

REVIEW PAPER

Overview on raspberry leaves and cohosh (*Caulophyllum thalictroides*) as partus preparatory

Ebrahim Alinia-Ahandani ^{1,*}, Farjad Rafeie ², Zahra Alizadeh-Tarpoei ³, Sahebeh Hajipour ⁴, Zeliha Selamoglu ⁵, Elifsena Canan Alp Arici ⁶

¹ Department of Biochemistry, Payame Noor University, Tehran, Iran

² Department of Biotechnology, University of Guilan, Rasht, Iran

³ Department of Biology, Faculty of Basic Sciences, University of Guilan, Iran

⁴ Department of Biology, Faculty of Science, Golestan University, Golestan, Iran

⁵ Department of Medical Biology, Faculty of Medicine, Nigde Ömer Halisdemir University, Campus, Nigde, Turkiye

⁶ Department of Obstetrics and Gynecology, Faculty of Medicine, Necmettin Erbakan, University of Meram, Konya, Turkey



Highlights

- Information of some medicinal herbs gathered from databases related medicinal plants effective in pregnancy and female fertility.
- Black cohosh root affect the immune system, reducing inflammation, nerve function and effect similar to the Estrogen.
- Red raspberry leaf tea increase fertility, reduce the intensity of contractions, increasing milk production.

Article Info

Receive Date: 23 April 2022

Revise Date: 27 May 2022

Accept Date: 14 June 2022

Available online: 19 June 2022

Keywords:

Cohosh
Pregnancy
Medicinal plants
Food
Review

Graphical Abstract



Abstract

The use of medicinal plants has increased worldwide. Most of consumers believe medicinal plants are of “natural” origin and therefore are safer helper to cure the disorders. We also know lots of herbs which are being used for pregnancy. In this research, information on mentioned herbs has been gathered through browsing databases from related sources by searching some keywords such as "medicinal plants effective in pregnancy and female fertility", "Cohosh medicinal plant and its positive and negative effects in pregnancy", and etc. Good findings have been found about the therapeutic effects of these effective medicinal plants, among which it can be said that black cohosh root contains several chemical compounds that can have therapeutic effects. Some of these chemical compounds affect the immune system and defend the body against diseases and reducing inflammation and can play a role similar to serotonin in brain and nerve function. Black cohosh also has an effect similar to the female hormone "Estrogen". Red raspberry leaf tea has been mentioned in traditional medicine as a substance that enhances women's health. It has been used to increase fertility, reduce the intensity of contractions, increasing milk production in lactating women, reduce morning sickness, and reduce the symptoms of premenstrual syndrome such as depression, muscle pain, and irritability. It has been used to help reduce pain and menstrual problems and heavy bleeding. This plant is considered as a natural treatment for menopause symptoms such as hot flashes and night sweats. At the end, by summarizing these methods, the best recommendations for using these medicinal plants were given.



doi: 10.22034/CAJPSI.2022.02.02

E-ISSN: 2783-1310

*Corresponding author: ebi.alinia@gmail.com (E. Alinia-Ahandani)

1. Introduction

Blue cohosh (*Caulophyllum thalictroides*), native to the forests of the eastern and central United States, has been traditionally and historically used as a feminine aid to treat amenorrhea, dysmenorrhea, and menorrhagia. One of its most important therapeutic properties is to induce labor, to ensure quick delivery, reduce labor pain and induce abortion. Medicinal use of plants for contraception during pregnancy to facilitate childbirth dates back to ancient times when the basis of herbal medicine was when plants used for such purposes were called birth preparations. The use of blue cohosh for this purpose was first introduced to white settlers by Native Americans, who referred to it as "squawroot" or "papoose root" and reportedly used it to facilitate the birthing process (Simpson et al., 2001; Towner et al., 1999; Parsons et al., 1999).

Raspberry (in English: Raspberry) is the general name of the edible fruit of several species of plants in the *Rubus* family, which are usually included in the subgenus *Idaeobatus*. This name is also attributed to the plant itself. Raspberry is a perennial plant with woody stems. Raspberries are one of the important commercial cultivars and are very prosperous in the agriculture of some countries such as Russia, Serbia, USA and Poland. They are also used to produce purees, jams, juices and dried fruits. The leaves of these plants are also used as tea. Until recently, most raspberries had red fruit and were hybrids of *Rubus idaeus* and *Rubus strigosus*. Now purple raspberries and golden or white raspberries are becoming popular. The most important role of raspberry is its effective medicinal compounds that act as an anti-cancer food. This property is due to the presence of antioxidants. Raspberries contain many polyphenols. Polyphenols are a group of antioxidants that have the ability to fight cancer, and according to recent research, many sources have shown that they have unique effects for nursing mothers as well as pregnancy. Due to its rich food basket, this plant can play a role in the prevention of cancers as well as the balance of the mother's hormones during pregnancy and even after the birth of the child. Another special anti-cancer agent of raspberries is vitamin K found in raspberries. One serving of raspberries has more than a third of the recommended daily requirement of vitamin K, which plays an important role in preventing and fighting cancer of the prostate, stomach, nose, colon, mouth, and liver (Pilcher et al., 1916; Napoli et al., 2000; Bayles, 2007; Vinks et al., 1982; Alinia-Ahandani, 2018; Alinia-Ahandani et al., 2019a).

2. Material and Method

In this research, information on raspberry and black and blue cohosh medicinal plants has been collected through searching databases such as Google Scholar, ScienceDirect, Scopus, SID, PubMed, Elsevier, Springer, etc. and it has also been tried by searching keywords such as "medicinal plants effective in pregnancy and female fertility", "Cohosh medicinal plant and its positive and negative effects in pregnancy", "Raspberry medicinal plant and how to use it during pregnancy", etc. In the following, according to the collected information, we tried to report the most important and most indicative properties about the investigated subject. Also, at the end, by stating the abstract and proposal in this field, actions should be taken for future research works.

3. Results and Discussion

Surveys show that about 7-45% of women use herbs during pregnancy. Articles published in reputable nursing and midwifery journals (eg, Journal of Nurse Midwifery, Obstetrics and Gynecology, and Clinical Obstetrics and Gynecology) indicate that a large number CNM use herbal medicine clinically or are interested in learning to do so (Rouhi-Boroujeni et al., 2015). Traditional uses are related to the past years (Lans et al., 2009). Not only is the use of herbal remedies common among pregnant women, water cohosh is also leading the way among medicinal herbs. One of the important studies by researchers to document the use of herbal preparations for cervical ripening, induction and augmentation of labor by CNMs. The authors conducted a national survey of 500 members of the American College of Nurse-Midwives (ACNM) by mailing an anonymous survey to every fifth name on the organization's membership list. Forty-eight nursing and midwifery education programs

were also surveyed to determine whether they formally or informally teach students about the use of herbal remedies for cervical ripening, induction, or augmentation of labor. Of a 34% response rate, 90 surveys were returned from CNMs who used herbal remedies to induce labor and 82 from CNMs who did not use herbal remedies to induce labor. Of the CNMs who used herbal remedies to induce labor, 64% used blue cohosh (castor oil was used by 93% and evening primrose oil by 60%; other herbs used included black cohosh by 45% and red raspberry by 63%) (Daglia et al., 2023; Hajipour et al., 2022; Selamoglu et al., 2022).

Nurse midwives working in private practice are more likely to use herbs to induce labor than those employed in hospitals. However, they were used in all settings. Seventy-eight percent of CNMs directly prescribed herbal remedies to induce labor, while 70% offered them indirectly to clients. Only 22% included them in their written practice protocols. Seventy-five percent of CNMs who used herbal remedies to induce labor used them first or instead of pitocin. Sixty-four percent of nursing education programs included teaching the use of herbal preparations to induce labor in their formal training programs, and 92% included informal discussions about the use of herbal preparations (Parsons et al., 1999; Alinia-Ahandani et al., 2022b).

Applied studies show that raspberries may help improve fertility in men and women by increasing vitamin C and magnesium, they argue that antioxidants and berries promote sperm health and protect against miscarriage. In a study conducted last year, researchers at the Lawrence Berkeley National Laboratory found a strong link between high vitamin C intake and improved sperm DNA quality. An analysis of 80 male volunteers found that those who consumed more vitamin C had 20% less DNA damage in their sperm than those who consumed less vitamin C. Medicinal plant researchers claim: similar damage to sperm DNA damage in younger men. This means that men who are prone to sperm DNA damage due to aging can do something about it. Reproductive nutrition consultant Juliet Wilson says: "The high level of folate (a type of B vitamin that promotes cell growth and fetal health) in raspberries is beneficial for pregnant women. During pregnancy, adequate levels of folate help prevent birth defects. In the baby's brain and spinal cord. Raspberries are not yet recognized as a nutrient among other berries, but raspberries have many nutrients that should not be overlooked, including a high content of vitamin C - one raspberry is the size of 173 grapes - which is a nutrient it is good. It is a source of folate and is known as a key component for fertility and early fetal development. In addition, raspberries are an excellent snack for weight loss, the high amount of fiber and low glycemic index (GL) absorb and ensure metabolism and help control hunger and satiety. As a result, researchers claim that for Fertility is also beneficial, as a healthy body weight helps balance sex hormones and increases the likelihood of pregnancy (Pilcher et al., 1916; Yao and Mills, 2016; Meletis and Barker, 2004; Adewoyin et al., 2017; Alinia-Ahandani et al., 2020b).

Basically, the leaves and roots of plants are used in medicinal treatments. Medicinal plant leaves have been used as a supplement for nutrition during pregnancy in many European countries for years. Recently, in the United States in medicine related to people and Southwest regions (Alinia-Ahandani et al., 2019; Steenkamp et al., 2001) focused on these goals. Some reported researches used raspberry during pregnancy and labour. Also, the use of raspberry and tea leaves during pregnancy and labour is mentioned. The active medicinal compounds in raspberries will be reviewed in this context in the following sections. There are several researches about raspberry leaves. Three of these animal studies were performed, one as an experiment on the basal trimester uterus after excision (Rouhi-Boroujeni et al., 2015). In a practical study, the results showed that raspberry leaves had positive effects in relaxing the uterine muscle of some animals such as cats. It was also mentioned that if the muscles are in the relaxation phase, contraction is induced in medicinal plants. Some other elements were isolated from raspberry leaves, few of which increased uterine contractions, while others started to relax the uterus (Napoli et al., 2000; Steenkamp et al., 2001; Khojastehfard et al., 2021).

A study involving postpartum women indicated positive and effective results in uterine contractions at frequency and strength levels. Most in the medical profession may be opposed to the use of raspberry leaves, thinking it may cause miscarriage or premature labor. Some sources could show this effect and it was related to the contractions that started in human uterine bands after they were hidden from the body (Anggraeni et al.,

2019; Farrag and Omar, 2018; Alinia-Ahandani et al., 2019b; Alinia-Ahandani et al., 2019d). Another retrospective studies demonstrated the safety of raspberry leaf as an herbal source for women and their babies during pregnancy. In addition, raspberry leaves have been used for many years to facilitate work. Blue cohosh is also used as a labor preparation drug seen in the literature. Recent studies have shown that the extract of the whole plant increases uterine tone, but decreases the level of contractions. Saponins are also responsible for increasing the range of contraction and cause a slight increase in speed (Bowman et al., 2021).

A few adverse events have been supported with the use of blue cohosh during pregnancy. Three cases of all were shown in the literature. In a case report study, a researcher used blue and black cohosh in a pregnant woman. He used a vegetarian diet to stimulate labor. The baby was on resuscitation, seizures, significant kidney loss, etc. In other cases, the child suffered injuries related to myocardial toxicity. Another report was of an infant who had a stroke possibly caused by his mother drinking blue cohosh tea to induce labor (Alinia-Ahandani et al., 2022a; Picciano and McGuire, 2008; Smith-Roe et al., 2022).

Caulosaponin causes coronary blood vessel constriction and direct myocardial toxicity. Unfortunately the knowledge on doses is lacking, and cardiotoxic impacts are due to much greater doses than would be found in doses commonly used in work. The herbs include amount of glycosides, caulosaponins and caulophyllosaponin, quinolizidine alkaloids (Sparteine) that have oxytocic features. A reduction in blood pressure with a relative promotion back to normal was seen in dogs' cases with large doses. There are vasoconstrictive influences or the saponins caulosaponins and caulophyllosaponin parts, that are uterine stimulants, and probably cause coronary vasoconstriction (Berger and DeGolier, 2008).

The existence of quinolizidine alkaloids containing sparteine in blue cohosh herbs may express both its oxytocic pose and toxicity. Sparteine named as an oxytocic medicine some days. Some herbs could be consumed to react hyperlipidemia in pregnancy period without any meaning both on mother or fetus. Recently, there are no reference standards for lipid parameters in pregnancy period, although it is clear that pregnancy is a state of insulin. In some other sources indicated severe hypertriglyceridemia which was associated with pancreatitis could be guided by omega-3 fatty acids, parenteral nutrition, plasmapheresis, and other lipid-lowering agents. These days, over 200 herbs have been recommended for treatment of hyperlipidemia (Rouhi-Boroujeni et al., 2017; Rauf et al., 2022; Alinia-Ahandani et al., 2019c). As with chemical medicines, herbs could cause permanent damage to fetus. Therefore, the high range usage expresses security in most cases, however high infant mortality may have hid negative aspect of the blue cohosh.

3.1. The active ingredient is red raspberry

Red raspberry contains many compounds that have a tremendous effect on human health. Phenolic compounds are present in plants that synthesize a total of several thousand different chemical structures characterized by aromatic hydroxylated ring(s). These compounds have important functions in plants. They also exhibit metabolic flexibility that enables plants to adapt to changing biotic and abiotic environments, imparting color, flavor, technological properties, and potential health-promoting benefits to plant products (Kam et al., 2019).

The most important health benefits of raspberry fruits are attributed to phenolic compounds such as flavonoids, phenolic acids and tannins. Raspberries are believed to have a higher antioxidant capacity than other fruits and vegetables. Polyphenols are a group of compounds that are exclusively synthesized by plants, especially for protection against ultraviolet radiation and the activity of pathogens. About 8000 plant polyphenol compounds have been identified so far, while only a few hundred compounds are found in edible plants. Phenolic compounds of plants can be divided into two general categories: 1) phenolic (exometallic) acids and their derivatives and 2) flavonoids (polyphenols). Phenolic acids and their derivatives, mainly esters, have more basic structures (Dimiņš and Augšpole, 2019; Alinia-Ahandani et al., 2020a).

The flavonoid class of compounds has a more complex molecular structure, usually heterocyclic with adsorbed phenolic ring(s). Flavonoids include anthocyanidins (water-soluble pigments, which are oxidized

flavonols), catechins, isoflavones, and proanthocyanidins. In addition, flavonoids are known as inhibitors of lipid peroxidation, platelet aggregation, capillary permeability and fragility, activity of cyclooxygenase and lipoxygenase enzymes, flavonoids as antioxidants, free radical absorbers or divalent cation chelators (Aug. Organization (WHO) emphasized the importance of the antioxidant activity of phenolic components, especially from small colorful fruits, for the prevention of major health problems such as cardiovascular diseases, diabetes, cancer and obesity. Raspberries are also an excellent source of vitamin C, an antioxidant. It is very strong with anti-cancer and immune-modulating properties and is known to prevent a wide range of diseases (Dimiņš and Augšpole, 2019).

3.2. The active ingredient is blue cohosh

Notably, most phytochemical and pharmacological studies have focused on *C. thalictroides* and *C. robustum* due to their important medicinal functions. Modern pharmacological studies have shown that triterpenes alkaloids and saponins are responsible for its main biological functions as an anti-inflammatory, analgesic, antioxidant, antibacterial, anti-acetylcholinesterase and anti-tumor.

To date, a systematic review of the chemistry, pharmacology and mechanisms of action of constituents from the genus *Caulophyllum*. In this review, different structures of alkaloids and saponins in the genus *Caulophyllum*, including natural compounds and synthetic derivatives of thaspin, have been described. Since most of the studies have been done on the mentioned species (Fig. 1). Future clinical studies are expected to be conducted on these species (Wen et al., 2011; Selamoglu, 2021; Madawala et al., 2022).

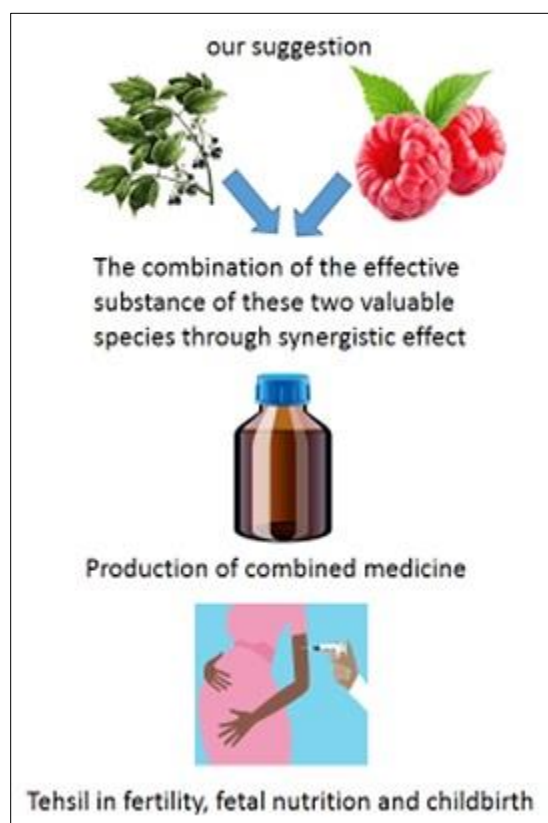


Fig. 1. Outline of clinical research proposal.

4. Conclusion

We reviewed many clinical studies on the medicinal compounds of red raspberry and blue cohosh and observed that there is a wide range of antioxidant compounds, especially phenols, in these valuable species. Since blue cohosh is effective in the birth process and red raspberry in fertility and fetal growth, as a result of the effective compounds of these species, they can be effective combined medicines in the fertility process until

delivery. Since the effective compounds of medicinal plants affect the dosage, the dosage of these compounds should be taken into consideration in the process of extraction and design of combined complementary medicines. Many studies have been conducted in the field of red raspberry and blue cohosh, but since both of these species play a role in fertility and childbirth, we suggest that research be conducted in this field by combining both plant species.

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How to cite this paper:

Alinia-Ahandani, E., Rafeie, F., Alizadeh-Tarpoei, Z., Hajipour, S., Selamoglu, Z., Canan Alp Arici, E., 2022. **Overview on raspberry leaves and cohosh (*Caulophyllum thalictroides*) as partus preparatory.** *Cent. Asian J. Plant Sci. Innov.*, **2**(2), 54-61.