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Research Article

Effects of Raspberry Leaf Tea (*Rubus idaeus l.*) in Labor: An Integrative Review

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Abstract

Introduction: Raspberry leaves are part of the Rosaceae family and are known for their therapeutic properties. One of the most studied species is *Rubus idaeus Linn* for its various effects on the human body as a facilitator of childbirth, aid in the treatment of diabetes and hypertension, among others.

Methodology: For the present study, PubMed, Medline and Science direct databases, in English and Portuguese, were used. After pre-selection of 75 articles related to the topic, of these, 6 were selected for data collection, including randomized clinical trial studies, retrospective cohort studies and laboratory tests in animals and pregnant women, and studies with women were excluded from this research. non-pregnant and postpartum women, as well as studies on other effects of raspberry leaves.

Results: After analysis, it was observed that the tests carried out in humans showed that the use of tea in pregnant women reduced the time of delivery, the artificial rupture of membranes and also the need for instrumental delivery. Antioxidants present in IR probably cause the death of cervical and myometrial cells, generating changes in conformation that influence the triggering of parturition processes.

Conclusion: Raspberry leaf is a well-known herb that has been traditionally used for decades against various ailments according to manuals and articles that are generally recognized as safe. However, evidence for efficacy is weak and identification of active constituents is scarce. Needing more studies in the area, considering the effectiveness and safety of the mother and baby.

Keywords: *Medicinal Plants; Phytotherapy; Pregnancy; Herbal Medicine; Complementary Medicine*

Abbreviations

RI: *Rubus idaeus;* LOX: Lipoxygenase

Introduction

Pregnancy is a period in a woman's life that requires more care related to health and nutrition. Healthy lifestyle habits help the mother and baby's well-being and can prevent complications during this period. Due to these redoubled care with health in the gestational period, many mothers choose herbal medicines because they believe they are safer, however, even with natural origin, this type of medicine can cause harm to the mother and the baby if used improperly, so it is of paramount importance. professional monitoring is important [1].

During the gestational period, it is common for discomforts and complications to occur that can be relieved, treated and/or prevented with the use of medicinal plants, however, it is very common that misuse occurs, without the follow-up of a professional, which is a worrying situation as there may be serious consequences [2].

Rubus species are part of the Rosaceae family and are known for their therapeutic properties. One of the most studied species is *Rubus idaeus Linn* for its various effects on the human body as a facilitator of childbirth, aid in the treatment of diabetes and hypertension, among others [3].

Raspberry leaf (*Rubus idaeus L.*) is an herbal medicine commonly used to assist in labor, especially in the last two months. Some studies indicate its positive effects on pain and shortening the time of childbirth, in addition to easing natural childbirth, often without the use of forceps, suction cups and cesarean section [4]. The *Rubus idaeus L* (RI) leaves have some active constituents that have biophysical effects on tissues, particularly smooth muscle, and can function as a stimulating and relaxing depending on the form and dose used [5].

A study conducted in 2006 with 500 pregnant women from a hospital in Australia to evaluate the use of herbal teas and supplements showed that the most used tea among them was raspberry leaf tea for shorten the childbirth [6].

The use of raspberry leaf can positively interfere with uterine contractions, making them more coordinated and facilitating labor [7]. In addition, its relaxing effects help control labor pains [4]. There are records in the literature of the use of raspberry leaf as tea, tincture, extract and tablet [7].

Aim of the Study

The present study aims to carry out an integrative review to describe the effects of raspberry leaves on labor, as well as the safety and efficacy described in the literature.

Materials and Methods

This research was carried out during March and April 2022. PubMed, Medline, ResearchGate and Science direct databases, were used to carry out the research. The descriptors used were registered at DeCS/MeSH, which were "raspberry leafs pregnancy", "raspberry leafs", "effects of raspberry leafs in pregnancy" and "*Rubus idaeus L*. and labor", in English and Portuguese.

The initial search had 75 articles related to the topic, of which 6 were selected after full text analyzed (2 studies conducted with animals, 3 with humans and 1 with humans and animals). After removing duplicates, 37 articles remained. Ten records were excluded after abstract read because they were for audiences other than pregnant woman; nine after full text analysis demonstrated that the effects described were not associated with the topic of this review, 11 as they were reporting on agriculture findings of the herb or other members of the *Rubus* family, and one as it was a theoretical discussion of the constituents and actions. This left 6 articles to be integrated for this review. The figure 1 is illustrating the process.

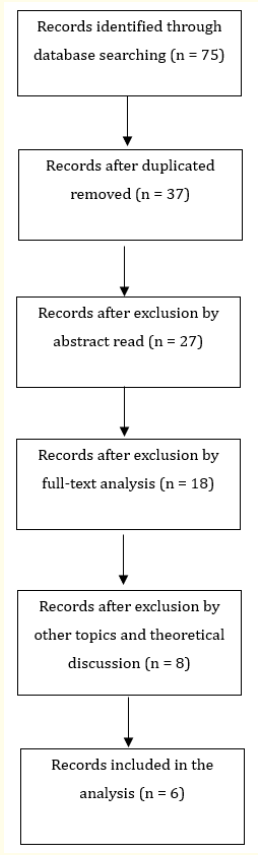

Figure 1: *Article selection flowchart.*

Inclusion criteria was based in study design, sample, methods, dose and form of raspberry leaf used where reported, so were included randomized clinical trial studies, retrospective cohort studies and laboratory tests in animals and pregnant women with the description of dose and form of presentation. The selected studies used the leaves of *Rubus idaeus* as tea [8-10], extract [9,11] tincture [8] and tablet [7,8].

Review articles, studies with non-pregnant and postpartum women, as well as studies on other effects of raspberry leaves, were excluded from this research. The search was not time-limited. For data collection, an instrument validated by Ursi [12] available in annex was used.

Results

Laboratory and animal studies

Laboratory and animal studies focused on analyzing the direct effects of raspberry leaf on uterine muscle. Zheng., *et al*. in 2010, performed a study using uterine tissue samples from pregnant and non-pregnant rats, subjecting them to cumulative additions of tea,

capsules and raspberry leaf extract. Additions were 1.0 mg/mL - 4.6 mg/ mL for tea, 1.0 mg/mL - 4.6 mg/ mL for capsules and 2.2 mg/ mL - 10.1 mg/ mL for extract. The results of this study showed that in the samples of the pregnant uterus, the stimulus of contractions had similar effects to oxytocin and when the combination of tea and oxytocin was used, the stimulus was greater than just oxytocin alone. Results showed too that the preparations didn't affect the ability of oxytocin to initiate contractions, but partially inhibited the pre-existing oxytocin-driven contraction at the highest concentration and had effects on pre-existing oxytocin-induced contractions [9]. A different result from that found by Bamford., *et al*. who, using crushed leaves infused in saline in uterine samples from rats and humans, described that in rats, no stimulus to contraction was observed, but inhibition of it, unlike in humans where there was stimulus [13].

Another study carried out with mice to evaluate the effects of raspberry leaves on the duration of parturition used leaf extract (1.68 mg/mL to 2.66 mg/mL) equivalent to that recommended for humans (1 to 2 cups per day) and found that higher doses reduced gestation time and litter size. Placebo and the group that ingested low-dose did not present significant differences in length gestation, unlike the group that used high doses. The high and low-dose concentration were 2.66 and 1.78 mg/mL, respectively. The placebo group received plain water [14].

These studies didn´t show significant differences that would be represent any risk between the control group and the group that used leaf extract.

Human studies

The study by Parsons., *et al*. with 108 pregnant women (52 as a placebo group) used raspberry leaves as tea, tablet and tincture with doses of 1 to 8 cups of tea or tablets or 1 dose of tincture per day, over 1 to 32 weeks in a continuous period. Some pregnant women started using RI at 8 weeks, but most started at 30 weeks. It was observed that the mothers who used the raspberry leaf had shorter childbirths, less artificial rupture of membranes, less need for forceps, cesarean section and instrumental labor, in addition to a greater number of term babies between them. No adverse effects or complications arising from the use of *Rubus idaeus* were recorded [8].

Similar effects were found by Simpson., *et al*. in a study carried out with 192 pregnant women (96 placebo group) using tablets with 1.2 mg/mL of RI extract from 32 weeks, where faster childbirths and reduced instrumental and artificial rupture of membranes. In this study, it was noticed that the number of vaginal deliveries was higher among women using raspberry leaf than in the placebo group, 62.4% of women using RI had natural labors and 50.6% of the placebo group [7].

A case study reported by Cheang., *et al*. demonstrated that in addition to properties capable of helping in labor, raspberry leaves also help in the control of blood glucose. The reported patient drank RI leaves tea twice a day for 3 days in the 32nd gestational week and did not report dietary changes and physical activity. The authors attributed the reduced glucose levels to tea use using Naranjo 's algorithm [15] to test the probability of tea effects. In this study, the effects related to the duration of labor were not accurate because the patient reduced the doses taken on her own from the 34th week onwards. This dose reduction generated postprandial hyperglycemia [10].

In none of the analyzed studies there was an adverse effect or risk for the mother or the baby. In the study conducted by Cheang., *et al*. a biopsy of the placenta and fetal membranes was performed, demonstrating normal characteristics, without any abnormality [10]. Parsons., *et al*. evaluated the safety of RI using the Apgar score after 5 minutes of birth, blood loss during the childbirth and maternal diastolic pressure. No significant differences were shown between the group using raspberry leaf and the control group [8].

Author, year	Search type	Sample	Form and dosage	Results
Bamford., *et al*. 1970	laboratory study	Uterine tissue from rats and humans, both with pregnant and non-pregnant samples.	Whole sheet crushed and infused in saline.	Inhibition of contraction in rats and stimulation of coordinated contraction in humans.
Parsons., *et al*. 1999	Retrospective cohort study	108 pregnant women (51 control group)	Leaves tea, pill, tea and pill and tincture. 1 to 8 cups of tea or tablets or 1 dose of tincture per day. Duration over 1 to 32 weeks in a continuous period.	Shorter deliveries, ↑ terms babies, ↓ artificial rupture of membranes, cesarean sections, and instrumental delivery without adverse effects.
Simpson., *et al*. 2001	Randomized Controlled Study	192 pregnant women (96 control group)	Pills from 32 weeks of gestation for both groups. The difference was the addition of 1.2g of raspberry leaf extract.	↓ duration of the second stage, ↓ instrumental delivery and artificial membrane rupture.
Zheng., *et al*. 2010	laboratory study	Uterine tissue of pregnant and non-pregnant rats	Cumulative additions of tea (1.0 mg/mL - 4.6 mg/mL), capsule (1.0 mg/mL - 4.6 mg/mL) and extract (2.2 mg/mL - 10.1 mg/mL).	Greater effect in pregnant uterus, stimulation of contractions with oxytocin-like effects. Combined tea and oxytocin treatment stimulated more contractions than oxytocin alone.
Cheang., *et al*. 2016	Case study	Pregnant woman with gestational diabetes	2 cups of tea for 3 days in the 32nd week.	↓ blood glucose
Hastings- Tolsma., *et al*. 2022	Laboratory study	27 mice (10 placebo group)	Leaf extract (1.68 mg/ml to 2.66 mg/ml). Dose used equivalent to that recommended for humans (1 to 2 cups per day).	Higher doses influenced the reduction of gestational time and litter size.

Table 1: *Summary of the results found.*

Discussion

Laboratory studies have identified that RI leaves have several constituents that have direct effects, mainly on smooth muscle [13]. Raspberry leaves have demonstrated effects for both relaxation and contraction of smooth muscles depending on the dose used, extraction method, tissue type and origin and pregnancy or non-pregnancy status of the uterine tissue [9]. The components of RI act on the uterine muscle stimulating more rhythmic and effective contractions for a faster and easier delivery, in addition, it acts on the tone of the uterus, helping to prevent miscarriages and postpartum hemorrhage [7]. Raspberry leaves can also help control pain during labor, as they have alkaloid components that strengthen the entire pelvic floor, including uterus and ovaries [16], this helps in muscle tonicity, the which consequently helps in pain control [7].

Although the mechanisms of RI leaves that influence labor are not yet fully clear, it is hypothesized that they are due to the bioactive compounds present in the leaves. Several phytochemicals derived from alkaloids, phenolics, terpenoids and glycosides, pro-inflammatory compounds, apoptosis inducers, influencers of enzymatic activity, etc. have been identified [17]. Due to this, it is assumed that the use of RI during pregnancy probably stimulates the activity of pro-inflammatory cytokines, vasodilation and apoptosis of cervical and myometrial cells, probably from flavonoids and catechins. Such bioactive compounds have the potential to play a key role in triggering childbirth processes [11].

Antioxidants present in RI probably cause the death of cervical and myometrial cells, generating changes in conformation that influence the triggering of parturition processes, thus triggering the signaling pathway of proteins that increase inflammation, inhibit cell growth and trigger cell cycle arrest [18]. Kaempferol has the ability to modulate signaling pathways related to cell apoptosis, this fact combined with the high bioavailability of quercetin and the promotion of inflammatory expression are possible influencers of IR in promoting parturition. Furthermore, quercetin influences the development of the endometrium during the peri-implantation period [19] in addition to promoting a reduction in cell proliferation and inducing apoptosis [20]. High doses of RI can stimulate AA (arachidonic acid) dependent proteins such as lipoxygenase (LOX) that produce pro-inflammatory cytokines. The LOX pathway is fundamental for the determination of prostaglandin synthesis, crucial in the stimulation of uterine contractions [14].

The studies with humans analyzed showed that the use of tea in pregnant women reduced the time of childbirth, the artificial rupture of membranes and also the need for instrumental labor [8]. However, it was reported by Simpson., *et al*. that the reduction in labor time was significant only in the second stage, the first stage time remained similar to the placebo group of the study [7]. As for membrane rupture, the reports by Parsons., *et al*. and Simpson., *et al*. were equivalent, both studies showed that the groups using tea had easier vaginal labor, without rupture and without the use of forceps compared to the placebo groups. Simpson., *et al*. reported that 54% of pregnant women who required artificial rupture of membranes were in the placebo group [7,8].

The studies showed no adverse effects or risks to mother and baby. Simpson., *et al*. reported that some pregnant women using the tea described nausea, diarrhea and vomiting but could not say whether they were the effects of *Rubus idaeus* or the pregnancy itself, since they are common symptoms in this period and also occurred with some in the placebo group [7]. Although there is no evidence in the literature of the risks of using tea for mother and baby.

A study by Makaji Ho., *et al*. showed that raspberry leaf has the potential to interact with other drugs. It was verified in this study that the female offspring of rats exposed to raspberry leaf exhibited alterations in the activity of the cytochrome enzyme (CYP). Investigating six commonly used herbs in pregnancy, including raspberry leaf, it was discovered that raspberry leaf (especially the ethanolic extract) is a powerful CYP inhibitor. This has implications for herb-drug interactions with the potential to cause unusual sensitivity to the effects of drugs at normal doses. Thus, the importance of observing the potential of drug interactions of raspberry leaf is notorious [21].

Furthermore, in another study, McLay, Izzati., *et al*. warned of the potential for herb-drug interactions where a cross-sectional survey of pregnant women (n = 889) in Scotland was conducted. They found that a high proportion (44.9%) of women taking prescription drugs also took natural and herbal preparations, and in these, they identified 34 herbal interactions in 12.7% of women. CYP inhibition by raspberry leaf has been cited as a potential mechanism in herb-drug interactions. Hypotheses associated with competition for absorption between raspberry leaf constituents (polyphenols) and iron were also raised, which may influence the occurrence of anemia in pregnant women who use tea. However, this has not been demonstrated in any studies of raspberry leaf use in pregnancy to date [5].

Study Limitations

The review had some limitations such as the low number of studies carried out in the area. In addition, as some studies have some time that were realized, the limitations of techniques and technology of analysis may have interfered with the knowledge of the components and mechanisms of action of the plant.

Conclusion

Based on all that was exposed, it was possible to observe that the use of *Rubus idaeus* leaves during pregnancy, especially after 30 weeks, can help with labor, making it faster and reducing the risk of ruptured membranes and instrumental childbirth. This result is of clinical significance for mothers, their babies and their midwives. Less intervention means a reduction in obstetrics and labor time and increased maternal satisfaction, which has been suggested to ease women's transition into motherhood.

The relevant experimental results evaluated in the present study of the effects of raspberry leaf tea in order to support the proposed indications and use during pregnancy did not demonstrate risks, however they are limited, although, more studies are needed in the area to better demonstrate its effectiveness and describe how it works, more specifically the possible adverse effects of the use of tea.

Conflict of Interest

Financial interest or any conflict of interest did not exist.

Annex 1

Instrument for data collection (validated by Ursi, 2005)

A. Identification	
Article title	
Journal title	
Authors	Name: Workplace: University graduate:
Country	
Language	
Year of publication	
B. Study Headquarters Institution	
C. Type of Publication	
D. Methodological Characteristics of the Study	
1. Type of publication	1.1 Research ( ) Quantitative approach ( ) Experimental design ( ) Quasi-experimental design ( ) Non-experimental design ( ) Qualitative approach 1.2 Do not search ( ) Literature review ( ) Experience report ( ) Others: _____
2. Research objective or question	

3. sample	3.1 Selection ( ) Random ( ) Convenience () Other: 3.2 Size (n) ( ) Initial ( ) Final 3.3 Features 3.4 Inclusion/exclusion criteria for subjects Studies in English, observational and
4. Data processing	
5. Interventions carried out	5.1 Independent variable _____ 5.2 Dependent variable _____ 5.3 Control group: yes ( ) no ( ) 5.4 Measuring instrument: yes ( ) no ( ) 5.5 Duration of the study _____ 5.6 Methods used to measure the intervention
6. Results	
7. Analysis	7.1 Statistical treatment_____ 7.2 Level of significance
8. Implications	8.1 The conclusions are justified based on the results_____ _____ _____ 8.2 What are the authors' recommendations _____ _____
9. Level of Evidence	
E. Assessment of Methodological Rigor	
Clarity in identifying the methodological trajectory in the text (method used, participating subjects, inclusion/exclusion criteria, intervention, results)	
Identification of limitations or biases	

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