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Effect of lignans on the quality of life of perimenopausal women

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The problems associated with the health of a woman in the second half of her life are one of the priority areas of modern medicine. The purpose of the study is to determine the efficacy and safety of the drug in comparison with placebo in patients of perimenopausal age. Materials and methods. A randomized study was conducted in 40 patients aged 38 to 55 years without chronic somatic and gynecological diseases. The 1st group included 20 women who were treated with the study drug (7-hydroxymatairesinol-lignan formula), the 2nd group included 20 placebo-controlled women (a similar dose of placebo). Conclusion. The results of the study showed that 7-hydroxymatairesinol has an effect on peripheral vasodilation, does not cause adverse reactions (drowsiness, weakness, reduced performance, does not lead to fluid retention), improves the general condition, causes a decrease in follicle-stimulating hormone, and has a positive effect on breast tissue. glands, increases sexual activity, affects weight loss, improves carbohydrate and lipid metabolism, as well as intracellular enzymatic activity of the liver. Key words: perimenopause, phytoestrogens, hot flashes, lignans. For citation: Serebrennikova K.G., Arutyunyan N.A. Effect of lignans on the quality of life of perimenopausal women. Gynecology. 2018; 20(3): 61–65. DOI: 10.26442/2079-5696_2018.3.61-65

The influence of lignans on the quality of life of women of perimenopausal age

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Abstract

Problems associated with the state of health of women in the second half of her life are one of the priorities of modern medicine. The aim of the study was to determine the efficacy and safety of the drug in comparison with placebo in patients of perimenopausal age.

materials and methods. A randomized study was conducted in 40 patients aged 38 to 55 years without chronic somatic and gynecological diseases. The I group included 20 women who underwent therapy with the test drug (7-hydroxymatairesinol-lignan formula), in the second group – 20 women, placebo-controlled (similar dose of placebo).

Conclusion. The results of the study showed that 7-hydroxymatairesinol has an effect on peripheral vasodilation, does not cause side effects (drowsiness, weakness, decreased efficiency, does not lead to fluid retention), improves general condition, causes a decrease in follicle-stimulant hormone, has a positive effect on breast tissue, increases sexual activity, affects weight loss, improves carbohydrate and lipid metabolism, as well as intracellular enzymatic activity of the liver.

Key words: perimenopause, phytoestrogens, hot flashes, lignans.

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Risks in women does not lose its significance both from the standpoint of improving the quality of life and from the standpoint of its impact on disease prevention. This is especially important at the present time, taking into account changes in the social and environmental situation and the growth of both diseases of the reproductive system and extragenital diseases [1, 2]. Perimenopause and late reproductive age in women aged

45–50 years are characterized by a gradual cessation of the menstrual cycle against the background of a decrease in ovarian secretion of estrogens and progesterone. During this period, the reproductive function of the female body declines and, together with a decrease in the levels of sex steroids, the frequency of signs and symptoms increases, which are traditionally considered clinical and biochemical markers of accelerated aging: overweight and obesity, hypercholesterolemia and hypertriglyceridemia, arterial hypertension, osteopenia and osteoporosis, as well as reduced quality of life [1-6].

According to many studies, the early symptoms of menopause - vasomotor symptoms, which include hot flashes and excessive sweating, which is intensely manifested at night, are associated with pathological afferentation of the central nervous system in the structure that regulates the activity of the hypothalamus-pituitary system. The reason for this is considered to be a decrease in the synthesis of inhibin in the granulosa cells of the follicles, which is the main regulator of the synthesis of follicle stimulating hormone (FSH) in the pituitary gland. An increase in FSH levels is noted long before the perimenopause with unchanged levels of luteinizing

hormone (LH) and the hormone estradiol in the blood [7]. As a result of changes in this system, there is a decrease in ovarian function, which leads to a violation of ovulation, the causes of anovulation are also undoubtedly associated with age-related changes in the late reproductive period.

In most patients, symptoms first appear with menstrual irregularities of the type of oligomenorrhea at the age of 45–47 years. About 70% of perimenopausal women complain about hot flashes and increased sweating of varying severity. In 80% of patients, hot flashes last more than 1 year, in 25-50% - more than 5 years, about 10% of women report the presence of hot flashes for 12 years after menopause. In a recently completed 13-year prospective cohort study, the median duration of moderate to severe hot flashes was 10.2 years [8, 9]. Nocturnal hot flashes cause sleep disturbance, which leads to irritability, tearfulness, and decreased performance [10, 11]. In perimenopause, a decrease in immune defense gradually progresses, non-infectious morbidity increases, meteorolability increases,

osteoporosis develops, degenerative changes in the cardiovascular system progress, metabolic disorders occur, body weight increases due to adipocyte hyperplasia. It has been established that the process of apoptosis of follicles is significantly accelerated after 37 years.

The development of safe methods for the prevention and treatment of menopausal syndrome, which is an integral medical, socio-economic problem, is becoming increasingly important due to the progressive increase in life expectancy and increasing

the need to provide the necessary level of its quality in women. Hormonal preparations (estrogens, combined estrogen-progestogen preparations, tibolone) are considered to be pathogenetically justified and most effective [12-15]. However, there are relative and absolute

contraindications for menopausal hormonal therapy (MHT). Absolute contraindications for MHT are, for example, vaginal bleeding of unknown nature, breast cancer, endometrial cancer, diseases manifested by thromboembolic syndrome, tardive cutaneous porphyria, pregnancy, and a number of other gynecological and extragenital diseases [16]. However, given that the use of MHT is limited due to the existing contraindications to its appointment, in the XX century, studies were conducted that made it

possible to scientifically substantiate the use of alternative methods of treating menopausal syndrome. One of these methods is phytotherapy based on plant materials rich in phytoestrogens [17, 18]. Phytoestrogens are plant compounds that, in their properties and action, are similar to estrogens, which have a selective effect in case of a lack of their own hormones, and eliminate the negative effects of

estrogen in excess. The mechanism of action of phytoestrogens is associated with physicochemical properties that allow them to bind to estrogen receptors, stimulating a specific cascade of reactions in the cell; their ability to influence the activity of enzymes of the aromatase system, stimulate the formation of globulins in the liver that bind sex steroids, and thus modulate the biological activity of endogenous estrogens. Phytoestrogens, having weaker properties compared to estrogens, can become a worthy alternative to conventional MHT [19]. Currently, phytoestrogens are classified as follows: isoflavones, lignans, coumestans, and drugs that act through the hypothalamic-pituitary system. Lignans are of particular interest. Lignans are phytoestrogens similar in their properties to estrogen, a mammalian enterolactone containing a phenolic ring. Lignarius is a purified active lignan 7-hydroxymatairesinol,

which is obtained from knots of Norway spruce (*Picea abies*). Norwegian spruce knots have been identified as a unique rich source of lignans. The content of hydroxymatairesinol reaches 84% of the

total amount of lignans [20]. Lignans have anti-inflammatory, antitumor, and antioxidant effects, strengthen cell structure, slow down the aging process, maintain a healthy weight by reducing appetite, regulate plasma cholesterol by increasing high density lipoproteins and reducing low density lipoproteins [21–24].

Objective : to determine the efficacy and safety of the herbal drug compared with placebo in patients of perimenopausal age.

Materials and Methods A

randomized study was conducted in 40 patients aged 38 to 55 years without chronic somatic and gynecological diseases. Group 1 included 20 women who were treated with the study drug (7-hydroxymatairesinol-lignan formula), group 2 included 20 placebo-controlled women (similar placebo dose). After the completion of the screening period and the final assessment of compliance with all selection criteria, the patients were randomized to receive therapy in one of 2 groups (in a ratio of 1:1).

Patients of the 1st group (n=20) received phytoestrogen, 7-hydroxymatairesinol, 2 capsules daily in the morning for 4 weeks (28 days). Each capsule of the drug contained lignan (7-hydroxymatairesinol) 30 mg, excipients: microcrystalline cellulose (but

sitel), capsule (gelatin, water, titanium dioxide dye). Patients of the 2nd group (n=20) received a placebo (30 mg of microcrystalline cellulose) in a regimen that mimics the regimen of taking a herbal preparation: 2 capsules daily in the morning for 4 weeks (28 days). Prior to the start of

therapy, all patients underwent a study of anamnestic data, such as height, body weight and body mass index (BMI), laboratory and instrumental research methods: clinical blood test, biochemical blood test, hemostasiogram, analysis of the level of sex and gonadotropic hormones (LH, FSH, estradiol, prolactin), urinalysis, microscopic examination of smears from the urethra, cervical canal and vagina for purity, oncocytological examination of the epithelium of the cervix and cervical canal, measurement of height and body weight, blood pressure, pulse, frequency of respiratory movements and body temperature, electrocardiography, transvaginal echography of the pelvic organs, mammography.

The severity of the climacteric syndrome was assessed in points according to the Green's climacteric scale. The Green Menopausal Scale provides a general assessment of the symptoms of menopause. Questions from this scale are used to assess and change different symptoms before and after menopause treatment. The severity of this or that symptom was determined on a 4-point scale: 0 points - no symptom, 1 - weak manifestation of the symptom, 2 - moderate manifestation of the symptom, 3 - pronounced manifestation of the symptom. The scale was assessed before the start of the drug and then after 1 and 2 months after the start of the study.

The Female Sexual Function Index (FSFI) was also assessed. The FSFI questionnaire assesses sexual function and related problems over the past 4 weeks. According to the FSFI questionnaire, the following domains are distinguished in sexual function: sexual desire, arousal, lubrication, orgasm, satisfaction, and pain during intercourse. Each question was scored from 0 to 5 points. Sexual desire was assessed by 2 questions – in terms of frequency and level of desire. Arousal was assessed by 4 questions: frequency, level, persistence, and satisfaction. Orgasm was assessed by 2 questions: frequency, difficulty to achieve, and satisfaction. Lubrication release was assessed by 4 questions - frequency, presence of problems, frequency of maintenance, and maintenance problems. Satisfaction was assessed by 3 questions - on the degree of closeness with a partner, sexual connection and general sexual life. Pain was assessed by 3 questions - the frequency of pain during and after vaginal penetration. For each of the 6 aspects, a separate score was calculated and by adding 6 partial points, a final score was obtained, which could take values from 2 to 36. At the end of the full course of therapy (4 weeks), a follow-up period of 4 weeks (28 days) was planned, cumulative effect and further examination was carried out, which was similar

to the examination earlier. All patients were included in the study after

obtain their informed consent to participate.

Statistical processing was performed using the Statistica 6.0 program. The statistical significance of differences was determined using nonparametric Mann–Whitney tests. Comparison of parametric variants after a preliminary check of the correctness of the distribution of samples was carried out on the basis of Student's t-test. Differences were considered significant at $p < 0.05$.

Results Patients

in menopause presented a wide range of complaints associated with vasomotor disorders: hot flashes of varying frequency and intensity, hyperhidrosis, neurovegetative symptoms - episodes of tachycardia and increased blood pressure, headaches and sleep disturbances, numbness of the feet or legs, psychoemotional

Table 1. The severity of climacteric syndrome in patients in perimenopause according to the Green's climacteric scale (points)

Index	1st group (n=20)			2nd group (n=20)		
	before treatment	1 month after treatment	2 months after treatment	before treatment	1 month after treatment	2 months after treatment
Physical condition symptoms	7.11±3.16	5.4±2.85*	5.36±1.3*	7.9±2.9	7.2±1.77	7.4±2.5
Psycho-emotional symptoms	14.8±7.4	10.08±3.3*	12.5±2.8*	14.23±5.48	12.6±3.04*	12.79±3.9*
Vasomotor symptoms	3.01±2.16	1.95±1.8*	2.02±0.7*	4.04±1.94	3.31±1.56*	3.67±1.5*
Total Symptom Score	24.9±6.32	17.43±3.7*	19.8±2.6*	26.17±5.07	23.1±2.43*	23.86±1.7*

*Here and further in Table. 2: there are significant differences in indicators before treatment and 1 and 2 months after treatment (p<0.05).

Table 2. Hormone levels in perimenopausal patients

Index	1st group (n=20)			2nd group (n=20)		
	before treatment	after 1 month after treatment	after 2 months after treatment	before treatment	after 1 month after treatment	after 2 months after treatment
LH, honey/ml	38.17±1.7	37.02±2.1	36.9±1.22	37.9±2.2	37.8±2.07	37.8±2.1
FSH, honey/ml	56.59±1.18	53.7±1.21*	50.1±1.08*	55.06±2.3	55.04±1.31	55.1±1.4
Estradiol, pmol/l	105.2±2.3	105.6±1.9	105.97±1.0	105.3±2.5	105.8±1.6	105.7±2.8
Prolactin, honey/ml	326.79±0.6	326.1±1.08	325.76±0.3	331.2±3.01	332.4±2.6	332.1±1.7

symptoms in the form of nervousness, labile mood, tearfulness and irritability. Patients' complaints were grouped and evaluated by scoring on the Green's menopausal scale (Table 1). As can be seen from Table. 1, despite the large number

of complaints about hot flashes and night sweats made by patients of the 2nd group (4.04±1.94), the average total indicator of menopausal disorders slightly differed between patients of the 1st and 2nd groups, which amounted to 24.9 ±6.32 and 26.17±5.07 points, respectively. The study of the components of the quality of life revealed

a positive correlation between the level of tension and nervousness, irritability, panic attacks, depression and the severity of the climacteric syndrome in patients of both groups. At the same time, the psychoemotional state and neurovegetative symptoms had the greatest influence on the change in the quality of life of patients in both groups. According to Table. Table 1 shows that, as expected, the most effective remedy for the relief of

menopausal disorders was therapy in patients of the 1st group (therapy with 7-hydroxymatairesinol), the maximum improvement was obtained 1 month after the start of the drug, which made it possible to reduce the total indicator of menopausal symptoms by 70% - by improving the indicators of symptoms of the physical condition, psycho-emotional, vasomotor symptoms, thereby leading to an improvement in the well-being and quality of life of patients. Patients noted good tolerability of the drug. Patients of the 2nd group, who received placebo, expressed dissatisfaction with the effectiveness of treatment in relation to the relief of symptoms of the psycho-emotional and physical state, only in 28% of cases there was a

positive effect of this drug on the Green's menopausal scale.

A comparative assessment of statistically significant changes based on the results of the FSFI questionnaire showed that an increase in the "desire" indicator was noted in 58.8% of patients in the 1st group. In patients of the 2nd group, there was no increase in the "desire" indicator. Comparative assessment of the indicator "excitement" showed a statistically significant change only in the 1st group in 37.3%. The "orgasm" domain changed statistically significantly during therapy only in patients of the 1st group - 41.7%. According to the indicator "release of lubricant" there was a statistically insignificant increase in indicators in all groups. Statistically significant results in the "satisfaction" domain were found in groups 1 and 2 in 58.6% and 20.2%, respectively. Patients of the 1st and 2nd groups were comparable in

age, anthropometric and clinical and laboratory parameters

lam. The mean age of women receiving herbal medicine was 46.3±1.2 years, those receiving placebo was 45.9±1.7 years (p<0.01). The patients did not differ statistically significantly in such indicators as height, body weight and BMI, which was 29.0±0.97 in group 1 and 28.14±1.2 in group 2 (p< 0.001). It was noted that 35% of patients in the 1st group showed a significantly significant decrease in BMI 2 months later (taking into account the cumulative effect) after treatment by 2.7 from the initial level.

It was noted that there were no significant differences between the groups in terms of systolic and diastolic blood pressure: in the 1st group it was 115±1.7/80±2.9 mm Hg. Art., in the 2nd - 116±1.02/82±0.4 mm Hg. Art. (p<0.001). It was found that the therapy had no effect on systolic and diastolic blood pressure, however, these indicators were not statistically significant (p<0.01). During the study, the levels of LH, FSH, estradiol and prolactin in the blood serum were determined (Table 2).

According to Table. 2, the levels of LH, estradiol and prolactin in patients of the 1st and 2nd groups before and after treatment practically did not differ. There was a significant decrease in FSH in patients of the 1st group (p<0.05), while the level of estradiol in the blood serum remained practically unchanged (p<0.001).

The study of hemostasiogram parameters (fibrinogen, soluble fibrin-monomer complexes, activated partial thromboplastin time, international normalized ratio, D-dimer, prothrombin index) showed the absence of a statistically significant positive and negative effect of tairesinol 7-hydroxymate on the hemostasis system as after 1 month , and after 2 months of observation. The effect of the drug on carbohydrate and lipid metabolism, as well as on the intracellular enzymatic activity of the

liver in blood serum was studied (Table 3). Comparative analysis of blood plasma glucose levels in patients of the 1st group revealed a significantly significant decrease in fasting glycemia: initially 6.1±1.22 mmol/l, after 2 months 5.2±0.74 mmol/l, and decrease in insulin from 13.8±1.59 to 9.4±0.14 mcU/l. As can be seen from Table. 3, the use of 7-hydroxymatairesinol led to an improvement in the lipid spectrum of the blood in the form of a decrease in the level of choleste

rin to 6.9 ± 0.12 mmol / l and triglycerides - up to 2.97 ± 0.28 mmol / l. A significantly significant decrease in the intracellular enzymatic activity of the liver (alanine aminotransferase) was noted in patients of the 1st group from 34.4±1.86 to 26.4±0.52 U/L. In the 2nd group (placebo), changes in the parameters of the carbohydrate and lipid spectrum of the blood were significantly insignificant.

Cytological examination of smears from the surface of the cervix and cervical canal of atypical

Index	1st group (n=20)			2nd group (n=20)		
	before treatment	1 month after treatment	2 months after treatment	before treatment	1 month after treatment	2 months after treatment
Glucose, mmol/l	6.1±1.22	5.8±1.01*	5.2±0.74**	5.98±1.9	5.8±1.27	5.8±1.2
Insulin, µU/l	13.8±1.59	10.6±1.32*	9.4±0.14**	12.7±2.2	11.9±2.05	12.3±1.9
Alanine aminotransferase, U/l	34.4±1.86	31.03±1.09*	26.4±0.52**	36.5±1.07	35.08±0.91	35.2±1.04
Aspartate aminotransferase, U/l	25.7±2.31	23.4±2.24	21.02±1.1	26.61±2.4	25.9±2.5	26.03±1.7
Triglycerides, mmol/l	3.96±0.44	3.5±0.3*	2.97±0.28**	3.59±0.81	3.61±0.37	3.4±0.72
Cholesterol, mmol/l	8.04±0.4	7.7±0.24*	6.9±0.12**	7.51±1.59	7.4±1.61	7.45±1.15
High density lipoprotein cholesterol, mmol/l	1.58±0.32	1.41±0.26	1.4±0.19	1.62±0.37	1.57±0.33	1.49±0.29
Low density lipoprotein cholesterol, mmol/l	4.13±0.81	4.15±0.55	3.9±0.28	4.45±0.72	4.01±1.62	4.22±0.9

There are significant differences in indicators: *before treatment and 1 month after treatment (p<0.01); **before treatment and 2 months after treatment (p<0.05).

cells were not detected in any case; in 5 (12.5%) patients, atrophic changes in ecto and endocervix cells were noted both before and after the treatment. During transvaginal ultrasound examination (ultrasound) of the pelvic organs in patients of groups 1 and 2, no pathological changes were detected. We performed a statistical analysis of the results of ultrasound of the pelvic organs before and after taking the drug, which showed that no significant changes were detected (p<0.01). At the same time, there were no cases of the formation of endometrial pathology and ovarian formations, uterine bleeding.

Mammography revealed a normal X-ray picture in 35% (n=7) in the 1st group and in 40% (n=8) in the 2nd group, fibro-fatty involution in 30% (n=6) and 24% (n=5), diffuse form of fibrocystic disease - in 35% (n=7) and 40% (n=8), respectively. No cases of malignancy were diagnosed. There were some changes in the structure of breast pathology detected by ultrasound, namely, the frequency of detection of fibro-fatty involution in the 1st group decreased due to an increase in the frequency of normal ultrasound picture (p<0.05). After 2 months in patients of the 1st group, there were no subjective complaints in 35.2% of patients. In 24.1% of cases, patients of the 1st group older than 45 years showed a good clinical effect, confirmed by ultrasound data. These changes affected only patients of the 1st group. Therefore, 7-hydroxy xymatairesinol has a positive effect on breast tissue.

Conclusion

Thus, as a result of the study, the ability of 7-hydroxymatairesinol to have an effect on peripheral vasodilation, which is the cause of autonomic reactions in women with menopausal syndrome, has been shown. The drug does not cause such adverse reactions as drowsiness, weakness, decreased performance, does not lead to fluid retention and weight gain. An interesting fact is that while taking 7-hydroxymatairesinol, the patients showed an

improvement in their general condition, namely, a significant relief in violation of sleep, memory, attention, mood, increased vitality and working capacity. At 2–4 weeks, there was an increase in sexual activity and libido, as well as an increase in orgasm. Taking 7-hydroxymatairesinol causes a decrease in FSH, while it does not affect the level of estradiol in the blood serum, which indicates the absence of

an estrogen effect of the drug components. According to mammography and ultrasound of the breast, it was revealed that taking 7-hydroxymatairesinol has a positive effect on breast tissue. When using 7-hydroxymatairesinol at a dosage of 60 mg (2 tablets) daily for 1 month in patients with metabolic syndrome in the perimenopausal period,

There is a good cumulative effect, which affects the decrease in body weight, and also significantly improves the indicators of carbohydrate, lipid metabolism and intracellular enzymatic activity of the liver. It should be

noted that during the entire period of the study of 7-hydroxymatairesinol, not a single undesirable effect associated with taking the drug was registered. Thus, during the study, 7-hydroxymatairesinol

was well tolerated and there were no side effects. According to the patients who took 7-hydroxymatairesinol, they have a need for its further use.

Literature/References 1.

- Yureneva S.V., Ilyina L.M., Smetnik V.P. *Aging of the female reproductive system: from theory to clinical practice. Part I. Endocrine and clinical characteristics of the stages of reproductive aging in women. Obstetrics and gynecology.* 2014; 3:21–7. / Yureneva SV, Ilyina LM, Smetnik VP *Starenie repro duktivnoj sistemy zhenshin: ot teorii k klinicheskoj praktike. Chast I. En dokrinnye i klinicheskie harakteristiki stadij reproduktivnogo stare niya zhenshin. Akusherstvo i ginekologiya.* 2014; 3:21–7. [in Russian]
2. Polotsky HN, Polotsky AJ. *Metabolic implications of menopause. Semin Reprod Med* 2010; 28(5): 426–34.
3. Khan UI, Wang D, Karvonen-Gutierrez CA et al. *Progression from metabolically benign to at-risk obesity in perimenopausal women: a longitudinal analysis of study of women across the nation (SWAN). J Clin Endocrinol Metab* 2014; 99(7): 2516–25.
4. Rees M. *EMAS position statements and clinical guides. Maturitas.* 2014; 77(4): 303–4.
5. Wu X, Cai H, Kallianpur A et al. *Age at menarche and natural menopause and number of reproductive years in association with mortality: results from a median follow-up of 11.2 years among 31,955 naturally menopausal Chinese women. PLoS One* 2014; 9(8): e103673.
6. Yousefzadeh G, Mahdavi-Jafari F, Shokoohi M et al. *Modulation of coronary artery disease risk factors by menopausal status: A population based study among Iranian women (KERCADRStudy). ARYA Atheroscler* 2013; 9(6):332–6. 7. Prilepskaya V.N. *Menopausal syndrome: innovations in menopausal therapy. breast cancer.* 2017; 25(2): 105–8. / Prilepskaya VN *Klimaktericheskiy sindrom: innovacii v menopauzalnoj terapii. RMZh.* 2017; 25(2): 105–8. [in Russian]
8. Heine R, Schmidt G, Knoch R et al. *Postmenopausal Hormone Therapy. J Clin Endocrinol Metab* 2010; 95(1):1–65.
9. Thorbjarnardottir T, Olafsdottir EJ, Valdimarsdottir UA et al. *Oral contraceptives, hormone replacement therapy and breast cancer risk: A cohort study of 16,928 women 48 years and older. Acta Oncol* 2014. 10. Gromova O.A., Torshin I.Yu., Limanov O.A. *Pathophysiology of vegetative-vascular paroxysms (hot flashes) during menopause in women and mechanisms of action of -alanine. New clinical and pharmacological concept. Gynecology.* 2010; 12 (2): 3. / Gromova OA, Torshin I.Yu., Limanov OA i dr. *Patofiziologiya vegetativno-sosudnykh paroksizmov (prilivy) v period menopauzy u zhenshin i mekhanizmy vozdeystviya -alanina. Novaya kliniko-farmakologicheskaya koncepciya. Gynecology.* 2010; 12 (2): 3. [in Russian]

11. Andricoula V, Prelevic G. Menopausal hot flashes revisited. *Climacteric* 2009; 12:3–15.
12. Gevorkyan M.A., Fatalieva K.Z. The role of hormone therapy in the prevention of menopausal metabolic syndrome. *Obstetrics, gynecology and reproduction*. 2009; 6:4–9. / Gevorkyan MA, Fatalieva KZ Rol gormonoterapii v profilaktike menopauzalnogo metabo licheskogo sindroma. *Akusherstvo, ginekologiya i reprodukcija*. 2009; 6:4–9. [in Russian] 13. Ledina A.V., Kulikov A.Yu. Complex treatment and prevention of estrogen dependent urogenital disorders: clinical aspects and pharmaco-economic analysis. *Pharmacoeconomics*. 2009; 1:13–8. / Ledina A.V., Kulikov A.Yu. Kompleksnoe lechenie i profilaktika estrogenzavisimyh urogenitalnyh rasstrojstv: klinicheskie aspekty i farmakoekonomicheskij analiz. *Farmakoekonomics*. 2009; 1:13–8. [in Russian] 14. Likhachev A.V., Galyanskaya E.G., Shevlyagina L.S., Polyanskaya I.B. Therapy of estrogen-deficient conditions in menopause. *Obstetrics, gynecology and reproduction*. 2008; 1:4–6. / Likhachev AV, Galyanskaya EG, Shevlyagina LS, Polyanskaya IB Terapiya estrogen-defitsitnyh sostoyanij v klimaktericheskom periode. *Akus herstvo, ginekologiya i reproduction*. 2008; 1:4–6. [in Russian] 15. Spiridonova N.V., Basina E.I., Krylova O.V. Comparative efficacy of various regimens for the treatment of menopausal disorders. *Obstetrics, gynecology and reproduction*. 2012; 3: 49–55. / Spiridonova NV, Basina EI, Krylova OV Akusherstvo, ginekologiya i reprodukcija. 2012; 3:49–55. [in Russian] 16. Von Wolff M., Stute P. *Gynecological endocrinology and reproductive medicine. Per. with him. Under total ed. E.N.Andreeva. M.: MEDpress-inform, 2017. / Von Wolff M., Shtute P. Ginekolo gicheskaya endokrinologiya i reproduktivnaya medicina. per. s German. Pod obsh. red. ENAndreevoj. M.: MEDpress-inform, 2017. [in Russian]*
17. Atkinson C, Franlencfeld C, Lampe J. Gut Bacterial Metabolism of the Soy Isoflavone Daidzein: Exploring the Relevance to Human Health. *Exp Biol Med* 2005; 230:155–70.
18. Manach C, Scalbert A, Morand C et al. Polyphenols: food sources and bioavailability. *Am J Clin Nutrition* 2004; 79:727–47.
19. Korennaya V.V. The use of phytotherapy and low-dose hormone replacement therapy in the treatment of menopausal syndrome. *AG info*. 2009; 4:44–8. / Korennaya VV Primenenie fitoterapii i nizkodozirovannoj zamestitelnoj gormonalnoj terapii v lechenii klimaktericheskogo sindroma. *AG info*. 2009; 4:44–8. [in Russian]
20. Aldercreutz H. Lignans and human health. *Crit Rev Clin Lab Sci* 2007; 44:483.
21. Gerstenmeyer E, Reimer S, Berghofer E et al. Effect of thermal heating on some lignans in flax seeds, sesame seeds and rye. *Food Chem* 2013; 138(2–3): 1847–55.
22. Udani JK, Brown DJ, Tan MO, Hardy M. Pharmacokinetics and bioavailability of plant lignan 7-hydroxymatairesinol and effects on serum enterolactone and clinical symptoms in postmenopausal women: a single-blinded, parallel, dose-comparison study. *J Am Coll Nutr* 2013; 32(6): 428–35.
23. Smeds AI, Eklund PC, Willfor SM. Chemical characterization of high-molecular mass fractions in a Norway spruce knotwood ethanol extract. *Phytochemistry* 2016; 130:207–17.
24. Yang D, Xiao CX, Su ZH et al. 7(S)-hydroxymatairesinol protects against tumor necrosis factor-mediated inflammation response in endothelial cells by blocking the MAPK/NF- κ B and activating Nrf2/HO-1. *Phytomedicine* 2017; 32:15–23.

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