FEMIMENS - EFFECTIVE AND SAFE ELIMINATION OF SYMPTOMS OF PRE-MENTAL SYNDROME, HYPERPROLACTINEMIA AND AGE-RELATED DYSHORMONAL DISORDERS

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Summary

The fast pace of life in today's society, environmental degradation, poor diet, work stress, and the growth of genital and extragenital pathologies affect the human adaptation mechanisms and cause the steady increased number of dishormonal disorders in the woman's reproductive system. The most common is premenstrual syndrome (PMS), which occurs in 75–95% of menstruating women [1]. 20–35% of them seek medical help due to severe symptoms [2, 3].

Premenstrual syndrome is a condition that occurs as a result of a complex of psychoemotional, endocrine and vegetovascular disorders 2–10 days before the onset of menstruation [4]. It is believed that the development of premenstrual syndrome is associated with the imbalance of sex hormones, such as estrogen and progesterone. In addition, different studies have established that fluctuations of these hormones concentration during the menstrual cycle are a decisive factor in the occurrence of PMS. Also, it has been proved that estrogens and progesterone have a significant modulating effect on the central nervous system due to their interaction with nuclear receptors. Estrogens and progesterone have a direct effect on the membrane of neurons and their synaptic function, not only in the centres responsible for the reproductive system, but also in the limbic brain regions that regulate emotions, behaviour and sleep [5].

Prolactin, which is a modulator of the action of many hormones, plays an important role in the pathogenesis of PMS. Prolactin contributes to the sodium-retarding effect of aldosterone and the antidiuretic effect of vasopressin. Special attention is paid to the cyclical production of prolactin: for example, there is a phenomenon of latent hyperprolactinemia, when the concentration of prolactin increases occasionally, such as after eating or stressful situations and while sleeping. The rest of the time the concentration of prolactin is within normal limits. It has been established that such fluctuations of prolactin can be the cause of the hormonal system imbalance as a whole [2, 3, 5].

Estrogens affect the activity of monoamine oxidase. This enzyme is involved in the oxidation of biogenic amines such as norepinephrine, epinephrine, serotonin and dopamine. The increased levels of epinephrine cause nausea, and the increased levels of epinephrine serotonin – tense anxiety, insomnia, palpitation, attention failure and fluid retention [6, 7].

In recent years, special attention in PMS pathogenesis has been paid to peptides of the intermediate lobe of pituitary gland, such as melanotropin and endorphins. Endogenous opioid peptides – P-endorphin and enkephalin are found not only in the cerebral cortex and pituitary gland, but also in other body tissues, including the adrenal glands, pancreas and gastrointestinal tract. Endorphins inhibit the secretion of lutein hormone and stimulate the release of prolactin by decreasing dopamine activity. By inhibiting central biogenic amines, endorphins can cause changes in mood and behaviour, and increased appetite and thirst as well. Breast engorgement, fluid retention, constipation and flatulence can be the result of the increased levels of prolactin and vasopressin, and their inhibitory effect on prostaglandin E1 in the intestine caused by endorphins [8, 9].

Hyperprolactinemia

The problem of hyperprolactinemia is still relevant at nowadays. It is primarily associated with the effect of the increased levels of prolactin on the genesis of infertility in women (about 30%) and men (15–20%). The prevalence of hyperprolactinemia in the population is 0.5% in women and 0.07% in men; so women are more than 7 times more likely than men. The highest frequency of this pathology is observed in women 25–40 years old [10]. In addition to infertility, hyperprolactinemia causes menstrual irregularities, libido disturbance, galactorrhea, neurological and psychoemotional disorders [11, 12].

Prolactin has a wide range of biological effects in the human body. Also it is a multifunctional hormone involved in the processes of follicular maturation and ovulation. Prolactin supports corpus luteum function and lactation during pregnancy; provides progesterone production; affects behaviour and stimulates parental reactions, as maternal instinct as well. Prolactin is a regulator of sexual function in men; it is necessary for the normal function of the testicles and the development of additional gonads. Prolactin synergistically acts with testosterone and luteinizing hormone; regulates the secretion of insulin and adrenal androgens [16].

It is known that the secretion of prolactin is under complex neuroendocrine control, which involves different factors: neurotransmitters and hormones of peripheral endocrine glands. To a greater extent, prolactin is synthesized and secreted by pituitary cells - lactotrophs. Dopamine, which is produced in the hypothalamus and enters the pituitary gland through the portal circulatory hypothalamic-pituitary tract, inhibits the secretion of prolactin by binding to lactotroph D2 receptors [13, 14]. Serotonin and norepinephrine increase prolactin secretion by reducing the activity of the tuberoinfundibular dopaminergic system (TIDA). Acetylcholine causes prolactin decrease and stimulates TIDA [14]. Excessive prolactin production in patients leads to the development of hyperprolactinemic hypogonadism. Under the influence of hyperprolactinemia, the production of the gonadotropin releasing factor in the hypothalamus is reduced. As a result the synthesis and secretion of gonadotropins - luteotropic (LH) and follicle-stimulating hormone (FSH) are inhibited. LH pulse activity, which is characterized for the normal functioning of the reproductive system, decreases.

Hyperprolactinemia also blocks the effects of gonadotropins at the level of target organs (gonads), which causes hypoestrogenemia, reduces the synthesis of progesterone, and stimulates the secretion of adrenal androgens. There are increased levels of dehydroepiandrosterone and dehydroepiandrosterone sulfate, which are also associated with the presence of prolactin

receptors in the reticular zone of adrenal cortex and the generality of hypothalamic regulation of synthesis and secretion of adrenocorticotropic and prolactin by the pituitary gland [15].

Hyperprolactinemia has the following clinical manifestations: shortening of the luteal phase and anovulatory cycles, opsenomenorrhea, oligomenorrhea, amenorrhea; infertility; luteal phase deficiency; uterine hypoplasia; galactorrhea; dishormonal diseases of the mammary gland, mastalgia and mastodynia; premenstrual syndrome; obesity; hirsute syndrome; osteopenia and osteoporosis [17].

Menopause is a physiological process of changes in the woman's reproductive system. These hormonal changes occurred in the body affect many processes, such as menstrual function, nervous system, gastrointestinal tract, bone and cardiovascular system. The menopause period is conditionally divided into premenopause (45 years to the onset of menopause), menopause (the last menstruation period), and postmenopause (from the last menstruation to the end of a woman's life) [18].

In premenopause, a gradual decrease in the level of sex hormones occurs. All these changes occur in the hypothalamus: there is a gradual decrease in its sensitivity to estrogen. There is the decreased release of follicle-stimulating and luteinizing hormones, which is accompanied by the first menstrual irregularities and the anovulatory cycle without ovulation. Atresia of follicles, destruction of their membranes, death of oocytes causing the decreased amount of secreted estrogen, are observed in the ovaries. Hypothalamus feedback, accompanied by the development of even greater hormonal imbalance, is disturbed. As a compensatory reaction by the adrenal glands, the production of adrenaline and norepinephrine increases, causing disturbances in the cardiovascular and nervous system. It is accompanied by high blood pressure, arrhythmia, "hot flashes", headache, dizziness, nausea, vomiting, weight gain and sexual dysfunction [19].

FEMIMENS - EFFECTIVE AND SAFE CORRECTION OF HORMONAL IMBALANCE

In case of menstrual irregularities, severe premenstrual syndrome, hyperprolactinemia and hormonal imbalance of menopause, the main method of treatment is a drug therapy. The priority is the prescription of dopamine receptor agonists that interact with dopamine D2 receptors located on the surface of pituitary cells and secreting prolactin. In response to this, the levels of cycloadenosine monophosphate and intracellular calcium are decreased. As a result the following reactions occur: the fast reaction wherein prolactin secretion decreases, and slow reaction wherein transcription of prolactin gene and its synthesis reduce. The antimitotic activity of dopamine receptor agonists leads to the restoration of menstrual function, ovulatory cycles, fertility, and the reduction in the size of tumours producing prolactin as well [20].

However, such therapy may be contraindicated in case of some cardiovascular diseases, endogenous psychosis, renal and hepatic failures. The therapy is accompanied by severe side effects and the rapid development of resistance [21].

Today, the use of dopamine receptor agonists of plant origin is recommended as an alternative therapy. Along with effectiveness, such therapy is safe and has better tolerance and excellent compliance.

FEMIMENS is a phytocomposition designed to correct hormonal imbalance in women. Femimens contains 4 components: Vitex agnus-castus extract - 125 mg, Withania somnifera extract - 100 mg, Zingiber ofcinale extract - 35 mg and Trigonella foenum-raecum extract - 30 mg. All components of Femimens are complementary.

VITEX AGNUS-CASTUS

As a result of randomized controlled trials and studies with a small sampling of patients, the evidence confirming the effectiveness and good tolerance of Vitex agnuscastus extract in the treatment of premenstrual syndrome, premenstrual dysphoric disorder and latent hyperprolactinemia was obtained (van Die M.D. et al., 2013).

Vitex extract components protect dopaminergic neurons and modulate dopamine receptor activity.

A study by S.E. Park et al. (2014) [23] has established that rutin extracted from Vitex agnuscastus protects dopaminergic neurons from damage by inhibiting proapoptotic JNK and p38 MAPK signalling pathways. Studies by W. Shen et al. (2012) and H.Q. Chen et al. (2008) have revealed that chlorogenic acid and luteolin inhibit excessive activation of microglia and thereby increase the survival of dopaminergic neurons [24, 25]. A study by B. Meier (2000) has shown that casticin, vitexilactone and rotundifuran, contained in the standardized fruit extracts of Vitex agnus castus, dose-dependently displace dopamine D2, D3, and D4 receptors [26].

The neuroprotective effect of rosmarinic acid was reported in the model of Parkinson's disease developed by J. Wang (2012): the action of rosmarinic acid provided the normalization of dopamine and tyrosine hydroxylase levels, as well as the restoration of the physiological ratio of Bcl-2/Bax proteins that regulate apoptosis [27].

The dopamine receptor modulation is due to the antihyperprolactin effects of Vitex extracts. In the experiment, intraperitoneal injections of extracts also significantly reduced the increased levels of testosterone that is similar to the action of dopamine receptor agonists [28].

Estrogen-modulating effect of Vitex agnus castus extract

Vitex agnus castus extract contains phytoestrogens and viticosterone flavone due to which it has a pronounced estrogen modulating activity [28]. The estrogenic effect of Vitex agnus-castus extract is carried out through interactions with estrogen receptors (ERa, ERb) and progesterone. This was confirmed by N.A. Ibrahim (2008): the administration of Vitex extract to rats with removed ovaries caused a significant increase of uterine mass, stimulated the increase of progesterone levels and the decrease of the levels of luteinizing hormone and prolactin. When using a specific antiestrogen inhibitor, the effect was significantly reduced [29]. Due to the effect of Vitex extract on estrogen activity it can be used for the treatment of premenstrual syndrome to alleviate the symptoms of menopause [27]. A randomized study by M.D. Van Die (2013) has shown that the effectiveness of Vitex agnus-castus extract was significantly higher than placebo. Vitex agnus-castus extract normalizes the excessive secretion of prolactin, the duration of the shortened luteal phase of the menstrual cycle, increases the level of progesterone and 17β-estradiol in the middle of the luteal phase [30, 31].

Antihyperprolactin effect of Vitex agnus castus extract

In clinical studies, the efficacy of Vitex agnus castus extracts in the treatment of mastalgia was reported. The efficacy was due to the inhibition of the excessive prolactin release by blocking dopamine D2 receptors in pituitary cells [30]. Analysis of the antihyperprolactinemic effects of Vitex extracts has shown that such effects are stimulated by the components of the flavonoid fraction of the extract, in particular flavonoid casticine [32].

Casticine dose-dependently inhibited the release of prolactin from pituitary cells upon stimulation with estradiol both in vitro and in vivo. These effects of casticin were associated with inhibition of ER receptor gene expression and increased ERb receptor gene expression. Casticine seemed to program pituitary cells to secrete normal prolactin levels rather than increased ones [33].

Analgesic and antidepressant properties of Vitex agnus castus extract

The analgesic and antidepressant properties of Vitex agnus castus are due to the influence of a number of components (vitexin, casticin, isoorientin, kempferol) on m- and d-opioid receptors. In particular, casticin, which is close in its effects to endorphins, is a selective agonist of d-opioid receptors. A study by D.E. Webster (2011) has shown that casticin has some similarities with endorphins [34].

Antitumor effects of Vitex agnus castus extract

The antitumor effects of Vitex extract are associated with the induction of apoptosis of cancer cells by increasing intracellular oxidation. A study by M. Weisskopf has established the cytotoxicity of Vitex agnuscastus extracts for breast cancer cells, gastric carcinoma (CATO-III), colon cancer (COLO 201), lung cancer (Lu-134-AH), promyelocytic leukemia HL-60, hyperplasia cells prostate and prostate cancer (BPH-1, LNCaP, PC-3) [54]. A study by X. Long (2008) has found that apigenin inhibits antiestrogen-resistant breast cancer cells [35].

Antimicrobial effects of Vitex agnus castus extract

Vitex agnus castus extract contains a significant amount of substances with bactericidal properties. Therefore, the extract exhibits a wide range of antimicrobial action (bactericidal, antimycobacterial, fungicidal, antiprotozoal). In particular, Vitex agnus castus essential oils are active against typical pathogenic and opportunistic bacteria (excluding Listeria). The effect is comparable with chloramphenicol and amoxicillin. The strains of Staphylococcus aureus [37], which are often resistant to most antibiotics, are the most sensitive to Vitex agnus castus. The antifungal activity of Vitex agnus castus leaf essential oil was observed for most strains of bacteria such as T.mentagrophytes, Microsporum Canis, Trichophyton Rubrum, M. gypseum and Epidermophyton floccosum [36].

Anti-inflammatory effect

Vitex extract prevents eosinophilic inflammation by reducing the secretion of eotaxin and the intensity of eosinophil migration [38]. Eosinophilia and lymphocytosis are significantly reduced against the background of a decrease in the levels of proinflammatory cytokines IL-4, IL-5, and TNF-α [39]. Extract components also inhibit cyclooxygenase in cytokine-mediated inflammation and reduce edema significantly [40]. Among the components of Vitex agnus castus extract, artemethine, penduletin and casticin directly modulate the metabolism of prostaglandins and also inhibit neutrophil chemotaxis [41].

WITHANIA SOMNIFERA

Ayurveda is the traditional Indian medicine, which was mentioned even 6000 years BC (Charak Samhita, 1949). Also, Withania somnifera known as “Indian winter cherry” or “Indian ginseng,” has been used as a tonic, aphrodisiac, diuretic, anthelmintic, astringent, hypothermic, and stimulating and anti-inflammatory remedy as well. It is one of the most important herbs in Ayurveda. Withania contains more than 80 types of phytochemical auxiliary asteroids, non-steroidal alkaloids, steroidal lactones and saponins, such as anaferin, anachigrin, hygrin, couscogyrin, tropin, pseudotropin, etc., amino acids such as aspartic acid, glycine, tryptophan, proline, alanine, tyrosine, hydroxyproline-valine, cystine, glutamic acid and cysteine, calcium, phosphorus, iron, flavonoids, starch, glycosides, dulcite and volatile oil (Smith DR et al., 2008; Direkvand-Moghadam A. et al., 2016; Rafieian-Kopaei M. et al., 2011).

Withania somnifera and treatment for infertility and sexual dysfunction

Numerous studies have shown that extracts of fruits, leaves, stems, and especially roots of Withania somnifera improve sperm quality, such as motility and sperm count in men (Mahdi AA et al., 2011; Ambiye VR et al., 2013; Gupta A . et al., 2013). Withania somnifera reduces the effect of chemical toxins on the testicles in men and on the ovaries in women (Sharma V. et al., 2011; Kumar A. et al., 2015; Belal NM et al., 2012; Shaikh NH et al., 2015; Patil RB 2012; Bhargavan D., 2015). In addition, Withania somnifera enhances folliculogenesis and spermatogenesis, as well as improves hormonal balance by normalizing the levels of luteinizing (LH) and follicle-stimulating hormones (FSH), testosterone (Kumar A. et al., 2015; Al-Qarawi A.A. et al., 2000; Nirupama M. et al., 2015; Kaspate D. et al., 2015). It is interesting to note that in the end of 8-week intake of Withania somnifera compared with a group of women taking a placebo, a significant advantage was observed ($p < 0.001$) when assessing parameters such as the index of female sexual behaviour and the index of female sexual distress in healthy women according to criteria such as the total index score, desire, orgasm, lubrication, and the total number of successful sexual contacts (Dongre S., Langade D. et al., 2015).

The exact mechanism of action of Withania somnifera on the reproductive system has not yet been fully revealed. However, it is believed that it is increasingly associated with the antioxidant properties of the plant. By acting like gamma-aminobutyric acid, which is a neurotransmitter in the central nervous system, Withania somnifera contributes to the improvement of hormonal balance (LH, FSH and testosterone) and activates detoxification processes (Jasuja ND et al., 2013; Shaikh N. et al., 2014). Withania somnifera, due to its metal ion content, facilitates enzyme activity, modifies oxidative stress and prevents cell apoptosis in the male reproductive system (Shukla K.K. et al., 2011).

Adaptogenic and anti-stress properties of Withania somnifera

Numerous studies have demonstrated the adaptogenic and anti-stress properties of Withania somnifera (Abbas and Singh, 2006; Kalsi et al., 1987; Singh et al., 1976, 1977, 1981, 1982, 1993a, 1993b; Singh, 1995a, 1995b, 2006, 2008). They have shown that the use of this plant increases physical endurance, prevents the stress-induced development of stomach ulcers, and reduces the risk of hepatotoxicity and mortality caused by using carbon tetrachloride (CCl4).

Effect of Withania somnifera on the nervous system

The positive effect of Withania somnifera on the intellectual potential, cognitive ability and memory is well known. It is best demonstrated in children with attention deficit disorders, in people with memory impairments cause by traumatic brain injury or long-term illness and in elderly population (Singh and Udupa, 1993). A study by Schliebs et al. (1997) has presented the results of experimental studies on the effects of Withania derivatives on cholinergic, glutamatergic and GABAergic receptors. The results of the study demonstrate the effect of Withania extract on cholinergic receptors in the cortical and basal parts of the forebrain, which partly explains the improved parameters in memory and learning ability [42].

Anti-inflammatory effect of Withania somnifera

Withania somnifera has an anti-inflammatory effect similar to that of hydrocortisone, which was demonstrated in experiments with carrageenan-induced edema in rats (al-Hindawi 1992) [42]. A study by Anbalagan K. (1988) has established that Withania somnifera extract leads to a significant reduction in inflammation, due to the decrease levels of serum proteins in the blood (α 2-glycoprotein, prealbumin and α 2-macroglobulin) [43]. A study by Begum V.H. (1987) has shown that in the course of using Withania somnifera, dissociation of oxidative phosphorylation occurs by significantly reducing ADP/O ratio in the mitochondria of granuloma tissue, which subsequently leads to the increased concentration of Mg^{2+}-dependent ATPase enzymes and the decreased activity of dehydrogenase succinate [43].

Antitumor effect of Withania somnifera

The antitumor effect of Withania somnifera has been revealed in sarcoma 180 (S-180) (Devi P.U., 1992). The ethanolic Withania somnifera extract at a dose of 400 mg/kg and higher with daily use within 15 days has decreased the tumour growth in mice [42, 43].

Antispasmodic effect of Withania somnifera

A study by Malhotra C.L. (1965) has shown that Withania somnifera exhibits an antispasmodic effect on the muscles of the intestines, uterus, trachea and blood vessels. Moreover, its effectiveness is similar to that of papaverine [41, 42].

ZINGIBER OFFICINALE

Zingiber officinale extract contains gingerols and shogaols, which are essential oils and phenolic compounds. They, due to the selective inhibition of cyclooxygenase-2 and 5-lipoxygenase enzymes, reduce the formation of prostaglandins, prostacyclins, thromboxane and leukotrienes and thereby provide the anti-inflammatory and analgesic effects of Zingiber officinale. At the same time, the important difference between ginger and many non-steroidal anti-inflammatory drugs (NSAIDs) is the absence of COX-1 inhibition that prevents gastrointestinal tract damage, including the occurrence of ulcers [4]. In addition, gingerols, being agonists of VR1 vanilloid receptors, provide an additional analgesic effect [44].

The analgesic effect of Zingiber officinale was demonstrated in patients with primary dysmenorrhea in a study of R. Mohammadbeigi (2011) and G. Ozgoli (2009). Its effectiveness at a daily dose of 1 g was comparable to that of ibuprofen and mefenamic acid [45, 46]. A study by S.O. Umeh (2013) has proved the androgenic activity of Zingiber officinale in male laboratory rats. The significantly increased testosterone levels were observed under the influence of phenolic compounds. However, such activity was not observed in female rats [47]. In vitro experiments have shown the ability of phenolic compounds to activate estrogen receptors with the same strength as Ural licorice [48].

TRIGONELLA FOETUM GRAECUM

Trigonella foetum graecum extract contains steroidal saponins, sterols, flavonoids (diosgenin, tigogenin, yamogenin, phytosterol), which are natural phytohormones. It is rich in potassium, phosphorus, magnesium, iron, calcium and vitamins (C, B1, B2, PP, folic acid). A study by S. Goyal (2016) has shown that diosgenin against the background of a pronounced inflammatory reaction significantly inhibits tumour necrosis factor (TNF-α) and pro-inflammatory cytokines IL-1 and IL-6, providing an anti-inflammatory effect [50]. As a precursor of progesterone, Trigonella foetum graecum extract stops progesterone-deficient states and normalises the balance of hormones [49, 51].

Trigonella foetum graecum saponins selectively inhibit tumour cell division, and can also activate apoptotic programs that cause programmed cell death. Both Trigonella foetum graecum extract and diosgenin isolated from it were able to inhibit the formation of aberrant foci of crypts, which can be regarded as precancerous lesions. A study by J. Raju (2004) has confirmed that diosgenin inhibits cell proliferation along with the induction of apoptosis, and inhibits the expression of proapoptotic BCL2 protein and thereby enhances the expression of the anti-apoptotic caspase-3 protein as well. Diosgenin also showed high antitumor activity in breast cancer [50]. The antidiabetic activity of Trigonella foetum graecum extract is confirmed in streptozotocin and alloxan diabetes mellitus. By acting on pancreatic β-cells polyphenols, Trigonella foetum graecum extract reduces blood glucose and normalizes the morphological state of acini and cytosol in the islets of Langerhans [51].

CONCLUSIONS

FEMIMENS is a phytocomposition designed to correct hormonal imbalance in women. Due to its balanced composition, FEMIMENS provides a polymodal pharmacological effect on the main pathogenetic links of premenstrual syndrome, hyperprolactinemia and age-related dishormonal disorders. Vitex agnuscastus extract has antihyperprolactin, dopamine and

estrogen modulating effects and exhibits analgesic, antidepressant, antiapoptotic, anti-inflammatory and antimicrobial effects. Withania somnifera has healing properties for infertility and sexual dysfunction, and exhibits calming, anti-inflammatory, antioxidant, antispasmodic, analgesic and immunomodulating effects, and improves cognitive performance and memory as well. Zingiber officinale extract has anti-inflammatory and analgesic effects that increase estrogen levels in women with insufficient production of these hormones. Trigonella foetum graecum extract exhibits anti-inflammatory, analgesic, antioxidant effects and increases progesterone levels.

The optimally selected composition of FEMIMENS, good tolerance and safety make it possible to recommend FEMIMENS for the following conditions:

- premenstrual syndrome, including premenstrual dysphoric disorder;
- hyperprolactinemia;
- age-related dishormonal disorders in perimenopausal period in women;
- anovulatory infertility, as well as infertility caused by insufficiency of the luteal phase;
- mastopathy;
- endometrial hyperplasia.

FEMIMENS is also can be used for:

- severe stress changes;
- autonomic homeostasis disturbance;
- some other reproductive health changes;
- to restore the menstrual cycle after abortion and other uterus interventions;

References are in editorial office

FEMIMENS
Capsules No.30

LIVE FULL LIFE!

Recommended for women[16]

- Involutive changes of the mammary glands [1, 15]
- Age-related dysgromonal conditions [5-10, 13, 14]
- In the presence of symptoms of premenstrual dysphoric disorders [11, 12]
- To reduce intensity and alleviate symptoms of PMS [3, 4, 13, 14]
- As an additional component to comprehensive correction of hyperprolactinemic conditions and age-related dysgromonal disorders [1, 2, 7-9]

References

1. Ibrahim E.N. et al., Transfuse Med, 2008.2. Van Die M.D. et al., Planta Med, 2013.3. Long Z. et al., Wei Sheng Yan, 2008. 4. Sohn S.H. et al., Neurotoxicology, 2009. 5. Langade D. et al., J Int Soc Sports Nutr, 2015. 6. Devi P.U. et al., Indian J Exp Biol, 1992. 7. Bhattacharya S.K. et al., European Journal of Operational Research, 1997. 8. Ghosal S. et al., Journal Article, 1989. 9. Schliebs R. et al., Neurochem Int, 1997. 10. Malhotra C.L. et al., Pharmacology, 1965. 11. Mohammadbeigi R. et al., Pak J Biol Sci, 2011. 12. Tatarchuk T.F. et al., Premenstrual syndrome, 2003. 13. Jagan M.R. et al., Cancer Epidemiol Biomarkers Prev, 2004. 14. Khanna S. et al., International Journal of Drug Development & Research, 2010. 15. Toxicol J. et al., J Med Toxicol, 2017. 16. Instructions for use of food supplement Femimens.

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