Prospects for the use of common rod (Vitex agnus-castus L.) as a source for obtaining medicines

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Prospects of using chest berry (Vitex agnus-castus L.) as a source of obtaining medicines

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SUMMARY

Currently, the use of medicinal plants as a source of biologically active substances for a mild effect on hormonal disorders associated with disruption in the work of the female reproductive system remains relevant. It has long been noted that the common twig plant (Vitex agnus-castus L.) is capable of exerting physiological effects similar to those of sex hormones, such as decreasing libido in men and relieving mastalgia symptoms in women. The dopaminergic activity of the common barnacle extract has been proven. The literature also describes the possibility of influencing the opioid system. Due to the various classes of secondary metabolites of the barnacle, namely: flavonoids, iridoids, terpenoids, it is capable of exerting antimicrobial, anti-inflammatory, anticarcinogenic effects, as well as affecting cognitive functions.

Key words: common prutnyak, sacred vitex, biologicallyactive substances, pharmacological properties.

RESUME

At present, the use of medicinal plants for soft influence on hormonal disorders of the female reproductive system remains relevant. It has long been noted that Vitex agnuscastus is able to exert physiological effects similar to that of sex hormones, such as reducing male libido and alleviating the symptoms of female mastalgia. The dopaminergic activity of Vitex agnus-castus L. was proved and the possibility of influencing the opioid system was also described in the literature. It is also able to provide antimicrobial, antiinflammatory, anti-carcinogenic action and also affect cognitive functions due to various classes of secondary metabolites of Vitex agnus-castus, such as flavonoids, iridoids, terpenoids.

Keywords: Vitex agnus-castus, chasteberry, biologically active substances, pharmacological properties.

Despite significant advances in the targeted chemical synthesis of active pharmaceutical ingredients, plants remain unique.

source of receipt biologically active compounds with the indisputable advantages of their use as prophylactic and therapeutic agents. Medicines based on total extracts and individual substances isolated from plants are successfully used to correct pathological conditions of various organs and systems of the human body, providing antioxidant, anti-inflammatory, antimicrobial, immunostimulating, hormone-like and other effects.

One of the topical areas of application of herbal medicinal products is the correction of disorders of the female reproductive system. The dynamic lifestyle of modern women, accompanied by stress, unbalanced nutrition and an unfavorable ecological situation in the urban environment, contributes to an increase in the frequency of occurrence of conditions associated with a violation of hormonal regulation and, as a consequence, with menstrual irregularities, mastopathy, etc. hormone therapy prescribed to relieve symptoms of menopause, urogenital disorders, cancer and metabolic disorders [1]. However, long-term use of hormonal drugs leads to an increased risk of coronary heart disease, strokes, venous thrombosis,

In the middle of the last century, it was found that some secondary plant metabolites, conventionally called "phytoestrogens", have hormone-like effects on the human body. Such substances contribute to the elimination of symptomatic manifestations of hormonal disorders, while they do not have side effects inherent in hormonal drugs [2, 3, 4]. In the last decade, this direction has been actively developing in terms of the search and study of new plant species that have a similar effect.

In this regard, the plant Prutnyak ordinary(Vitex agnus-castus L.) of the Vervain family (Verbenaceae), also known asthe name "Vitex sacred", "Abraham's tree", "Monastic pepper".

Common prutnyak is a shrub that reaches a height of six meters. The branches are tetrahedral, the leaves are compound, consisting of 5–7 lanceolate leaves. Small, light purple flowers are located at the ends of branches in the form of spike-shaped inflorescences up to 20 cm long. The fruit is a dark brown drupe of a round shape, 3-5 mm in size, covered from 2/3 to 3/4 of a pubescent, grayish-green calyx. By the time of full ripening, the fruits have a wrinkled surface. Each of the four cotyledons contains oblong seeds.

In nature, the prutnyak grows from the Mediterranean to the Black Sea coast, in the southern part of Asia. In Russia, it can be found on loamy and stony soils, the plant is listed in the Red Book of the Krasnodar Territory. Prutnyak is successfully cultivated as a food and ornamental plant [5].

In folk medicine, the aerial part of the rod is used to relieve the symptoms of premenstrual syndrome and menopause, and the broth has a mild sedative effect [6]. The dried fruits of this plant were used as a spice instead of allspice. It was later observed that eating fruits

common prutnyak helps to reduce sexual desire, which was used by the monks, from where the name "Agnus-castus" (from Latin "innocent lamb") came from. In Turkey, common use of barnacle to prevent premature birth, as well as a diuretic [7].

As a medicinal plant, common twig is included in the European Pharmacopoeia 7.0, 8.0 and 9.0 and the American Herbal Pharmacopoeia, where the mature dried fruits of the plant are described as medicinal plant raw materials. Also, this plant is used in homeopathy [8, 9, 10].

CHEMICAL COMPOSITION

According to the literature, various classes of chemical compounds were found in various parts of the common rod plant: flavonoids, iridoids, terpenoids [11, 12].

Dried unripe fruits contain 0.76% essential oil, ripe - 0.72%, in the leaves - 0.56%. Over 98.5% of the essential oil components were identified by gas chromatography with a mass selective detector, which amounted to over 70 compounds. Prevailing in terms of the ratio of components in total are α-pinene, α-terpenyl acetate, sabinene, β-myrcene, p-cymene, limonene, 1,8-cineole, α-terpineol, trans-β-caryophyllene, trans-β-farnesene, caryophyllene oxide, (E, Z) -geranyl, linalool, sklaren [13].

Along with this, the presence of iridoids was established in this plant - a group of biologically active substances (BAS) with various pharmacological effects, including anti-inflammatory and hypoglycemic ones [14, 15, 16, 17].

Column chromatography from a methanol extract of flowers was used to isolate acubin, agnuside, musaenosic acid and 6'-O-phydroxybenzoyl massenosic acid, agnucastoside A, agnucastoside B, and agnucastoside C [18]. Acubin and agnuside have also been found in fruits [19].

Terpenes, represented by vitexylactone, rotundifuran, 6,7-diacetoxy-13-hydroxy-labda-8,14-diene, are one of the pharmacologically significant classes of compounds in the fruit of the cane. At the Swiss Federal Institute of Technology, these compounds are obtained in pure form. The substances were isolated from the hexane extract by preparative chromatography on silica gel in a gradient mode with a hexane-ethyl acetate mixture. From 80 grams of crushed fruits, vitexylactone 3 mg, rotundifuran 4 mg, 6b, 7b-diacetoxy-13-hydroxy-labda-8,14-diene - 5 mg were obtained. Further studies have shown that the last two compounds have dopaminergic activity [20].

In a study carried out on a cell culture containing recombinant human D2 dopamine receptors, it was found that terpene-containing fractions of the dry extract of the common rod BNO-1095 have an affinity for these receptors, which confirms the dopaminergic effect of the common rod [21].

In the same study, the interaction of some flavonoids (pendulatin, apigenin) of the cane extract with

estrogen receptors. Along with this, other flavonoids have also been identified in the fruits of common willow: casticin, isovitexin, orientin, gomorintin [22].

PHARMACOLOGICAL PROPERTIESstudied

Most pharmacological activity standardized extracts of common prutus fruits: "BNO-1095", which is a dry extract (10: 1), and "Ze 440" - a dry extract less stable in composition (6-12: 1), obtained by extraction of fruits with ethyl alcohol 70% and 60%, respectively, the first was used at a dosage of 4 mg, the second - 20 mg [23].

Extracts are used orally in the form of tablets or in the form of drops, but the literature also describes the use of the extract of the cane fruit in the form of a nanoemulsion for better absorption in the intestine. Experiment Resultsin vitro indicate a significant increase in the rate of solubility and absorption multicomponent rod extract in this form [24].

Recently, there has been interest in the study of cannabis due to the assumption that it can influence cognitive functions.

In a study by Allahtavakoli, Mohammad et al. [25] studied the ability to memorize in rats with ovariectomy. The result was positive in the groups using the ethanol extract of the common rod or estradiol, in both groups there was an increase in the expression of genes for α-estrogen receptors.

The most widely studied effect of the common rod extract on the regulation of the level of sex hormones, in particular, for the relief of premenstrual syndrome (PMS) [26, 27, 28]. PMS is a complex symptom complex, manifested by vascular, neuropsychic and endocrine changes in the female body. The frequency of its manifestation in women reaches 80–95%, and in about 5% of cases it is severe. Today, it is believed that estrogens play a leading role in the pathogenesis of PMS, namely, their level and ratio. Estrogens, in turn, stimulate an increase in prolactin levels, high concentrations of which contribute to the appearance of edema and mastalgia [29].

The exact mechanism of action of PMS extract on PMS, as well as the full etiology of PMS, has not been sufficiently studied. Undoubtedly, an important role in this effect is played by the dopaminergic and estrogenic activity of biologically active substances in the fruit of the cane [30, 31].

Along with this, some researchers have suggested another mechanism that contributes to the relief of PMS symptoms - the effect on opioid receptors. In a study [32], the affinity of the secondary metabolites of cannabis fruit to opioid receptors was studied. The experiment was carried out on a cell culture with a cloned human opioid receptor. To neutralize the effect of fatty acids on the course of the experiment and obtain a false positive result, the authors processed the raw material with petroleum ether before extraction with 90% methanol. The obtained positive result of this study is important for understanding the mechanisms of action of biologically active substances in cannabis, since, as is known, the system of endogenous opiates is less active during PMS.

and at the same time is able to strongly influence the psychological state and perception of pain.

Proven and definitely significant pharmacological effect, rendered by the fruits of the cane is a decrease in the level of prolactin. In a study by Kilicdag EB et al. [33], in which 40 women with cyclic mastalgia and 40 women with mild prolactinemia took part, it is indicated that the extract of cannabis fruit (Agnucaston) shows similar results with bromocriptine in alleviating mastalgia and reducing the level of prolactin in the blood, but in contrast to bromocriptine no side effects were observed in the patients. These properties are especially important, since good tolerance and the absence of toxicity are especially important for long-term courses of taking such drugs.

In 2017, a meta-analysis of studies on the efficacy of barnacle extract for the treatment of PMS was published, using different dosages, from 8 to 41 mg, and treatment regimens: every day or 6 days before menstruation. As a result of the studies carried out, the efficacy of the treatment with an extract of the common barnacle in this pathological condition has been reliably confirmed [34].

In the literature, other effects are also described that the extracts of the cane fruit have. So, for example, onSalmonella typhimurium has been studied as antimutagenic the activity of the alcoholic extract and essential oil of the cane. A positive dose-dependent effect of both components has been established, which, probably, can lead to a decrease in the risk of developing malignant neoplasms [35].

The experiments also confirmed the antibacterial [36] and antifungal activity of the common barnacle [37]. The methanol extract of the fruit demonstrates a significant inhibition of the growth of mycelium of the fungus in experiments.in vitro and ontomato seedlings. It is assumed that the effect was achieved due to increased expression of plant defense genes [38]. A similar study was carried out on apples [39] with the cannabis essential oil, in the course of which it was found that the components of the essential oil 1,8-cineole and α-pinene have antibacterial and fungistatic effects.

APPLICATION IN MEDICINE

At present, the drug of the company Bionorica "Cyclodinone" is registered in the register of drugs of the Russian Federation in the form of a liquid extract and tablets, the active pharmaceutical substance of which is the extract of the fruit of the cane. Published clinical studies on the use of this drug confirm that the common rod extract has dopaminergic effects, good tolerance, can be used for the treatment of premenstrual syndrome, and also has a positive effect on psychoemotional premenstrual symptoms and somatic complaints, in particular mastodynia [40].

"Cyclodynon" (Cyclodynon) was registered for the first time in Germany and is currently being sold in Europe on an over-the-counter sale. In the Russian Federation, this drug was registered in 2005 under the trade name Agnucaston, and in 2006 it was re-registered as Cyclodinone.

CONCLUSION

Thus, the fruits of the common prutnyak are promising plant raw materials for detailed study and development on its basis of domestic medicines for the correction of disorders of the female reproductive system as part of the implementation of the import substitution program.

LITERATURE

1. Abeer Y. Ibrahim, Samah A. El-Newary, Eman R. Youness, Amr MM Ibrahim, Walaa A. El Kashak. Protective and therapeutic effect of Vitexagnus-castus against prostate cancer in rat // Journal of Applied Pharmaceutical Science Vol. 7 (12), pp. 133-143, December, 2017.

2. Torshin I.Yu., Gromova O.A., Limanova O.A. Systematic analysis of the composition and mechanisms of molecular action of standardized extracts Vitex Agnus-castus // Difficult patient. - 2015. - No. 1-2. -
vol.13. - pp. 19–28.

3. Vysotskaya I.V., Letyagin V.P. Pharmacological effects and molecular mechanisms of action of a medicinal phytopreparation based on Vitex agnus-castus // Mammology. - 2017. - No. 1. - volume 13. - pp. 14–19.

4. Wuttke V., Jarri G., Zaydlova-Wuttke D., Uvarova E.V., Devyatchenko T.F., Gumenyuk E.G., Pogodin O.K., Levenets S.A. Therapeutic possibilities of extracts from the tree of Abraham (Vitex Agnus-castus) in gynecological practice // Problems of reproduction. - 2009. -
No. 4. - P.53–58.

5. Zamotailov A.S., Litvinskaya S.A. Red Data Book of the Krasnodar Territory. - 2007.

6. Lavrenov V.K., Lavrenova G.V. Encyclopedia of Medicinal Plants traditional medicine. - SPb .: Publishing house "Neva", 2003 - 46 p.

7. Mohamed Latoui, Bahar Aliakbarian, Alessandro A. Casazza, Mongi Seffen, Attilio Converti, Patrizia Perego. Extraction of phenolic compounds from Vitexagnus-castus L. // Food and Bioproducts Processing, October 2012, Pages 748–754.

8. German homoeopathic pharmacopoeia, 2003 Medpharm Scientific Publishers, Stuttgart, Germany.

9. European Pharmacopoeia 9.0.

10. Upton Roy. American herbal pharmacopoeia.American Herbal Pharmacopoeia, 2011.

11. Chen Shao-Nong et al. Phytoconstituentsfrom Vitexagnus-castus fruits.Fitoterapia 82.4 (2011): 528-533.

12. Ajay Kumar Meena, Niranjan US, Rao MM, Padhi MM, Ramesh Babu. A review of the important chemical constituents and medicinal uses of Vitex genus // Asian Journal of Traditional Medicines, 2011,
6 (2). - R.54-60.

13. Stojković Dejan et al. Chemical composition and antimicrobial activity of Vitexagnus-castus L. fruits and leaves essential oils. Food Chemistry 128.4 (2011): 1017-1022.

14. Hayder B. Sahib, Adeeb A. AL-Zubaudy, Shallal M. Hussain, Ghaith Ali Jasim, Ban J. Qasim, sawsan S. Al Rawi Acute Toxicity of Vitexagnuscastus Methanol Extract // Int. J. Pharm. Sci. Rev. Res., 26 (2), May-Jun 2014; Article No. 22, Pages: 123-128 /

15. Ramírez-Cisneros M.Á. et al. In vitro COX-1 and COX-2 enzyme inhibitory activities of iridoids from Penstemonbarbatus, Castillejatenuiflora, Cresentiaalata and Vitexmollis // Bioorganic & medicinal chemistry letters. - 2015. - T. 25. - No. 20. - P.4505-4508.

16. Bas Esperanza et al. Inhibition of the pro-inflammatory mediators' production and anti-inflammatory effect of the iridoidscrovalentinoside // Journal of ethnopharmacology 110.3 (2007): 419–427.

17. Sundaram R. et al. Antihyperglycemic effect of iridoid glucoside, isolated from the leaves of Vitexnegundo in streptozotocin-induced diabetic rats with special reference to glycoprotein components // Phytomedicine. - 2012. - T. 19. - No. 3. - P. 211–216.

18. Kuruüzüm-Uz Ayse et al. Glucosides from Vitexagnus-castus.Phytochemistry 63.8 (2003): 959-964.

19. Li Shenghong et al. Compounds from the fruits of the popular European medicinal plant Vitexagnus-castus in chemoprevention via NADP (H): Quinone oxidoreductase type 1 induction. Evidence-Based Complementary and Alternative Medicine 2013 (2013).

20. Hoberg Eva et al. Diterpenoids from the fruits of Vitex agnus-castus // Phytochemistry 52.8 (1999): 1555-1558.

21. Jarry Hubertus et al. In vitro assays for bioactivity-guided isolation of endocrine active compounds in Vitex agnus-castus. Maturitas 55 (2006): S26 – S36.

22. Mari Angela et al. Metabolic profiling of Vitexagnuscastus leaves, fruits and sprouts: Analysis by LC / ESI / (QqQ) MS and (HR) LC / ESI / (Orbitrap) / MS n. Journal of pharmaceutical and biomedical analysis 102 (2015): 215-221.23. 10.1016 / j.phymed.2012.08.006.

23. Schellenberg R., Zimmermann HR, Drewe J. Dose-dependent efficacy extract of Vitex agnus-castus ZE 440 in patients with premenstrual syndrome // Reproductive endocrinology. - 2016. - No. 4 (30). - P.111-118.

24. Yong-Jiang Li, Xiong-Bin Hu, Xiu-Ling Lu, De-Hua Liao, Tian-Tian Tang, Jun-Yong Wu, Da-Xiong Xiang. (2017) Nanoemulsion-based delivery system for enhanced oral bioavailability and Caco-2 cell monolayers permeability of berberine hydrochloride. Drug Delivery 24: 1, pages 1868-1873 /

25. Allahtavakoli, Mohammad et al. Vitexagnuscastus extract improves learning and memory and increases the transcription of estrogen receptor α in hippocampus of ovariectomized rats. // Basic and clinical neuroscience 6.3 (2015): 185.

26. Zahid Hina, Ghazala H. Rizwani and Sumaira Ishaqe. Phytopharmacological review on Vitex agnus-castus: a potential medicinal plant. // Chinese Herbal Medicines 8.1 (2016): 24–29.

27. Vitex agnus-castus. Monograph / Alternative Medicine Review Volume 14, one Number 2009. [Electronic resource] - Access mode: http://www.altmedrev.com/publications/14/1/67.pdf. [Date of treatment 12/29/2017].

28. Vitex agnus-castus. A Systematic Review of Adverse Events / Claudia Daniele Joanna Thompson CoonMax H. Pittler Edzard Ernst // Drug Safety April 2005, Volume 28, Issue 4, pp 319-332.

29. Horrobin DF Prolactin: physiology and clinical significance / Horrobin DF -

Lancaster: MTP Press Ltd., 1973 - p.503-507].

30. Wuttke W. et al. Chaste tree (Vitexagnus-castus) –pharmacology and clinical indications. Phytomedicine 10.4 (2003): 348-357.

31. Artymuk N.V., Ustinova T.A., Vlasova V.V. Experience with Vitex Agnus-castus in the complex of treatment of patients with polycystic ovary syndrome and infertility // Russian Bulletin of Obstetrician-Gynecologist. - 2011. - No. 2. - P.65–68.

32. Webster DE et al. Activation of the μ-opiate receptor by Vitexagnus-castus methanol extracts: Implication for its use in PMS. Journal of ethnopharmacology 106.2 (2006): 216-221.

33. Kilicdag EB et al. Fructusagnicasti and bromocriptine for treatment of hyperprolactinemia and mastalgia // International Journal of Gynecology & Obstetrics 85.3 (2004): 292-293.

34. Schulte P. et al. The treatment of premenstrual syndrome with preparations of Vitex Agnus-castus (Chaste-berry): A systematic review and meta-analysis // European Psychiatry 41 (2017): S907 – S908.

35. Sarac Nurdan, Aysel Ugur and Burak Sen. In vitro antimutagenic activity of Vitexagnus-castus L. essential oils and ethanolic extracts. Industrial Crops and Products 63 (2015): 100-103.

36.Bashir Ahmad, Sadiq Azam, Shumaila Bashir, Achyut Adhikari and Iqbal Choudhary M. Biological activities of a new compound isolated from the aerial parts of Vitexagnuscastus L. // African Journal of Biotechnology Vol. 9 (53), pp. 9063–9069, 27 December, 2010.

37. Antifungal activity of Vitexagnuscastus-in vitro study / G. MOHANDASS, K. SUGUNA DEVI and AMALORPAVARA // Biomedical & Pharmacology Journal Vol. 3 (1), 187-190 (2010) /

38. Švecová E. et al. Antifungal activity of Vitex agnus-castus extract against Pythium ultimum in tomato. Crop protection 43 (2013): 223-230.

39. Stojković Dejan et al. Chemical composition and antimicrobial activity of Vitex agnus-castus L. fruits and leaves essential oils // Food Chemistry 128.4 (2011): 1017-1022.

40. The value of common barnacle in gynecological endocrinology / Source: Wuttke W., Seidlova-Wuttke D., Jarry H., Artymuk N. Der Stellenwert des Monchspfeffers (Vitex agnus-castus). Zeitschriftfur Phytotherapie 2010; 31: 294-298. Per. Mikhail Firstov // Reproductive endocrinology. - 2013. - No. 1 (9). - P.58–62.

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