A review of antifertility folkloric plants tested in laboratory animals

Damasceno, D. C.[1,2] , Volpato, G. T.[2] , Lemonica, I. P.[3]

[1]Faculdade de Medicina de Marília (FAMEMA), Av. Aziz Atallah s/n, CEP. 17519-030, Marília, SP. (E-mail:decaito@bol.com.br). [2]Laboratório Experimental de Obstetrícia, Depto. de Ginecologia e Obstetrícia, Faculdade de Medicina de Botucatu - UNESP, CEP. 18618-000, Botucatu, SP. [3]Laboratório Experimental de Teratologia, Departamento de Farmacologia, IBB, UNESP, CEP. 18618-000, Botucatu, SP.

RESUMO: O uso de princípios naturais como terapia alternativa, em países onde grande porcentagem da população não tem acesso à assistência médica, é muito difundido. Esses princípios naturais são usados como alimento ou remédio e, até mesmo, como agentes contraceptivos. É necessário estabelecer uma relação entre os costumes populares e as informações atuais sobre a origem das substâncias antifertilidade, e conhecer seus mecanismos de ação. Os agentes antifertilidade podem atuar em muitas áreas como hipotálamo, hipófise, ovário, oviduto, útero (incluindo endométrio, miométrio e cérvix) e vagina, interferindo na síntese e liberação de hormônios (folículo-estimulante, luteinizante, esteróides), na ovulação, no transporte da célula ovo e no processo de implantação. O objetivo deste trabalho é chamar a atenção para o amplo uso de plantas, popularmente usadas como abortivas, e verificar se o efeito dessas plantas é compatível ao encontrado nos animais de laboratório. Para isso foi realizada uma revisão de literatura, incluindo diversas plantas popularmente utilizadas como abortivas, as quais foram testadas em animais de laboratório para confirmar seu efeito.

Palavras-chave: Plantas medicinais, comportamento contraceptivo, hormônios, animais de laboratório.

ABSTRACT: A review of anti-fertility native folklore plants in laboratory animals. The use of natural active principals is widespread among a great proportion of the rural population, or by people who do not have easy access to medical assistance. These active principles are used as food or medicines, and even for purposes of contraception. It becomes necessary to establish a relationship between the folklore habits and current information on the nature of anti-fertility substances, and knowledge of their mechanisms. Anti-fertility agents may exert their actions in a number of areas, (hypothalamus, anterior pituitary, oviduct, uterus, and vagina), inhibiting synthesis and/or liberation of hormones (follicle-stimulating, luteinizing, and steroid hormones), ovulation, ovum transportation, and implantation process. Therefore, a review of literature was carried out, including of several plants used by women as abortifacient and anti-fertility agents to compare their effects with those obtained among laboratory animals.

Key-words: Medicinal herbs, plant, fertility, anti-fertility, hormones, animals

INTRODUCTION

The population explosion is posing an alarming concern all around the world, even threatening the survival of mankind. How to control the birth rate is a problem which has drawn the attention of political leaders and governments and also scientists; not only from the highly populated dovoloping countries but also from many industrialized countries. Population of countries which support the family planning needs new and effective contraceptive agents and/ or methods that have a minimum of side reactions, providing a maximum protective effect (Sethi *et al.*, 1991). The use of natural principles as an alternative therapy, in countries where a large percentage of the population does not have access to medical assistance, is widespread (Di Stasi *et al.*, 1989).

The plant extracts are traditionally used by the majority of the disadvantaged population, living mainly in the countryside, or by the people who leave the countryside to live on the city. In order to establish the relationship between the folk habits and current information on the nature of anti-fertility substances and the way they act, it is necessary to: identify botanically the species used; search the literature for the already known chemical components of these species, or to characterize them, in this work ; to try to discover the pharmacological basis that could justify the empirical use of those plants (Weniger, 1982). Nevertheless, there is little information about the toxic effects of many of these plants that are frequently used in the cure of diseases, but it is extremely important to know the effect of these plant extracts. It is of importance that there be an exact botanical classification *of* the plants for pharmacological research, since insignificant mistakes in this matter can lead to the study of

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similar plants with different chemical components (Ramos *et al.*, 1992).

Almost every pharmacological category of drugs has, as prototype, a substance of natural origin; thus it is reasonable to believe that the plant kingdom should yield an effective anti-fertility drug. The problem underlying the search for natural anti fertility drugs, basically concerns the choice of species of higher plants that should be examined in an animal system for their potential anti-fertility effects. There appears to be only three paths to follow, i. e., 1) test plants that have folkloric reputation of being used by women as oral contraceptives, 2) test plants that are known to contain components that theoretically could affect the female cycle to produce anti-fertility effects, or that contract the uterus potentially, and 3) make a random collection-mass screening of all available plants for anti-fertility effects. The first two of these methods appear to be the most practical and realistic ones (Farnsworth et al., 1975). The present report is a review of published literature on the anti-fertility activity of Brazilian medicinal plants. Several plants have been examined for anti-fertility activity. Many of them showed a positive activity while some did not show any. Thus, the purpose of this review is to draw attention to the large use of plants, popularly used as abortive, and to verify if the employment of these plants is in agreement with tests made with laboratory animals.

Anti-fertility Mechanisms

The World Health Organization has set up a Task Force on plants for fertility regulation, the strategic plan of which is to identify novel drug prototypes found in plants which have been alleged to have fertility regulating properties (Sethi *et al.*, 1991).

Anti-fertility agents that prevent ovulation and/or fertilization are commonly referred to as contraceptive agents, whereas those that act after implantation have been called abortifacients. The term interceptive has been used by some workers to refer to compounds that act after the occurrence of fertilization, but prevent the embryonic implantation process (Morris & Wagenen, 1973). Most of the plants are used in cases of presumed pregnancy. But it is difficult or impossible to distinguish between their contraceptive or abortive properties, since their more or less regular use may change the duration of the menstrual cycle and nothing enables one to determine if the patient is pregnant or is experiencing a simple delay of menses. Some plants species are used in cases of recent pregnancy, as well as in cases of advanced pregnancy, up to third or fourth month (Weniger, 1982).

Although the physiological and pharmacological mechanisms are important for implantation process, we should consider others factors involved during an investigation using plants like: sensibility of the animals, dose of herb extract used, period and route of administration of the extract given to the animals (Nishimura & Tanimura, 1976). According to Claeson *et al.* (2000), vasicine, a chemical component of the *Adhatoda vasica*, administered intraperitoneally (2.5, 5 and 10 mg/kg body weight) in rabbits caused abortifacient activity after parenteral administration, while no activity was observed after oral administration. This experiment showed that different routes of administration presented different results. Claeson *et al.* (2000) also verified that hamsters that intraperitoneally received 5 mg of vasicine/kg body weight, after day 7 of pregnancy, presented a failure pregnancy or abortifacient activity, but the rats given the vasicine in same dose and period of administration showed no anti-implantation effect. Thus, the difference of sensibility of the animals is very important for an investigation, as verified in the paper cited.

In general, there are a great many abortifacient plants and the chemical structure of their active principles varies widely. Therefore, there also must be several action mechanisms. There is a number of areas within the female mammalians organs where substances that have anti-fertility effects may exert their action(s); these areas are the hypothalamus, anterior pituitary, ovary, oviduct, uterus (including the endometrium, myometrium, and cervix), and vagina. A given compound may exert its anti-fertility effects in more than one of these areas and not necessarily by the same pharmacological mechanism. Conversely, different compounds may act in the same area to inhibit fertility but in some cases by different mechanisms (Farnsworth *et al.*, 1975).

A review of literature was carried out and it included several plants having folkloric reputation as abortive and anti-fertility agents. The search of the literature extends though 2001. The sources of references included Biological abstracts, Pubmed, Lilacs, and books of herbal and/or medicinal plants. It was intended to list the folkloric medicinal plants used by women as contraceptives or for anti-fertility activities, and to correlate the effects of these plants in laboratory animals. The Table I presents the names of these plants, whose substances were under tests for crude extracts and were injected in vivo, by different administration route, without control of specific topic effects.

In this section, we cited some areas within the female mammal where the plants having anti-fertility effects may exert their action.

Pituitary gland-hypothalamus

The hypophysis secretes a number of important hormones for the reproduction. In the anterior hypophysis, gonadotropic hormones are secreted,

such as LH (luteinizing hormone) and FSH (follicle-stimulating hormone). The hypothalamus produces the GnRH (gonadotropin-releasing hormone), which promotes the liberation of the LH and FSH. These hormones are important for the growth of follicles after menstruation and also for ovulation. After the occurrence of ovulation, the LH also induces the ruptured follicle to form the endocrine corpus luteum. The granulosa cells of the ruptured follicular wall begin to proliferate and give rise to the cells of the corpus luteum. With this viewpoint, two basic mechanisms can be considered for the performance of the substances in these areas (Farnsworth *et al.*, 1975):

- Interference of a normal hormonal function of the hypothalamus and pituitary by steroids, non-steroids with anti-gonadotropic activity, and by steroid antagonists
- Interference of the neural impulse for the hypothalamus

Several plant extracts are used by folk medicine and they may act on the hypothalamus, such as *Juniperus communis* and *Physalis alkekengi* fruit extracts (Table I). These extracts were respectively administered by oral and intraperitoneal routes of administration on rats. Both presented an anti-fertility effect, and the authors verified that these plants interfered with the hypothalamus, suggesting a possible action mechanism (Prakash *et al.*,1994; Vessal *et al.*, 1991).

Ovary

The chemical substances may exert their anti-fertility effects at ovarian level by the inhibition of the ovulation and the synthesis of steroids. The corpus luteum secretes large quantities of estrogen and progesterone, while the inibin hormone presents a negative feedback for the liberation of LH and FSH. The performance of the substance in the corpus luteum can interfere with the synthesis of steroids. Some substances also can act impeding the ovulation, for example, the prostaglandin. These substances reach the corpus luteum and decrease the ovarian secretion of progesterone.

Rivea hypocrateriformis is an example of plant that reaches the ovarian structure. The ethanol extract of the aerial parts of this plant when tested in female albino rats caused anti-fertility activity due to the anti-progestational effect, which might act as inhibitor either in the biosynthesis of progesterone or in the receptor binding (Shivalingappa *et al.*, 2001).

There is folk information regarding women seated briefly above a bath of the plant *Inula viscosa* three days after copulation, or had administered ground leaves through the anus for abortifacient purpose. However, no experimental studies have been found supporting the reputed pregnancy terminating action of *I. viscosa*. An experimental study showed that an aqueous extract of leaf of this plant caused a significant reduction in the number of corpus luteum and of progesterone blood levels (Dafni *et al.*,1984; Al-Dissi *et al.*, 2001).

Choudhur *et al.* (1991) administered an ethanolic extract of *Piper betle* (1g/kg) in rats and observed a decrease in the activity of the responsible enzyme for the synthesis of steroid hormones. Besides that, this plant diminishes the number of corpus luteum. The authors concluded that these explanations might probably justify the folkloric use of *Piper betle* to cause abortion.

Oviduct

A normal embryonic implantation in the uterus depends on the exact time of embryonic arrival on the uterus. However, if there are complications in the ovum transportation in the oviduct, there will be some miscues during the implantation. The substances that have the ability of altering the motility of the oviduct, may be able to inhibit the fertility and the embryonic implantation, as verified by Singh *et al.* (1993) (Table I), when administered the ethanol extract of *Ixora finlayconiana* (1g/kg) in rats in the first day of pregnancy.

Boling and Blandau (1971) demonstrated that smooth musculature of the reproductive tract exhibits maximum contractility under estrogenic influence, and it has been related that several plants possess estrogenic activity.

Estrogen and progesterone can also alter fertility. The estrogen increases the synchronized beating of the cilia on the oviduct wall, carrying the ovum on the direction of the uterus, and it also relaxes the isthmus for the passage of the ovum. Therefore, an altered dose of these hormones can increase or decrease the exact arrival time of the zygote in the uterus. The isthmus of rabbits, rats and humans possess a rich sympathetic innervation, maintaining the sphincter tonus of the isthmus, promoting the ovum retention. So, the substances that affect the SNA sympathetic can interfere with fertility (Farnsworth *et al.*, 1975).

Lemonica *et al.* (1996) verified that *Rosmarinus officinalis* aqueous extract (Table I) interfered with the oviduct movements and consequently with ovum transport, or with the uterine condition related to ovum implantation. Damasceno and Lemonica (1999) showed that the rats treated with 260 mg/kg of *R. officinalis* aqueous extract presented embryotoxic effect and 1040 mg/kg promoted a longer embryo retention in the oviduct. Similarly, Almeida and Lemonica (2000) showed that leaf extract of *Coleus barbatus* (boldo) caused an anti-implantation effect, as shown in Table I.

Table I – Antifertility plants evaluated in experimental animals

Plant Name	Popular Name	Part	Type of Extract	Dose	Route of Administration	Species	Structure	Reference
Abrus precatorius	Jequiriti	Seeds	PE	150 mg/kg	-	Rats/Mice	O	Zia-Ul-Haque *et al.* (1993)
Acacia catechu	Catechu	Fruit	PE	100-500mg/kg	oral	Rats	-	Garg & Garg (1970)
Acalypha indica	Erva daninha	Whole plant	PE and ET	300-600 mg/kg	oral	Rats	U	Hiremath *et al.* (1999)
Adhateda vasica	-	Leaf	vasicine	5 mg/kg	ip	hamster	U	Claeson *et al.* (2000)
Ailanthus excelsa	Árvore celeste	Leaf and Stem bark	ET	250 mg/kg	oral	Rats	-	Dhanasekaran *et al.* (1993)
Ambrosia artemisiifolia	Ambrosia americana	Plant	W	-	-	Rat	T	Mats *et al.* (1987)
Anona squamosa	Pinha	Seed	W	100mg/kg	oral	Rats	-	Mishra *et al.* (1979)
Aristolochia indica	Papo de Peru	Roots	ET	50 mg/kg	oral	Mouse	-	Pakrashi & Pakrashi (1979)
Artemisa absintum	Losna	Leaves	ET	200 mg/kg	oral	Rats	-	Rao *et al.* (1988)
Ateleia glazioviana	Timbo de palmeira	Leaf	W	100mg/kg	i.p.	Rats	-	Marona *et al.* (1992)
Azadirachia indica	Cinnamomo ou Nimbo	Seeds	HE	100% fraction (NS101/H)	oral	Rats	-	Mukherjee & Talwar (1999)
Cannabis sativa	Maconha	Leaves	W	125-200-400-800 mg/kg	oral	Rats	-	Sethi *et al.* (1991)
Carica papaia	Mamoeiro	Fruits	PE	500 mg/kg	oral	Rats	-	Garg (1974)
Cassia fistula	Cannafistula verdadeira	Seeds	W	500 mg/kg	oral	Rats	U	Yadav and Jain (1999)
Cinnamomum zeylanicum	Canela	Leaf	W and CH	70 mg/kg	oral	Rats	-	Lemonica & Macedo (1994)
Citrulus colocynthus	Coloquintida verdadeira	Leaf	ET and BZ	-	-	Rats	-	Prakash *et al.* (1985)
Citrus hystrix	Limeira da Pérsia	Fruit peel	ET and CH	100 mg for 5g/kg	oral	Rats	U	Piyachaturawat et al. (1985)
Coleus barbatus	Boldo	Leaf	ETW	880 mg/kg	oral	Rats	O or T	Almeida and Lemonica (2000)
Coriandrum sativum	Coentro	Seeds	W	250-500 mg/kg	oral	Rats	O	Al-Said *et al.* (1987)
Crotoncajucara	Cajucára	Bark	t-dehydrocrotonin	25-50 mg/kg		Rats	U	Luna Costa *et al.* (1999)
Cuminun cyminum	Cominho	Seeds	W	250 and 500 mg/kg	oral	Rats	O	Al-Kamis *et al.* (1988)
Daucus carota	Cenoura	Seeds	ET	50 to 250 mg/kg	oral	Rats	U	Bhatnagar *et al.* (1995)
Dimorphandra mollis	Barbatimão	Pods	ETW	2 g/kg of dried plant	oral	Rats	-	Langeloh *et al.* (1991)
Gossypiun herbaceum	Algodão	Seeds	W	200 mg/kg	oral	Rats	-	Nath *et al.* (1997)
Hibiscus rosa sinensis	Mimo-de-vênus	Flowers	BZ	1 mg/kg	oral	Mouse	O	Pakrashi *et al.* (1986)
Himathanthus sucuuba	Sucuuba	Stem bark	W	40 mg/day	oral	Rats	-	Guerra & Peters *et al.* (1991)
Inula viscosa	-	Leaf	W	1.86 mg/kg	oral	Rats	O	Al-Disse *et al.* (2001)
Ipomoea fistulosa	Algodão bravo	Aerial parts	ET	100 mg/kg	oral	Rats	-	Mishra *et al.* (1979)
Ixora finlaysoniana	Ixora branca	Aerial parts	ET	250-500-1000 mg/kg	oral	Rats	O or T	Singh *et al.* (1993)
Jatropha curcas	Pinhão-de-purga	Fruit	Different extracts	Different doses	oral	Rats	-	Mishra *et al.* (1995)
Juniperus communis	Zimbro	Needles	-	4.5-5.5 kg/d	oral	Cattle	U or T	Gardner *et al.* (1998)
		Fruit	B	100- 400 mg/kg	oral	Rats	H or O	Prakash *et al.* (1994)
Kigelia pinnata	Madeira ídolo	Plant	ET	-	-	Rats	-	Prakash *et al.* (1985)

Mentha arvensis	Hortelã	Seeds	W	175 mg/kg	oral	Rats	O	Sethi *et al.* (1989)
Murraya paniculata	Jasmim Laranja	Roots	ET	100 mg/kg	oral	Rats	O	Choudhuri *et al.* (1990)
Nelumbo nucifera	Lotus do Egito	Seeds	PE	3 mg/kg	i.p.	Mice	O	Mazumber *et al.* (1992)
Nigella sativa	Nigela	Seeds	HE	2 g/kg	oral	Rats	U	Keshri *et al.* (1995)
Ocymum sanctum	Margericão	Leaves	PE, BZ, E, AC	1 mg/kg	oral	Rats	-	Batta *et al.* (1971)
Paeonia officinalis	Erva de Santa Rosa	Leaves	W	175 mg/kg	oral	Rats	-	Sethi *et al.* (1989)
Phillanthus amarus	Quetra-pedra	Whole plant	ET	100 mg/kg	oral	Mice	O	Rao and Alice (2001)
Physalis alkekengi	Camapú	Fruits	W	1ml/day	i.p.	Rats	H or U	Vessal *et al.* (1991)
Piper betle	Nenta	Leaves	ET	1 g/kg	oral	Rats	O	Choudhuri *et al.* (1990)
Pisum sativum	Ervilha	Seeds	m-xylohy-droquinilone	20-30% of diet	oral	Rat	-	Sanyal (1956)
Ricinus comunis	Mamão	Seeds	ME	600 -1.2 mg/kg	subcutaneous	Rats	-	Okwuasaba *et al.* (1991)
Rivea hipocrateriformis	-	Aerial parts	ET	200-400 mg/kg	oral	Rats	O	Shivalingappa *et al.* (2001)
Rosmarinus officinalis	Alecrim	Aerial parts	W	130mg/kg 1040 mg/kg	oral oral	Rats Rats	O or T T	Lemonica *et al.* (1996)
Ruta graveolens	Arruda	Leaves	ET	125 mg/kg	oral	Rats	-	Rao *et al.* (1988)
Schubertia multiflora	Angélica de Rama	Roots	ET	80 mg/kg	oral	Rats	-	Rao *et al.* (1988)
Sida carpinifolia	Vassourinha	Whole plant	ME	20 mg/rat	oral	Rats	U	Kholkute & Munshi (1978)
Sida linifolia	Guaxuma	Leaves	ET	25 mg/kg	oral	Rats	-	Nwobodo *et al.* (1996)
Sida veronicaefolia	Guarchumba	Aerial parts	ET	different doses	different routes	Rats	U	Lutterodt (1988)
Spondias mombin	Cajazeira	Leaves	W	750-1500mg/kg	i.p.	Mice	-	Offiah & Anyanwu (1989)
Stevia rebaudiana	Caá-ehé/ Stévia	Weeds	W	5ml/kg	oral	Rats	-	Planas & Kuc (1968)

Types of extract: W=aqueous; PE=petroleum ether; ET= ethanol; E= ether; CH= chloroform; BZ= benzene; B= butanolic; ME= methanol; AC= acetone; HE= hexane; ETW= ethanol-water.
Structures: H=hypothalamus; O=ovary; T= oviduct; U= uterus.

Uterus

In the uterus, the estrogen will have the function of altering the endometrium, bringing on a proliferation of the stroma and a great development of glands. The progesterone stimulates the endometrial layer to thicken further and to form glandular structures and increased vasculature, that are necessary for the nutrition of the zygote, which is in division. It also diminishes the uterine contractions, helping to impede the excretion of the ovum implanted. Therefore, the substances that act altering the concentration of estrogen and progesterone may have an anti-implantation or abortifacient effect, likewise the substances that stimulate the uterine contraction (Guyton and Hall, 1997).

Hiremath *et al.* (1999) investigated the petroleum ether and ethanol extracts of the *Acalypha indica* (weed) in female rats and found to be an effective agent to cause significant anti-implantation activity and suggested an estrogenic effect of this plant. This effect was observed in morphological studies of the uterus morphometry. This paper appears contradictory because an early embryo needs an edematous uterine wall , vascularized, to support the growth of the embryo implanted, which is realized by a high estrogenic level.

The Table I shows some plants that act in the uterus such as *Citrus hystrix.* According to Piyachaturawat *et al.* (1985) the rats treated with alcohol and chloroform extracts of the *Citrus hystrix* presented the blastocysts excreted due to an increase of uterine contractions, and this fact might to justify the use of this plant for the Brazilian women as an abortifacient.

It is a common misconception that "all that is natural is good", and a number of highly toxic compounds have been isolated from plants. The lack of information about other toxic effects of many plants used as abortifacient justify the investigation about their wide use. Before these medicinal plants may be used in humans, further scientific research is required. Toxicological and clinical studies, that support the use of these plants, confirm that anti-fertility activity study should be made. On the other hand, we would like to suggest further chemical-pharmacological studies using plants that would lead us to identification of the responsible substance(s) for the anti-fertility effect, and the mechanism by which the plant extract influences in the reproduction.

CONCLUSION

From the data presented in Table I, it can be seen that a number of plants are known to have a folkloric reputation for use as abortifacient or contraceptive during the pregnancy. But the plant extracts frequently have not had their effects confirmed in laboratory animals. This fact might be related to differences of sensibility in, and between, species, the treatment periods which the women and the experimental animals are undergoing, the dose employed and the preparation of the plant extract used. Furthermore, the species of plants used can contain different isolated active compounds. Presumably, these active principles might produce anti-fertility effect or exhibit no action on the reproductive functions.

REFERENCE

Al-Dissi, N.M.; Salhab, A.S.; Al-Hajj, H.A. Effects of *Inula viscosa* leaf extracts on abortion and implantation in rats. **Journal of Ethnopharmacology,** v.77, p.117-121, 2001.

Al-Kamis, K.I., Al-Said, M.S., Islam, M.W., Tariq, M., Parmar, N.S., Ageel, A.M. Antifertility, anti-implantation and abortifacient activity of the aqueous extract of *Cuminum cyminum.* **Fitoterapia**, v.59, p.5-10, 1988.

Almeida, F.G.C.; Lemonica, I.P. The toxic effect of *Coleus barbatus* B. on the different periods of pregnancy in rats. **Journal of Ethnopharmacology,** v.73, p.53-60, 2000.

Al-Said, M.S., Al-Kamis, K.I., Islam, M.W., Parmar, N.S., Tariq, M., Ageel, A.M. Post-coital antifertility activity of the seeds of *Coriandrum sativum* in rats. **Journal of Ethnopharmacology,** v.21, p.165-173, 1987.

Batta, S.K., Santhakumari, G. The antifertility effect of *Ocimum sanctum* and *Hibiscus rosa sinensis.* **Indian Journal of Medical Research**, v.59, p.777-781, 1971.

Bhatnagar, U. Post-coital contraceptive effects of an alcoholic extracts of the *Daucus carota* Linn. seed in rats. **Clinical Drug Investigation**, v.9, p.30-36, 1995.

Boling, J.L., Blandau, R.J. Egg transport through the ampullae of the oviducts of rabbits under various experimental conditions. **Biology of Reproduction**, v.4, p.174-184, 1971.

Choudhuri, D., Adhikary, P., Banerji, J., Jana, S., Chatterjee, A. Pregnancy interceptive effect of *Piper betle.* **Fitoterapia**, v.58, p.397-401, 1990.

Claeson. U.P.; Malmfors, T.; Wikman, G.; Bruhn, J.G. *Adhatoda vasica*: a critical review of ethnopharmacological and toxicological data. **Journal of Ethnopharmacology.** v.72. p.1-20. 2000.

Dafni, A.; Yaniv, Z.; Pelevich, D. Ethnobotanical survey of medicinal plants in Northen Israel. **Journal of Ethnopharmacology,** v.10, p.295-310, 1984.

Damasceno, D.C., Lemonica, I.P. Embryotoxicity and anti-implantation effects of rosemary *(Rosmarinus officinalis* L.) extract in pregnant rats within preimplantation period. **Revista Brasileira de Toxicologia,** v.12, p.47-54, 1999.

Dhanasekaran, S., Suresh, B., Sethuraman, M., Rajan, S., Dubey, R. Antifertility activy of *Ailanthus excelsa* Linn. In female albino rats. **Indian Journal of Experimental Biology**, v.31, p.384-385, 1993.

Di Stasi, L.C., Santos, E.M.G., Santos, C.M., Hiruma, C.A. **Plantas Medicinais na Amazônia.** São Paulo: Editora Unesp, 1989.

Farnsworth, R.N., Bingel, A.S., Cordell, G.A., Crane, F.A., Fong, H.H.S. Potencial value of plants as source of nem antifertility agents. Journal of Pharmacological Science, **v.64, p.535-598, 1975.**

Gardner, D.R., Panter, K.E., James, L.F., Stegelmeier, B.L. Abortifacient effects of lodgepole pine (*Pinus contorta*) and common juniper (*Juniperus communis*) on cattle. **Veterinary and Human Toxicology**, v.40, p.260-263, 1998.

Garg, S.K., Garg, G.P. Antifertility effect of oil from few indigenous plants on female albino rats. **Indian Journal of Medical Research,** v.59, p.302, 1970.

Garg, S.K. Antifertility effect of oil from few indigenous plants on female albino rats. **Planta Medica,** v.26, p.391-393, 1974.

Goonasekera, M.M., Gunawardana, V.K., Jayasena, K., Mohammed, S.G., Balasubramaniam, S. Pregnancy terminating effect of *Jatropha curcas* in rats. **Journal of Ethnopharmacology**, v.47, p.117-123, 1995.

Guerra, M.O., Peters, V.M. Screening for reproduct toxicity in rats of a decoction of *Himathanthus sucuuba* stem bark. **Journal of Ethnopharmacology**, v.34, p.195-199, 1991.

Guyton, A.C., Hall, J.E. **Tratado de Fisiologia Médica**. Rio de Janeiro: Guanabara-Koogan, 1997.

Hiremath, S.P.; Rudresh, K.; Badami, S; Patil, S.B.; Patil, S.R. Post-coital activity of *Acalypha indica* L. **Journal of Ethnopharmacology,** v.67, p.253-258, 1999.

Keshri, G., Singh, M.M., Lakshmi, V., Kamboj, V.P. Post-coital contraceptive efficacy of the seeds of *Nigella sativa* in rats. **Indian Journal of Physiology and Pharmacology,** v.39, p.59-62, 1995.

Kholkute, S.D., Munshi, S.R. Antifertility activity of indigenous plants *Sida carpinifolia* and *Podocarpus brevifolius* Stapf in female rats. **Indian Journal of Experimental Biology**, v.16, p.696-698, 1978.

Langeloh, A., Maidana-Leguizamon, F., Dalsenter, P. Potencial abortivo e infertilizante de plantas brasileiras contaminantes ocasionais de pastagens de bovinos e outros herbívoros de interesse econômico. **Pesquisa Veterinária Brasileira,** v.12, p.11-18, 1991.

Lemonica, I.P., Macedo, A.M.R.B. Abortive and/or embryototoxic effect of *Cinnamomum zeylanicum* leaf. **Fitoterapia**, v.65, p.431-434, 1994.

Lemonica, I.P., Damasceno, D.C., Di Stasi, L.C. Study of the embryotoxic effects of an extract of rosemary *(Rosmarinus officinalis* L.). **Brazilian Journal of Medical and Biological Research,** v.29, p.223-227, 1996.

Luna Costa, A.M.; Silva, J.C.; Campos, A.R.; Rao, V.S.; Maciel, M.A.; Pinto, A.C. Antioestrogenic effect of trans-dehydrocrotonin, a nor-clerodane diterpene from *Croton cajucara* Benth. in rats. **Phytotherapy Research**, v.13, p.689-691, 1999.

Lutterodt, G.D. Abortifacient properties of an extract from *Sida veronicaefolia*. **Journal of Ethnopharmacology,** v.23, p.27-37, 1988.

Marona, H.R.N., Langeloh, A., Schenkel, E.P. Atividade abortiva de *Ateleia glazioviana* (Leg. Papilionoideae) em ratas. **Pesquisa Veterinária Brasileira**, v.12, p.81-83, 1992.

Mats, M.N., Bogatkna, V.F., Vishnyakov-Yu, S. Contraceptive activity of an extract from *Ambrosia artemisiifolia*. **Rastitel Research**, v.23, p.125-129, 1987.

Mazumder, U.K., Gupta, M., Pramanik, G., Mukhopadhyay, R.K., Sarkar, S. Antifertility activity of *Nelumbo nucifera* in mice. **Indian Journal of Experimental Biology**, v.30, p.533-534, 1992.

Mishra, A., Dogra, J.V.V., Singh, J.N., Jha, O.P. Post-coital antifertility activity of *Annona squamosa* and *Ipomoea fistulosa*. **Planta Medica**, v.35, p.283-285, 1979.

Morris, J.M., Van Wagenen, G. Interception: The use of postovulatory estrogens to prevent implantation. **American Journal of Obstetrics and Gynecology**, v.115, p.101-116, 1973.

Mukherjee, S., Talwar, G.P. Early post implantation contraceptive effects of a purified fraction of neem (*Azadirachta indica*) seeds, given orally in rats: *communis*. **Fitoterapia**, v.65, p.248-252, 1994.

Nath, D., Sethi, N., Srivastava, S., Jain, A.K. Teratogenic evaluation of a indigenous antifertility medicinal plant *Gossypium herbaceum* in rat. **Fitoterapia**, v.68, p.137-139, 1997.

Nishimura, H., Tanimura, T. ***Clinical Aspects of the Teratogenicity of Drugs.*** New York: American Elsevier Publishing Company, 1976.

Nwobodo, E.O., Nwafia, W.C., Ezeigbo, J.C., Onwughalu, J. The post-coital contraceptive activity of *Sida linifolia*. **Fitoterapia**, v.67, p.291-293, 1996.

Offiah, V.N., Anyanwu, I.I. Abortifacient activity of an aqueous extract of *Spondias mombin* leaves. **Journal of Ethnopharmacology**, v.26, p.317-320, 1989.

Okwuasaba, F.K., Osunkwo, U.A., Ekpenyong, K.I., Onwukeme, K.E., Olaynka, A.O., Uguru, M.O., Das, S.C. Anticonceptive and estrogenic effects of a seed extract of *Ricinus communis* var. minor. ***Journal of Ethnopharmacology,*** 34: 141-145. (1991).

Pakrashi, A., Pakrasi, P. Antifertility efficacy of the plant *Aristilochia indica* Linn. on mouse. **Contraception,** v.20, p.49-54, 1979.

Pakrashi, A., Bhattacharya, K., Kabir, S.N., Pal, A.K. Flowers of *Hibiscus rosea-sinensis*, a potential source of contragestive agent III: Interceptive effect of benzene extract in mouse. ***Contraception,*** v.34, p.523-536, 1986.

Piyachaturawat, P., Glinsukon, T., Chanjarunee, A. Antifertility effect of *Citrus hystrix*. **Journal of Ethnopharmacology**, v.13, p.105-110, 1985.

Planas, G.M., Kuc, J. Contraceptive properties of *Stevia rebaudiana*. **Science**, v.162, p.1007, 1968.

Prakash, A.O., Saxena, V., Shukla, S., Tewari, R.K., Mathur, S., Gupta, A., Sharma, S., Mathur, R. Anti-implantation activity of some indigenous plants in rats. ***Acta of European Fertility***, v.16, p.441-448, 1985.

Prakash, A.O., Sisodia, B., Mathur, R. Biological profile of butanolic extract of dried fruits of *Juniperus communis*. **Fitoterapia**, v.65, p.248-252, 1994.

Ramos, R.R., Alarcon-Aguilar, F., Lara-Lemus, L., Flores-Saenz, I.L. Hypoglycemic effect of plants used in Mexico as antidiabetics. **Archieve of Medical Research**, v.23, p.59-64, 1992.

Rao, M.V.; Alice, K. M. Contraceptive effects of *Phillanthus amarus* in female mice. **Phytotherapy Research**, v.15, p.265-267, 2001.

Rao, V.S.N., Menezes, M.A.S., Gadelha, M.G.T. Antifertility screening of some indegenous plants of Brazil. **Fitoterapia,** v.59, p.17-20, 1988.

Sanyal, S. **Acta Endocrinologica**, v.28 (Suppl), p.72-78, 1956.

Sethi, N., Nath, D., Singh, R.K., Srivastava, R.D. Antifertility and teratogenic activity of *Cannabis sativa* in rats. **Fitoterapia**, v.62, p.69-71, 1991.

Sethi, N., Nath, D., Singh, R.K., Srivastava, R.K. Antifertility and teratogenic activity of some indigenous medicinal plants in rats. **Fitoterapia**, v.61, p.64-67, 1989.

Shivalingappa, H.;; Satyanarayan, N.D.; Purohit, M.G. Antiimplantation and pregnancy interruption efficacy of *Rivea hypocrateriformis* in the rat. **Journal of Ethnopharmacology,** v.74, p.245-249, 2001.

Singh, M.M., Chowdhury, S.R., Kulshreshtha, D.K., Kamboj, V.P. Antigestagenic activity of *Ixora finlayconiana* in rats. **Contraception,** v.48, p.178-191, 1993.

Vessal, M., Mehrani, H.Á., Omrani, G.H. Effects of an aqueous extract of *Physalis alkekengi* fruit on estrus cycle, reproduction and uterine creatine kinase BB-isozyme in rats. **Journal of Ethnopharmacology,** v.34, p.69-78, 1991.

Weniger, B. Plants of Haiti used as antifertility agents. **Journal of Ethnopharmacology**, v.6, p.67-84, 1982.

Yadav, R.; Jain, G.C. Antifertility effect os aqueous extract of seeds of *Cassia fistula* in female rats. **Advances in Contraception**, v.15, p.293-301, 1999.

Zia-Ul-Haque, A., Qazi, M.H., Hamdard, M.E. Studies on the antifertility properties of active components isolated from the seeds of *Abrus precatorius*. **Pakistan Journal of Zoology**, v.15, p.144-146, 1983.