Sci Tech
العلوم والتكنولوجيا
Science Today
ISSN: 3078-994X

Medicinal Plants in Pregnancy: A Brief Review of the Risks to Fetal Development

Ubirajara Lanza-Júnior[1*], Maitê de Mello e Castro[1], Candida Aparecida Leite Kassuya[1], Fábio Morato de Oliveira[2], Cátia Rezende[3], Shafaq Nisar[4]

[1]Faculty of Health Sciences-Federal University of Grande Dourados-UFGD, Brazil.

[2]Laboratory of Medical Genetics, Federal University of Jataí-UFJ Brazil.

[3]Paulista University-Araraquara, São Paulo, Brazil.

[4]Department of Chemistry, University of Agriculture, Faisalabad, Pakistan.

Abstract

During fetal organogenesis, exposure to natural and/or synthetic chemical agents can have devastating effects on the developing fetus, including congenital malformations, embryotoxicity, and fetal death. Despite contraindications to the use of certain chemicals during pregnancy, many pregnant women use medicinal plants to alleviate unwanted symptoms inherent to the development of the gestational period, such as nausea, vomiting, and abdominal pain, among others. This practice is unfortunately supported by the false idea that the use of natural substances is incapable of causing harm to the health of the pregnant woman or the fetus. This study aims to systematically identify medicinal plants commonly used in South America and their secondary metabolites that may pose risks to fetal development if consumed during pregnancy. By investigating these plants and their secondary metabolites, we aim to improve the understanding of their potential embryotoxic effects and provide valuable insights for clinical practices related to herbal remedies during pregnancy. The search for articles was carried out in the databases PubMed (NCBI), Virtual Health Library (VHL), Scientific Online Electronic Library (SciELO), Medical Literature Analysis and Retrieval System Online – MedLine (PubMed), Scientific Electronic Library – SciELO and Latin American and Caribbean Literature in Health Sciences – LILACS. Although the use of medicinal plants to relieve discomfort related to the development of pregnancy is an ancient practice, the use of the medicinal plants presented in this work should be avoided by pregnant women, as they are plants endowed with secondary metabolites that can cause embryotoxic, teratogenic and abortifacient effects.

Keywords: Pregnancy, medicinal plants, folk medicine, fetal malformations, fetal death

Full length article **Corresponding Author*, e-mail: *ubirajaralanzajunior@gmail.com, Tel: +551899678,* doi# 10.71111/Science today/1-25-2-2-st-1

1. Introduction

During the critical phase of fetal organogenesis, exposure to chemical agents—whether of natural or synthetic origin—can lead to significant adverse outcomes, including congenital malformations, embryotoxicity, or even fetal death. In many Latin American countries, it is quite common for pregnant women to use medicinal plants to alleviate various discomforts related to pregnancy, including nausea, constipation, flatulence, weight gain, hormonal fluctuations, sleep disorders, depression, heartburn, and muscle pain, among others [1-4]. Medicinal plants are used in South American countries mainly because of several factors, such as the popular belief that they are devoid of adverse effects, socioeconomic difficulties, including limited access to public health services, unemployment, and the high cost of conventional medicines [4-5]. In this way, the use of medicinal plants reflects a complex interaction between traditional practices and modern health challenges. Many women perceive these natural substances as safer alternatives to allopathic medicines, which are often viewed as potentially harmful during pregnancy.

However, although use of these plants is most often undertaken without supervision of a qualified professional, it is essential to approach this practice with caution due to the lack of comprehensive safety data on their effects on maternal and fetal health [6-7]. Thus, continued research and education are crucial to address potential risks associated with use of herbal remedies during pregnancy. Although certain chemical agents are explicitly contraindicated during pregnancy, there is a worrying gap in knowledge about the

potential risks associated with several substances derived from medicinal plants or consumption of medicinal plants in food form in large quantities or over a prolonged period, especially during pregnancy. This lack of awareness, together with inadequate medical advice and insufficient technical-scientific information, can result in serious detrimental effects on embryonic development [7-8]. Main objective of this study was to systematically identify medicinal plants prevalent in South America (mainly in Brazil) and their secondary metabolites, may pose risks to fetal development.

2. Methodology

The present work is a literature review where the identification of articles of interest was performed using the PubMed databases of the US National Library of Medicine (https://pubmed.ncbi.nlm.nih.gov/), database Medical Literature Analysis and Retrieval System Online (MEDLINE), Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature on Health Sciences (LILACS), and the search tool attached to the Virtual Health Library (VHL). The Institutional Repository of different Brazilian Universities for researching articles along with theses, dissertations, and monographs also consulted. The predefined keywords “Pregnancy”, “Medicinal plants”, “Folk medicine”, “Fetal malformations”, “Fetal death” were used in the searches. The search expression was the Boolean operator "AND", limiting the searches to words of the title or abstract of articles, in English, Portuguese and Spanish, studies with human beings and/or experimental animals, as well as *in vivo* studies and/or *ex-vivo*. To ensure the quality of the articles, only indexed publications were included in this database, comprising articles that presented titles and abstracts on theme and excluding those that did not meet these conditions.

3. Results and discussion

Different morphophysiological adaptations occur throughout the development of pregnancy and can lead to discomforts such as nausea, constipation, flatulence, weight gain, hormonal changes, sleep disorders, heartburn, and lower back and pelvic pain, which appear from the first week of pregnancy and can persist throughout the gestational period in many women [5-9]. The gestational period that runs from fertilization to the 57th day of gestation is one in which several cell divisions occur. During this period, the embryo is most susceptible to the action of teratogenic and embryotoxic agents [10-12]. In this context, health conditions of pregnant women have been target of special attention, since, at this stage, women become especially sensitive and concerned about well-being of the fetus, becoming vulnerable to advice and guidance from friends and family regarding “home remedies” seen as beneficial and without health risks [4-13]. To alleviate the discomforts that arise during pregnancy, many pregnant women seek alternative treatment in medicinal plants, as they believe that, because they are natural, they are free of harmful effects on pregnancy, despite the lack of robust data on their safety and efficacy [1-2]. However, some plants used in empirical medicine can determine embryotoxic, teratogenic, and abortifacient effects, requiring special care in their use, since plants are usually chemically complex and may contain toxic substances in addition to their biologically active principles [2-3-14-15].

Pregnant women should use medicinal plants with same care as they would with allopathic medicines, always accompanied by prior medical knowledge [16]. Occurrence of embryotoxicity is directly related to maternal exposure to toxic xenobiotics, cause disorders in embryonic development, where this embryotoxicity may or may not be reversible, depending on regenerative capacity of damaged tissue, and may result in abortion [17-18]. In turn, teratogenicity occurs when a chemical agent can irreversibly alter structural or functional development of embryo or fetus and can occur throughout the gestational period. In turn, exposure to xenobiotics during pregnancy may determine occurrence of teratogenicity, which is characterized mainly by irreversible changes in structural or functional development of embryo or fetus and may occur throughout gestational period. Teratogenic xenobiotics cause selective malformation of some target organs, such as those directly linked to the formation of lower and upper limbs [19-21] and it is possible that many secondary metabolites of plants, such as alkaloids, flavonoids, coumarins, terpenes and anthraquinones, represent risk during pregnancy [22-24]. Different medicinal plants used in empirical medicine during pregnancy contain many of these secondary metabolites in their composition.

The use of these plants as medicine during pregnancy can have devastating effects on the fetus, as demonstrated in Table 1. Alkaloids are present in many plant species described in Table 1. Plants such as *Plectranthus barbatus* (Falso boldo), *Symphytum officinale* (Confrei), *Rosmarinus officinales* (Alecrim), *Solanun crinitum* (Jurubeba), *Peumus boldus* (Boldo do Chile), *Punica granatum* (Romã), *Echinodorus macrophyllus* (Chapéu-de-Couro), *Brunfelsia uniflora* (Manacá), and *Camellia sinensis* (Chá-verde) are rich in these metabolites, which makes the consumption of these plants during pregnancy a high-risk practice since the literature reports that in addition to being teratogenic, these secondary metabolites of plants can determine embryotoxic and abortifacient effects [25-29]. Some morphological characteristics of plants rich in alkaloids in their constitution and commonly found in different regions of different Brazilian states are shown in Figure 1. Among the types of alkaloids, pyrrolizidines stand out, which when hepatically biotransformed by CYP450, generate highly reactive and toxic compounds that can determine occurrence of hepatotoxicity and related diseases [30-33].

During pregnancy, the main pathophysiological implication determined by ingestion of pyrrolizidine alkaloids is teratogenicity, due to ability of these substances to bind to the DNA molecule and cause interference in cell differentiation, devastatingly damaging fetal development [34-35]. In South America and mainly in Brazil, it is not uncommon to observe that some pregnant women use plants such as *Aloe vera* (Babosa), *Rhamnus purshiana* (Cáscara sagrada), *Cassia angustifolia* (Sene), *Handroanthus impetiginosus* (Ipê roxo) to reduce weight gain during pregnancy. Some characteristics of these plants can be observed in figure 2 these species are rich in anthraquinones, Table 1, which have laxative, anti-inflammatory, antioxidant, & antihistamine action, in addition to being vasoconstrictors. Laxative action is predominant therapeutic activity of these species, as anthraquinones stimulate contraction of smooth muscle of intestine, increasing peristalsis. Main risk to health of pregnant women and which related to indiscriminate use of these compounds is abortion, as these substances are

capable of inducing an increase in activity of uterine smooth muscle, which results in intense uterine contractions.

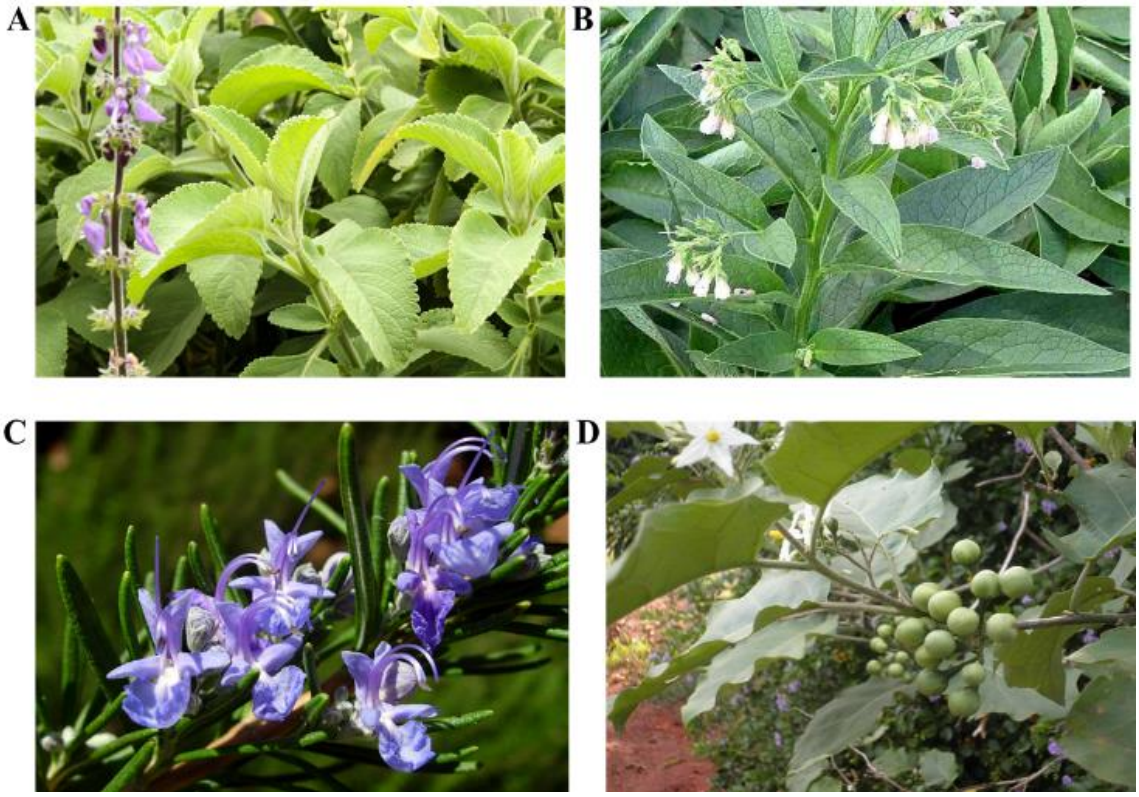

Figure 1. Medicinal plants rich in alkaloids and easily found in Brazilian household gardens. (A) *Plectranthus barbatus* (falso boldo), a species used against inflammatory and respiratory disorders. (B) *Symphytum officinale* (Confrei), known for its traditional use in wound healing and anti-inflammatory properties. (C) *Rosmarinus officinales* (Alecrim), traditionally used to treat inflammatory conditions. (D) *Solanum crinitum* (Jurubeba), used in folk medicine to treat digestive system disorders.

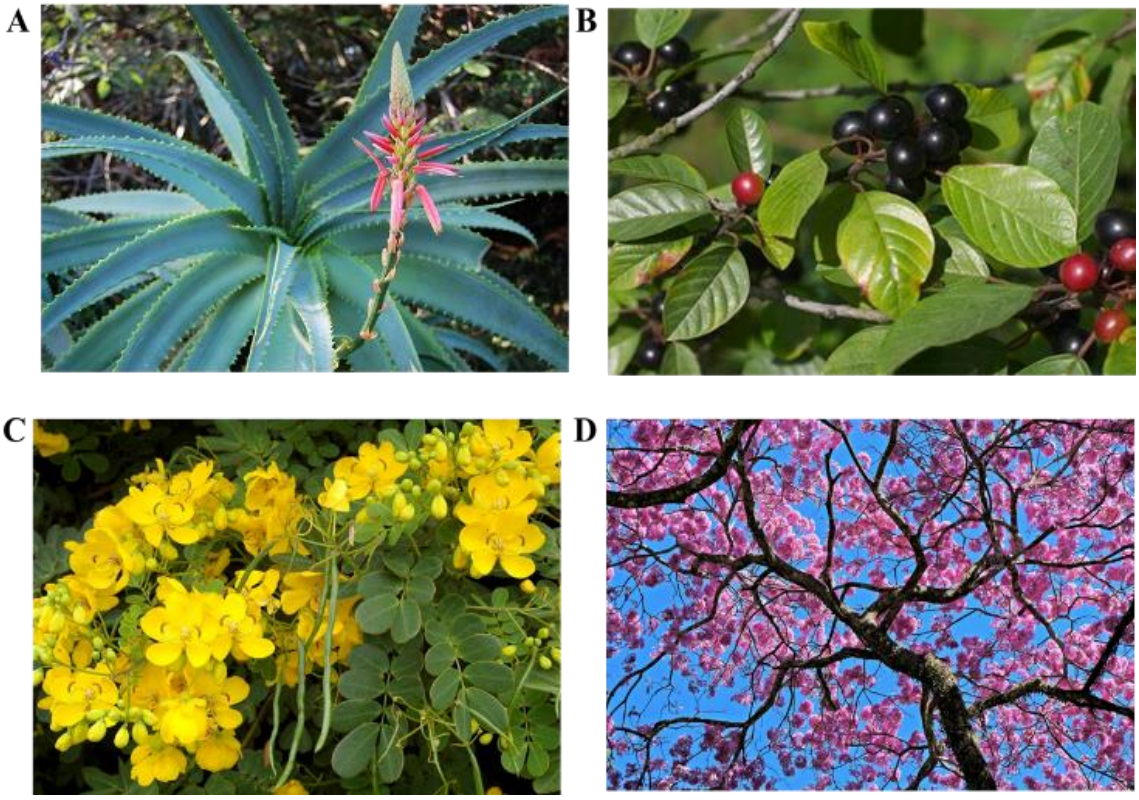

Figure 2. Plants rich in anthraquinones in their compositions. (A) *Aloe vera* (Babosa) a species used in the treatment of skin and gastrointestinal system diseases. (B) *Rhamnus purshiana* (Cáscara sagrada), a plant used empirically against gastrointestinal disorders. *Cassia angustifolia* (Sene), a species used in folk medicine as a laxative. (C) *Handroanthus impetiginosus* (Ipê roxo), A

species used empirically for various therapeutic purposes in South America, especially in Brazil.

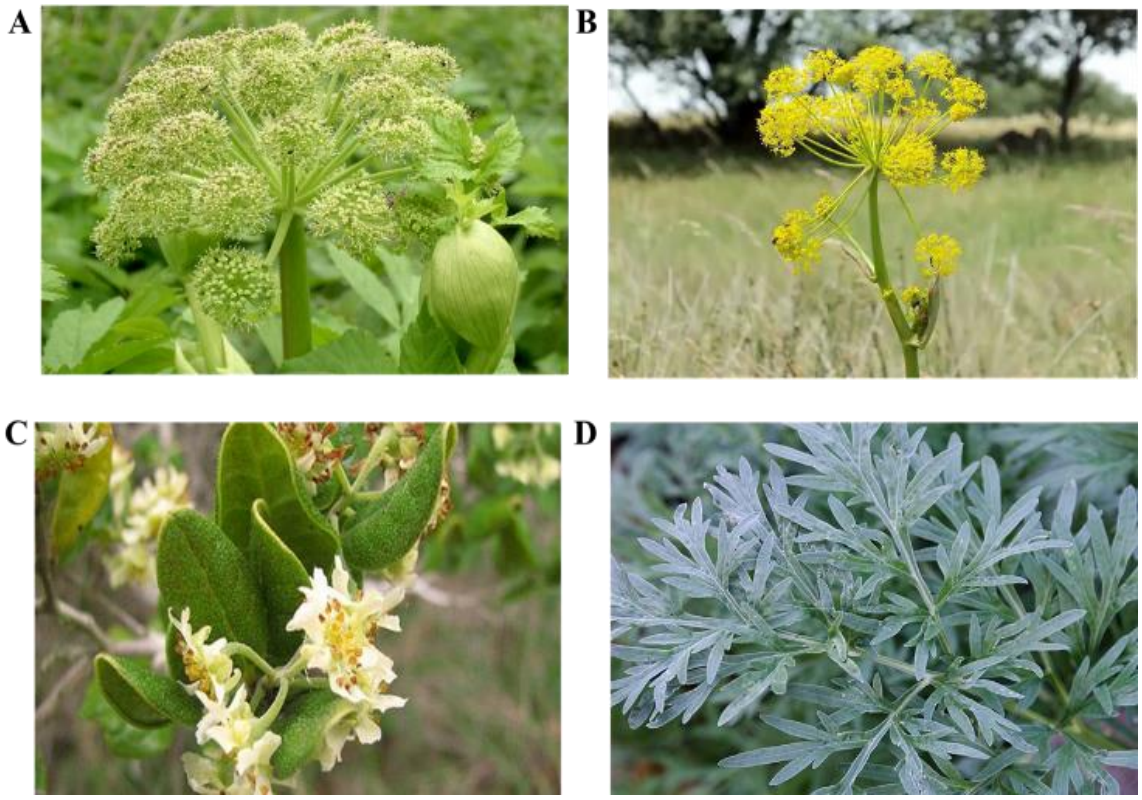

Figure 3. Some morphological characteristics of plants rich in coumarin, endemic in different regions of different Brazilian states. (A) *Angelica archangelica* (Erva-dos-anjos), popularly used in gastric and central nervous system disorders. (B) *Ferula assafoetida* (Assa-fétida), popularly used against infections and diabetes. (C) *Peumus boldus* (Boldo-do-Chile), a species used against indigestion. (D) *Artemisia vulgaris* (Losna) popularly used against inflammatory pain.

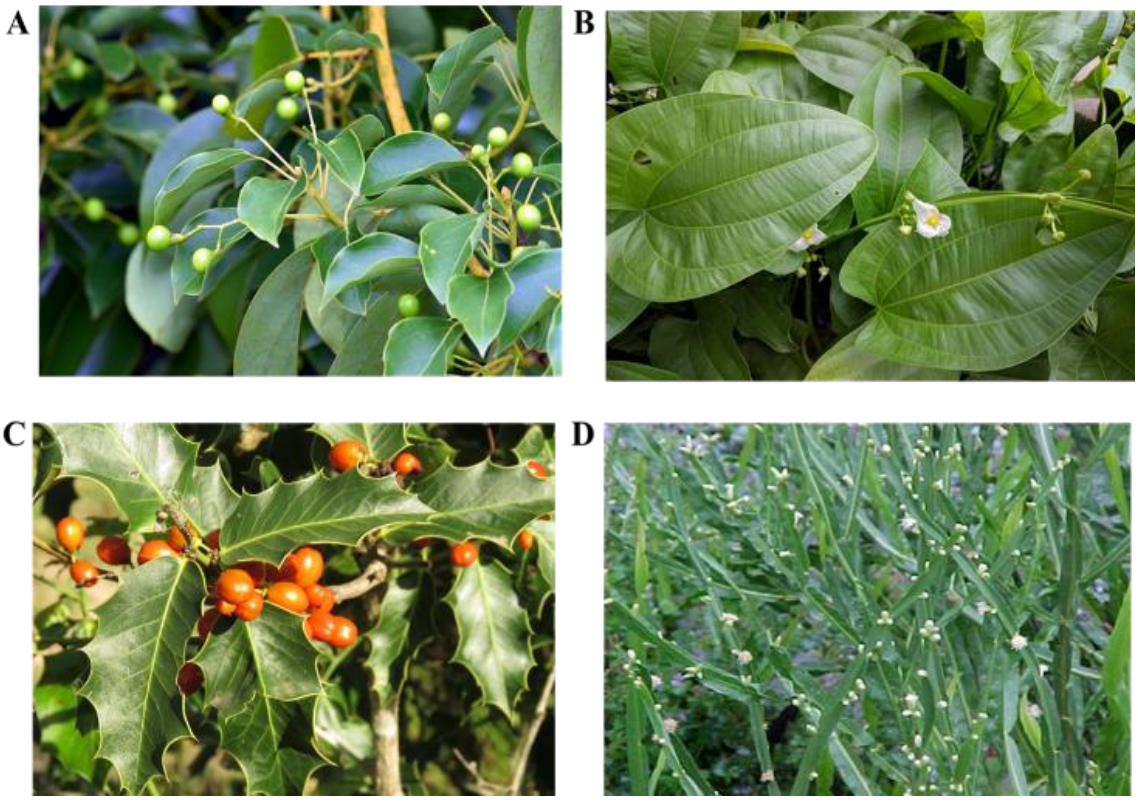

Figure 4. Plants rich in terpenoids in their compositions. (A) *Cinnamomum camphora* (Cânfora) a species popularly used against inflammatory pain. (B) *Echinodorus macrophyllum* (Chapéu-de-couro), a plant used empirically used as an anti-inflammatory. (C) *Maytenus ilicifolia* (Espinheira santa), plant used popularly against gastritis. (D) *Baccharis trimera* (Carqueja) a species popularly

used against digestive system disorders.

Table 1. Medicinal plants and their secondary metabolites that are potentially harmful to fetal development

Scientific name/popular name in Brazil	Use according to folk medicine	Raw Plant Materials	Secondary metabolites	Harmful effects on fetal development	References
***Aloe* sp/Babosa**	Burns and skin conditions, and gastrointestinal system disorders	Leaves and sap	Anthraquinones	Abortifacient and mutagenic	[36-60-97]
***Angelica archangelica*/Erva-dos-anjos**	Gastric discomfort and anxiety	Flowers	Volatile oils, coumarins, and flavonoids	Abortifacient and teratogenic	[48-49-59]
***Artemisia vulgaris*/Losna**	Anti-inflammatory, antiparasitic	Leaves and roots	Coumarins, tannins, terpenes	Teratogenic and embryotoxic	[44-61]
***Baccharis trimera*/Carqueja**	Food indigestion and gastric disorders	Leaves	Flavonoids and terpenes	Abortifacient	[43-62]
***Brunfelsia uniflora*/Manacá-de-cheiro**	Inflammatory symptoms	Leaves, roots and stems	Alkaloids	Abortifacient	[26]
***Cassia angustifolia*/Sene**	Constipation	Leaves	Anthraquinones an flavonoids	Abortifacient	[34-49]
Cinnamomum verum/Canela	Inflammatory symptoms	Stem	Phenolic acids, flavonoids, terpenes, aldehydes and glycosides	Embryo loss and fetal malformation	[49-51-65]
Cymbopogon citratus/Capim cidreira	Inflammatory symptoms	Leaves	Geranial, geraniol, geranyl acetate, citronellal, citronellol, germacrene and elemol	Developmental toxicity and abortifacient effects	[51-53-66-68]
***Echinodorus macrophyllus/* Chapéu-de-Couro**	Acute and chronic inflammatory conditions	Leaves	Alkaloids, flavonoids and triterpenes	Abortifacient	[44-69-70]
***Eucalyptus globulus*/Eucalipto**	Pediculosis	Leaves	Terpenes and flavonoids	Abortifacient	[37-71-72]
***Ferula assafoetida*/Assa fétida**	Antiviral and hyperglycemia	Leaves	Coumarins and terpenes	Emmenagogue, abortifacient and teratogenic	[44-45-73-74]
Ginkgo biloba/Ginko	Blood circulation disorders	Leaves, fruits and seeds	Flavonoids and coumarins	Abortifacient and teratogenic	[17-75-76]
***Handroanthus impetiginosus/* Ipê roxo**	Depression, inflammatory symptoms and bacterial infections	Leaves	Anthraquinones, flavonoids and tannins	Teratogenic and abortifacient	[4-49-94-96]
***Lantana camara/* Camará, chumbinho**	Inflammatory disorders	Leaves	Flavonoids and terpenes	Teratogenic	[26-54-77]
***Luffa operculata*/Bucha paulista**	Rhinitis and rhinosinusitis	Fruits	Terpenes	Abortifacient and embryotoxic	[9-13-19-34-55-78-79]
***Matricaria recutita/* Camomila**	Inflammatory symptoms, gastrointestinal, and liver disorders	Leaves and flowers	Flavonoids and terpenes	Abortifacient	[19-80]
***Maytenus ilicifolia/* Espinheira santa**	Ulcer and gastritis	Leaves, bark and roots	Terpenes	Abortifacient	[9-55-81]
***Mentha piperita*/Hortelã**	Digestive disorders	Leaves	Lignans, terpenes, flavonoids and p-coumarinic acid	Teratogenic	[4-55-56-82-83]

***Peumus boldus*/Boldo do Chile**	Gastrointestinal disorders	Leaves, roots and stems	Alkaloids	Embryotoxic, abortive and teratogenic	[26-84]
***Plectranthus barbatus*/Falso boldo**	Respiratory and inflammatory disorders	Leaves	Alkaloids, diterpenes and coumarins	Abortifacient	[57-85]
***Punica granatum*/Romã**	Gastric ulcers and diarrhea	Seeds, bark, fruit, trunk and root bark	Alkaloids	Embryotoxic	[56-86]
***Rhamnus purshiana*/ Cáscara sagrada**	Constipation	Leaves and fruits	Anthraquinones	Emmenagogue, abortifacient, genotoxic	[19-40-87]
***Rosmarinus officinales*/ Alecrim**	Inflammatory symptoms	Leaves and branches	Terpenes and flavonoids	Abortifacient	[4-88]
***Solanun crinitum*/ Jurubeba**	Gastric and liver disorders	Fruits, roots, leaves and flowers	Alkaloids	Abortifacient	[26-89-92]
***Symphytum officinale* Confrei**	Inflammatory symptoms	Leaves	Alkaloids and terpenes	Abortifacient	[26-34-93]

In addition, this class of secondary metabolites has been shown to have mutagenic activity and, therefore, can interfere with the replication of fetal cells devastatingly [36]. Plants rich in anthraquinones and commonly found in many regions of different Brazilian states are shown in Figure 2. The flavonoids shown in Table 1 are found in plants such as *Rosmarinus officinalis* (Alecrim), *Polianthes tuberosa* (Angelica), *Peumus boldus* (Boldo-do-Chile), *Lantana camara* (Camará), *Matricaria recutita* (Camomila), *Baccharis trimera* (Carqueja), *Echinodorus macrophyllum* (Chapéu-de-couro), *Eucalyptus globulus* (Eucalipto), *Ginkgo biloba* (Ginkgo), and *Punica granatum* (Romã) [19-24-26-37]. Therefore, the use of these plants rich in flavonoids should be avoided by pregnant women, especially in the last trimester of pregnancy, as the anti-inflammatory action of these metabolites can alter fetal cardiac function, resulting from the inhibition of production of prostaglandins produced by the placenta, which have the function of keeping open the arterial duct that connects the pulmonary artery to the aorta. After seven months of gestation, this duct depends on prostaglandins to remain open. Its closure can interrupt blood flow, leading to fetal death [38]. Coumarins are phenolic compounds that have anticoagulant, anti-inflammatory, antidiarrheal, antiseptic, and antioxidant effects [39].

These phenolic compounds are present in species such as *Angelica archangelica* (Erva-dos-anjos), *Ferula assafoetida* (Assa-fétida), *Peumus boldus* (Boldo-do-Chile), *Artemisia vulgaris* (Losna), *Ruta graveolens* (Arruda), and *Ginkgo biloba* (Ginkgo), as described in Table 1. Coumarins are vitamin K antagonists and, as such, inhibit the synthesis of coagulation factors II (prothrombin), VII, IX, and X, as well as proteins C and S, disrupting the homeostasis of the coagulation cascade. These metabolites interact synergistically with synthetic anticoagulants, such as heparin, increasing the risk of bleeding or thromboembolic events. Coumarins are considered teratogenic when used in the first trimester of pregnancy and, in some cases, can cause abortion [39- 41]. Figure 3 shows some morphological characteristics of plant species rich in coumarins and easily accessible to the Brazilian population. In turn, terpenoids are abundant secondary metabolites in the plant kingdom, being the metabolites with the greatest presence in the species presented in Table 1. Many compounds of this class are used in the pharmaceutical industry, as they present a wide variety of biological properties, such as antimicrobial, antifungal, antiviral, hypoglycemic, analgesic, anti-inflammatory, and antiparasitic effects [42-43]. In this context, terpenoids are present in products based on *Cinnamomum camphora* (Cânfora), *Echinodorus macrophyllum* (Chapéu-de-couro), *Maytenus ilicifolia* (Espinheira santa), *Baccharis trimera* (Carqueja), *Rosmarinus officinalis* (Alecrim), *Mentha piperita* (Hortelã), *Matricaria recutita* (Camomila), *Artemisia vulgaris* (Losna), *Ferula assafoetida* (Assa-fétida), and *Eucalyptus globulus* (Eucalipto).

Many of these products derived from these plants are consumed by pregnant women for the rapid treatment of symptoms such as nausea, vomiting, constipation, flatulence, heartburn, colds, flu, anxiety, and depression [44-46]. Some morphological characteristics of plants rich in terpenoids and commonly found in many regions of different Brazilian states are shown in Figure 4. Terpenoids can determine harm to the health of pregnant women, such as spontaneous abortion due to the relaxation of the uterine muscles, which makes it difficult for the embryo to attach. Effects such as embryotoxicity and teratogenicity are also described in the literature [43-47]. In this context, it is clear that the use of medicinal plants as an alternative to conventional medicines, although it may be seen as a viable solution, presents significant risks that require a careful and scientific approach. In some populations in Brazil, popular knowledge about the use of medicinal plants is passed down from generation to generation, and it is usually an accessible and culturally accepted practice. However, the inappropriate use of these plants can result in harmful effects for both the mother and the fetus, which can be represented mainly by teratogenic, embryotoxic, and abortifacient risks. In addition, the lack of scientific knowledge about the dosage and safe administration of preparations obtained from these plants, as well as their botanical identifications carried out incorrectly, can result in poisoning and aggravation of these risks.

4. Final considerations

Due to sociocultural factors or not, self-medication with medicinal plants by pregnant women, even in the

absence of proof regarding the efficacy and safety of these substances, can be a high-risk practice for both maternal and fetal health. This concern applies even too many plants that have been consumed for centuries without any reports or consensus in the literature on their potential harm to human health. Therefore, the use of medicinal plants as an alternative therapy for various undesirable physiological changes during pregnancy should be avoided, or in cases of extreme necessity, should be monitored by a qualified professional.

References

[1] H.B. Im, R. Ghelman, C.F.S. Portella, J.H. Hwang, D. Choi, S.K. Kunwor, S.D.T.d.A. Moraes, D. Han. (2023). Assessing the safety and use of medicinal herbs during pregnancy: a cross-sectional study in São Paulo, Brazil. Frontiers in Pharmacology. 14: 1268185.

[2] A.M. Da Silva, A.L. Horsth, É.d.S. Timóteo, R.J. Faria, P.S. Bazoni, E.F. Meira, J.B.R. Dos Santos, M.R.R. Da Silva. (2023). Use of medicinal plants during COVID-19 pandemic in Brazil. Scientific Reports. 13(1): 16558.

[3] P. Yazbek, J. Tezoto, F. Cassas, E. Rodrigues. (2016). Plants used during maternity, menstrual cycle and other women's health conditions among Brazilian cultures. Journal of Ethnopharmacology. 179: 310-31.

[4] L.E. Gorril, E. Jacomassi, S.E.M. Junior, P.R. Dalsenter, A.G. Junior, E.L.B. Lourenço. (2016). Risco das plantas medicinais na gestação: uma revisão dos dados de acesso livre em língua portuguesa. Arquivos de Ciências da Saúde da UNIPAR. 20(1):67-72.

[5] M.d.O.P. Lima, M.A. Tsunechiro, I.C. Bonadio, M. Murata. (2017). Sintomas depressivos na gestação e fatores associados: estudo longitudinal. Acta Paulista de Enfermagem. 30: 39-46.

[6] N. Bernstein, M. Akram, Z. Yaniv-Bachrach, M. Daniyal. (2021). Is it safe to consume traditional medicinal plants during pregnancy? Phytotherapy Research. 35(4): 1908-1924.

[7] Y.M. Balbontín, D. Stewart, A. Shetty, C.A. Fitton, J.S. McLay. (2019). Herbal medicinal product use during pregnancy and the postnatal period: a systematic review. Obstetrics & Gynecology. 133(5): 920-932.

[8] S. Balarastaghi, M. Delirrad, A. Jafari, M. Majidi, M. Sadeghi, H. Zare-Zardini, G. Karimi, A. Ghorani-Azam. (2022). Potential benefits versus hazards of herbal therapy during pregnancy; a systematic review of available literature. Phytotherapy Research. 36(2): 824-841.

[9] E.d.C. Coutinho, C.B.d. Silva, C.M.B. Chaves, P.A.B. Nelas, V.B.C. Parreira, M.O. Amaral, J.C. Duarte. (2014). Gravidez e parto: O que muda no estilo de vida das mulheres que se tornam mães? Revista da Escola de Enfermagem da USP. 48: 17-24.

[10] S. Zhang, R. Yang, M. Zhao, S. Li, N. Yin, A. Zhang, F. Faiola. (2024). Typical neonicotinoids and organophosphate esters, but not their metabolites, adversely impact early human development by activating BMP4 signaling. Journal of Hazardous Materials. 465: 133028.

[11] M.J. Park, J.-P. Chae, D. Woo, J.Y. Kim, Y.C. Bae, J.Y. Lee, S.Y. Lee, E.J. Nam, S.-W. Nam. (2024). Ibuprofen-induced multiorgan malformation during embryogenesis in Xenopus laevis (FETAX). Biochemical and biophysical research communications. 703: 149565.

[12] T. Ismail, H. Lee, Y. Kim, H.Y. Ryu, D.H. Cho, Z.Y. Ryoo, D.S. Lee, T.K. Kwon, T.J. Park, T. Kwon. (2023). PCNB exposure during early embryogenic development induces developmental delay and teratogenicity by altering the gene expression in Xenopus laevis. Environmental Toxicology. 38(1): 216-224.

[13] R.A.M. Borges, V.B. Oliveira. (2015). Riscos associados ao uso de plantas medicinais durante o período da gestação: uma revisão. Revista Uniandrade. 16(2): 101-108.

[14] C.R.F. de Araújo, F.G. Santiago, M.I. Peixoto, J.O.D. de Oliveira, M. de Sousa Coutinho. (2016). Use of medicinal plants with teratogenic and abortive effects by pregnant women in a city in Northeastern Brazil. Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics. 38(03): 127-131.

[15] J. Wiesner, W. Knöss. (2017). Herbal medicinal products in pregnancy− which data are available? Reproductive Toxicology. 72: 142-152.

[16] H.G. Rodrigues, C. Meireles, J. Lima, G. Toledo, J. Cardoso, S. Gomes. (2011). Efeito embriotóxico, teratogênico e abortivo de plantas medicinais. Revista brasileira de plantas medicinais. 13: 359-366.

[17] M. Carvalho, A. Melo, C. Aragão, F. Raffin, T. Moura. (2013). Schinus terebinthifolius Raddi: chemical composition, biological properties and toxicity. Revista brasileira de plantas medicinais. 15: 158-169.

[18] Y. Kim, J. Kim, O.J. Kim, W.C. Kim. (2014). Intoxication by angel's trumpet: case report and literature review. BMC research notes. 7: 553-555.

[19] G.M.G. Arcanjo, M. Medeiros, R. Azevedo, T. Rocha, S. Griz, K. Mousinho. (2013). Estudo da utilização de plantas medicinais com finalidade abortiva. Rev Eletr Biol. 6(3): 234-250.

[20] A.M. Andrade, A.A. Ramalho, S.P. Opitz, F.A. Martins, R.J. Koifman. (2017). Farmacocinética e mecanismos de teratogenicidade dos medicamentos na gestação: uma revisão da literatura. Infarma-Ciências Farmacêuticas. 29(2): 100-107.

[21] X.H. Wang, L.Y. Fan, S. Wang, Y. Wang, L.C. Yan, S.S. Zheng, C.J. Martyniuk, Y.H. Zhao. (2017). Relationship between acute and chronic toxicity for prevalent organic pollutants in Vibrio fischeri based upon chemical mode of action. Journal of Hazardous Materials. 338: 458-465.

[22] T. Fotland, J. Paulsen, T. Sanner, J. Alexander, T. Husøy. (2012). Risk assessment of coumarin using the bench mark dose (BMD) approach: Children in Norway which regularly eat oatmeal porridge with cinnamon may exceed the TDI for coumarin with

several folds. Food and Chemical Toxicology. 50(3-4): 903-912.

[23] R. Samavati, E. Ducza, J. Hajagos-Tóth, R. Gaspar. (2017). Herbal laxatives and antiemetics in pregnancy. Reproductive Toxicology. 72: 153-158.

[24] F.C. Silva, A.B. Ribeiro, P. RIBIEIRO. (2017). Avaliação da qualidade de plantas medicinais comercializadas no município de Imperatriz, Maranhão. 13(2): 1-9

[25] K.C.d.S. Costa, S.B. Bezerra, C.M. Norte, L.M.N. Nunes, T.M.d. Olinda. (2012). Medicinal plants with teratogenic potential: current considerations. Brazilian Journal of Pharmaceutical Sciences. 48: 427-433.

[26] S. Campos, C. Silva, P. Campana, V. Almeida. (2016). Toxicidade de espécies vegetais. Revista brasileira de plantas medicinais. 18: 373-382.

[27] M. Wink. (2016). Alkaloids: Toxicology and health effects.

[28] S. Izcara, N. Casado, S. Morante-Zarcero, D. Pérez-Quintanilla, I. Sierra. (2022). Miniaturized and modified QuEChERS method with mesostructured silica as clean-up sorbent for pyrrolizidine alkaloids determination in aromatic herbs. Food chemistry. 380: 132-189.

[29] S. Rizzo, R. Celano, A.L. Piccinelli, M. Russo, L. Rastrelli. (2023). Target screening method for the quantitative determination of 118 pyrrolizidine alkaloids in food supplements, herbal infusions, honey and teas by liquid chromatography coupled to quadrupole orbitrap mass spectrometry. Food chemistry. 423: 136306.

[30] R. Teschke, N. Vongdala, N.V. Quan, T.N. Quy, T.D. Xuan. (2021). Metabolic toxification of 1, 2-unsaturated pyrrolizidine alkaloids causes human hepatic sinusoidal obstruction syndrome: The update. International journal of molecular sciences. 22(19): 10419.

[31] Z. Huang, Z. Wu, X. Gu, L. Ji. (2024). Diagnosis, toxicological mechanism, and detoxification for hepatotoxicity induced by pyrrolizidine alkaloids from herbal medicines or other plants. Critical Reviews in Toxicology. 54(2): 123-133.

[32] J. Glück, J. Waizenegger, A. Braeuning, S. Hessel-Pras. (2020). Pyrrolizidine alkaloids induce cell death in human heparg cells in a structure-dependent manner. International journal of molecular sciences. 22(1): 202.

[33] B. Tábuas, S. Cruz Barros, C. Diogo, C. Cavaleiro, A. Sanches Silva. (2024). Pyrrolizidine Alkaloids in Foods, Herbal Drugs, and Food Supplements: Chemistry, Metabolism, Toxicological Significance, Analytical Methods, Occurrence, and Challenges for Future. Toxins. 16(2): 79.

[34] M.A. Medeiros, F. Riet-Correa, F.P. Dantas, J.R. Santos, R.M. Medeiros, Efeitos teratogênicos de Prosopis juliflora em ratos e análise da toxicidade das vagens. In SciELO Brasil: 2014; Vol. 34, pp 1089-1093.

[35] B.-E. Van Wyk, M. Stander, H. Long. (2017). Senecio angustifolius as the major source of pyrrolizidine alkaloid contamination of rooibos tea (Aspalathus linearis). South African Journal of Botany. 110: 124-131.

[36] V. Freitas, R. Rodrigues, F. Gaspi. (2014). Propriedades farmacológicas da Aloe vera (L.) Burm. f. Revista brasileira de plantas medicinais. 16: 299-307.

[37] N. Souza Maria, M.M.P. Tangerina, V. Silva, W. Vilegas, M. Sannomiya. (2013). Plantas medicinais abortivas utilizadas por mulheres de UBS: etnofarmacologia e análises cromatográficas por CCD e CLAE. Revista brasileira de plantas medicinais. 15: 763-773.

[38] P. Zielinsky, A.L. Piccoli Jr, I. Vian, A.M. Zílio, A.A. Naujorks, L.H. Nicoloso, C.W. Barbisan, S. Busato, M. Lopes, C. Klein. (2013). Restrição materna de polifenóis e dinâmica ductal fetal na gestação normal: um ensaio clínico aberto. Arquivos Brasileiros de Cardiologia. 101: 217-225.

[39] S. Weigt, N. Huebler, R. Strecker, T. Braunbeck, T.H. Broschard. (2012). Developmental effects of coumarin and the anticoagulant coumarin derivative warfarin on zebrafish (Danio rerio) embryos. Reproductive Toxicology. 33(2): 133-141.

[40] F. Lussana, M. Coppens, M. Cattaneo, S. Middeldorp. (2012). Pregnancy-related venous thromboembolism: risk and the effect of thromboprophylaxis. Thrombosis research. 129(6): 673-680.

[41] C.d.F. Viegas, C.H. Franciscon, M.d.P. Lima. (2014). Abordagem Etnobotânica em uma empresa do Polo Industrial de Manaus. Volume 3, Pags. 51-58.

[42] M. Oliveira, A. Barreto, L.Q. Júnior, A. Guimarães. (2014). Aplicação de terpenos como agentes analgésicos: uma prospecção tecnológica. Revista Geintec-Gestão Inovação E Tecnologias. 4(4): 1292-1298.

[43] D. Montesano, G. Rocchetti, P. Putnik, L. Lucini. (2018). Bioactive profile of pumpkin: An overview on terpenoids and their health-promoting properties. Current Opinion in Food Science. 22: 81-87.

[44] T.K. Karam, L. Dalposso, D.d. Casa, G. De Freitas. (2013). Carqueja (Baccharis trimera): utilização terapêutica e biossíntese. Revista brasileira de plantas medicinais. 15: 280-286.

[45] M. Messias, M. Menegatto, A.C.C. Prado, B.R.d. Santos, M.F.M. Guimarães. (2015). Uso popular de plantas medicinais e perfil socioeconômico dos usuários: um estudo em área urbana em Ouro Preto, MG, Brasil. Revista brasileira de plantas medicinais. 17(1): 76-104.

[46] G. Lopes, E. Pinto, L. Salgueiro. (2017). Natural products: an alternative to conventional therapy for dermatophytosis? Mycopathologia. 182: 143-167.

[47] L. Kristanc, S. Kreft. (2016). European medicinal and edible plants associated with subacute and chronic toxicity part I: Plants with carcinogenic, teratogenic and endocrine-disrupting effects. Food and Chemical Toxicology. 92: 150-164.

[48] S. Roman, A. Dambros, A. Rosset, M. Pistore, A. Schimid, R. Cansian. (2014). Toxicidade materna e reprodutiva de extrato hidroalcoólico de Sonchus

oleraceus L. em ratos wistar. Rev Perspect. 38: 69-77.

[49] Y. Wang, P.d.B. Harrington, P. Chen. (2020). Metabolomic profiling and comparison of major cinnamon species using UHPLC–HRMS. Analytical and bioanalytical chemistry. 412: 7669-7681.

[50] D. Kennedy, A. Lupattelli, G. Koren, H. Nordeng. (2016). Safety classification of herbal medicines used in pregnancy in a multinational study. BMC complementary and alternative medicine. 16(1): 102.

[51] M. McGuffin, C. Hobbs, R.Upton, A. Goldberg. (1997). Botanical safety handbook. CRC Press.

[52] C.E. Ekpenyong, E.E. Akpan, N.E. Daniel. (2014). Phytochemical Constituents, Therapeutic Applications and Toxicological Profile of Cymbopogon citratus Stapf (DC) Leaf Extract. Journal of Pharmacognosy and Phytochemistry. 3(1): 133-141.

[53] SDED Saúde. (2002). Resolução - SES/RJ No 1757 de 18/02/2002. Editor E. D. Saúde. Rio de Janeiro: Legislação e Políticas Públicas.

[54] G.K. Traesel, F.F. de Lima, A.C. Dos Santos, R.I.C. Souza, D.T. Cantadori, C.R. Kretschmer, V.J. Navarini, S.A. Oesterreich. (2017). Evaluation of embryotoxic and teratogenic effects of the oil extracted from Caryocar brasiliense Cambess pulp in rats. Food and Chemical Toxicology. 110: 74-82.

[55] L. Rodrigues da Silva, L.d.V. Martins, I. Bantim Felicio Calou, M.d.S. Meireles de Deus, P.M.P. Ferreira, A.P. Peron. (2015). Flavonóides: constituição química, ações medicinais e potencial tóxico. Acta toxicológica argentina. 23(1): 36-43.

[56] N. Anhesi, L.G. Da Rosa, A.C. Pereira, A. De Melo. (2016). Uso de Plantas Medicinais na Gestação. RETEC. 9(2): 101-109.

[57] M.D. de Sousa Ferreira, E.K.F. Batista, I. dos Santos Farias, L.F. Santos, J.M.G. de Oliveira, S.M.M. de Sousa Silva. (2017). Avaliação fitoquímica e toxicológica dos extratos do fruto de Buchenavia sp. Acta Brasiliensis. 1(2): 17-22.

[58] M.S. Ali-Shtayeh, R.M. Jamous, R.M. Jamous. (2015). Plants used during pregnancy, childbirth, postpartum and infant healthcare in Palestine. Complementary Therapies in Clinical Practice. 21(2): 84-93.

[59] A. Kaur, R. Bhatti. (2021). Understanding the phytochemistry and molecular insights to the pharmacology of Angelica archangelica L.(garden angelica) and its bioactive components. Phytotherapy Research. 35(11): 5961-5979.

[60] H. Svitina, R. Swanepoel, J. Rossouw, H. Netshimbupfe, C. Gouws, J. Hamman. (2019). Treatment of skin disorders with Aloe materials. Current pharmaceutical design. 25(20): 2208-2240.

[61] X. Feng, S. Cao, F. Qiu, B. Zhang. (2020). Traditional application and modern pharmacological research of Artemisia annua L. Pharmacology & therapeutics. 216: 107650.

[62] A.C.S. Rabelo, D.C. Costa. (2018). A review of biological and pharmacological activities of Baccharis trimera. Chemico-Biological Interactions. 296: 65-75.

[63] P. Weimer, L.M. Spies, R. Haubert, J.A.S. de Lima, R.W. Maluf, R.C. Rossi, E.S. Suyenaga. (2021). Anti-inflammatory activity of Brunfelsia uniflora root extract: phytochemical characterization and pharmacologic potential of this under-investigated species. Natural Product Research. 35(24): 6122-6128.

[64] R. Samavati, E. Ducza, J. Hajagos-Tóth, R. Gaspar. (2017). Herbal laxatives and antiemetics in pregnancy. Reproductive Toxicology. 72: 153-158.

[65] P. Ranasinghe, S. Pigera, G.S. Premakumara, P. Galappaththy, G.R. Constantine, P. Katulanda. (2013). Medicinal properties of 'true'cinnamon (Cinnamomum zeylanicum): a systematic review. BMC complementary and alternative medicine. 13: 275.

[66] M.N. Boukhatem, M.A. Ferhat, A. Kameli, F. Saidi, H.T. Kebir. (2014). Lemon grass (Cymbopogon citratus) essential oil as a potent anti-inflammatory and antifungal drugs. Libyan Journal of Medicine. 9(1): 25431.

[67] J. Leite, V.S. Maria De Lourdes, E. Maluf, K. Assolant, D. Suchecki, S. Tufik, S. Klepacz, H.M. Calil, E. Carlini. (1986). Pharmacology of lemongrass (Cymbopogon citratus Stapf). III. Assessment of eventual toxic, hypnotic and anxiolytic effects on humans. Journal of Ethnopharmacology. 17(1): 75-83.

[68] A.C.M. Hacke, E. Miyoshi, J.A. Marques, R.P. Pereira. (2020). Anxiolytic properties of Cymbopogon citratus (DC.) stapf extract, essential oil and its constituents in zebrafish (Danio rerio). Journal of Ethnopharmacology. 260: 113036.

[69] D.C. Fernandes, B.P. Martins, G.P. Da Silva, E.N. Da Fonseca, S.V.M. Santos, L.S.M. Velozo, C.R.M. Gayer, K.C.C. Sabino, M.G.P. Coelho. (2021). Echinodorus macrophyllus fraction with a high level of flavonoid inhibits peripheral and central mechanisms of nociception. Journal of Traditional and Complementary Medicine. 12(2): 123-130.

[70] L.C. Lopes, F. Albano, G.A.T. Laranja, L.M. Alves, L.F. Martins e Silva, G.P. De Souza, I.M. Araujo, J.F. Nogueira-Neto, I. Felzenszwalb, K. Kovary. (2000). Toxicological evaluation by in vitro and in vivo assays of an aqueous extract prepared from Echinodorus macrophyllus leaves. Toxicology Letters. 116(3): 189-98.

[71] M. Avello, P. Fernández, M. Fernandez, B. Schulz, M. De Diego, S. Mennickent, P. Novoa, E. Pastene. (2016). Pediculicide effect of a Eucaliptus globulus L formulation. Revista chilena de infectologia: organo oficial de la Sociedad Chilena de Infectologia. 33(4): 433-437.

[72] R. Tardugno, F. Pellati, R. Iseppi, M. Bondi, G. Bruzzesi, S. Benvenuti. (2018). Phytochemical composition and in vitro screening of the antimicrobial activity of essential oils on oral pathogenic bacteria. Natural Product Research. 32(5): 544-551.

[73] W. Perera, J.A. Liyanage, K. Dissanayake, H. Gunathilaka, W. Weerakoon, D. Wanigasekara, W. Fernando, R. Rajapaksha, R. Liyanage, B.T. Perera. (2021). Antiviral potential of selected medicinal herbs and their isolated natural products. BioMed research international. 2021(1): 7872406.

[74] S. Kumar, A. Mittal, D. Babu, A. Mittal. (2021). Herbal medicines for diabetes management and its secondary complications. Current diabetes reviews. 17(4): 437-456.

[75] J. Nawrot, J. Gornowicz-Porowska, J. Budzianowski, G. Nowak, G. Schroeder, J. Kurczewska. (2022). Medicinal herbs in the relief of neurological, cardiovascular, and respiratory symptoms after COVID-19 infection a literature review. Cells. 11(12): 1897.

[76] R. Kumar, S. Malik, R. Tiwari, S.B. Zhautivova, A.H. Rakhimovna, T. Raj, P. Kumar. (2021). Pathophysiology of cardiovascular diseases and the role of vitamins, and herbal extracts in the reduction of cardiovascular risks. Cardiovascular & Hematological Agents in Medicinal Chemistry (Formerly. 19(2): 175-186.

[77] A.A. El-Banna, R.S. Darwish, D.A. Ghareeb, A.M. Yassin, S.A. Abdulmalek, H.M. Dawood. (2022). Metabolic profiling of Lantana camara L. using UPLC-MS/MS and revealing its inflammation-related targets using network pharmacology-based and molecular docking analyses. Scientific Reports. 12(1): 14828.

[78] M.A.M. Miyake, M. Caniello, A.P.S. Balbani, O. Butugan. (2003). Inquérito sobre uso de plantas medicinais para tratamento de afecções otorrinolaringológicas entre pacientes de um hospital público terciário. Revista Brasileira de Otorrinolaringologia. 70(1): 43-55.

[79] B. Niggemann, C. Grüber. (2003). Side-effects of complementary and alternative medicine. Allergy. 58(8): 707-716.

[80] A. El Mihyaoui, J.C. Esteves da Silva, S. Charfi, M.E. Candela Castillo, A. Lamarti, M.B. Arnao. (2022). Chamomile (Matricaria chamomilla L.): a review of ethnomedicinal use, phytochemistry and pharmacological uses. Life. 12(4): 479.

[81] S.B. do Nascimento, M. de Lima Nascimento, L.L. de Araújo, F.M. de Oliveira, M. do Carmo Vieira, J.M. Duarte-Almeida, J.M. Siqueira, I. da Costa César, H. Derendorf, W.V. de Castro. (2020). Evaluation of the effects of Maytenus ilicifolia on the activities of cytochrome P450 3A and P-glycoprotein. Current Drug Metabolism. 21(4): 281-290.

[82] M. Babaeian, M. Naseri, M. Kamalinejad, F. Ghaffari, F. Emadi, A. Feizi, N.H. Yekta, P. Adibi. (2015). Herbal remedies for functional dyspepsia and traditional Iranian medicine perspective. Iranian Red Crescent Medical Journal. 17(11): e20741.

[83] M. Mahboubi. (2021). Mentha spicata L. essential oil, phytochemistry and its effectiveness in flatulence. Journal of Traditional and Complementary Medicine. 11(2): 75-81.

[84] B. Salehi, J. Sharifi-Rad, J. Herrera-Bravo, L.A. Salazar, C. Delporte, G.V. Barra, M.-E. Cazar Ramirez, M.D. López, K. Ramírez-Alarcón, N. Cruz-Martins. (2021). Ethnopharmacology, phytochemistry and biological activities of native chilean plants. Current pharmaceutical design. 27(7): 953-970.

[85] C.W. Lukhoba, M.S. Simmonds, A.J. Paton. (2006). Plectranthus: A review of ethnobotanical uses. Journal of Ethnopharmacology. 103(1): 1-24.

[86] S. Adiga, P. Trivedi, V. Ravichandra, D. Deb, F. Mehta. (2010). Effect of Punica granatum peel extract on learning and memory in rats. Asian Pacific Journal of Tropical Medicine. 3(9): 687-690.

[87] J. Fairbairn. (1976). Biological assay and its relation to chemical structure. Pharmacology. 14(1): 48-61.

[88] M.I. Yatoo, A. Gopalakrishnan, A. Saxena, O.R. Parray, N.A. Tufani, S. Chakraborty, R. Tiwari, K. Dhama, H.M. Iqbal. (2018). Anti-inflammatory drugs and herbs with special emphasis on herbal medicines for countering inflammatory diseases and disorders-a review. Recent patents on inflammation & allergy drug discovery. 12(1): 39-58.

[89] K. Nurit-Silva, R. Costa-Silva, I.J. Basílio, M.d.F. Agra. (2012). Leaf epidermal characters of Brazilian species of Solanum section Torva as taxonomic evidence. Botany. 90(9): 806-814.

[90] K. Nurit, M. Agra, I. Basílio. (2007). Estudo farmacobotânico comparativo entre Solanum paniculatum L. e Solanum rhytidoandrum Sendtn.(Solanaceae). Revista Brasileira de Biociências. 5(1): 243-245.

[91] D.C. Endringer, Y.M. Valadares, P.R. Campana, J.J. Campos, K.G. Guimarães, J.M. Pezzuto, F.C. Braga. (2010). Evaluation of Brazilian plants on cancer chemoprevention targets in vitro. Phytotherapy Research. 24(6): 928-933.

[92] M.G. Brandão, G.P. Cosenza, C.F. Grael, N.L. Netto Junior, R.L. Monte-Mór. (2009). Traditional uses of American plant species from the 1st edition of Brazilian Official Pharmacopoeia. Revista Brasileira de Farmacognosia. 19(2A): 478-487.

[93] J. Seigner, M. Junker-Samek, A. Plaza, G. D 'Urso, M. Masullo, S. Piacente, Y.M. Holper-Schichl, R. de Martin. (2019). A Symphytum officinale root extract exerts anti-inflammatory properties by affecting two distinct steps of NF-κB signaling. Frontiers in Pharmacology. 10: 289.

[94] F.G.G. De Miranda, J.C. Vilar, I.A.N. Alves, S.C.d.H. Cavalcanti, Â.R. Antoniolli. (2001). Antinociceptive and antiedematogenic properties and acute toxicity of Tabebuia avellanedae Lor. ex Griseb. inner bark aqueous extract. BMC pharmacology. 1: 6.

[95] A.E. Freitas, M. Moretti, J. Budni, G.O. Balen, S.C. Fernandes, P.O. Veronezi, M. Heller, G.A. Micke, M.G. Pizzolatti, A.L.S. Rodrigues. (2013). NMDA Receptors and the L-Arginine–Nitric Oxide–Cyclic Guanosine Monophosphate Pathway Are Implicated in the Antidepressant-Like Action of the Ethanolic

Extract from Tabebuia avellanedae in Mice. Journal of medicinal food. 16(11): 1030-1038.

[96] A. Fernandez, I.E. Cock. (2020). Tabebuia impetiginosa (Mart. Ex DC. Mattos) bark extracts inhibit the growth gastrointestinal bacterial pathogens and potentiate the activity of some conventional antibiotics. Pharmacognosy Communications. 10(2): 75-82.

[97] M. Al-Fatimi. (2019). Ethnobotanical survey of medicinal plants in central Abyan governorate, Yemen. Journal of Ethnopharmacology. 15(241): 111973.