tsk}_{chest}[^{\circ}C]$ | ns | ns | ns- | ns | ns | ns | | |
| $\Delta Tsk_{arm} [^{\circ}C]$ | ns | r=23 | ns | ns | ns | ns | | |
| $\Delta Tsk_{thigh} [^{\circ}C]$ | ns | ns- | ns | ns | r=0.27 | ns | | |
| WOMEN | | | | | | | | |
| Δ Tsk _{chest} [°C] | r=-0.26 | nss | ns | ns | r=-0.24 | ns | | |
| Δ Tsk $_{arm}$ [°C] | r=-0.28 | ns | ns | ns | ns | ns | | |
| Δ Tsk _{thigh} [°C] | r=-0.56 | r=-0.26 | r=-0.39 | r=-0.62 | ns | ns | | |

A significant, inversely proportional correlation was observed between increases in skin temperature (ΔTsk) measured on the thigh (Tsk_{thigh}), on the arm (Tsk_{arm}) and on the chest (Tsk_{chest}), and the increase in (Δ)SBP after consumption of TSE. Correlations at the level of significant changes were noted in the studied group of females (Table 3), but not males.

DISCUSSION

The results of the conducted study showed that a single dose of the compound TSE containing p-synephrine, caffeine, EGCG, guarana and piperine did not significantly affect the cardiovascular function (heart rate). However, after its consumption the range of blood pressure fluctuations at rest significantly increased. The systemic changes concerning SBP/DBP were more prominent in males, while changes in local skin temperatures were manifested more in the studied group of females. Despite the fact that the absolute values of the assessed indicators did not significantly differ between the consumption of TSE and placebo, there were significant differences in the increases (fluctuations) of the tested variables in males and females. The increases in local skin temperatures were inversely proportional to the changes in systolic blood pressure, and the strong correlation between the two tested variables was revealed after consumption of TSE only in the women's group.

The applied TSE is a multi-ingredient preparation containing many substances with a thermogenic effect. It contained the greatest amounts of tyrosine, which is an endogenous amino acid used for the synthesis of noradrenaline and dopamine, and of p-synephrine, which has an effect similar to ephedrine, but without AR stimulation [24]. Caffeine contained in the preparation is a recognised, safe thermogenic agent used for body weight regulation [2]. Caffeine influences thermogenesis by inhibiting the phosphodiesterase involved in cyclic AMP (cAMP) degradation [2], thereby prolonging the effect of the catecholamine activity. Caffeine has been shown to increase the metabolic rate up to three hours after its consumption [1, 25]. The ratio of synephrine to caffeine in the consumed preparation amounted to 1:10 and was similar to the proportion used in the study by Astrup et al. [12]. The cited authors assessed the effectiveness of ephedrine and caffeine on the cardiovascular function and

the effectiveness of ephedrine and caffeine on the cardiovascular function and noted that taking them in the above proportions stimulates the cardiovascular function the most (20:200mg). Furthermore, the subjects consumed a dose of EGCG (275mg/pp) along with the TSE preparation. This is a known optimal dose of EGCG used to increase the oxidation of macronutrients [26]. Caffeine and EGCG increase the concentration of catecholamines in the blood and prolong their effects in the body [27]. However, a possible side effect of green tea consumption is a slight increase in blood pressure, which was shown in the study by Berube-Parent et al. [26]. All ingredients taken together with the TSE product influence the thermogenesis process by using adrenergic stimulation in its pathway and prolonging the effect of the SNS neurotransmitters on the cells [8, 28]. Still one should remember that also other components of the Thermo Speed supplement exert their own biological effects and can also weaken/strengthen or induce similar effects to caffeine activity. Ryan et al. [29] claim that a particular combination of the ingredients of the supplement may potentiate the effects of caffeine by influencing the effectiveness of its activity in the body.

Few studies were aimed at evaluating hemodynamic and temperature changes in men and women after a single dose of a multi-ingredient preparation containing multiple thermogenic stimulants; therefore, it is difficult to assign the observed effects only to one of them. Interestingly, the consumption of p-synephrine in this study (20mg in females and 30mg in males) was low compared to other studies in which the dose of synephrine ranged from 12 to 100 mg [24, 28, 30]. Synephrine exhibits some structural similarity to ephedrine [31, 32], but its effect is not accompanied by side effects in the form of changes in the cardiovascular function, because it has a weak affinity of binding to $\alpha 1$, $\alpha 2$, $\beta 1$ and $\beta 2$ adrenergic receptors [24, 30]. However, synephrine activates \$3 adrenergic receptors, which can be responsible for an increased use of fat in energy processes and increased production of endogenous heat. In the study by Ratamess et al. [28] it was shown that consumption of 103 mg of p-synephrine did not result in changes in SBP or HR during 3 hours of controlled calm seating. Synephrine usually does not cause changes in blood pressure or the heart rate, but in combination with other components, it can stimulate the cardiovascular system similarly to SNS activation. The quantities of single doses of caffeine consumed with TSE were equivalent to 200 mg in women and 300 mg in men. In their study [12], Astrup et al. observed small and insignificant changes in blood pressure and the heart rate after consumption of 100 and 200 mg of caffeine. However, after consumption of 400 mg of caffeine, the systolic and diastolic blood pressure significantly increased, on average by 6.3 mmHg. In the study by Robertson et al. [33] 250 mg of caffeine was given to people who were not accustomed to drinking coffee. In these subjects, systolic blood pressure increased by 10 mmHq 1 h after consumption of caffeine. The heart rate values decreased after the first hour and then after 2 hours increased above the values at rest. Catechins of green tea, especially EGCG, are a highly regarded safe thermogenic agent with a broad spectrum of activity [27, 34, 35]. Adverse reactions after consumption of green tea were rarely reported after consumption of optimal doses of EGCG. Green tea, containing both tea catechins and caffeine, can act at different stages of sympathetic signalling, exerting thermogenic effects [36]. Only in the study by Berube-Parent et al. [26] there was a negligible increase (7 mmHg) in systolic and diastolic blood pressure (5 mmHg) up to 24 hours after EGCG consumption, but no increase in the heart rate was observed in that study. The results of the present study remain consistent with the previously described

effects of bioactive thermogenic agents [7], which are usually accompanied by blood pressure changes without significant changes in the heart rate values [37]. Thermogenesis induced by these substances is believed to trigger non-specific stimulation of adrenergic receptors, which may be accompanied by adverse effects [38], including changes in cardiovascular activity.

In the light of the conducted studies, it was revealed that TSE strongly modifies peripheral blood flow, but this effect varies between males and females. The tone of the choke vessels muscularis is an important determinant of blood pressure and local blood flow. It is controlled by mediators of the sympathetic system and blood vessels endothelium. Noradrenaline is the main sympathetic neurotransmitter that narrows blood vessels by acting on α -adrenergic receptors. It is also a strong agonist of β 1-adrenergic receptors, but it has a much weaker effect on β2 receptors [39, 40]. β2 (but not β1) agonists fed into women's humeral artery dilated the choke vessels of the forearm, partly by activating the L-arginine/nitric oxide (NO) pathway [39]. Vasoconstriction was observed when ligands were bound to α -adrenergic receptors, whereas binding to the $\beta1$ adrenergic receptor resulted in increased cardiac contractility and HR [32]. Kneale et al. [19] observed differences in sensitivity to norepinephrine and the effectiveness in narrowing of choke vessels between males and females. The results of their study showed that there were gender differences in the expression of different adrenergic receptors and levels of receptor proteins in men and women, which could partly explain the different efficiency of activity of bioactive components on blood vessels in men and women.

The thermogenic effectiveness of supplements is particularly associated with activation of β3 AR receptors in brown adipose tissue (BAT), associated with initiation of a signalling pathway involving UCP-1 proteins and increased production of endogenous heat. The presence of uncoupling protein-1 (UCP-1), called thermogenin, whose task is to disperse energy in the form of heat, in the mitochondria of these cells is a characteristic feature of brown tissue cells. Therefore, this protein is a thermogenesis regulator, deciding about the amount of energy generated in the form of heat [41]. The effectiveness of the supplement in inducing thermogenesis in humans depends on the subjects' age [42], gender [21, 43, 44,], individual characteristics [45, 46, 47], the dose [48] and the time of consumption of the supplement [49, 50], interactions/ antagonism between metabolic effects of its components and biological activity of metabolites and their clearance and environmental conditions [45, 51]. The substances contained in the TSE preparation were not selective agonists of β3-AR receptors and were additionally likely to stimulate β1 and β2 receptors, causing effects in the form of changes in the peripheral blood flow [39].

β2-AR receptors predominate in blood vessels, the stimulation of which leads to vasodilation, thereby reducing the total peripheral resistance and lowering blood pressure. Therefore, differences in the reactivity of AR receptors and their different concentration in men and women could affect the differences in the body's responses to the consumption of the supplement. Kneale et al. [19] investigated inter-gender differences in the primary and agonistic blood flow in the forearm stimulated by albuterol (a selective β2-adrenergic receptor agonist) and demonstrated that it is a stronger vasodilator in females than in males. The results of the study by Freedman et al. [20] indicate different β-adrenergic sensitivity in various types of blood vessels in humans in vivo.

There is evidence that men show greater activity of SNS at rest than women, who may exhibit increased sympathetic activity [52]. Therefore, this increased SNS activity in men may possibly contribute to a weaker response of β -adrenergic receptors in males than in females. The concentration of $\beta 2$ -adrenergic receptors and the activity of adenylyl cyclase associated with the receptor is greater in women's lymphocytes in comparison to males and varies depending the menstrual cycle phase [53]. If smooth muscle cells of the endothelial blood vessels have similar characteristics, this could explain the gender differences in the reactivity of the skin blood vessels to bioactive agents in women and a greater increase in the temperature of the arm and thigh in the conducted study in women.

The applied thermogenic supplement induced a significantly weaker increase in internal temperature in the female subjects and a significant increase in the skin temperature during six hours of guiet seating. The study reported an almost 1.0°C increase in the skin temperature in the 15th minute after administration of the supplement. The increased Tsk remained stable until the end of experiment, especially in the group of female subjects. The significant increase in Tsk was reported in the peripheral parts of the body in both women and men (the 45th minute of the experiment). The environmental conditions (thermoneutral) in which the experiment was conducted and the (resting) state in which the subjects remained throughout the experiment indicate that the Tsk changes observed in the current study could be primarily a consequence of the activity of the TSE supplement. Given that the change in internal temperature at rest may occur when the amount of the produced endogenous heat or the magnitude of heat dissipation is altered, it seems reasonable to believe that the lower values of internal temperature observed during the experiment in the women's group were due to greater heat dissipation from the body connected with a higher gradient of skin temperature/environment temperature (the distal-proximal skin-temperature gradient DPG). DPG is associated with peripheral vasodilation, which provides greater blood flow to distant areas of the skin, promoting the loss of heat through cutaneous blood vessels (arterial and venous anastomoses and capillaries) [54].

CONCLUSIONS

In summary, it should be noted that a single dose of TSE has a weak effect on the systemic cardiovascular function at rest; nevertheless, depending on gender, it is accompanied by a better local blood supply to the skin, which manifests itself in the increase in the skin temperature, especially in women. The results of the current study are complementary to the performance characteristics of the effect of a compound thermogenic agent on the body, indicating its different effectiveness of a single dose in women and men and its strong effect on improving local blood supply to the skin.

LIMITATIONS

A single dose of administered TSE and a small number of both test groups is a limitation in a broader interpretation of the results obtained in this study. Therefore, drawing conclusions based on our findings on the causes and consequences of hemodynamic changes and body temperatures after consumption of a single dose of the TSE preparation is limited and requires further detailed studies comprising larger groups of subjects.

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