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Effects of Fennel Supplementation on Biochemical Blood Indices in Females During Climacteric Period – Preliminary Reports

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Keywords
Foeniculum vulgare Mill., women, herbal medicine

Abstract
Introduction: The menopausal period in women, also called climacteric, is the time when several hormonal changes take place and gonadal functions disappears. Although medicinal such as Fennel plants (*Foeniculum vulgare Mill*.) feature a relatively weaker effect than synthetic drugs, they are more commonly applied in different societies or ethnical groups due to the lower probability of side effect occurrence during the climacteric period in females.
Objectives: The aim of the work was to assess blood biochemical indices in menopausal women and quality of life after fennel supplementation.
Materials and methods: The research included 10 females aged 43-69 years with observed climacteric symptoms. Blood was taken twice (before fennel seed supplementation and after it) on an empty stomach, in the morning. Selected biochemical blood indices were tested in all the participants.
Results: Comparing the examined group results before and after fennel supplementation, statistically significant changes were found for the following indices: HCT [%], MCV [fl], MCHC [g/dl], CHCM [g/dl], HDW [g/dl] and Basophils [%]. No changes were observed for: RBC [10^{12}/l], HGB [g/dl], MCH [pg], RDW [%], WBC [10^9/l], neutrophils [%], lymphocytes [%], monocytes [%], eosinophils [%], LUC [%], neutrophils [10^9/l], lymphocytes [10^9/l], monocytes [10^9/l], eosinophils [10^9/l], basophils [10^9/l], LUC [10^9/l], PLT [10^9/l], MPV [fl], PCT [%], PDW [%], iron [umol/l], ASPAT [U/l], ALAT [U/l], total cholesterol [mmol/l], cholesterol HDL [mmol/l], cholesterol LDL [mmol/l], urea [mmol/l], creatinine [umol/l], eGFR [ml/min/1,732], alpha-Amylase [U/l] or Lipase [U/l].
Conclusions: Fennel (*Foeniculum vulgare Mill*.) favours women's health and may eliminate unbearable climacteric symptoms. Our research confirmed the occurrence of differences in blood morphology test results in females after fennel supplementation in relation to the results of tests performed before it.

INTRODUCTION

Fennel (*Foeniculum vulgare Mill*.) is a two-year medicinal plant belonging to the *Apiaceae* family. It is a resilient, umbellate plant of yellow flowers and feathery leaves. Its fruit comprise dry seeds. Fennel is believed to be an indigenous species occurring within the region of the Mediterranean Sea. It has also widely spread and settled mainly on dry soils nearby sea shores and on rivers embankments[1]. Fennel appears in a few varieties that differ according to morphology of fruit and chemical composition[2]. In medicine, fennel fruit (*Foeniculi fructus*) and fennel oil (*Foeniculi aether oleum*) are applied. The grown fruit of fennel are collected in September. They are rich in flavonoids (derivatives of quercetin and kaempferol), stigmasterol, fatty oils, protein and carbohydrates, and comprise approximate-

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ly 2-6% of essential oil[3]. Fennel oil is composed of anethole (20-90%), fenchone (10-30%), and also transanethole, camphene, p-Cymene, Myrcene, α- as well as β-felandren γ-Terpinene, Pinene and estragole. The oil found in fennel fruit features a relaxing effect on the smooth muscles of the digestive system as well as secretolytic properties and antimicrobial activity. In medicine, it is used in disorders linked to the digestive system. Fennel oil is also applied in the cosmetic industry, and due to its typical scent of aniseed, as an additive for flavouring food. In traditional medicine, the preparations including fennel oil were used for healing wounds whereas the herb and fruit were believed to be an aphrodisiac. Ancient Rome, Egypt and Asia used materials obtained from fennel. The plant positively affected the process of lactation in women, stabilised irregular menstruation, increased libido and was also applied for treating digestive system disorders and diseases of the kidneys and bladder[4,5]. Moreover, it features antioxidant[4], antithrombotic, anticancer, antidiabetic[6], antimicrobial, antibacterial, antifungal and acaricidal[7] properties. In the latest studies, it has been reported that consumption of fennel may alleviate typical symptoms of menopause (flushing, cold perspirations) and it also improves memory and has anxiolytic effect[8]. Fennel fruit extracts are prepared mainly for infants to prevent the occurrence of colic and bloating[9]. Fennel, consumed in any form, was recommended in the medieval period to improve skin colour, also adding a pleasant scent to it. It was additionally used for fresh breath and clear sight as well as improving the mood and supporting digestive processes (reduction of bloats and gastric problems)[10,11]. Fennel fruit extract was applied in treating insomnia (and other sleep-related problems). It was given to women during heavy labours and also was recommended for general strengthening of the body[12]. The menopausal period in women, also called climacteric, is the time when several hormonal changes take place and gonadal functions disappear. Menopause affects changes in women's mental, physical and sexual spheres[13]. It frequently lasts for even fifteen years starting at the age of 45. WHO symbolically divided climacteric into three periods: pre-menopause – the transition period, perimenopause – the period around menopause and postmenopause[14]. In other words, climacteric can be presented as two periods: the one lasting approximately six years before the last menstruation and the other one lasting about six years after the final menstruation[15].

A rapid decrease in ovary function is observed about six months before the onset of menopause[16]. The ovaries then lose sensitivity to hypothalamic stimuli and subsequently produce less androgen and oestrogen[17]. This results in lengthening menstrual cycles. When the concentration of oestrogen is so low that proliferation of uterus mucosal cells is no longer possible, bleeding stops. In the postmenopausal period, the synthesis of oestrogen takes place mainly on peripheral way (extra-glandular aromatisation of androgen to oestrogen)[18]. Climacteric is a physiological period that is genetically programmed. During menopause, menstrual disorders, decreased secretion of oestrogen (hypoestrogenism) with consequences due to cessation of ovarian function, as well as disorders in the somatic and mental spheres are observed. The cessation of oestrogen production by the ovaries results in metabolic disorders and increases the risk of life-threatening diseases. Menopausal symptoms vary individually. Their severity and type are influenced by the concentration of sex hormones (including hormonal supplementation) and the state of physical and mental health, as well as the condition of social relations[14]. The symptoms of menopause can be divided into early and late. Early symptoms of menopause include: hot flashes, palpitations, mood swings, irritability, sleep disturbances, frequent headaches (migraines), menstrual disorders, and vaginal dryness[19,20,21]. Late symptoms comprise: atrophic changes in the genitourinary system, as well as related sexual dysfunctions, diseases of the cardiovascular system, musculoskeletal ailments and osteoporosis. The above symptoms are experienced by women from different populations at different frequencies and intensities (genetic predisposition and the action and influence of external factors play an important role)[17,22,23].

OBJECTIVES

The aim of the work was to assess biochemical indices of the blood and quality of life after supplementation with fennel in women during the climacteric period. The following research question was formulated in order to realise the aim:

- Did fennel supplementation in women during the climacteric period influence changes in biochemical indices of the blood: morphology, iron, liver tests, lipidogram, renal and pancreas profiles and quality of life?

Research hypothesis

On the basis of the objectives, the following research hypothesis was formulated:

- Supplementation with fennel in climacteric women affects the biochemical indices of blood and quality of life.

MATERIAL AND METHODS

Characteristics of study group

A healthy group of women with menopausal symptoms was selected for the study. The study sample consisted of 10 women aged 43-69. The control group comprising 10 women, aged 45-65, also took part in the study. Qualification to the groups was carried out by random division (Table 1). The inclusion criteria for the study were female gender, age between 43 and 69 years, with menopausal symptoms, a medical certificate confirming that there were no contraindications for participation, and the respondent's voluntary consent to be included in the project. The exclusion criteria were unregulated cardiovascular diseases, diabetes, oncolog-

Table 1

Anthropometric data of subjects

Group	Age (years)	Body mass (kg)	Body height (cm)	BMI
Study group	52±7.88	68.3±9.46	166.7±4.86	24.51±2.55
Control group	51±6.23	64.5±7.98	164.4±4.18	23.78±1.93

ical treatment, mental disorders and/or the inability to move independently. In order to exclude other factors that could influence the studied variables, the participants could not take part in other forms of training during the research project.

The participating women were recruited from the family members of our students with menopausal symptoms. Out of 28 eligible individuals, eight were excluded due to either failure to meet inclusion criteria or lack of consent to participate. As a result, the study group, comprising women with menopausal symptoms (n = 10), included 10 females supplementing fennel twice a day for two weeks. Similarly, the control group (n = 10) was composed of 10 females with menopausal symptoms but without fennel supplementation.

The extract was prepared by the research team following the traditional recipe: a teaspoon of fennel seed (ecologically grown in France), smashed before use, poured over with boiling water and then poured through a strainer after 10-15 min. The liquid prepared in such a manner was consumed by the women twice a day for two weeks.

In order to analyse selected biochemical indices of the blood, venous blood was taken from the participants. The first tests took place on 28th June 2021 and the second on 12th July 2021 after the completed period of supplementation with fennel. The examined subjected filled out a questionnaire concerning the influence of fennel supplementation on their physical and mental state. The questionnaire concerned only the study group (the control group did not complete the questionnaire) and was anonymous. Blood was collected at the University of Physical Education in Kraków, in the morning hours, on empty stomach, and from the elbow vein in the amount of 4 ml into BD Vacutainer® test tubes from K2EDTA. This was done at the Laboratory of Blood Physiology by a certified nurse and following laboratory standards.

The collected blood was analysed at the Unit of Clinical Analysis and Biochemistry, Oncology Centre (11 Garncarska Street) in Kraców.

The volunteers were informed about the procedures and purpose of the research in detail, and about the possibility of resigning from participation at any stage without giving reason. All the examined participants were asked not to alter their nutrition habits, taken medicines or level of physical activity during the experiment. All volunteers provided written consent for participation in the study, as well as for the use of personal data and research results for scientific purposes. The research was approved by the Bioethical Commission at the Regional Medical Chamber in Kraków No. 212/KBL/OIL/2022.

Measurement of morphological blood indices

Complete blood morphology was performed with the use of the ADVIA 2120i analyser (Siemens Healthineers). The following blood indices were determined:

1. RBC [10^{12}/l] –red blood cell count (erythrocytes);
2. HGB [g/dl] – haemoglobin;
3. HCT [%] – haematocrit;
4. MCV [fl] – mean corpuscular volume;
5. MCH [pg] – mean corpuscular haemoglobin;
6. MCHC [g/dl] – mean corpuscular haemoglobin concentration;
7. CHCM [g/dl] – cell haemoglobin concentration mean;
8. RDW [%] – red blood cell distribution width;
9. HDW [g/dl] – standard deviation for haemoglobin concentration in red blood cells;
10. WBC [10^9/l] – white blood cell count;
11. Neutrophils [%];
12. Lymphocytes [%];
13. Monocytes [%]
14. Eosinophils [%];
15. Basophiles [%];
16. LUC [%] – large unstained cells;
17. Neutrophils [10^9/l] –neutrophil count;
18. Lymphocytes [10^9/l] – lymphocyte count;
19. Monocytes [10^9/l] – monocyte count;
20. Eosinophils [10^9/l] – eosinophil count;
21. Basophils [10^9/l] –basophil count;
22. LUC [10^9/l] – large unstained cells;
23. PLT [10^9/l] – platelets;
24. MPV [fl] – size of blood cells;
25. PCT [%] – plateletcrit;
26. PDW [%] – platelet distribution width.

Measurement of biochemical indices

Iron, liver tests and lipidogram

Biochemical indices of the blood were measured in the plasma with the use of the Roche/Hitachi Cobas c501, module 6000 biochemical analyser:

1. Iron [umol/L];
2. AspAT [U/L] – aspartate transaminase;
3. AlAT [U/L] – alanine transaminase;
4. Total cholesterol [mmol/L];
5. HDL [mmol/L] – cholesterol HDL;
6. LDL [mmol/L] – cholesterol LDL.

Renal indices

Renal profiles were defined using the calorimetric method implementing a reagent set and the Cobas c 311 (Roche DiTagnostics) Analyser. The device automatically calculates the analytical activity of a given substance for each sample.

The following indices were determined:

1. Urea [mmol/l];
2. Creatinine [mmol/l];
3. eGFR [ml/min/1.73m^2] – index of glomerular filtration.

Pancreatic indices

Pancreatic profiles were determined using the kinetic method from EPS, following IFCC, in the Roche Cobas c501 analyser.

The following indices were determined:

1. Alpha-Amylase [U/l];
2. Lipase [U/l].

Questionnaire

The anonymous questionnaire was directed towards women in the menopausal period who were exposed to a two-week supplementation with fennel in the form of tea:

1. Have you noticed improvement in your general well-being?
- Yes
- No
- Hard to say
2. Have you noticed a change in your mood?
- Yes
- No (go to question 4)
3. Has your mood changed in comparison to the situation before supplementation?
- Significantly improved
- Improved
- Worsened
- Significantly worsened
4. Have you noticed a change in your sleep quality?
- Yes
- No (go to question 6)
5. Has your sleep changed in comparison to the situation before supplementation?
- Significantly improved
- Improved
- Worsened
- Significantly worsened
6. Have you noticed memory improvement (e.g. better memorisation, better concentration, easy focusing)?
- Yes
- No
- Hard to say
7. Have you noticed a lower frequency of night perspiration during sleep?
- Yes
- No
- Hard to say
8. Has the frequency of flushing occurrence decreased?
- Yes
- No
- Hard to say
9. Has flushing intensity decreased?
- Yes
- No
- Hard to say
10. Have you observed lower perspiration?
- Yes
- No
- Hard to say
11. Do you think your skin odour has improved (does it smell nice)?
- Yes
- No
- Hard to say
12. Has the odour from the mouth improved?
- Yes
- No
- Hard to say
13. Have you observed improvement in your skin appearance (e.g. the skin became lighter, brighter or smoother)?
- Yes
- No
14. Do you experience decreased digestive discomfort (e.g. reduction of heartburn, diarrhoea, bloating and constipation)?
- Yes
- No
15. Have you noticed any other effects resulting from supplementation with fennel that have not been mentioned above?
- Yes
- No

Analysis of statistical data

The data were presented in the form of mean values and standard deviations of medians and quartiles I and III, depending on assessment of the variable distribution. Normality of distribution was verified based on the Shapiro-Wilk test.

Dependent variables were compared using the Student's *t*-test for related variables and if not applicable, the Wilcoxon test was used. Independent variables were compared via the Student's *t*-test for unrelated variables or with the U Mann Whitney test in case of lack of normal distribution of variables. The level of significance was assumed as $p \leq 0.05$. The analyses were performed with the use of the Statistica 13 package (Tibco Software Inc., USA).

Points were assigned to the survey data (0 – 'no', 1 – 'hard to say', 2 – 'yes'). The Wilcoxon test and Spearman's R correlation coefficient were used for statistical calculations.

RESULTS

Overall results

Changes were found for morphological indices such as: HCT [%], MCV [fl], MCHC [g/dl], CHCM [g/dl], HDW [g/dl] and basophils [%], whereas no changes were observed for the remaining morphological and biochemical blood indices in the examined group compared to the results before and after fennel supplementation (Table 2).

Changes were found for the following morphological indices: HGB [g/dl], MCH [pg], RDW [%], monocytes [10^9/l] and lipase [U/l], whereas no changes were observed for the remaining morphological and biochemical blood indices in the examined group comparing the results before fennel supplementation and to the control group (Table 2).

Changes were noted for morphological indices: MCH [pg], MCHC [g/dl], CHCM [g/dl], RDW [%] [%], monocytes [10^9/l] and Lipase [U/l], whereas no changes were observed for the remaining morphological and biochemical blood indices in the examined group compared to the results after fennel supplementation and to the control (Table 2).

Graphic analysis of morphological indices in examined group comparing results before and after fennel supplementation

HCT [%]

Changes were observed in study group 1 (before fennel supplementation) in comparison to group 2 (after fennel supplementation): an increase in HCT [%] by 3.6% was registered in the examined individuals after supplementation (Figure 1, Table 2).

Table 2

Values of blood morphological and biochemical parameters in supplemented (SG) and control (CG) groups before and after fennel supplementation, considering interactions between groups (p int) and changes over time (p pre-post)

Variables	Group	Pre					Post					p value
		$\bar{x}$	SD	Me	Lower quartile	Upper quartile	$\bar{x}$	SD	Me	Lower quartile	Upper quartile	Pre-Post
RBC [10^{12}/l]	SG			4.590	4.440	4.700			4.585	4.400	4.730	0.260
	CG			4.530	4.150	4.580			4.530	4.150	4.580	
	p int			0.540					0.514			
HGB [g/dl]	SG	13.120	0.405				13.200	0.726				0.694
	CG	13.689	0.533				13.689	0.533				
	p int			**0.017***					0.116			
HCT [%]	SG	38.900	1.541				40.300	1.855				**0.047***
	CG	40.300	1.552				40.300	1.552				
	p int			0.065					1.000			
MCV [fl]	SG			84.350	83.400	90.000			86.250	85.100	91.600	**0.008***
	CG			88.600	86.200	92.400			88.600	86.200	92.400	
	p int			0.724					0.288			
MCH [pg]	SG			28.500	28.400	30.200			28.700	28.100	30.000	0.154
	CG			30.500	29.500	31.100			30.500	29.500	31.100	
	p int			**0.041***					**0.027***			
MCHC [g/dL]	SG	33.760	0.368				32.770	0.811				**0.009***
	CG	33.933	0.596				33.933	0.596				
	p int			0.450					**0.002***			
CHCM [g/dl]	SG	35.060	0.414				33.62	0.995				**0.001***
	CG	34.778	0.909				34.778	0.909				
	p int			0.388					**0.017***			
RDW [%]	SG	13.320	0.461				13.270	0.414				0.551
	CG	12.600	0.394				12.600	0.394				
	p int			**0.002***					**0.002***			
HDW [g/dl]	SG	2.504	0.167				2.450	0.122				**0.044***
	CG	2.472	0.141				2.472	0.141				
	p int			0.661					0.717			
WBC [10^9/l]	SG	6.071	1.547				6.169	1.468				0.846
	CG	5.083	1.077				5.083	1.077				
	p int			0.129					0.086			
Neutrophils [%]	SG	55.230	5.170				54.900	7.727				0.877
	CG	55.456	7.201				55.456	7.201				
	p int			0.938					0.874			
Lymphocytes [%]	33.000	4.992					32.930	7.239				0.966
	33.422	6.321					33.422	6.321				
				0.873					0.877			
Monocytes [%]	SG	6.120	0.983				6.310	1.097				0.651
	CG	5.556	0.968				5.556	0.968				
	p int			0.225					0.132			
Eosinophils [%]	SG			3.400	2.500	4.500			2.900	2.000	3.200	0.678
	CG			2.600	2.100	3.700			2.600	2.100	3.700	
	p int			0.462					0.838			
Basophiles [%]	SG	0.600	0.283				0.840	0.337				**0.021***
	CG	0.800	0.312				0.800	0.312				
	p int			0.161					0.792			
LUC [%]	SG			1.750	1.500	1.900			1.850	1.700	2.200	0.093
	CG			1.700	1.600	1.900			1.700	1.600	1.900	
	p int											

Neutrophils [10^9/l]	SG	3.334	0.859				3.423	1.071				0.817
	CG	2.830	0.741				2.830	0.741				
	p int			0.191					0.183			
Lymphocytes [10^9/l]	SG	2.030	0.695				2.003	0.542				0.803
	CG	1.696	0.468				1.696	0.468				
	p int			0.241					0.206			
Monocytes [10^9/l]	SG	0.367	0.092				0.386	0.105				0.631
	CG	0.282	0.071				0.282	0.071				
	p int			**0.039***					**0.024***			
Eosinophils [10^9/l]	SG			0.210	0.140	0.240			0.150	0.140	0.200	0.507
	CG			0.150	0.090	0.200			0.150	0.090	0.200	
	p int			0.178					0.462			
Basophils [10^9/l]	SG			0.040	0.020	0.050			0.050	0.030	0.070	0.075
	CG											
	p int											
LUC [10^9/l]	SG	0.104	0.028				0.119	0.040				0.181
	CG	0.091	0.029				0.091	0.029				
	p int			0.337					0.101			
PLT [10^9/l]	SG	263.500	76.042				252.700	47.981				0.427
	CG	272.444	53.986				272.444	53.986				
	p int			0.774					0.410			
MPV [fl]	SG			9.900	9.400	10.300			10.200	8.600	10.600	0.726
	CG			9.300	9.000	9.800			9.300	9.000	9.800	
	p int			0.270					0.540			
PCT [%]	SG	0.262	0.064		0.262	0.064	0.248	0.030				0.394
	CG	0.256	0.040				0.256	0.040				
	p int			0.799					0.649			
PDW [%]	SG	53.540	7.768				53.800	8.401				0.793
	CG	54.667	7.895				54.667	7.895				
	p int			0.758					0.820			
Iron [umol/L]	SG				8.600	8.200	13.800		12.000	9.400	15.700	0.799
	CG				14.000	11.200	17.600		14.000	11.200	17.600	
	p int			0.221					0.307			
AspAT [U/L]	SG				21.750	18.200	26.200		18.650	16.200	22.200	0.139
	CG				20.200	19.100	23.900		20.200	19.100	23.900	
	p int			0.967					0.307			
AlAT [U/L]	SG	21.930	10.318				18.610	8.698				0.111
	CG	23.856	8.124				23.856	8.124				
	p int			0.660					0.194			
Total cholesterol [mmol/L]	SG			4.770	4.220	5.760			4.590	3.970	5.750	0.919
	CG			4.880	4.760	5.190			4.880	4.760	5.190	
	p int			0.596					0.540			
HDL [mmol/L]	SG	1.515	0.353				1.533	0.338				0.880
	CG	1.472	0.303				1.472	0.303				
	p int			0.781					0.686			
LDL [mmol/L]	SG	2.971	0.946				3.101	0.987				0.594
	CG	3.564	0.841				3.564	0.841				
	p int			0.168					0.289			
Urea [mmol/l]	SG	4.705	1.212				4.676	1.156				0.908
	CG	5.068	0.980				5.068	0.980				
	p int			0.486					0.439			
Creatinine [mmol/l]	SG			69.500	58.200	80.600			69.250	63.300	79.200	0.214
	CG			65.000	59.600	69.000			65.000	59.600	69.000	
	p int			0.903					0.288			

eGFR [ml/ min/1,73m2]	SG			80.500	66.000	90.000			80.500	66.000	87.000	0.173
	CG			80.000	79.000	89.000			80.000	79.000	89.000	
	p int			0.744					0.540			
Alpha-Amylase [U/l]	SG	49.940	14.863				52.040	12.527				0.188
	CG	52.478	9.468				52.478	9.468				
	p int			0.667					0.933			
Lipase [U/l]	SG	33.500	11.163				31.110	6.180				0.411
	CG	42.444	5.328				42.444	5.328				
	p int			**0.043***					**0.001***			

$\bar{x}$ – mean; *SD* – standard deviation; Me – median; *p* – * statistically significant value ($p<0.05$]; RBC – red blood cell count (erythrocytes); HGB – haemoglobin; HCT – haematocrit; MCV – mean corpuscular volume; MCH – mean corpuscular haemoglobin; MCHC [g/dl] – mean corpuscular haemoglobin concentration; CHCM – cell haemoglobin concentration mean; RDW – red blood cell distribution width; HDW – standard deviation for haemoglobin concentration in red cells; WBC – white blood cell count; LUC – large unstained cells, Neutrophils –neutrophil count; Lymphocytes –lymphocyte count; Monocytes –monocyte count; Eosinophils –eosinophil count; Basophils –basophil count; LUC – large unstained cells; PLT – platelets; MPV – mean platelet volume; PCT – plateletcrit; PDW – platelet distribution width; AspAT – aspartate transaminase; AlAT – alanine transaminase; HDL – cholesterol HDL; LDL – cholesterol LDL; eGFR –glomerular filtration index.

MCV [fl]

Changes were noted in study group 1 (before fennel supplementation) in comparison to group 2 (after fennel supplementation): an increase in MCV [fl by 2.23% was registered in the examined participants after supplementation (Figure 2, Table 2).

MCHC [g/dl]

Changes were detected in study group 1 (before fennel supplementation) in comparison to group 2 (after fennel supplementation): a decrease in MCHC [g/dl] by 2.93% was registered in the examined subjects after supplementation (Figure 3, Table 2).

CHCM [g/dl]

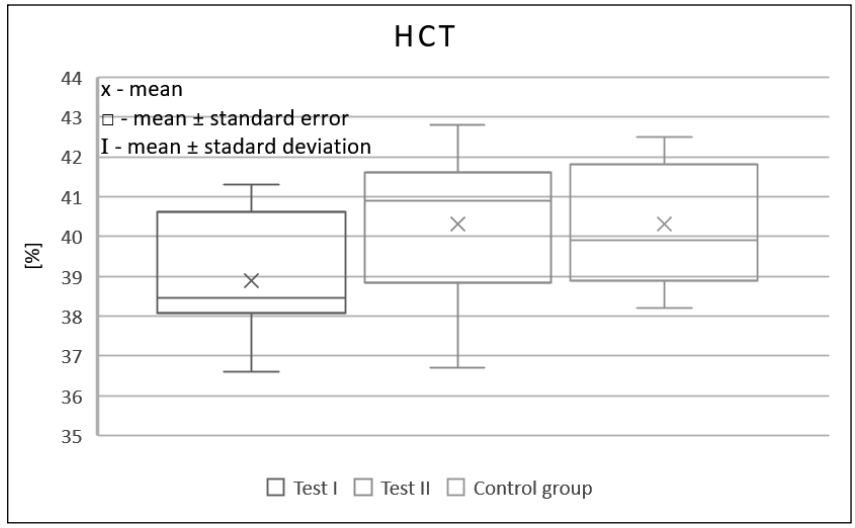
Changes were observed in study group 1 (before fennel supplementation) in comparison to group 2 (after fennel supplementation): a decrease in CHCM [g/dl] by 4.11% was registered in the examined participants after supplementation (Figure 4, Table 2).

HDW [g/dl]

Changes were observed in study group 1 (before fennel supplementation) in comparison to group 2 (after fennel supplementation): a decrease in HDW [g/dl] by 2.16% was registered in the examined persons after supplementation (Figure 5, Table 2).

Basophils [%]

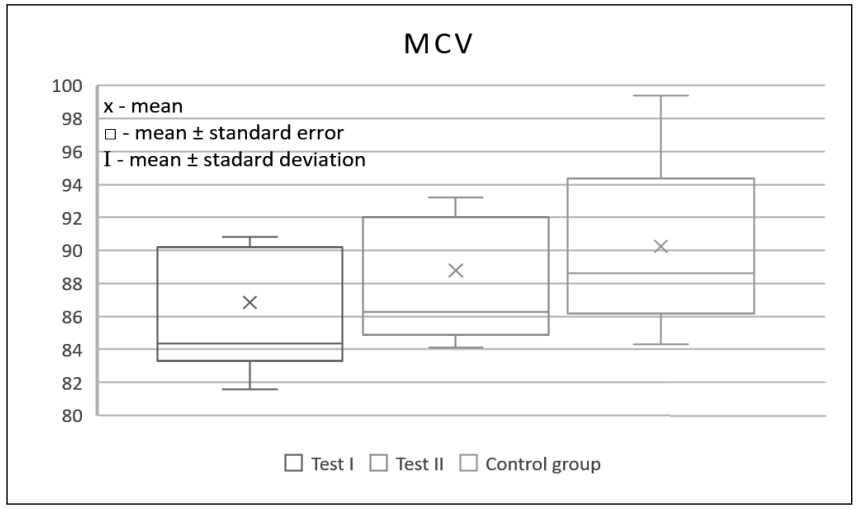
Changes were observed in study group 1 (before fennel supplementation) in comparison to group 2 (after fennel supplementation): an increase in basophils [%] by 40% was



p-value = 0.047

Figure 1

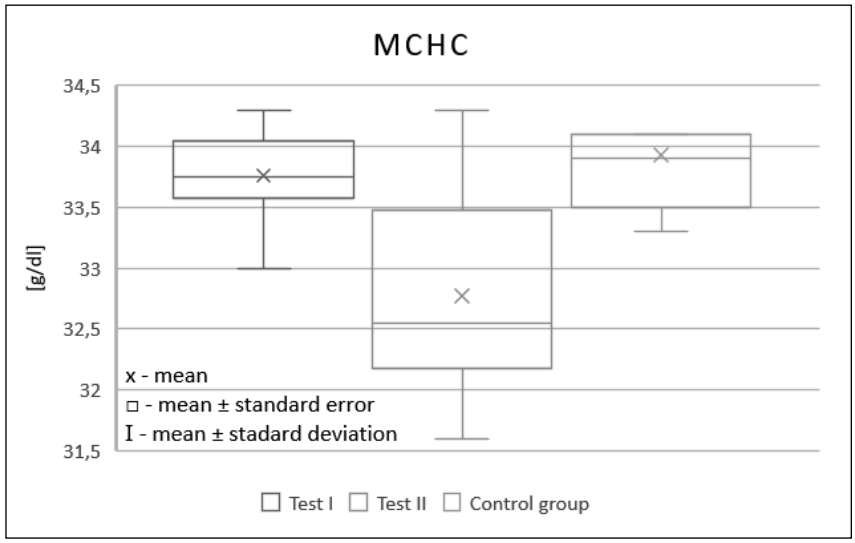
Changes in haematocrit (HCT [%]) before (pre) and after (post) fennel supplementation.



p-value = 0.008

Figure 2

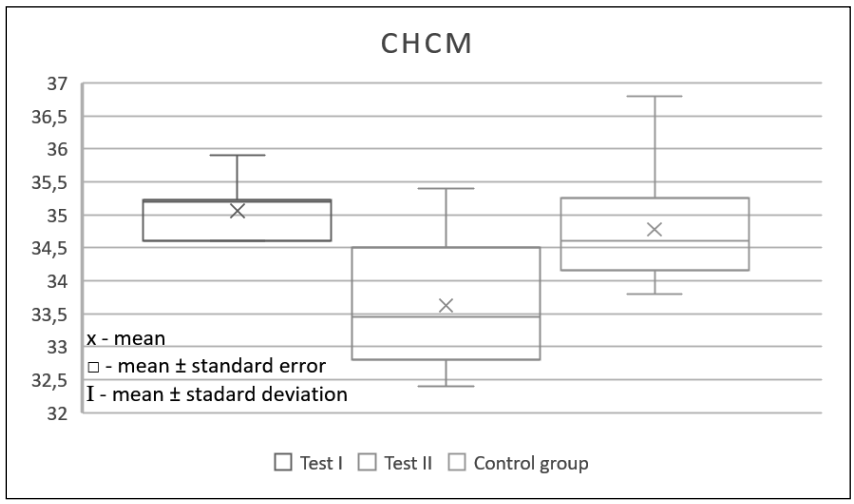
Changes in mean corpuscular volume (MCV [fl]) before (pre) and after (post) fennel supplementation.



p-value = 0.009

Figure 3

Changes in mean corpuscular haemoglobin concentration (MCHC [g/dl]) before (pre) and after (post) fennel supplementation.



p-value = 0.001

Figure 4

Changes in cell haemoglobin concentration mean (CHCM [g/dl]) before (pre) and after (post) fennel supplementation.

registered in the examined individuals after supplementation (Figure 6, Table 2).

Questionnaire

The analysis of the questionnaire confirmed changes related to the following questions: improvement in general well-being, improvement in mood, change in sleep quality, improvement in memory, reduction in the frequency of night perspirations, reduction in the frequency and intensity of hot flashes, reduction in perspiration, improvement in skin odour, improvement in odour from the mouth, improvement in skin appearance (smooth skin), reduction of digestive ailments (improved intestinal motility, reduction of constipation) and other effects resulting from supplementation with fennel (reduced nervousness and calmness, fatigue) (Table 3).

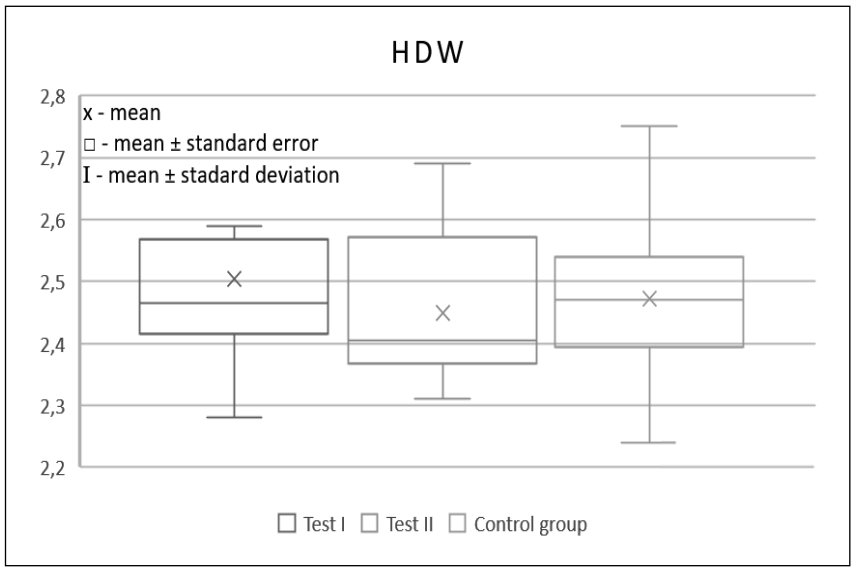
Correlation between questionnaire responses and morphological parameters

Significant positive correlations were found between: HDW level [g/dl] and general well-being, neutrophil level [%] and skin odour, monocyte level [%] and skin appearance, LUC level [10^9/l] and skin odour, urea level [mmol/l] and sleep quality, as well as RBC level [10^{12}/l] and memory. In contrast, negative correlations were found between: CHCM level [g/dl] and excessive perspiration, lymphocyte level [%] and skin odour, lymphocyte level [10^9/l] and skin odour, urea level [mmol/l] and skin odour, MCV level [fl] and mood, eosinophil level [10^9/l] and general well-being, LUC level [%] and skin odour, eosinophil level [10^9/l] and mouth odour as well as skin appearance, and iron level [umol/l] and mouth odour (Table 4, Table 4.1, Table 4.2)

DISSCUSION

The aim of the work was to assess the influence of supplementation with fennel on biochemical indices in women during the climacteric period and quality of life. A literature overview allows to indicate a lack of detailed information on the issue. Although medicinal plants feature relatively weaker effects than synthetic drugs, they are more commonly applied in different societies or ethnical groups due to their lower probability of side effects. A positive effect of *Foeniculum vulgare* was demonstrated in previous research by Abbas et al.[24] and El Araby et al.[25] on the number of white and red blood cells which was also observed in the current study conducted by the author. There were also studies on changes in lipid profile[26,27,28]. On the basis of the authors' own research, no statistically significant changes were found in the above listed indices[24,25,26,27,28].

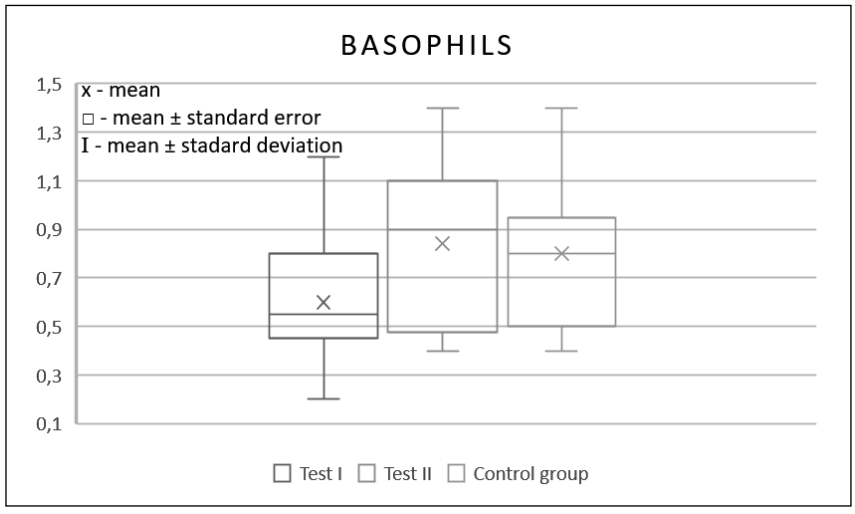
According to the research conducted by Mansouri et al.[29], fennel extract significantly increased the number of red blood cells in rats. Plants, due to their oxidation properties, may eliminate the negative influence of free radicals which cause destruction of cell membraned in red cells[29]. In the study by Faudale et al.[30], it was found that phenolic compounds isolated from aqueous extracts of fennel present absorption activity and ability to remove free radicals. Sim-



p-value = 0.044

Figure 5

Changes in standard deviation for haemoglobin distribution width (HDW [g/dl]) before (pre) and after (post) fennel supplementation.



p-value = 0.021

Figure 6

Changes in basophils [%] before (pre) and after (post) fennel supplementation.

ilar results were obtained by Oktay et al.[31]. Aqueous and ethanol extracts of fennel feature strong anti-oxidation properties due to absorption of free radicals and the ability to chelate metals. This results in the protection of the cell membrane in red cells against oxidising agents and lengthening their life. In the research carried out by Abbas et al.[24] on albino rabbits (one control group and two study groups supplemented with fennel, respectively, fennel seeds made up 2% and 4% of their diet), the authors showed that diet enriched with *Foeniculum vulgare* significantly increased haemoglobin concentration in the examined groups. The erythrocyte count increased in both examined groups. A significant increase in leukocytes was noted in the group with a 4% share of fennel in their diet. Increased values of haemoglobin and haematocrit were also demonstrated in the research. An increase in some indices of blood cells (i.e. mean concentration of haemoglobin in red cells) was observed in both examined groups with fennel supplementation[24]. In the research on rats conducted by El Araby et al.[25] it was shown that diet supplementation in the form of fennel seeds increased number of red cells, haemoglobin content and HCT [%] as well as monocyte count.

There have been studies conducted on animals to investigate the influence of fennel on changes in lipid profile. In the study by Helal et al.[26], hyperlipidaemia in rats was observed. It was also found that fennel may have had influence on lowering the total level of lipid to the normal level. The mechanism regarding such activity of fennel may result from its anti-oxidation properties[26].

In the research by Fatiha et al.[28] a methanol extract of fennel was administered to rats, and it lowered total cholesterol, LDL fraction and triglycerides. It was demonstrated that the fennel extract may have anti-atherosclerotic and hypolipidemic effects[28]. Afiat et al.[27] conducted a study on short-term treatment with fennel and its results on lipid profile in post-menopausal women. The double-blind, randomised, placebo controlled trials included 60 women. The examined females were randomly assigned to groups (treated group and placebo group). Their blood was taken twice: at the beginning and after three months of treatment with fennel. The indices measured in the research comprised: total cholesterol, cholesterol fractions and triglycerides. The results did not present significant differences between groups in the levels of triglycerides, total cholesterol or LDL and HDL cholesterol fractions, whereas a significant borderline improvement was observed in HDL fraction in the group supplemented with fennel. However, the level of LDL cholesterol fraction[27] was lower in women supplemented with fennel.

In the present study, while comparing indices of the red cell system in the examined group before and after supplementation with fennel, it was found that HCT increased by 3.6% and MCV by 2.23%, whereas MCHC decreased by 2.93%, CHCM by 4.11% and HDW by 2.16 %. In the research, it was noted that an increase in the HDW index results in

Table 3

Changes in reported menopausal symptoms before and after fennel supplementation

Question	Baseline point value (before supplementation period)	Final point value (after supplementation period)	*p*-value
1	0	13	0.014*
2	0	12	0.000*
3	ns	ns	ns
4	0	14	0.000*
5	ns	ns	ns
6	0	12	0.014*
7	0	11	0.000*
8	0	12	0.014*
9	0	12	0.014*
10	0	14	0.014*
11	0	9	0.000*
12	0	11	0.000*
13	0	10	0.000*
14	0	12	0.000*
15	0	8	0.000*

ns – non-significant; * level of statistical significance $p \leq 0.05$.

Table 4

Correlations for variables with distribution close to normal

Morphological parameters	General well-being (applies to question 1)	Sleep quality (applies to question 5)	Excessive perspiration (applies to question 10)	Skin odour (applies to question 11)	Skin appearance (applies to question 13)
CHCM [g/dl]	-0.432	0.288	**-0.687***	-0.189	-0.458
HDW [g/dl]	**0.644***	0.041	0.432	-0.189	-0.458
Neutrophils [%]	0.369	-0.120	0.497	**0.708***	0.084
Lymphocytes [%]	-0.361	0.188	-0.451	**-0.727***	-0.118
Monocytes [%]	0.411	-0.448	-0.029	0.157	**0.686***
Lymphocytes [10^9/l]	-0.423	0.317	-0.030	**-0.739***	-0.288
LUC [10^9/l]	0.078	0.075	0.217	**0.637***	0.151
Urea [mmol/l]	-0.613	**0.637***	-0.041	0.055	**-0.667***

*level of statistical significance $p \leq 0.05$

Table 4.1

Correlations for distribution of variables other than normal

Morphological parameters	General well-being (applies to question 1)	Mood (applies to question 3)	Memory (applies to question 6)	Night perspiration (applies to question 7)	Occurrence of hot flashes (applies to question 8)
RBC [10^{12}/l]	-0.217	0.543	**0.740***	0.141	0.506
MCV [fl]	0.086	**-0.657***	-0.623	-0.347	-0.545
MCH [pg]	-0.118	-0.583	-0.428	-0.726	-0.817
LUC [%]	0.222	-0.142	0.235	0.200	0.039
Eosinophils [10^9/l]	**-0.753***	0.156	-0.197	-0.319	-0.039
Iron [umol/l]	-0.422	0.077	-0.078	-0.451	-0.351

*level of statistical significance $p \leq 0.05$.

Table 4.2

Correlations for variables with distribution other than normal

Morphological parameters	Intensity of hot flashes (applies to question 9)	Excessive perspiration (applies to question 10)	Skin odour (applies to question 11)	Odor from mouth (applies to question 12)	Skin appearance (applies to question 13)
RBC [10^{12}/l]	0.506	0.110	0.283	-0.347	-0.104
MCV [fl]	-0.545	-0.578	-0.592	0.090	0.104
MCH [pg]	-0.817	-0.716	-0.382	-0.327	-0.104
LUC [%]	0.039	0.111	**-0.708***	-0.090	0.385
Eosinophils [10^{9}/l]	-0.039	-0.084	-0.120	**-0.709***	**-0.811***
Iron [umol/l]	-0.351	-0.522	-0.238	**-0.667***	-0.489

*level of statistical significance $p \leq 0.05$.

improved general well-being. In the authors' research, comparing the group after the period of supplementation with fennel and the control group, changes were also observed for the MCHC and CHCM indices.

No significant changes were noticed for RBC, HGB, MCH, RDW or iron. Changes in the red cell system in climacteric women may result from many factors, including diet. Maintaining a proper level of erythrocyte indices is supported by a diet rich in iron, vitamins B12 and B6, folic acid and amino acids. Fennel contains polyphenols and vitamin C that inhibit the aging process and also decrease the negative influence of free radicals on the cell membrane, also in red cells. Anethole, the main component of fennel, features anti-oxidation properties. Such activity may explain the increase in haematocrit and the index concerning the mean volume of red cells. Lowered MCHM, CHCM and HDW indices and a lack of statistically significant changes for RBC, HGB, MCH, RDW and iron may by caused by a deficiency of iron in the diet of the examined women. According to observations and examinations, the level of iron in women has recently worsened, especially in developed countries. The level of haemoglobin in the blood is affected by factors such as health condition, season of the year, temperature or barometric pressure. In research, it has been indicated that the level of haemoglobin also fluctuates under the influence of the outside environment (i.e. dust and gas contamination in one's surroundings). Examining the group after the supplementation period and the control, statistically significant changes were noted for RDW and MCH. Fennel, introduced in the diet, improves cell oxygenation and the functioning of the red blood cell system[24,29,32,33].

In the examined group, an increase in the number of basophils by 40% was observed after the fennel supplementation period. This may prove an increase in immunity. Coumarins, flavonoids, triglycerides and sterols found in *Foeniculum vulgare* indicate antimicrobial, antipyretic and immunomodulatory activity. Anethole contained in the plant features strong anti-inflammatory and anti-bacterial effects. In the studies by Dua et al.[3] and Kaur et al.[34], it was confirmed that fennel plays an important role in eliminating bacterial, fungal, viral and parasitic infections. Fennel seeds are a rich source of nitrite, therefore, they may significantly influence and modulate vascular functions[3,24,29,33,34,35,36].

In the authors' own research, no changes were found for WBC, neurocytes, lymphocytes, monocytes, eosinophils or LUC before or after the supplementation period. However, statistically significant changes in monocytes were noted between the group after the period of supplementation with fennel and the control group. In the studies by Abbas et al.[24] and El Araby et al.[25], the influence of fennel on the above listed blood indices was demonstrated. The duration of fennel supplementation in the mentioned trials was approximately one month. It may be assumed that in the authors' own research, statistically significant changes for the indices were not observed because of the period of supplementation was too short[24,26].

In the present research, no changes in PLT, MPV, PCT or PDW indices were noted. The main function of platelets is participation in haemostasis processes. The central role of platelets in inflammatory reactions and immunological responses has been indicated in the latest reports. Some symptoms of menopause are, among others, mood swings, frequent headaches, susceptibility to stress and irritability. Recently, the influence of stress on rheological blood parameters and immunological processes has been observed. A reaction to stress occurs so that the body adapts to metabolic and immunological functions, enabling the organism to survive in a situation of external threat[37,38].

In the research by Kwiatkowski et al.[39], fennel lengthened the blood coagulation time in the examined group. The researchers applied oil isolated from fennel which contained high concentrations of phenol compounds and coumarins that feature anti-coagulant and thrombolytic properties. In the present research, the patients were supplemented with an infusion prepared from fennel seeds containing from 2 to 6% of essential oil, so no statistically significant differences were observed for PLT, MPV, PCT or PDW indices[39].

After the period of supplementation with fennel in the research group, no statistically significant changes were

found for urea, creatinine, eGFR, ASPAT, ALAT, total cholesterol, LDL, HDL, alpha-Amylase or lipase. In the authors' research, comparing the group after the period of fennel supplementation with the control group, statistically significant changes were shown for lipase. In the research by El-Araby et al.[25], Afiat et al.[27] and Farid et al.[35], there were changes observed for renal, hepatic and lipid profiles. The supplementation period in the studies ranged from one to a few months. The lack of statistically significant changes for urea, creatinine, eGFR, ASPAT, ALAT, total cholesterol, LDL and HDL that was observed in the authors' own research may result from the short period of supplementation and small research group. In the studies by El-Araby et al.[25], Afiat et al.[27] and Farid et al.[35], no statistically significant differences were observed for pancreatic profile, and the same results were confirmed in the present study[25,27,35].

Summarising, in recent studies, there is a lack of reports on changes in biochemical blood indices among menopausal women subjected to *Foeniculum vulgare* supplementation.

Fennel contains a high number of phytoestrogens (non-steroidal, plant-based, polyphenolic compound of structure similar to 17β-estradiol), therefore, it is able to reduce and relieve symptoms of climacteric, such as: hot flashes, sleep disorders, anxiety, bad mood, palpitations, perspiration, mood swings, irritability, problems with concentration and memory, vertigo, headaches and lowered libido. In the survey, the women examined in the current study confirmed improvement in general well-being and mood, as well as improved sleep quality. The subjects also indicated a reduction in perspiration and digestive discomfort after the period of supplementation with fennel (improvement in intestinal peristalsis and reduction of constipations)[14,17,18,22,23,40].

The study results obtained in this work are among the few reporting on fennel supplementation's effect on morphological and biochemical blood indices in menopausal women. The above study contains limitations in the form of a small number of subjects, short time of supplementation and lack of a control group. The collected data were based on a self-reported questionnaire and the studied women's answers. Therefore, it seems justified to carry out further research and analyses concerning the issue.

CONCLUSIONS

1. Fennel (*Foeniculum vulgare* Mill.) is a plant that, due to the content of many precious components (including phytoestrogens), features, among others, antioxidant, anti-inflammatory and anti-microbial effects, and can also be acknowledged as a supplement supporting women's health which is reflected in the blood biochemical indices.
2. Knowledge of processes connected with the occurrence of climacteric that take place in a woman's organism as well as a proper diet can contribute to the elimination of irritating symptoms of menopause and general improvement in a woman's physical and mental condition in the period of climacteric.
3. The planned main study is feasible based on the results of the pilot study, but can have some experimental errors regarding the inclusion and exclusion criteria.

Conflicts of interest
The authors declare no conflict of interest.

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