POTENTIAL RISKS TO PREGNANT DUE USE OF MEDICINAL PLANTS

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ABSTRACT

The use of medicinal plants with therapeutic purposes is an ancient practice spread throughout the population for healing and disease prevention. This practice has increased due to the belief that "natural" product is safe. From this mistaken idea, pregnant women often seek natural alternatives to treat symptoms resulting from pregnancy, believing that medicinal plants have no harmful effects on the fetus. However, numerous research show that medicinal plants are not without risks to health and may cause toxicity. Faced with this problem, this study aimed to describe the risks of indiscriminate use of medicinal plants, as a warning, not only for pregnant women, but also to healthcare professionals, so that they orient to the public on the safe use these products.

KEYWORDS: Medicinal plants, pregnancy, abortion.

1. INTRODUCTION

Pregnancy is an event full of changes. An experiment in which the mother is overwhelmed with intense feelings that can make room for unconscious contents of the mother. Pregnant women have sought ways to provide a safe and healthy pregnancy, seeking their welfare and the baby¹.

During pregnancy, the care in relation to health must be doubled, since the exposure of pregnant women to risks, environmental or biological factors can cause complications for both mother and the fetus².

The use of medicinal plants as a therapeutic resource for the prevention, treatment and cure of this disease is a practice since the dawn of humanity, seeking in nature, the cure for your ills³.

Leite *et al.* $(2008)^4$, argue that the prevalence of medication use is considered high among all strata and for various classes of drugs. Mainly the drugs frequently used by pregnant women, children and the elderly, do not have sufficient toxicological studies to age and physiological condition. In many cases, the choice of

drug to be used is made or repetition of an old or indication of lay people (neighbors, relatives, friends, clerks pharmacy) recipe, featuring self-medication.

In recent years have also seen a significant increase in products considered by natural population. The concept of natural is related to what is produced by nature, not featuring fireworks, mixture or composition, being something of vegetable origin. Thus, natural products are said to be synonyms of beneficial and safe products, following the popular saying "*natural product does no harm to health*". This synonym is inadequate, and an erroneous idea of the population, since the medicinal plants are considered xenobiotic agents, i.e. foreign compounds that the human body can indeed bring many complications if used improperly⁵.

Pregnant women deserve a special focus overall population which encourages the use of medicinal plants, because they believe that will not cause harm to the fetus⁶. However, especially during the first trimester of pregnancy can occur from congenital malformations, even a spontaneous miscarriage⁷.

Some medicinal plants have teratogenic and abortifacient potential and its systemic use is contraindicated in the first trimester of pregnancy, by being able to cross the placental barrier and may thus affect the fetus⁸.

Many people use medicinal plants as an aid for health care practice⁹. This increase in consumption of medicinal plants, has happened for advertising and promotion in the media and the economic crisis affecting the country, related to the difficult access of the population to health care, ranging from hospital care until obtaining tests and drugs. It is also due to easy access to this type of product that has great marketing in public places such as health food stores and pharmacies³.

Many plants are known to be teratogenic and abortifacient. However, lack of information and publicity can make use of a simple "*natural medicine*" a serious problem.

Therefore, this study aimed to establish the likelihood of the use of medicinal plants by pregnant women, presenting their potential teratogenic and abortifacient effects, in order to warn of the risks that they are exposing themselves doing the indiscriminate use or even routine these plants.

2. MATERIAL AND METHODS

This study was conducted through a literature review, through the electronic bibliographic databases Google Scholar, Medline and SciELO, using the following keyword combinations: medicinal plants; abortion; pregnancy.

3. LITERATURE REVIEW

During pregnancy, a series of physiological changes that are due to period and may cause unpleasant symptoms occurs to pregnant women. These changes occur due to hormonal factors that change the physiological patterns of functioning of a woman's body, in order to tailor it to the maternal-fetal complex own organic needs and childbirth¹⁰.

Based on these changes, symptoms such as nausea, vomiting, constipation and urinary system disorders, with increased frequency of urination, are reasons that can often lead to pregnant women using drugs to relieve these symptoms, they may, be conventional or vegetable origin. It is noteworthy that before using any medication during pregnancy, a detailed analysis of each specific situation must be made, taking into account the risk-benefit¹².

The main guidance for pregnant women, it would be no use of any medicine, but there is no way to seal the risks of drug therapy in pregnant women, because like most of the population, the mother is also subject to variations requiring drug interventions¹³.

Medicinal plants are significantly important for maintaining the health of the population. From various studies reported in the literature, there is proof of the therapeutic action of plants that are popularly used by a knowledge diffused over several generations¹⁴.

According to WHO (World Health Organization) medicinal plant is "any plant that has, in one or more organs, substances that can be used for therapeutic purposes or which are precursors of semisynthetic drugs"¹⁵.

The aid for research, technological development and innovation based on Brazilian biodiversity, according to the epidemiological needs of the population, provides an important challenge for the National Policy on Medicinal Plants and Herbal Medicines (NPMP). The NPMP was approved in 2006, encouraging the rational use of medicinal plants and herbal¹⁶. In Brazil, the National Agency for Sanitary Vigilance is the main organ responsible for the regulation of these products¹⁷.

The therapy from medicinal plants have been used in various ways for treatment, prevention and cure of diseases. The most common form is tea, which can be prepared by extractive techniques such as infusion, decoction or maceration. Other homemade preparations like syrups, compresses, poultices, baths and potions can also be included as a treatment¹⁸.

The correct identification of medicinal plants is of utmost importance, since many plants have similarities with each other, and are many popular names, making it difficult to choose¹⁶. So do not know the safety of its use when a mistaken identification of the plant, intentional or accidental tampering and other contaminants occurs⁵.

In addition to checking the plant, there must be conditions for collection and proper storage, since the plant produces secondary metabolites that represent a chemical connection between medicinal plants and the environment around. Thus, the synthesis of plants can be sensitized by different environmental conditions, the main factors being the day/ night cycle, seasons, temperature, age and plant growth, water availability, ultraviolet radiation, nutrients, altitude and air pollution, can have lower or higher concentrations of its assets²⁰.

Medicinal plants when used during pregnancy have constituents that can cross the placenta, reach the fetus, and promote serious problems such as teratogenicity, embryo toxicity and even abortion²¹.

Teratogens integrate environmental, physical, chemical and biological agents may cause congenital malformation²². Teratogenic effect on the fetus depends on what stage it is, the association between dose and effect, the maternal fetal genotype and specific pathogenic mechanisms of each agent²³. Thus, the teratogenic effects of the drug for therapeutic purposes, can cross the placenta, reach the fetus, and lead to harmful effects²⁴.

Embryo toxicity it is a change in embryonic development, dependent doses that do not affect the maternal organism. The reaction of the embryo is related to exogenous agents, most often with the same genetic constitution²⁴.

Abortion is the termination of pregnancy, the death of the embryo or fetus, from a stimulation of uterine contraction. Among the most used means abortifacient, highlight the infusions and teas made from medicinal plants²⁵.

Accordingly, it can be seen that self-medication is indiscriminate alarming, since in most cases no knowledge of the toxicity of the plant. Thus, there may be health risks if there is no assurance that the expected pharmacological properties are obtained, without side effects or adverse²⁶.

In Brazil, the State of Rio de Janeiro is one of the few states that has a law that contraindicate the use of

herbal medicines by pregnant women. This state has a resolution-SES/ RJ No. 1757 of February 18, 2002, which still considers toxic, teratogenic and abortifacient the most varied species of plants with medicinal effects

purpose²⁷. According Mengue *et al.* (2001)¹², plants with reports of abortive action or any other suspected risk during pregnancy are: arruda, cinnamon, horsetail, bushing, Bilberry, purple ipe, herv of Saint Mary, jeriquiti spring mint, *Parthenium sp*, melon of Saint Caetano, pinion-to-purge, Hypericum, poeja, me-nobody-can, among other.

The use of laxatives, because of problems of constipation is very common in pregnant women. This problem is related to the physiological changes resulting from pregnancy, as the action of specific hormones on intestinal motility²⁸. Plants that effect with stimulant laxative anthraquinones has in its composition, senna (*Senna alexandrina* Mill - Fabaceae) is the laxative antanoide most used worldwide. Anthraquinones induce uterine contractions²⁹, causing the increase in uterine blood flow, thereby enabling the risk of fetal loss. The same can also reach the breast milk and cause unwanted effects, such as diarrhea, the baby³⁰.

Regarding stimulants of the central nervous system, there is caffeine, which is present in coffee beans (Coffea arábicaL. - Rubiaceae), yerba mate (Ilex paraguariensisSt.-Hil - Aquifoliaceae family), tea- black and green tea (Camellia sinensis(L.) - Theaceae family), cola (Cola nitida (Vent) Schott & Endl -.. Sterculiaceae family) and guarana (Paullinia cupana Kunth - Sapindaceae family). Caffeine can cross the placental barrier, reducing blood flow to the placenta. Thus, their intake during pregnancy may be associated with fetal growth retardation, with a reduction in weight of newborn babies³¹. However, this fact is contradictory, according Clausson et al. (2002)³¹ and Bracken et al. (2003)³², this reduction can be confused with the effects of nicotine on the fetus, since smoking is related to the ingestion of large amounts of beverages containing caffeine.

Another species of medicinal plant with its action in the central nervous system is popularly cognized as hiperico or St. John's Wort (*Hypericum perforatum* L. –Guttiferae family) being used in the treatment of mild to moderate depression, having a profile superior to synthetic antidepressants reasonableness. There is disagreement among authors regarding the risks of using hiperico during pregnancy^{33,34}. However, Gregoretti *et al.* $(2004)^{35}$ reported from experiments in animals receiving extracts of *H. perforatum* during pregnancy, their offspring had severe kidney and liver damage. These lesions were also seen in pups whose mothers received only extracts during breastfeeding. Other studies that examined changes in growth, development, physical maturation and cognitive capacity of animals that were exposed to extracts hiperico during the prenatal period, showed no differentiation with respect to the animals who received placebo in the same period²⁹. However, studies to date are not sufficient to ensure the safe use of this plant during pregnancy.

According Tsui *et al.* (2001)³⁶, the main problem reported by pregnant women is sick. The ginger (*Zingiber officinale* Roscoe – Zingiberaceae family) is used to relieve morning sickness in pregnant women. In studies, it was administered ginger pregnancy in rats, it was observed that ginger above could cause loss of normal embryo, but also increase the weight of the remaining fetuses²⁹. While studies of the toxic potential of ginger in pregnancy, some authors advocate its use. According to Amorim (2013)³⁷, ginger may be more effective in treating nausea and vomiting in pregnancy, when compared to placebo. Already Belew (1999)³⁸, said pregnant women in India make use of ginger in food; there are no reports of adverse effects, and the use of the same in Chinese medicine for nausea, no contraindication.

The Ruta graveolens L. - Rutaceae Family recommended in folk medicine, as the plant that "force menstruation", is one of the most used by women for contraception or induced abortion³⁹. Contains toxic and photosensitive substances. Your handling can cause dermatitis if exposure to the sun, besides presenting abortive activity 40. Starting at experiments in rats, anti-fertility and/ or contraceptive activity was observed when administered to an animal an extract of different plant parts. The ingestion of alcoholic extract, at high doses for rats during the pre-implantation period change caused cells from the blastocyst by reducing the number of cells and delaying embryonic development. It was also observed that when administered in the early organogenesis, the extract could cause fetal death²⁹. Thus, if discouraging also been found that the use rue during pregnancy is extremely contraindicated its use in inducing abortion.

The Peumus boldus Molina - Monimiaceae family, known as bilberry-true, is originally from Chile and is commonly confused with the false Boldo (Coleus barbatus Benth Andrews - Lamiaceae), Brazil¹⁹. Bilberry is indicated as choleretic and cholagogue, being used in the treatment of hepatic disorders in general. In some experiments, in which the crude extract were administered the Peumus boldus to female rats from gestation was observed anatomical abnormalities in the fetus and in blastocysts⁴¹. Also was observed that the false-bilberry when administered to animals in the pre-implantation causes a large increase in embryonic loss. The falsebilberry presents a likely mechanism for the anti-implantation action with relaxing effect on tubal mobility, which interferes with the transport of the embryo to the uterus and its subsequent deployment⁴².

The plant popularly known as bush "buchinha", a lit-

tle bush (*Luffa operculata* (L.) Cogn. – família Cucurbitaceae), is distinguished among the ten most used plants as abortion in Brazil³⁹. His dried fruit are indicated for rhinitis and sinusitis, being administered through inhalation and nasal drops solution, with recommendations for use that cause poisoning. Poisonings were recorded related to abortion attempts among women 19 to 26 years, and these records kept by the Toxicological Information Center of Santa Catarina State, between 1984 and 1997⁴³. Recently, studies have shown that the result of decoction (decoction) of buchinha administered to female mice during the embryo implantation, the rate decreases denatalidade²⁹.

The Symphytum officinale L. - Boraginaceae family, known as consolide or confreié originally from Europe and Asia. In countries of origin, the roots were used consolidates with healing purpose in outdoor use. More known as comfrey was popularly used to treat asthma, hepatitis, diabetes, gastritis and rheumatism, in an internal use⁴⁰. In Brazil, in 1992 after the Ministry of Health (Ordinance No. 19, 30/01/1992) has banned evidence of their toxicity, the internal use of comfrey, restricting the indication of its products to external use, topic application⁴⁴. From studies in rats, the roots and leaves of comfrey, showed carcinogenic and hepatotoxic action when administered chronically. Its toxicity is attributed to the presence of pyrrolizidine alkaloids, compounds known for their carcinogenic activity, hepatotoxic, teratogenic and mutagenic⁴⁵.

The vine species known as "thousand-men" or vine "jarrinha" (*Aristolochia triangularis* Cham. – Aristolochiaceae family), is known for its wide variety of indications, such as stomach problems, fever, diarrhea, convulsions, anorexia and also has antiseptic and anti-inflammatory properties. Several authors of books on folk medicine attach to species of this genus, mutagenic, and carcinogenic effects abortifacients. After studies of the vine "thousand-men," noted the presence of toxic components, leading to banning the trade of products containing these components, even in highly diluted preparations used in homeopathy¹².

Melon of St. Caetano (*Momordica charantia* L. – Cucurbitaceae family) is known for his action emenagoga, anthelmintic and purgative⁴⁰. Tests on mice have shown that from the administration of glycoproteins (alpha and beta momorcharina) isolated from the seeds, the induction of abortion and inhibitory action on cell proliferation of the endometrium occurs and myometrium. In the study, intraperitoneal administration of beta-momorcharina the fourth and sixth days of gestation caused an inhibition of pregnancy; disrupts the pre-implantation and embryonic development, by blocking the incubation of embryos through the pellucid zone, the decrease in the incidence of effective attachment of the blastocyst, reduced growth of the trophoblast and suspend the development of the inner cell mass¹².

The ginkgo biloba (Ginkgo biloba L. - Ginkgoaceae family) is indicated for cognitive disorders, recent memory loss, dizziness, headache, and emotional lability with anxiety, improving erectile dysfunction secondary to antidepressant treatments, increase peripheral blood flow in patients with diabetes mellitus, and improving the impaired hearing of patients by poor blood circulation in the ears. Can also decrease fertility between men and women. Thus, its use should be avoided by couples who want to have children. In turn, the adverse reactions related to pregnancy are hemorrhagic disorders, which can be result of chronic use of ginkgo as a result of increased hemorrhagic potential probably associated with the reduction of platelet aggregation by inhibiting the PAF (Platelet Aggregation factor) by "ginkgolides" components⁴⁶.

4. CONCLUSION

The easy acceptance by the population of medicinal plants has led to a potential danger of self-medication. The main problem is related to using the belief that plant products are free of toxicity and adverse reactions, as they are natural.

The consumption of homemade dressings using parts of plants from many plant species known and seemingly harmless can cause us serious of the health of the mother and fetus. Thus, there is need for further information to pregnant women about the harmfulness of some medicinal plants administered during pregnancy. It is up to health professionals such as physicians, pharmacists, nurses, among others, be prepared to provide such clarification to the population.

REFERENCES

- [1] Zucco F, Barreto SJ. Fisioterapia na gravidez de risco. Revista Fisio & Terapia, Rio de Janeiro. 2001; 6(29).
- [2] Ministério da Saúde. Secretária de Atenção à Saúde. Departamento de Ações Programáticas Estratégicas. Gestação de alto risco: manual técnico. 5º ed. Brasília: Editora do Ministério da Saúde. 2010.
- [3] Veiga Junior VF, Pinto AC, Maciel MAM. Plantas medicinais: cura segura? Química Nova 2005; 28(3):519-28.
- [4] Leite SN, Vieira M, Veber AP. Estudos de utilização de medicamentos: uma síntese de artigos publicados no Brasil e América Latina. Ciência e Saúde Coletiva 2008; 13:793-802.
- [5] Campesato VR. Uso de plantas medicinais durante a gravidez e risco para malformações congênitas. [Tese] Doutorado em Genética e Biologia Molecular. Porto Alegre: Universidade Federal do Rio Grande do Sul. 2005.
- [6] Weier KM, Beal M. Complementary therapies as adjuncts in the treatment of postpartum depression. J Midwifery Womens Health 2004; 49(2):96-104.
- [7] Pires AM, Araujo OS. Percepção de risco e conceitos sobre plantas medicinais, fitoterápicos e medicamentos alopáti-

Openly accessible at http://www.mastereditora.com.br/bjscr

cos entre gestantes. Revista Baiana Saúde Pública 2011; 35(2):320-33.

- [8] Rio de Janeiro (Estado). Resolução SES Nº1757, de 18 de fevereiro de 2002. Contraindica o uso de Plantas Medicinais no Âmbito do Estado do Rio de Janeiro e dá outras providências. Diário Oficial do Estado do Rio de Janeiro, 20 de fevereiro de 2002, Ano XXVII. Nº33. Parte I.
- [9] Badke MR, Budó MLD, Silva FM, Ressel LB. Plantas medicinais: o saber sustentado na prática do cotidiano popular. Escola Anna Nery Revista de Enfermagem 2011; 15(1):132-39.
- [10] Reis GFF. Alterações fisiológicas maternas da gravidez. Rev Bras Anest 1993; 43(1):3-9.
- [11] Pinheiro P. Enjoos e vômitos na gravidez: tratamento e causas. [acesso 4 agost. 2014] Disponível em: http://www.mdsaude.com/2010/07/enjoo-nauseas-vomitos -gravidez.html
- [12] Mengue SS, Mentz LA, Schenkel EP. Uso de plantas medicinais na gravidez. In: Sanseverino VTM, Spreitzer TD, Schüler-Faccini L. Manual de Teratogênese. Porto Alegre: Editora da Universidade/UFRGS 2001; 423-50.
- [13] Mello SCCS, Pelloso SM, Carvalho MDB, Oliveira NLB. Uso de medicamentos por gestantes usuárias do Sistema Único de Saúde. Acta Paulista de Enfermagem 2009; 22.
- [14] Leite SN. Além da medicação: a contribuição da fitoterapia para a saúde pública [dissertação]. São Paulo: Departamento de Saúde Materno-Infantil da Faculdade de Saúde Pública/USP; 2000.
- [15] World Health Organization. Bulletin of the World Health Organization. Regulatory situation of herbal medicines. Geneva: WHO, 1998. [acesso 10 agost. 2014] Disponível em: http://www.who.int/en/
- [16] Macedo EV, Gemal AL. A produção de Fitomedicamentos e a Política Nacional de Plantas Medicinais e Fitoterápicos. Rev. Bras. Farm 2009; 90(4):290-97.
- [17] Brasil. Agência Nacional de Vigilância Sanitária. Resolução RDC nº 17, de 24 de fevereiro de 2000. Dispõe sobre o registro de medicamentos fitoterápicos.
- [18] Faria GF, Ayres A, Alvim NA. O diálogo com gestantes sobre plantas medicinais: contribuições para os cuidados básicos de saúde. Rio de Janeiro 2004; 26(2):292.
- [19] Mengue SS, Mentz LA, Schenkel EP. Uso de plantas medicinais na gravidez. In: Anseverino ATV, Spreitzer DI, Schüler-Faccini L. Manual de Teratogênese. Porto Alegre: Editora da Universidade 2001; 422-50.
- [20] Neto LG, Lopes NP. Plantas medicinais: fatores de influência no conteúdo de metabólitos secundários. São Paulo 2007; 30(2):347-81.
- [21] Brasil. Resolução SES nº1757, de 18 de fevereiro de 2002. Contraindica o uso de Plantas Medicinais no Âmbito do Estado do Rio de Janeiro e dá outras providências. Diário Oficial do Estado do Rio de Janeiro, 20 fev. 2002; 27(33):Parte I.
- [22] Embiruçu EK, Sorte NB, Vidal R, Lessa L, Panão E, Mota AC, et al. Risco teratogênico: a percepção em diferentes segmentos da população. Revista de Ciências Médicas e Biológicas 2005; 4(3):201-7
- [23] Schüler-Faccini L, Leite JCL, Vieira MT, Sanseverino, Peres RM. Avaliação dos teratógenos na população brasileira. Ciência & Saúde Coletiva 2002; 7(1):65-71.
- [24] Rodrigues HG, Meireles CG, Lima JTS, Toledo GP, Cardoso JL, Gomes SL. Efeito embriotóxico, teratogênico e

abortivo de plantas medicinais. Rev Bras Pl Med. Botucatu 2011; 13(3):359-66.

- [25] Moreira LMA, Dias AL, Ribeiro HBS, Falcão CL, Felício TD, Stringuetti C, et al. Associação entre o uso de abortifacientes e defeitos congênitos. Rev Bras Ginecol Obstet. 2001; 23(8):517-21.
- [26] Veiga VF. Estudo do consumo de plantas medicinais na região Centro-Norte do Estado do Rio de Janeiro: aceitação pelos profissionais de saúde e modo de uso pela população. Revista Brasileira de Farmacognosia 2008; 308-13.
- [27] Secretaria de Saúde do Estado do Rio de Janeiro (Rio de Janeiro). Resolução nº 1757, de 18 de fevereiro de 2002. Diário Oficial do Estado do Rio de Janeiro, 20.02.2002.
- [28] Kawaguti FS, Klug WA, Fang CB, Ortiz JÁ, Capelhucnick P. Constipação na Gravidez. Rev Bras Coloproct. Janeiro/Março 2008; 28(1):46-9.
- [29] Clarke JH, Rates SM, Bridi R. Um alerta sobre o uso de produtos de origem vegetal na gravidez. Infarma 2007; 19(1/2):41-8.
- [30] Shulz V, Hansel R, Tyler VE. Fitoterapia Racional: Um Guia de Fitoterapia para as Ciências da Saúde. Barueri: Manole 2002; 386.
- [31] Clausson B, Granath F, Ekbom A, Lundgren S, Nordmark A, Signorello LB, et al. Effects of caffeine exposure during pregnancy on birth weight and gestational age. Am J Epidemiology 2002; 155(5):429-36.
- [32] Bracken MB, Triche EW, Belanger K, Hallenbrand K, Leaderer BP. Association of maternal caffeine consumption with decrements in fetal growth. Am J Epidemiology 2003; 157(5):456-66.
- [33] Bahls SC.Tratamento fitoterápico da depressão. J Bras Psiquiatr 2001; 50:389-96.
- [34] Ratz AE, Von Moos M, Drewe J. St. John's wort: a pharmaceutical with potentially dangerous interaction. Schweiz Rundsch Med Prax 2001; 90:843-49.
- [35] Gregoretti B, Stebel M, Candussio L, Crivellato E, Bartoli F, Decorti G. Toxicity of Hypericum perforatum (St. John's wort) administered during pregnancy and lactation in rats. Toxicol Appl Pharmacol. 2004; 200(3):201-5.
- [36] Tsui B, Dennehy CE, Tsourounis C. A survey of dietary supplement use during pregnancy at an academic medical center. Am J Obstet Gynecol. 2001; 185(2):433-7.
- [37] Amorim A, Ferreira ART, Carrapiço E. Gengibre no tratamento da náusea e vômito da gravidez: Revisão baseada na evidência. Acta Obstet Ginecol Port 2013; 7(2):103-08.
- [38] Belew C. Herbs and Childbearing woman. J Nurse Midwifery 1999; 44(3):231-52.
- [39] Mengue SS, Schenkel EP, Mentz LA, Schmidt MI. Especies vegetales utilizadas por embarazadas con el objeto de provocar la menstruación (Encuesta a siete ciudades de Brasil). Acta Farmacéutica Bonaerense 1997;16(2):251-8.
- [40] Ritter MR, Sobierajski GR, Schenkel EP, Mentz LA. Plantas usadas como medicinais no município de Ipê, RS, Brasil. Revista Brasileira de Farmacognosia 2002;12(2):51-62.
- [41] Almeida ER, Melo AM, Xavier H. Toxicological Evaluation of the Hydro-alcohol Extract of the Dry Leaves of Peumus boldus and boldine in Rats. Phytotherapy Research 2000; 14(2):99-102.
- [42] Almeida FCG, Lemonica IP. The toxicity of Coleus barbatus B. on the different periods of pregnancy in rats. J Ethnopharmacol 2000; 73(1-2):53-60.

Openly accessible at http://www.mastereditora.com.br/bjscr

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- [43] Schenkel EP, Zannin M, Mentz LA, Bordignon SAL, Irgang B. Plantas tóxicas. In: Simões CMO, Schenkel EP, Gosmann G, Mello JCP, Mentz LA, Petrovick PR. Farmacognosia da Planta ao Medicamento. 5 Ed. Porto Alegre/Florianópolis: Editora da UFRGS/ Editora da UFSC, 2003.
- [44] BRASIL (1992) Ministério da Saúde. Secretaria Nacional de Vigilância Sanitária. Portaria SNVS nº 19 de 30/01/1992. Proíbe o uso de confrei (Symphytum officinale L.) em preparações para o uso interno. Diário Oficial da União, 03/02/1995.
- [45] Silva CM, Bolzan AA, Heinzmann BM. Alcalóides Pirrolizidínicos em espécies do gênero *Senecio*. Quim. Nova 2006; 29(5):1047-53.
- [46] Silva TFO, Marcelino CE, Gomes AJPS. Utilizações e interações medicamentosas de produtos contendo o *Ginkgo biloba*. Colloquium Vitae jan/jun 2010; 2(1):54-61.

