Risks and benefits of use of medicinal plants during pregnancy: a review

Riscos e benefícios do uso de plantas medicinais durante a gravidez: uma revisão

Beneficios del uso de plantas medicinales durante el embarazo: una revisión

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ABSTRACT
The administration of drugs or any substances in order to minimize the discomfort of the gestational period can compromise the good development of the new being in formation or even cause abortion. This study aimed to realize an integrative literature review on the prevalence of the use of medicinal plants by women during pregnancy. Between November 2019 and September 2020, a survey was performed in the Scielo database and in CAPES journals with the descriptors “medicinal plant during pregnancy”, “ethnobotany and pregnant women” and their correspondents in Portuguese: “planta medicinal durante a gravidez”; “etnobotânica e gestantes”. Among the articles published in the period from 2001 to 2020, 50 studies were appropriated in the inclusion and exclusion criteria being selected for this review. All studies (100%) were conducted through interviews. One of these studies is of a multinational character. The medicinal plants most commonly used by pregnant women are Lippia alba (lemongrass -79.5%), Peumus boldus Molina (boldo -41%), Pimpinella anisum (fennel -28%) and Matricaria recutita (chamomile -28%).

Keywords: medicinal plants, gestation, abortive, toxicity, teratogenicity.

RESUMO
A administração de medicamentos ou qualquer substância com o objetivo de minimizar o desconforto do período gestacional pode comprometer o bom desenvolvimento do novo ser em formação ou até mesmo causar aborto. Este estudo teve como objetivo realizar uma revisão integrativa da literatura sobre a prevalência do uso de plantas medicinais por mulheres durante a gravidez. Entre novembro de 2019 e setembro de 2020, foi realizada uma pesquisa na base de dados Scielo e em revistas da CAPES com os descritores "planta medicinal durante a gravidez", "etnobotânica e gestantes" e seus correspondentes em português: "planta medicinal durante a gravidez"; "etnobotânica e gestantes". Entre os artigos publicados no período de 2001 a 2020, foram selecionados 50 estudos que atenderam aos critérios de inclusão e exclusão para esta revisão. Todos os estudos (100%) foram conduzidos por meio de entrevistas. Um desses estudos tem caráter multinacional. As plantas medicinais mais comumente utilizadas por mulheres grávidas são Lippia alba (erva-cidreira - 79,5%), Peumus boldus Molina (boldo - 41%), Pimpinella anisum (funcho - 28%) e Matricaria recutita (camomila - 28%).

Palavras-chave: plantas medicinais, gestação, abortivo, toxicidade, teratogenicidade.
RESUMEN
La administración de medicamentos o cualquier sustancia con el fin de minimizar las molestias del periodo gestacional puede comprometer el buen desarrollo del nuevo ser en formación o incluso causar aborto. Este estudio tuvo como objetivo realizar una revisión bibliográfica integrativa sobre la prevalencia del uso de plantas medicinales por parte de las mujeres durante el embarazo. Entre noviembre de 2019 y septiembre de 2020, se realizó una búsqueda en la base de datos Scielo y en revistas de CAPES con los descriptores "planta medicinal durante el embarazo", "etnobotánica y mujeres embarazadas" y sus equivalentes en portugués: "planta medicinal durante a gravidez"; "etnobotânica e gestantes". Entre los artículos publicados en el período de 2001 a 2020, se seleccionaron 50 estudios que cumplían con los criterios de inclusión y exclusión para esta revisión. Todos los estudios (100%) se realizaron a través de entrevistas. Uno de estos estudios es de carácter multinacional. Las plantas medicinales más utilizadas por las mujeres embarazadas son *Lippia alba* (hierba luisa - 79.5%), *Peumus boldus* Molina (boldo - 41%), *Pimpinella anisum* (hinojo - 28%) y *Matricaria recutita* (manzanilla - 28%).

Palabras clave: plantas medicinales, gestación, abortivo, toxicidad, teratogenicidad.

1 INTRODUCTION

The research and the teaching about the development of medical practice from its inception to the modern health care system that we have today is based on the history of cure. In this context, the use of medicinal plants is inserted at different times in the history, serving as an instrument of cure for human illnesses (Leite, 2009).

The history reveals that a growing number of species used in traditional medicine have been incorporated into medical prescriptions for the treatment of health problems. It is estimated that the number of superior plant species described may reach up to 750,000 and that 119 chemical substances extracted from plants indicated for medicinal purposes are obtained from about 90 species. Of these chemical compounds, about 75% are derived from plants used in traditional medicine (Brasil, 2006; Dutau, 2004; Rangel; Bragança, 2009). Even with the globalization of the chemical industry and the use of synthetic medicines, products derived from medicinal plants still hold a share of the world market; 14 billion of an estimated total of 280 billion dollars, about 5% of the world market for pharmaceutical products (Carvalho et al., 2007).

Considering that pregnancy is a period in a woman's life that requires special care, especially in the first trimester of pregnancy, being considered the most critical, the systematic use of some medicinal plants during this period is contraindicated due to their toxic, teratogenic...
and abortive potential, found in them. Certain plants have their active principles capable of crossing the placental barrier, which can harm the fetus (Oliveira, 2011).

The indications for the use of herbal medicines during pregnancy may vary between regions and countries, and may be related to the mother or child (Illamola et al. 2020). Herbal medicines can sometimes be used as part of maternal care to treat pregnancy-related problems and often to improve the well-being of the mother and/or fetus (Haji; Holst, 2020).

The belief that what is “natural” is synonymous with “safe”, makes many pregnant women resort to the use of medicinal plants to treat various symptoms and illnesses that may arise during the gestational period (Rangel and Bragança 2009). Like the whole population, they are subject to some illnesses that require them to use some type of medicine or plants. Thus, this therapy during the pregnancy period has been a reason for studies to estimate the risk/benefit of this use for mother and fetus (Campesato, 2005).

The most commonly reported indications are nausea and vomiting, urinary tract infections, preparation for and/or facilitation of childbirth, common cold or flu, gastrointestinal problems (eg, constipation, flatulence), pain conditions, improvement in fetal outcomes, prevention of abortion, anxiety relief, treatment and/or prevention of anemia, and treatment of edema (Ahmed et al. 2018b; Illamola et al. 2020; John; Shantakumari, 2015; Kennedy et al. 2013).

In addition to the use of plants to relieve pregnancy symptoms, the use of these by pregnant women is also due to their effectiveness, low cost compared to allopathic medicines, the easy to acquire them (which can be collected in the garden of the user’s house), finally making its use practical, easy and cheap (Faria et al. 2004).

The most worrying adverse effects that can cause harmful damage to the fetus and the mother are embryotoxicity, which is the disturbance in embryonic or fetal development by dosages that do not affect the maternal organism and the teratogen, composed of environmental agents, chemical, physical and biological that can cause obstetric and/or fetal abnormalities. This action depends on several factors, such as the conceptus’ stage of development, dose-effect relationship and maternal-fetal genotype. Among the most used abortifacients are teas and infusions of medicinal plants (Arcanjo et al. 2013).

However, the use of herbal medicines during pregnancy raises specific concerns because many herbal products are marketed specifically for symptoms that commonly occur during
pregnancy, such as nausea and vomiting (Allaire et al. 2000; Broussard et al. 2010). An important fact is that the association between plants and the teratogenic or embryotoxic effect is scarce, however, the relationship between the abortive effect and plants is most frequently (Rodrigues, 2011).

Thus, considering the lack of data from randomized clinical trials about the efficacy and safety of the use of herbal medicines during pregnancy, it is necessary to investigate the risks of using medicinal plants by women during their gestational period.

2 MATERIAL AND METHODS

The study was conducted from November 2019 to September 2020. In the Scielo database and CAPES journals, 50 published articles were selected from 2001 to 2020 and had as descriptors the words “medicinal plant during pregnancy”, “ethnobotany and pregnant women” and its correspondents in Portuguese: “medicinal plant during pregnancy”; “ethnobotanica and pregnant women”. The journals used were: Revista Brasileira de Plantas Medicinais, Arq. Cienc. Saúde UNIPAR, Infarma, T&C Amazônia, Obstet Gynecol., Química Nova, Rev Gaúcha Enferm., Revista Eletrônica de Biologia., Revista Brasileira de Farmácia, Revista Brasileira de Farmacognosia, Diálogos & Ciência, Rev Visão Acadêmica, Cogitare Enfermagem, BioFar, Revue Française d’Allergologie ET d’Immunologie Clinique, Acta Sci Health Sci, Complement. Altern. Med, Pharmacoepidemiol. Drug Saf. In the analyzed articles, all studies were conducted through interviews.

3 RESULTS AND DISCUSSION

The selected articles aimed to investigate the risks of using medicinal plants during the gestational period, showing the plant species that may entail some risk and/or benefit during this period. Exceptionally in recent years, there has been a more constant search and a more special consideration for herbal medicine. We can’t rule out the scenario which the provision of health care to the populations has been passing through, as well as the inexistence of resources available in public health systems. These factors combined with the possibility of having access to
treatment without such high drug costs, have made people search for alternative therapies more often.

Rangel and Bragança (2009) performed a study whose objective was to analyze representations formed about the use of medicinal plants by pregnant women in outpatient treatment, where the categories of conception and reasons for the use, or not, of the plants were verified. The authors reported that a total of 39 plants were mentioned 133 times and the most used species were: *Lippia alba* (lemon balm - 79.5%), *Peumus boldus* (boldo - 41%), *Pimpinella anisum* (Fennel - 28% ) and *Matricaria recutita* (chamomile -28%).

It is noteworthy that the study participants use a large number of plants and are mostly unaware of their risks and benefits, as well as the scientific parameters that guide the actions in treatments (Rangel and Bragança 2009). Through the data obtained from this study, it was possible to verify that the knowledge acquired by the users has been transmitted in a hereditary way, that is, from generation to generation. Thus, it can be observed that this acquired knowledge, although accepted, can lead to and to induce inappropriate or ineffective use. In the group that did not use herbal medicines, lack of knowledge about herbal medicine, or the understanding of plants as dangerous, that is, harmful to the fetus is identified.

Above all, the aforementioned authors found difficulties in identifying and safely administering the plants and a certain degree of mystification, in addition to the use of ineffective and potentially toxic substances, thus highlighting the value of dialogue between doctor and patients, with attention to the possible medicinal use of plants.

Costa et al. (2010), realized a study whose purpose was to know the practices of the use of medicinal plants among pregnant women at a Health Center in Florianópolis during pregnancy, in which it became possible to know the practice of the use of medicinal plants among pregnant women in the Lagoa da Conceição community.

This study describes a survey realized with 16 pregnant women. Of these, fourteen (14) stated that they had already made use of medicinal plants at some point in their lives, and of these, four (4) abstained from using medicinal plants during their pregnancy. It is highlighted that among the sixteen (16), two (2) never used these therapeutic resources (Costa et al. 2010).

The above authors observed that the use of medicinal plants is a common practice among pregnant women, and the knowledge and indication of their use are mainly through popular knowledge. With this study it was found that among the most used plants are *Matricaria recutita*
(chamomile) and *Lippia alba* (lemon balm), reporting their use as a tranquilizer and the main form of preparation was tea made through infusion.

The indication and guidance by health professionals was mentioned only once, which is why the authors emphasize the need to train these professionals so that they can act effectively and safely against the practice of using medicinal plants., in addition to highlighting the importance of analysis of local practices by professionals so that they can plan appropriate health actions.

Among the plants most mentioned by the pregnant women interviewed in this study, we can mention: *Matricaria recutita* (chamomile-7) and *Lippia alba* (lemon balm-3). Less frequently, *Cymbopogon citratus* (DC.) Stapf (lemon grass/lemon grass), *Mentha spicata* L. (mint), *Pimpinella anisum* L. (fennel), *Melissa officinalis* L. (melissa) were also mentioned., *Foeniculum vulgare* Mill. (fennel) and *Ilex paraguariensis* var. *dentata* A.St.-Hil. (mate herb). Additionally, some herbal medicines were mentioned, such as: *Citrus sinensis* (L.) Osbeck (orange essential oil-1) and *Cymbopogon citratus* (DC.) Stapf (lemongrass essential oil-1).

According to Gorril et al. (2016), although these species are contraindicated in the gestational period due to embryotoxic, teratogenic and abortifacient risks, they are commonly consumed by pregnant women due to the fact that they are more affordable, as they are unaware of their unwanted effects during the gestational period and because they believe that consumption of natural products is less harmful to the mother's organism and fetal (Clarke et al. 2007; Faria et al. 2004; Gorril et al. 2016; Rodrigues et al. 201; Silva et al. 2012).

According to Campesato (2005), boldo (*Peumus boldus* Molina) is quite common in Brazil and is used in the treatment of liver disorders, having collagenous properties, its volatile oil contains irritating terpenes and is therefore considered the most toxic, and its not safe administration during the gestational period (Campesato, 2005; Rangel; Bragança, 2009).

According to Silva (2014), it is evident the use of chamomile (*Matricaria chamomilla*) in the second trimester among other plants to treat heartburn; a common symptom at this stage of pregnancy, according to a study realized in São Carlos city, in São Paulo with pregnant women attended at the high-risk outpatient clinic of Maternity Santa Casa in 2012 (Suzuki, 2013).

Under this aegis, Veiga Junior et al. (2005), report that the use of rue (*Ruta Graveolens* L.) can cause severe bleeding, irritation of the oral mucosa, as well as epidermal inflammation. In this context, Castro (2006) reports that the extract of rue leaves (*Ruta graveolens* L.) causes
abortion, and its internal use (high doses) can cause hyperemia of the respiratory organs, with consequent severe bleeding, corroborating with Veiga Júnior (2005). The Herbal Therapeutic Index -HTI (2008) warns that rue extract is a potassium channel blocker, according to Rodrigues et al. (2011), this extract has an embryotoxic and teratogenic effect in the post-implantation period, corroborating the data contained in Table 1.

In this context, Silva (2014) highlights that Arab doctors were the first to use senna (*Senna alexandrina* Mill) for medicinal purposes, since the 9th century BC, until then senna has an important role in traditional medicine (Hti, 2008). Its overdose causes severe cramps, vomiting, nausea and electrolyte disturbances (Corrêa, 2008).

<table>
<thead>
<tr>
<th>SCIENTIFIC NAME</th>
<th>RECOMMENDATION</th>
<th>ADVERSE EVENTS REPORTED</th>
<th>COMMON PREPARATIONS</th>
<th>REFERENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Zingiber officinale</em> Roscoe</td>
<td>Nausea, vomiting</td>
<td>Drowsiness, reflux, vomiting, heartburn, headache, abdominal discomfort, prepartum delivery, smaller head circumference of the newborn.</td>
<td>Ginger tea, chew raw ginger</td>
<td>(Dante et al. 2014; Holst et al. 2011; Trabace et al. 2015)</td>
</tr>
<tr>
<td><em>Valeriana officinalis</em> L.</td>
<td>Sleep disorders</td>
<td>Diarrhea.</td>
<td>Root decoction, capsules</td>
<td>(Bent et al. 2006)</td>
</tr>
<tr>
<td><em>Rubus idaeus</em> L.</td>
<td>Nausea, increased milk production, induction of labor</td>
<td>Hypoglycemia, higher percentage of cesarean deliveries compared to non-users.</td>
<td>Raspberry leaf tea, capsules</td>
<td>(Al -Ramahi et al. 2013; Cheang et al. 2016; Nordeng et al. 2011)</td>
</tr>
<tr>
<td><em>Matricaria chamomilla</em> L. <em>Chamaemelum nobilis</em> (L) Al.</td>
<td>Gastrointestinal irritation, insomnia, joint pain, relaxation</td>
<td>Gastrointestinal irritation, insomnia, joint pain, relaxation</td>
<td>Chamomile tea prepared with dried flowers</td>
<td>(Al -Ramahi et al. 2013; Silva et al. 2018; Trabace et al. 2015)</td>
</tr>
<tr>
<td><em>Mentha piperita</em> L.</td>
<td>Nausea, vomiting, flatulence, indigestion, irritable bowel syndrome</td>
<td>Heartbeat, dry mouth, belching, rash, dizziness, headache.</td>
<td>Leaf tea, oil extract</td>
<td>(Alammar et al. 2019; Al-Ramahi et al. 2013)</td>
</tr>
<tr>
<td><em>Allium sativum</em> L.</td>
<td>Pre-eclampsia prophylaxis, preterm birth prophylaxis, improving the immune system.</td>
<td>Fetal odor, nausea</td>
<td>Eat raw garlic, garlic tea, garlic juice</td>
<td>(Laelago, 2018; Myhre et al. 2013; Ziaei et al., 2001)</td>
</tr>
<tr>
<td><em>Cucurbita pepo</em> L.</td>
<td>Nutritional supplement, cough, fever, common cold, headache, gastrointestinal irritation, heartburn, edema,</td>
<td>No adverse events were identified in the literature.</td>
<td>Seed decoction, leaf juice (mixed with milk)</td>
<td>(Adnan et al. 2017; Ahmed et al. 2018b)</td>
</tr>
</tbody>
</table>
### Gymnathemum amigdalinum (Delle) Sch. Bip.
- Nausea, vomiting, fever, constipation, increased appetite, pelvic floor muscle strengthening, malaria, anemia.
- Uterine motility stimulation
- Leaf soup, fresh leaves are washed and squeezed in clean water and the water is extracted to dry.

### Ricinus communis L.
- Labor induction.
- Nausea, abdominal pain, uterine rupture
- Leaves or roots soaked in hot or cold water, usually drunk at the start of work.

### Garcinia kola Heckel
- Nausea, vomiting.
- Weight loss, prolonged sleep duration, increased libido
- Chewing the seeds

### Ocimum lamifolium Hochst. ex. Benth
- Headache, fever, inflammation and back pain, common cold, cough, eye infections
- No adverse events were identified in the literature.
- Oral decoction of crushed leaves, leaf juice drunk or snorted or used as eye drops

### Azadirachta indica A. Jus
- Inducing childbirth, malaria, pain, hemorrhoids, improving fetal development
- Vomiting, metabolite acidosis, encephalopathy
- Body covered with crushed leaves, neem leaf tea, oral neem husk extracts

### Ruta chalepensis L
- Nausea, vomiting, common cold, abdominal discomfort
- Sedation, drowsiness
- Leaf tea, leaf juice

### Aloe vera (L.) Burm. f
- Digestive problems, constipation, skin treatment
- Itching, skin rash
- Topical gel, lotion, leaf tea, leaf juice

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**Source:** HAJJ and HOLST, 2020

Thus, a study indicates that the consumption of senna-based laxatives can cause toxicity, especially in patients who use the plant infusions continuously and chronically (Manso, 2013). In this context, Table 1 can be identified, containing the species most cited by the authors consulted in this review, highlighting their risks, popular names, scientific, scientific use/popular indication, scientific, used part and references (Corrêa, 2008; Itf, 2008; Manso, 2013; Silva, 2014).

It is worth noting that in the multinational study by Kennedy *et al.* (2013), in 9,459 pregnant women from 23 countries in Europe, North and South America and Australia, it was identified that the most used herbal medicines were *Zingiber officinale* Roscoe (ginger), *Vaccinium oxycoccus* L. *Vaccinium macrocarpon* Aiton L. (cranberry), *Valeriana officinalis* L. (valeriana), *Rubus idaeus* L. (raspberry leaf), *Matricaria chamomilla* L. (chamomile) and *Mentha piperita* L. (peppermint) (Kennedy *et al.* 2013).
The scientific literature on the use of medicinal plants during pregnancy reports that many species are commonly used by the population, especially Ruta graveolens L. (arruda), Salvia officinalis L. (salvia), Punica granatum L. (pomegranate), Datura suaveolens Humb. & Bonpl. ex Willd. (belladonna), Allium sativum L. (garlic), Aloe ferox Mill. (aloe/aloe), Angelica archangelica L. (angelica), Arnica montana L. (arnica), Cinnamomum camphora (L.) J.Presl (camphor), Symphytum officinale var. bohemicum (F.W. Schmidt) Pres. (comfrey), Eucalyptus globulus Labill. (eucalyptus), Rosmarinus officinalis L. (rosemary) Zingiber officinalis Rosc. (ginger), Cassia angustifolia Vahl, (sene), Hibiscus rosa-sinensis L. (hibiscus), Baccharis genistelloides var. trimera (Less.) Baker (gorse), Peumus boldus Molina (Chile bollocks), Luffa operculata (L.) Cogn. (loofah), Artemisia vulgaris var. indicates (Willd.) Maxim. (Mugwort) and Hibiscus sabdariffa L. (hisbiscus) (Souza et al. 2013).

Suzuki (2013) highlights that during pregnancy, physiological changes usually occur intrinsic to this period, which causes a range of unpleasant symptoms and discomfort to the pregnant woman, such as: nausea, vomiting, anorexia, picamalacia (intake of substances with little or no nutritional value, edible or not), breast congestion, heartburn, constipation, edema, cramps, nausea and dizziness. These notes justify the indiscriminate use of medicinal plants in an attempt to minimize the discomfort felt (Suzuki et al. 2013).

According to Hajj and Holst (2020), in a study – realized in 2004 – investigated the use of herbal medicines during pregnancy among 400 Norwegian women, it is evident that approximately 40% of the 144 users of herbal medicines consumed herbal products (see Table 1 – to consult the most commonly used herbal medicines during pregnancy: indications, reported adverse events, and preparations) that were potentially harmful or lack information about their safety in pregnancy (Hajj; Holst 2020; Nordeng; Havnen 2004).

Similarly, in a large multinational study that classified 126 different herbal medicines used in pregnancy according to their safety, only 28 herbs (22.2%) were considered safe for use in pregnancy based on current literature (Kennedy et al. 2013).

According to Hajj and Holst (2020), most recently, a systematic review done in sub-Saharan Africa, which aimed to determine whether the use of herbal medicines during pregnancy was associated with adverse maternal or child outcomes, found that the topical use of Almond oil (Prunus dulcis (Mill.) DA Webb) was significantly associated with preterm birth, oral raspberry leaf (Rubus idaeus L.) with caesarean section and licorice (Glycyrrhiza glabra L.)
heavy consumption (greater than 500 mg/week) with early preterm birth (Hajj; Holst, 2020; Balbontin et al. 2019).

4 CONCLUSION

With this survey, it is observed that the use of medicinal plants by pregnant women is very common, especially those with a calming effect such as *Lippia alba* (lemon balm) and *Matricaria chamomilla* (chamomile), and with antiemetic action such as *Mentha piperita* L. (pepper mint). Thus, it is essential to better elucidate its method of preparation and use, interaction with other drugs and origin of medicinal plants, in order to offer greater safety for its use during pregnancy.

It is expected that more research will be realized in order to contribute with more clarification on the subject in question, as the investigation of which herbs pregnant women use highlights the importance of conducting controlled preclinical studies, as well as risk assessment and benefits of the consumption of medicinal plants during all events that constitute embryogenesis, as well as in the gestational and postpartum period.
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