

Medicinal plants with potential anti-fertility activity: A review

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Abstract

Medicinal plants is a common word which can utter in everyone's mouth that are helpful in treating many diseases which cannot be done by even allopathic medicine. Among those the birth control and at the same time increasing the fertility in human beings are both become major problems nowadays. This review presents updated information gathered on scientifically proved medicinal plants used for the anti-fertility activity. This study provides the information on botanical name, family, parts used, solvents used, and their chemical constituents present in plants. In spite of rapid progress and spread of modern medicine and surgery, faith in and popularity of traditional methods has not decreased. There are a large number of studies which supports the anti-fertility effects of traditional herbal medicines. The aim of this review is to highlight the work on anti-fertility of plant origin. The present paper also involves various plant drugs and their bioactive extracts involved in the anti-fertility mechanism. This article may help investigators to identify medicinal plants responsible for the anti-fertility activity.

Key words: Anti-fertility plants, herbal medicines, estrogens

INTRODUCTION

The extraordinary growth of the world population stands as one of the significant events of the modern era to think over. The current world population is around 6.46 billion and especially that of India is around 1.1 billion. One of the critical problems of the developing countries like in India is the geometrical increase in human population.

Today, we understand that our sheer numbers have increased so much that they are straining Earth's capacity to supply food, energy, and raw materials. Advances in medicine and public health have led to a significant decrease in mortality and an increased life expectancy. This population explosion will have a negative impact on our economic policies and would simultaneously misbalance our socio-economic infrastructure. Thus, the control of human fertility in the sense of its limitation is the most important and urgent of all biosocial and medical problems confronting mankind today.

The development of new fertility regulating drugs from medicinal plants is an attractive proposition, because from times immemorial, humans have relied on plants and their products

as sources of drugs and therapeutic agents, although in recent times, synthetic drugs are used extensively in modern medicine systems. However, many modern medicines are developed through the clues obtained from phytochemical studied. Moreover, the phytochemicals are even are important resources for medicinal uses. The plant products are becoming more popular than the synthetic drugs, in recent times. It is mainly attributed to their low toxicity and long-standing experience of the use of these drugs in ethnic medicine system like Ayurveda. Family planning has been promoted through several methods of contraception, but due to serious adverse effects produced by synthetic steroidal contraceptives, attention has now been focused on indigenous plants for possible contraceptive effect. Although contraceptives containing estrogen and progesterone are effective and popular, the risks associated with the drugs have triggered the need to develop contraceptives drugs from medicinal plants. Hence, there is a need for searching suitable products from indigenous medicinal plants that could be effectively used in the place of pills.

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THE PHYSIOLOGY OF FEMALE REPRODUCTIVE SYSTEM

The principal organs of the human female reproductive tract are the ovaries, the fallopian tubes, the uterus, and the vagina. Reproduction begins with the development of ova in the ovaries, a single ovum is expelled from an ovarian follicle into the abdominal cavity in the middle of each monthly sexual cycle, this ovum then passes through one of the fallopian tubes into the uterus, and if it has been fertilized by a sperm, it implants in the uterus where it develops into a fetus, a placenta, and fetal membrane.

The ovarian hormones play an important role in pregnancy; the different ovarian hormones are estrogen and progesterone. Estrogen is mainly secreted by the growing follicles and progesterone mainly by the corpus lutea.

When pregnancy occurs the ordinary ovarian cycle is suspended, and the hormone relaxin is secreted by corpus lutea and placenta ensures uterine quiescence and prevents the early abortion of the pregnancy.

FEMALE HORMONAL SYSTEM

- A hypothalamic-releasing hormone, luteinizing hormone (LH) releasing hormone
- The anterior pituitary hormones, follicle-stimulating hormone (FSH), and LH, both of which are secreted in response to the releasing hormone from the hypothalamus
- The ovarian hormones, estrogen, and progesterone, which are secreted by the ovaries in response to the two hormones from the anterior pituitary gland.

The various hormones are not secreted in constant amounts throughout the female monthly sexual cycle but instead are secreted at drastically different rates during different parts of the cycle.^[1]

Estrogens

Estrogens are a class of steroid hormones linked principally with the control of female sex organ responsiveness and of reproduction. The important endogenous estrogens are 17 β -estradiol, estrone, and estriol. The most potent biogenic form is 17 β -estradiol. Estrogens are biosynthesized in the ovary.

Estrogenic compounds derived from plants are termed phyto-estrogens. The major chemical groups of phyto-estrogens are classified as flavonoids, (flavones, flavanones, and isoflavanoids) coumastrans, lignans, and myoestrogens.

These compounds interacting with the estrogenic receptor exert estrogenic activity, such as uterotrophic effect, sterility

or disruption of normal reproductive processes occurs in farm animals grazing in pastures with plant sources high in phyto-estrogens. In humans cancer protective properties have been associated with phyto-estrogens.^[2]

Physiology of Estrogens

Estrogens are required for the normal maturation of the female. They stimulate the development of vagina, uterus, and uterine tube as well as the secondary sexual characteristics. They stimulate the development of stroma and ductal growth in the breast. They contribute to the growth of the axillary and pubic hair and later the distribution of body fat. Estrogen also plays an important role in the development of endometrial lining. Estrogens stimulate the synthesis of enzymes and growth factors, leading to uterine growth and differentiation. In the liver, estrogens alter the circulating levels of proteins such as transcortin (cortisol binding globulin), thyroxin-binding globin, sex hormone-binding globin, transferrin, rennin substrate, and fibrinogen. This leads to increased circulating levels of thyroxin, estrogen, testosterone, iron, copper, and other substances. Estrogens enhance the coagulability of blood. Alterations in the composition of the plasma lipids caused by estrogens are characterized by an increase in the high-density lipoproteins and a reduction in plasma cholesterol level. Plasma triglycerides levels are increased.^[3]

Mechanism of Action of Estrogen

Estrogen may act on the hypothalamic center to inhibit the secretion of gonadotropin releasing factor thereby preventing pituitary gonadotropin secretion and the resultant ovulation. The transport of ova through the tubules is either accelerated or inhibited so that the ovum enters the unprepared uterus where it is degenerated or expelled. Administered estrogens also alter the delicate balance of estrogen and progesterone required for implantation of the blastocyte in the endometrium.

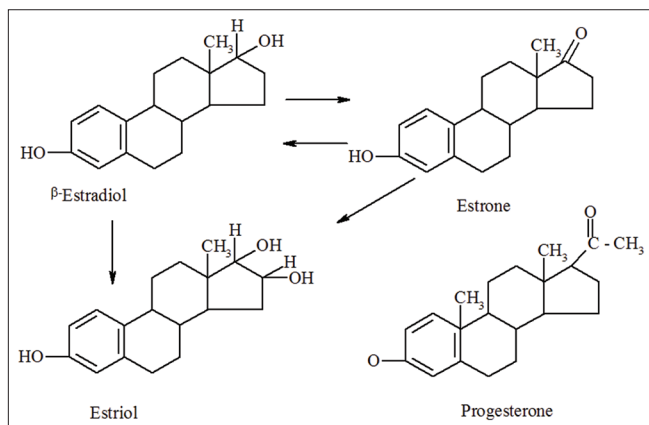
Estrogens also induce the formation of hormonal receptors necessary for the interaction of the different hormones. Most of the actions of estrogens are mediated by the activation of intracellular receptors.^[4]

Estrogens exert their action by inducing specific physiologic response until the estrogenic receptors. The estrogenic receptor resides in the nucleus, and the hydrophobic estrogenic compounds readily diffuse through the cellular and nuclear membrane to bind and subsequently activate the estrogenic receptors. The activated form of the estrogenic receptors can then stimulate the transcription of estrogen responsive genes.

Chemistry of the Estrogen

The estrogens are secreted in major quantities only by the ovaries though minute amounts are also secreted by

the adrenal cortices. Only three estrogens are present in significant quantities in the plasma of the human female: β -estradiol, estrone, and estriol. The principal estrogen secreted by the ovaries is β -estradiol. Small amounts of estrone are also secreted. Estriol is an oxidative product derived from estradiol and estrone, the conversion occurring mainly in the liver. The estrogenic potency of β -estradiol is 12 times that of estrone and 80 times that of estriol.^[1]



THE IMPORTANT BIOLOGICAL ACTIVITIES OF ESTROGEN^[5]

Stimulation of growth of both the myometrium and endometrium.

- Maintenance of a thick vaginal mucosa and indirectly the acidic vaginal pH. Stimulation of cervical glands to secrete copious quantities of viscous mucous,
- Stimulation of breast growth and development,
- Deposition of subcutaneous fat, which results in a characteristic feminine habitus,
- Regulation of gonadotropin secretion including both "negative" and "positive" feedback,
- Sensitization of the ovaries to gonadotropins, and
- Retardation of linear body growth in association with facilitation and epiphysis closure.

Ovarian Cycle^[1]

The normal reproductive years of the female are characterized by monthly rhythmic changes in the rates of secretion of the female hormones and corresponding changes in the ovaries and sexual organs as well. This rhythmic pattern is called the female sexual cycle (or less accurately, the menstrual cycle). The duration of the cycle averages 28 days. It may be as short as 20 days or as long as 45 days even in completely normal women though abnormal cycle length is occasionally associated with decreased fertility.

The two significant results of the female sexual cycle are: First, only a single mature ovum is normally released from

the ovaries each month. Second, the uterine endometrium is prepared for implantation of the fertilized ovum at the required time of the month.

After puberty, when FSH and LH from the anterior pituitary gland begin to be secreted in large quantity, the entire ovaries together with the follicle within them begin to grow.

Disturbance of the natural steroid hormone balance can successfully disorganize the co-ordinate events involved in ovulation, ovum transport, and implantation. Thus, compounds possessing estrogenic, progestation, and anti-estrogenic or anti-progestational activity may also exhibit anti-fertility activity.^[6]

ROLE OF SPERMS IN FERTILIZATION

Semen is the complete discharge of the male during normal ejaculation. It consists of seminal plasma, spermatozoa and usually some cells cast off from the lining of the reproductive ducts and glands. Seminal plasma consists of the secretion of the prostate, seminal vesicles, bulbourethral glands and epididymis, the chief contribution being from the prostate and seminal vesicles. The seminal plasma serves as a food source and vehicle for the spermatozoa.

Testicular or epididymal sperm is inactive but quickly become active in seminal plasma (or saline). The role of the high content of hyaluronidase in sperm is not entirely understood, but histochemical studies indicate that it breaks down the egg coating and aids the sperm in penetrating the egg.^[7,8]

The production of spermatozoa occurs in the seminiferous tubules of the testis, which are controlled by hormones from the anterior pituitary gland. LH stimulates the interstitial cells of Leydig to produce testosterone. Testosterone is responsible for the appearance and maintenance of secondary sex characteristics. The male accessory sex organs are the organs adopted for transfer of live spermatozoa from males to female. Sperm must remain in the female tract for several hours to acquire the ability to penetrate ovum-capacitation.^[8]

As early as the 19th century B.C. the Egyptians were mixing honey, natron (Sodium carbonate) and crocodile dung to form a vaginal contraceptive paste. During the middle Ages, rock salt and alum were frequently used as vaginal contraceptives. The spermicidal must be inserted deep into the vagina (usually with an applicator). They must be used just before intercourse and reused if intercourse is to be repeated. The ideal vaginal contraceptive must be non-toxic and non-irritating to both partners. The spermicidal agents also provide significant protection against venereal disease transmission. Modern spermicidal reagents or vaginal contraceptives fall into three categories.^[9]

Table 1: Anti-fertility activity of some medicinal plants

Common name	Botanical name	Activities	Plant parts used
Chirmi	<i>A. precatorius</i>	Reduces sperm motility and density	Seed
Shikakai	<i>A. concinna</i>	Spermicidal and sperm coagulating activities	Stem bark
Kadakadi	<i>A. aspera</i>	Spermicidal action	Root
Bael	<i>A. marmalos</i>	Resist process of spermatogenesis and decrease sperm motility	Whole plant
Bhutala	<i>C. roxburghii</i>	Anti-estrogenic activity	Bark
Caster	<i>C. aromatic</i>	Anti-estrogenic activity	Rhizomes
Aaghada	<i>A. aspera</i>	Anti-implantation activity	Root
Perumaram	<i>A. excels</i>	Abortifacient activity	Leaf, stem, bark
Tree spinach	<i>C. conitifolius</i>	Contraceptive activity	Leaves
Cumin	<i>C. cyminum</i>	Anti-estrogenic activity	Leaves
Wild carrot	<i>D. carota</i>	Anti-implantation activity	Rhizomes
Yarrow	<i>A. folium</i>	Spermicidal action	Stem bark
Hemorrhage plant	<i>A. africana</i>	Reduces the hormone level	Seeds
Thunder god vine	<i>T. wilfordii</i>	Estrogenic activity	Stem
Ylang-ylang	<i>C. odorata</i>	Decrease epididymal sperm motility, sperm count in and abnormality in sperm morphology	Dried root
Phang	<i>R. hypocrateriformis</i>	Irregular estrous cycle with shortened estrus and metestrus	Aerial part of plant
Desert broom	<i>C. aphylla</i>	Potential male contraceptive	Flower
Varuna	<i>C. nurvala</i>	Significant anti-fertility effects	Stem bark
Papaya	<i>C. papaya</i>	Causes infertility and irregular estrous cycles	Fruits
Snake gourd	<i>T. cucumerina</i>	Estrous cycle showing a significant increase in estrus and metestrus phase	Whole plant
Muktajhuri	<i>A. indica</i>	Significant anti-implantation activity	Leaves
Golden shower	<i>C. fistula</i>	Anti-implantation activity	Seeds
Sesban	<i>S. sesban</i>	Inhibit the ovarian function	Seeds
Fenugreek	<i>T. foenum graecum</i>	Anti-estrogenic and anti-fertility activity	Seeds
Horehound	<i>B. undulate</i>	Negative effects on fertility and pregnancy	Flowers

A. concinna: *Acacia concinna*, *A. precatorius*: *Abrus precatorius*, *A. aspera*: *Achyranthus aspera*, *A. marmalos*: *Aegle marmalos*, *C. roxburghii*: *Croton roxburghii*, *C. aromatic*: *Curcuma aromatic*, *A. aspera*: *Achyranthus aspera*, *A. excels*: *Ailanthus excels*, *C. conitifolius*: *Cnidioscolousa conitifolius*, *C. cyminum*: *Cuminum cyminum*, *D. carota*: *Daucus carota*, *A. folium*: *Achillea mille folium*, *A. africana*: *Aspilia Africana*, *T. wilfordii*: *Tripterygium wilfordii*, *C. odorata*: *Cananga odorata*, *R. hypocrateriformis*: *Rivea hypocrateriformis*, *C. aphylla*: *Capparis aphylla*, *C. nurvala*: *Crataeva nurvala*, *C. papaya*: *Carrica papaya*, *T. cucumerina*: *Trichosanthes cucumerina*, *A. indica*: *Acalypha indica*, *C. fistula*: *Cassia fistula*, *S. sesban*: *Sesbania sesban*, *T. foenum graecum*: *Trigonella foenum graecum*, *B. undulate*: *Ballota undulate*

1. Surface active/sulfhydryl binding agents

E.g.

- i. Non-oxynol - I.U.S.P. (Delfen, Immolin)
- ii. Otoxynol U.S.P. (Koromex).

2. Bactericides

E.g.

- i. Phenyl mercuric acetate (Lorophyn)
- ii. Benzenthonium chloride
- iii. Methylbenzenthonium chloride
- iv. Phenyl mercuric borate.

3. Acids

E.g., Boric acid, tartaric acid, phenols, etc.

Contraception is literally the prevention of conception but generally is taken to mean the prevention of pregnancy.^[10]

A number of plants have been reported to have anti-fertility properties by various workers such as:

***Curcuma longa* (Zingiberaceae)**

C. longa Linn., commonly known as turmeric, Indian saffron or Haldi is a perennial herb cultivated throughout India and is widely used as an antibiotic in folk medicines and as spices. Its tubers, rhizomes, and oil, have great importance. *C. longa* also possesses anti-mutagenic and anti-carcinogenic properties.^[11]

Phenolic diketone, curcumin (diferuloylmethane) (3-4%) is responsible for the yellow and comprises curcumin I (94%), curcumin II (6%), and curcumin III (0.3%).^[12]

***Abrus precatorius* Leguminosae (Fabaceae)**

The plant *A. precatorius* Linn., popularly known as Rosary pea found throughout India in hedges and bushes in exposed areas.^[13] Usually, seeds are used against leucoderma, wounds, alopecia, asthma, tubercular glands, leprosy, fever, ulcer, and tumor.^[14]

Precatorine, trigonelline, choline, and abrine are present in the seeds. Abricin and abridin, two steroids were also reported in the seeds; the latter exhibited anti-fertility property.^[15]

***Barleria prionitis* (Acanthaceae)**

B. prionitis L. is commonly known as Vajradanti. In indigenous system of medicine in India, the aerial parts (stem, leaf, and flower) are used in fever, toothache, inflammation, as diuretic, and gastrointestinal disorders; bark in a whooping cough as an expectorant; the whole plant and especially the roots are used as a tonic.^[16] Leaves, stem, and root of *B. prionitis* possess antibacterial and anti-inflammatory activities.

From the aerial parts of *B. prionitis*, one new phenylethanoid glycoside, barlerinoside along with six known iridoid glycosides, namely, shanzhiside methyl ester, 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester, barlerin, acetylbarlerin, 7-methoxydiderroside, and lupulinoside were isolated.^[17]

***Achyranthes aspera* (Amaranthaceae)**

A. aspera Linn. is an abundant indigenous herb in India. It is traditionally being used as an abortifacient. The ethanol extract of the root was screened for anti-fertility activity in proven fertile female albino rats and 83.3% anti-implantation at 200 mg/kg body weight and given orally on days 1-7 of pregnancy.^[18]

***Nelumbo nucifera* (Nelumbonaceae)**

N. nucifera has been used as an anti-fertility agent in females by the local tribals of Rajasthan, India. Oral administration of *N. nucifera* extract brought about a significant decline in the weight of ovary, protein, and glycogen level, however, cholesterol level increased significantly. In addition, the diestrous phase of the estrous cycle was found to be prolonged. These results suggest that *N. nucifera* has the anti-estrogenic nature without altering the general physiology of the female rats.^[19]

***Azadirachta indica* (Meliaceae)**

The seed oil of *A. indica* is used in traditional medicine for its anti-diabetic, spermicidal, anti-fertility, antibacterial, and

wound a significant reduction in the number of normal single layered follicles and follicles in various stages of follicular development in treatment with *A. indica*.^[20]

***Ocimum gratissimum* (Lamiaceae)**

O. gratissimum is widely used in folk medicine for several conditions because of its high medicinal value and, therefore, calls for its toxicological screening. *O. gratissimum* caused no significant effect on the serum levels of the hormones studied. However, sperm count and motility were decreased, while the percentages of abnormal sperm cells, sperm debris, and primordial cells were increased the dose and time dependently.^[21]

***Strychnos potatorum* (Loganiaceae)**

The treatment of *S. potatorum* extract did not bring any body weight loss, whereas, the weight of testes, epididymides, seminal vesicle, and ventral prostate were decreased significantly. Reduced sperm count and motility resulted in suppression of fertility by 91.81%. *S. potatorum* seed possesses suppressive effects on male fertility and could be useful in the development of male contraceptive agent. However, further studies are needed.^[22]

***Dendrophthoe fallata* (Loranthaceae)**

Analysis of vaginal smears revealed that all animals were cycling; although the length of the diestrous was longer in *D. Fallata* extract treated groups. In post coital testing, the extract was found to be more effective in causing significant anti-implantation activity and reduction in the number of litters born. The extract also exhibited weak estrogenic activity when given alone, and when ethinyl estradiol, it exhibited slight anti-estrogenic activity in immature ovariectomized rats. All observation suggests that the extract has an anti-fertility effect and it safe at effective doses employed in the study.^[23]

***Rumex steudelii* (Polygonaceae)**

The methanolic extract of the roots of this plant were investigated for their anti-fertility activity in female rats, and oral lethal dose 50 (LD₅₀) was determined in mice. The extract reduced significantly the number of litters. It also produced an anti-fertility effect in a dose dependent manner, and the contraceptive effect was manifested for a define period of time. Furthermore, the extract prolonged significantly the estrous cycle and the diestrous phase of the rats. The oral LD₅₀ of the extract was found to be 5 g/kg in mice. Thus, the extract has an anti-fertility effect.^[24,25] The plants that are shows potent antifertility effect are summarized in Table 1

CONCLUSION

The list of medicinal plants used as anti-fertility agents presented in this review is useful practitioners. This list is best used only as a preliminary screening of potential anti-fertility plants, not as a definitive or complete list of the anti-fertility plant.

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