REVIEW ARTICLE

# Plant origin contraceptives: phytochemistry, mechanism of action, and side effects

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## Abstract

This review examines the effects of plant origin various contraceptives on ovulatory events, egg transport, toxic action on eggs, end of implantation stages, and implantation through hypothalamic and pituitary controls. Plant-origin products modify the hormonal environment of fertilized eggs or developing ovums by the use of steroids and other chemicals. These herbal contraceptives affect spermatogenesis and lowers down the number of spermatocytes, intromission, and ejaculation frequencies. These also inhibit sperm production in males and obstruct fertilization in females. These herbal agents successfully obstruct reproduction and control the production, release, and action of hormones. Plant natural products work by blocking the effects of anti-androgens, which affect menstruation and pregnancy, cause birth, and birth control. This review explains the anti-fertility action of many plant species with active ingredients. It is important to understand the long-term effects of plant natural products on body metabolism to prevent undesired toxicity to other organs. These might have more effective role in the regulation of fertility and breakdown of pregnancy. These could be used for long-term family planning equally by both male and female partners. There is a great need for effective, reversible, and safe contraceptives for men and women, but the mechanisms of action of plant extracts and active compounds have yet to be determined.

**Key words:** Birth and birth control, male contraceptives, menstruation, pregnancy, termination of implantation

## INTRODUCTION

Plants are used worldwide for the treatment of various human ailments since time immemorial. For centuries, plants and plant-based products have been used as a valuable natural source of medicines for treating various ailments.[1] Literature showed these were used in traditional/folkloric system of medicine for centuries for contraception or fertility control by ancient people without knowing their active principles.[2] Besides, fertility controls that these plant materials were used for the treatment of other diseases, where they were found to put adverse effects on reproductive, neurological, developmental, and metabolism in the body. In Ayurveda, so many plant-based drugs and formulations are available which have been standardized and its ethnopharmacological values are known but chemistry is still lacking. Later on, its active principles were explored and characterized that it leads to development of several life-saving drugs, which are in clinical use today. These herbal contraceptives mainly control spermatogenesis and oogenesis. These steroidal and non-steroidal anti-fertility substances; interfere in ovulatory events; egg transport; toxic action on eggs; termination of implantation stages; and implantation.[3] However, several commonly used plants have been reported to adversely affect male reproductive functions in wildlife and humans [Figure 1].

Plant natural products are used for the treatment of reproductive health problems and the management of reproduction is almost universal. In females, these stimulate blood flow and increase uterine contraction and terminate pregnancy. These are believed to warm the blood and increase its flow and irritate the uterus that helps to evacuate its contents.[4] Medicinal plants may prove useful in developing plant-based contraceptive strategies for regulation of male

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fertility. These natural products are either modulators of spermatogenesis: and act as male contraceptive.[5] These should be anti-spermatogenic in action and successfully control fertility and do not show toxicity in other organs. These plant natural products might be non-invasive in administration, non-hormonal in action, non-toxic and that is relatively long-acting. To date, no natural-based male contraceptive is available in the commercial market, mostly due to the difficulty in reversing the effects of these products in male fertility.[5] Mostly, people use synthetic steroidal agents, which impose many side effects, and affect the health of user if he or she uses them as anti-fertility substances [Figure 1].

These plant-origin products are centered around the mechanisms involved in modifications in the hormonal environment of the fertilized egg or developing ovum by steroidal and other chemicals.[3] Herbal preparations affect gonadal functions mainly both spermatogenesis and steroidogenesis [Figure 1]. These cause a decrease in the motility of ejaculated spermatozoa and inhibit spermatogenesis by affecting spermatocyte production also act as spermicides, sperm immobilizers, and inactivate sperm immediately on deposition in the vagina [Figure 1]. There is an immense need of herbal contraceptives to replace the synthetic contraceptives because they impart side effects. Such contraceptives would be especially useful in those cases where hormonal contraceptive agents are contraindicated [Figure 2].

Plant natural products are administered orally as infusion or as powder, paste or fresh juice, or extract to control fertility. Most of these plant substances/materials slow down the pre-ovulatory, pre-implantation, and post-implantation anti-fertility mechanisms. These severely affect the hypothalamus-pituitary functions [Figure 1]. It finally influences the operational mechanisms in ovary and oviduct. These act at cellular level to obstruct menstruation, conception, and pregnancy and help to control fertility and birth control. Most of these plants, that is, *Hibiscus tiliaceus* (*Malvaceae*), and *Dendrobium* sp. an orchid are supplemented with milk, sweet potato, cooked papaya fruit, and lightly boiled edible ferns (*Cyathea* sp., *Diplazium* sp., *Tectaria latifolia*, Microlepia speluncae, and *Hypolepis* sp.). These act as abortive agents. For fertility control natural products from *Asplenium nidus*, *Hemigraphis reptans*, *Dysoxylum gaudichaudianum*, *Omalanthus nutans*, *Pemphis acidula*, *Ipomoea* sp., *Merremia peltata*, or *Ficus adenosperma* are used with coconut.[6] *H. reptans, A. nidus. D. gaudichaudianum* and O. *nutans* were act as abortive agents.[6]

Hence, many Indian origin plants showed anti-fertility potential with their active principles could not formulated as established medicine.[7] However, its bio-organic natural products such as terpenoids, alkaloids, glycosides, phenols, and other compounds act as contraceptives.[8] From higher plants, lithospermic acid, m-Xylohydroquinone, coronaridine, rutin, and rottlerin active antifertility bio-organic candidates have been isolated and tested. Besides these volatile oils, quinine and castor oil, and sparteine have been investigated abortifacient agents for the inhibition of fertility. However, these were not found successful because of its side effects. Some active compounds, isolated from about various plant species, have been reported to possess significant anti-fertility potential.[9] There is a vast array of unexploited plants having a traditional role in fertility regulation. Furthermore, the mechanisms of action by which plant extracts and their active compounds exert anti-fertility effects must be investigated and established to avoid failures [Table 1].[9]

Females for contraception for steroidal contraceptives and other physical devices are used. Estrogens and progestins mini pills are used in various combinations to intervention in reproductive function both centrally and peripherally. These inhibit release of gonadotrophin and prevent ovulation. These

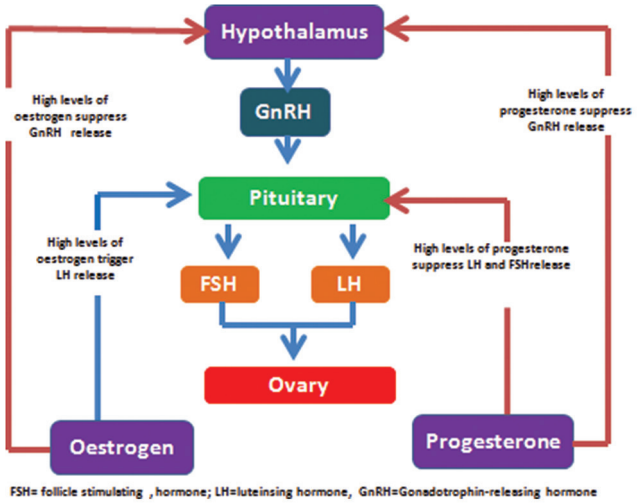


**Figure 1:** Role of hypothalamus-pituitary functions in fertility

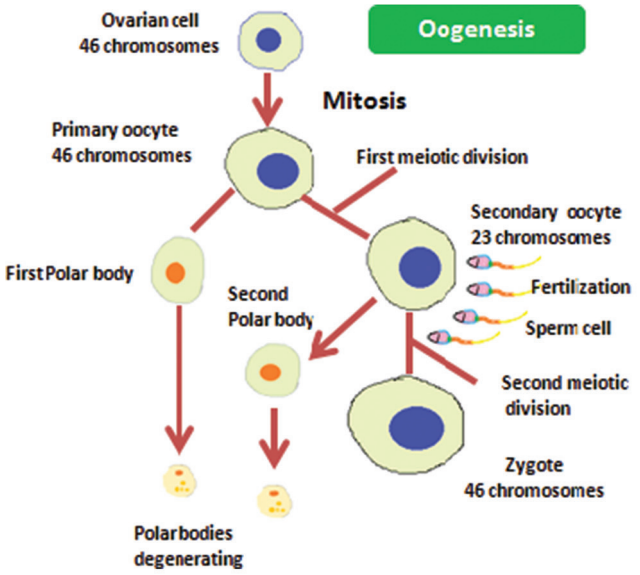


**Figure 2:** Process of oogenesis and spermatogenesis

**Table 1:** Plant origin anti-fertility/contraceptive agents

| Common name | Scientific name | Family | Plant part used | Biological effect |
|---|---|---|---|---|
| Desert date | *Balanites roxburghii* | *Zygophyllaceae* | Fruits Juice, | Contraceptive juice |
| Neem | *Azadirachta indica* | *Meliaceae* | Seed powder | Contraceptive |
| Common night glory | *Rivea hyopcrteriformis* | *Convolvulaceae* | Aerial parts extract | Contraceptive |
| Malai Vembu | *Melia azesarach* | *Meliaceae* | Aerial parts | Fresh juice |
| Danti | *Jatrophus curcas* | *Euphorbiaceae* | Fruits | Fresh juice |
| Common Rue | *Ruta gravelens* | *Rutaceae* | Aerial parts | Infusion taken orally |
| Long piper | *Piper longum* | *Piperaceae* | Leaf | Infusion taken orally |
| Bilva | *Aegle marmelos* | *Rutaceae* | Leaf | Infusion taken orally |
| Brahmi | *Bacopa monnieri* | *Scrophulariaceae* | Plant | |
| Christmas bush | *Alchonea ocrdifolia* Schum. and Thonn. | *Euphorbiaceae* | Leaf bark/roots/bark | Infusion taken orally |
| Tulsi or Basil | *Ocimum viride* Willd | Labiateae | Leaf | Infusion taken orally |
| hog plum or amra | *Spondias mombin* Linn | *Anacardiaceae* | Leaf | |
| Ashanti pepper | *Piper guineensis* Schum. and Thonn. | *Piperaceae* | Leaf/seed | Infusion taken orally |
| Papita | *Carica papya* Linn | *Caricaceae* | Leaf/roots/bark | Fresh extarct |
| Neem | *Azadirachta indica* A Juss | *Meliaceae* | Leaf/bark | Fresh extarct |
| Dombwe | *Heteromorpha trifoliate* | *Apiaceae* | root | Powder mixed with porridge |
| Schkuhria pinnate | *Dwarf marigold* | *Ateraceae* | Whole plant | Infusion taken orally |
| Vernonia amygdalina | *Dwarf marigold* | *Ateraceae* | Root | Infusion taken orally |
| Sausage tree | *Kigelia africana* | *Bignoniaceae* | Root bark | Powder mixed with porridge |
| Castor oil plant | *Ricinus communis* | *Euphorbiaceae* | Root and leaf | Peeled whole seed taken orally once a year |
| Snow berry | *Securinega virosa* | *Euphorbiaceae* | Roots | Powder or infusion taken orally |
| Bakota plum | *Flacourtia indica* | Flacourtiaceae | Root leaf | Powder or infusion taken orally |
| Callindra | *Derris brevipes* | Papillionaceae | Root | Powder or infusion taken orally |
| Aagadha | *Achyranthes aspera* | Amarnthaceae | Root | Powder with water |
| Betel pepper | *Piper betel* | *Piperaceae* | Root | Powder with water |
| Fenugreek | *Trigonella foenum gracum* | Fabaceae | Seed | Powder with water |
| Lostus | *Nelumbo nucifera* | *Nymphaeaceae* | Seed | Powder with water |
| Honeysuckle miteletoe | *Dendrophthoefalcate* | *Loranthaceae* | Aerial parts | infusion taken orally |
| Ambusi | *Oxalis corniculata* | *Oxalidaceae* | Whole plant | infusion taken orally |
| Nata Karanja | *Caesalpinia bonduc* | *Caesalpiniaceae* | Root and bark | infusion taken orally |
| *Christmas bush* | *Alchonea ocrdifolia* Schum. and Thonn. | *Euphorbiaceae* | Leaf /bark/roots/bark | Fresh juice |
| Ram *tulsi* | *Ocimum viride* Willd | Labiateae | Leaf | Infusion taken orally |
| *hog plum* | *Spondias mombin* Linn | *Anacardiaceae* | Leaf | Infusion taken orally |
| Piper | *Piper guineensis* Schum. and Thonn. | *Piperaceae* | Leaf/seed | Infusion taken orally |
| Paipta | *Carica papya* Linn | *Caricaceae* | Leaf/roots/bark | Infusion taken orally |
| Neem | *Azadirachta indica* A Juss | *Meliaceae* | Leaf/bark | Fresh juice |

also hamper follicular maturation and impair its nourishment, due to pituitary gonadotropin secretion inhibition [Figure 3]. Today, there is no solution of rising world population and cases of unintended pregnancy become big issue with serious ramifications for women, their families, and society, including abortion, infertility, and maternal death. At global level various concepts, behaviors and practices relating to menstruation, pregnancy, birth, and birth control are prevalent. Most of them are not suitable for both men and women. These contraceptives are toxic to both men and women There is a search for new, safe, effective, and reversible contraceptive methods for family planning. Search for an effective, feasible, and safe male contraceptive has been one of the major public health challenges. Infertility, a couple's inability to conceive after 1 year of unprotected regular intercourse, is an important issue in the world. The use of natural products in the treatment of infertility has been considered as a possible alternative to conventional therapies.[10] There is a dire need of plant origin contraceptive that may be non-invasive in administration, non-hormonal in action and non-toxic.[11]

## SOURCE OF INFORMATION

For writing this comprehensive research review on "plant origin anti-fertility agents mainly contraceptives," various databases were searched. For the collection of relevant information specific terms such as medical subject headings and keytext words, such as herbal "contraceptives" and its use in anti-fertility control published till 2023 were explored out in MEDLINE. There are more than 200 plants and their bio-organic constituents who exhibited contraceptive properties were collected. Most specially for retrieving all articles pertaining to the traditional uses of plant natural products/extracts/compounds for fertility control in animal models were searched in, electronic bibliographic databases, and abstracts of published studies with relevant information on the male and female contraception were collected.

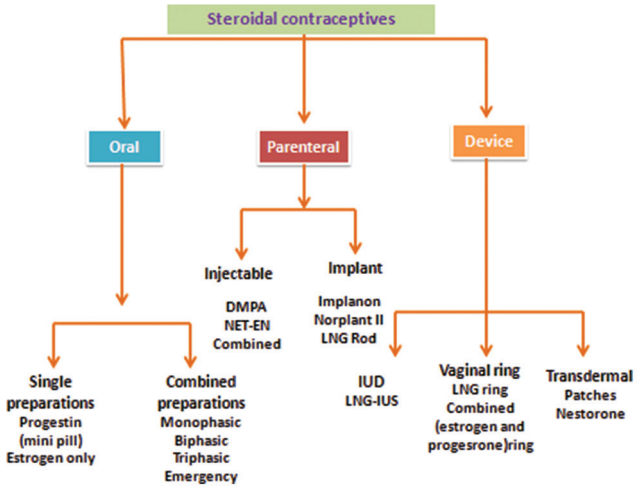


**Figure 3:** Types and use of steroidal other contraceptives

Furthermore, references cited by the studies on the present topic were exhaustively searched. Relevant terms were used individually and in combination to ensure an extensive literature search. For updating the information about a subject and incorporation of recent knowledge, relevant research articles, books, conferences proceedings, and public health organization survey reports were selected and collated based on the broader objective of the review. The present review aimed to systematically analyze published data on plant-origin contraceptives: its use and side effects. This was achieved by searching databases, including SCOPUS, Web of Science, and EMBASE, Pubmed, Swissprot, Google searches," and Cochrane library were searched. From this common methodology, discoveries and findings were identified and summarized in this final review.

## PHYTOCHEMISTRY OF PLANT ORIGIN CONTRACEPTIVES

Hence, many medicinal plants possess contraceptive activity, among them *Bulbine latifolia*, *Pouzolzia mixta*, *Salsola tuberculatiformis*, *Securidaca longipedunculata*, and *Typha capensis* have shown a decrease in mount, intromission, and ejaculatory frequencies. These inhibit implantation and impose contraceptive effects. These also displaced glucocorticoids and impose prolonged diestrus or negative effects on vitality, motility, and sperm production. *B. latifolia* and *P. mixta* of South African origin possess contraceptive agents for both males and females.[12] *C. fistula* contains flavonoids which reversibly suppresses fertility in male rats.[13] These obstruct reproduction and control of hormone production, release, and action [Table 2].[14]

## MEDICINAL PLANTS USED AS ANTI-FERTILITY AGENTS

Herbal contraceptives are obtained from various plant parts including leaves, roots, fruits (15%), seeds, stem/stem bark, and flowers. Plants, their parts, and extracts possess phyto-constituents which are traditionally used for anti-implantation, abortifacients, contraception, emmenagogue, and sterilization purposes.[8] These are used in fertility regulation.[8] Plant synthesizes a vast array of chemicals; few of them are saponins, ecdysterone, achyranthine, and inokosterone. Alpha-chlorohydrin Calotropin alpha amyrin beta amyrin acacic acid lactone, lupeol acetate, rutin, thevetigenin platycodin D (PD), bougainvinones, pinitol, quercetagetin, quercetin, and terpinolene, Triptolide, a diterpene triepoxide, Thevetigenin, luteolin, juniperin rutin, kaempferol, and scutellarein oxymethyl-anthraquinones, margosic acid, azadir-achtin, polysaccharides, nimbine, nimbidinate, nimbidol, oil, and nimbidin, limonoid glycosides, limonene, geranial, neral, ichangin 4-beta-glucopyranoside, nomilinic acid, and 4-beta-glucopyranoside, plumbagin,

**Table 2:** Medicinal plants showing anti-implantation and anti-ovulatory activity

| Common name | Scientific name | Family | Plant part used | Treatment/dose |
|---|---|---|---|---|
| **Anti-implantation activity** | | | | |
| Desert Horse | *Trianthema portulacastrum* | *Aizoaceae* | Stem leaf | Extract 2–5 mL twice per day |
| Lasura | *Cordia dichotoma* | *Boraginaceae* | Bark | Powder mixed with porridge |
| Sojava/Jewel of opar | *Talinum paniculatum* | *Dioscoreaceae* | Root and leaf | Powder mixed with porridge |
| Barna and Varuna | *Crataera nurvela* | *Capparidaceae* | Stem and Bark | Infusion taken orally |
| Nag Champa | *Artbotrys odoratissimus* | *Annonaceae* | Leaf | Infusion taken orally |
| Wood sorrel | *Oxalis corniculata* | *Oxalidaceae* | Whole plant | Powder mixed with porridge |
| Kaila Spati | *Couroupta guiancensis* | *Lecythidaceae* | Bark | Powder mixed with porridge |
| Moss rose/parsley | *Portulaca oleracea* | *Portulaceae* | Aerial parts | Extract 2–5 mL twice per day |
| Jiwanti/Dodi | *Leptadenia reticulate* | *Asclepiadaceae* | whole plants | Extract 2–5 mL twice per day |
| Haldi | *Curcuma aromatic* | *Zingiberaceae* | Rhizome | Extract 2-5 ml twice per day |
| Nata Karanja | *Caesalpinia bonduc* | *Caesalpiniaceae* | Root and bark | Powder mixed with porridge |
| Water Willow | *Justicia simplex* | *Acanthaceae* | Root | Fresh extract or infusion |
| Calliandra brevipes | *Derris brevipes* | *Papillionaceae* | Root | Fresh extract or infusion |
| Golden Shower | *Cassia fistula* | Caesalpiniaceae | Seeds | Powder mixed with porridge |
| Chinese lantern | *Dichrostachys cinerea* | *Mimosoideae* | Root | Infusions are taken |
| Buffalo thorn | *Ziziphus mucronata* | *Rhamnaceae* | Root bark | Fresh extract or infusion |
| Makoni tea | *Fadogia ancylantha* | *Rubiaceae* | Root | Fresh extract or infusion |
| Olat kambale | *Abroma angusta* (L)L.f. | *Sterculiaceae* | Roots | Fresh extract or infusion |
| Aaghada | *Achyranthes aspera* L. | *Amranthaceae* | Whole plant, Stem bark | Fresh extract, powder |
| Adulsa | *Adhatoda vasica* Nees. | *Acanthaceae* | Leaves | Powder mixed in hot water |
| Papai | *Carica papaya* L. | *Caricaceae* | Latex of green fruit Seeds | Fresh extract or infusion |
| Gajar | *Daucus carota* L. | *Apiaceae* | Seeds | Powder mixed in hot water |
| Deokapashi | *Gossipium herbacium* L. | *Malvaceae* | Stem, Roots &Seeds | Fresh extract or infusion |
| Bhringaraja kula | *Artemisia vulgaris* | *Asteraceae* | Leaf | Methanolic extract |
| Asiatic Witchweed | *Striga orobanchioides* | *Orobanchaceae* | Leaf | Ethanolic extract |
| *Chicory* | *Cichorium intybus* | *Asteraceae* | Seed | Ethanolic extract |
| Amar Bel | *Cuscuta reflexa Roxb.* | *Convolvulaceae* | Stem and leaf | Ethanolic extract |
| Manjistha plant | *Rubia cordifolia* | *Rubiaceae* | Leaf | Ethanolic extract |
| Chorat | *Urtica diocia* | *Urticaceae* | Root | Leaf Ethanolic extract |
| *Devil's Cotton* | *Abroma augusta* | *Sterculiaceae* | Leaf | Petroleum ether |
| *Turmeric* | *Curcuma longa* | *Zingiberaceae* | Rhizome | Petroleum ether |
| *Lal chitrak* | *Plumbago rosea* | *Plumbaginaceae* | Leaf | Acetone extract |
| Ghikanvar | *Aloe barbadensis* | *Asphodelaceae* | Sap | Aqueous extract |
| *Indian* Mallow | *Abutilon indicum* | *Malpighiaceae* | Leaf | Aqueous methanolic extract |
| **Medicinal plants with anti-ovulatory activity** | | | | |
| Betel nut | *Areca catechu* | *Arecaceae* | Nut | Aqueous extract |
| Dhak ki-be | *Rivea hyopcrteriformis* | *Convolvulaceae* | Aerial parts | Aqueous extract |

isoshinanolone, trans-cinnamic acid, vanillic acid, beta-sitosterol, 4-hydrox-ybenzaldehyde, and plumbagic acid, glycosides and cardenolides, diterpine acid, resin, volatile oil which have shown anti-fertility activity. Few well-known families are *Fabaceae*, *Asteraceae*, *Euphorbiaceae*, *Apiaceae* and Labiateae [Table 1 and Figure 4].

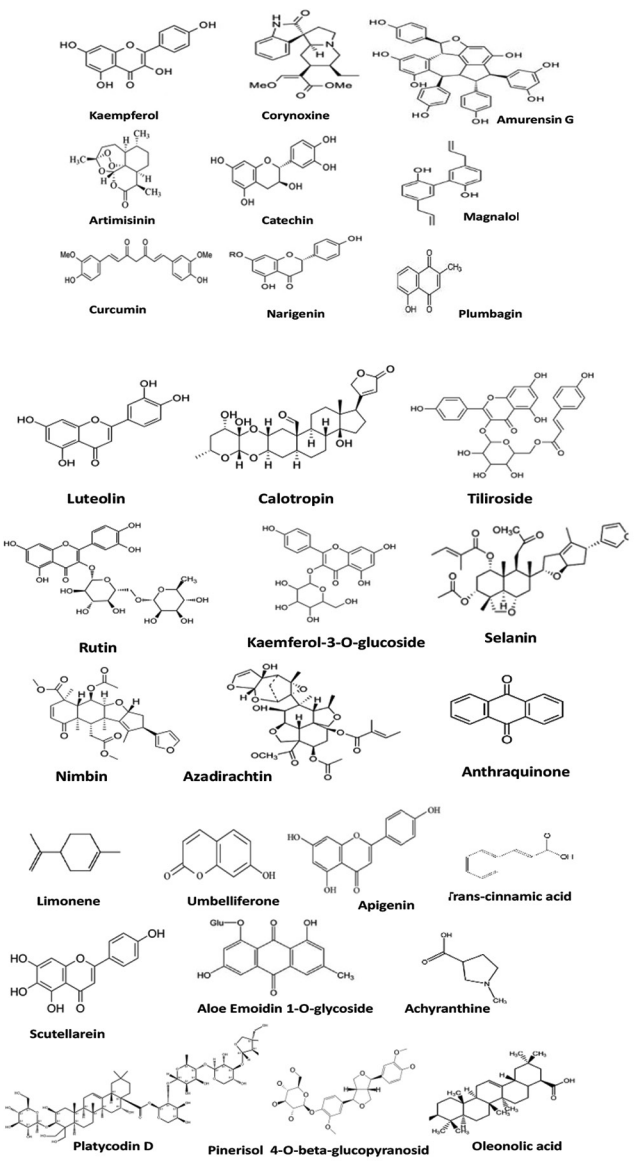


**Figure 4:** Important anti-fertility compounds isolated from various plant species

## REGULATION OF FEMALE FERTILITY

Contraception is one of the most important tools for controlling a rapidly expanding population. Women have a wide range of contraceptive options while men have limited options except for condoms and vasectomies. As a result, the responsibility for family planning falls on the woman. In recent years, there has been a lot of research into the feasibility of male hormonal contraceptives. Hormonal contraceptives also have effects on your ovaries, your cervical mucus, and your fallopian tubes. Progesterone and estrogen stimulation of your cervical mucus make it difficult for your sperm to enter your cervix. Continued use of OC makes endometrium a difficult environment for sperm to implant and stimulates further embryonic growth glandular atrophy and interstitial decidualization.[15]

## ORAL CONTRACEPTIVES

For contraception both progestogen (norethindrone, norethynodrel, ethynodiol diacetate, or norgestrel) and estrogen (ethinyl estradiol or mestranol) are prescribed in different amounts and activities. Women's bodies naturally contain both of these hormones. Estrogens and progestins come in a wide variety of forms, and various pharmaceutical companies sell pills with various combinations. Moreover, combination of steroid hormones causes intervention in reproductive function both centrally and peripherally. Ovulation is prevented by inhibiting the release of gonadotropin. These demonstrate follicular maturation impairment, and the primary mechanism of action of OCs is ultimately pituitary gonadotropin secretion inhibition.[15] Due to glandular atrophy and stromal decidualization brought on by prolonged OC use, the endometrium becomes unfavorable to implantation and subsequent embryonic development.[15] Use of oral contraceptives set a lower pregnancy rate of <0.2%/100 women after a year. However, combined oral pill was found the most effective form of contraception. Comparatively, sequential oral contraceptives should only be used by women who have amenorrhea because they are less effective and have more side effects [Table 1].

These medications function similarly. Women who take these oral contraceptives every day at roughly the same time of day only take mini pills, which contain progestin. When doses are missed frequently, oral contraceptives are not an effective method of birth control. Women who smoke and are over 35 should not take combination oral contraceptives because they have a higher risk of blood clots. They also come in grip of high blood pressure, high cholesterol, and face risk of CVDs, strokes, and migraines. These also might face bad consequences of breast cancer [Table 1].

Normally contraceptives are used to get rid of pregnancy and to regulate fertility, but these impose negative effects. In women, these give rise endometriosis, polycystic ovarian syndrome, acne, uterine fibroids, heavy or irregular periods, painful periods, and premenstrual syndromes. However, using oral contraceptives causes women to have altered atherogenic index, elevated serum lipids, abnormal liver function, and thromboembolism. The central nervous system is also altered by these. These raise the risk of elevated body weight, hypertension, and cerebral vascular accidents. Women experience severe phases of amenorrhea, oligomenorrhea, and hypertension, myomata of the uterus, depression, and epilipsy. Hyperlipidemia, gestational diabetes, liver disease, and coronary artery disease are all brought on by oral contraceptive therapy [Table 1].

## ANTI-OVULATION ACTIVITY

Natural plant products show anti-fertility properties in animal models, they effectively prevent ovulation and

interfere with the estrous cycle.[16] These anti-fertility agents derived from plants also affect females, inhibiting ovulation, implantation of eggs, destroying zygotes, and inducing abortions. It inhibits testosterone, stops spermatogenesis in men, and has an impact on organ gonadotrophin or sperm mortality. Furthermore, indomethacin demonstrated anti-implantation properties. A small number of nonsteroidal anti-inflammatory medications are also used to prevent female reproduction.[17] Many of these therapeutic plants regulate reproduction by acting through an anti-zygotic mechanism.[8] In rats, spermicidal activity from *Hibiscus rosa-sinensis* flower extract slowed down spermatogenesis and the activity of accessory reproductive organs.[18] In Sprague-Dawley rats, an alcoholic extract of neem flower disturbed the estrous cycle and partially blocked ovulation [Table 2].[19]

In addition to being utilized for nutrition, the following plant species have anti-fertility properties: *Polygonum hydropiper* Linn, *Citrus limonum*, *Piper nigrum* Linn, *Juniperis communis*, *Achyranthes aspera*, *Azadirachta indica*, *Tinospora cordifolia*, and *Barleria prionitis. P. hydropiper* Linn (family *Polygonaceae*) leaves contain acetic acid, beldianic acid, tannin, essential oil, and oxymethyl-anthraquinones which primarily exhibit antiovulatory effects when it comes to antifertility. In experimental animals, its root extracts successfully prevent ovulation.[13] Piper betel (PB) Linn leaf extracts, both aqueous and methanolic, have an impact on the estrous cycle of female albino rats.[20] The antiestrogenic properties of PB leaves may be attributed to their flavonoid and saponin contents.[20] Flowers of the *H. rosa-senensis* plant have been shown to have similar antiovulatory effects. It also affects the male rat's estrous cycle and reproductive organs.[21,22] It causes a prolonged menstrual cycle and irregular estrous cycle.[23] *H. rosa-senensis* significantly reduces estrogen activity and has a strong contraceptive effect in female rats.[23] More precisely, its low dose causes human female menustration to be stimulated, but an overdose causes the pregnancy to end (abortion).[24] It also significantly cut down plasma progesterone levels.[25,26] In addition, *H. rosa-senensis* is used to help with childbirth, lessen menstrual cramps, and relieve fever, inflammation, and headaches.[27] In North-east Indian states, *H. rosa-senensis* flowers may be used as a contraceptive method for family planning and birth control [Tables 2 and 3].[28] Its floral benzene extract prevents mouse implantation.[29]

Mice treated with benzene extract from *H. rosa-senensis* flowers showed anti-estrogenic properties. While ethanolic root extract exhibits estrogenic and anti-fertility properties.[28,30] In addition, it reduced the number of epididymal sperm and testis spermatogenic elements.[22] It dramatically reduced the production of sperm and increased the infertility of male rats [Table 1].[26,31] Certain plants function as abortive agents, including *H. reptans*, *A. nidus*, *D. gaudichaudianum*, *O. nutans*, and *P. acidula*.[7]

The active ingredients of *Bougainvillea spectabilis* (Family: *Nyctaginaceae*) include pinitol, quercetagetin, quercetin, and terpinolene.[32] Its decoction and aqueous extract exhibit anti-fertility properties.[32] Similar to this, male albino rats treated with an ethanolic extract of *Salsola imbricata* Forsk exhibit contraceptive effects. Polyphenols, specifically flavonoids and phenolic acids, quercitrin (12.692%) and coumaric acid (4.251%), are present in it [Figure 1]. This is true that prolonged oral administration of this medication results in a slight reduction in testis weight but a significant decrease in sperm count [Tables 2 and 3].[33]

Fruit extracts from *Terminalia chebula* (Contracept-TM) significantly reduced spermiological activity in aqueous extracts. According to Ghosh *et al*. (2017), its polyherbal formulation might be more effective at causing hypo-testicular activity.[34] Similarly, PD is a saponin that is derived from *Platycodon grandiflorum*.[35] It exhibits spermicidal and contraceptive activity. It damages sperm's head and separates tail membranes. In female rat, it stops fertility without imposing negative effects on rat vaginal tissue.[35]

*Jatropha verigata* (*Euphorbiaceae*) is a shrub; its fruits are traditionally used for birth control by local women. Its fruit methanol extracts exhibit estrogenic activity and successfully prevent embryo implantation.[36] Plants such as *Mondia whitei, Acalypha villicaulis*, *Combretum illairii*, *Erythrina abyssinica, Pappea capensis, Rhus vulgaris*, and *Warburgia ugandensis* are the most commonly used, while the most commonly used organs for making decoctions (69%), are roots (44.9%), leaves (21.8%), stem and root barks (16.7%) of shrubs (35%), trees (31%), herbs (26%), and climbers (8%). Among the plants that help raise testosterone levels and produce pro-sexual stimulatory effects in male rats are *Citropsis articulata*, *Cola acuminata, Ekebergia capensis*, *Plumbago zeylanica*, *Tarenna graveolens, Urtica massaica,* and *Zingiber officinale* [Table 2].[37]

## ANTI-IMPLANTATION ACTIVITY

Numerous plant species, such as *Cordia dichotoma* and *Trianthema portulacastrum*, *Talinum paniculatum* Nurvela Crataera, *The* odoratissimus artbotrys*, Oxalis corniculata, Guiancensis Couroupta*, *Oleracea portulaca*, *The Leptadenia reticulata,* aromatic *Curcuma, Caesalpinia bonduc* Simplex justice *Derris Brevipes, Cassia fistula, Astragalus* cinerea*, Ziziphus mucronata Fadogia ancylantha*, *Adhatoda vasica* Nees, *A. aspera L., Abroma angusta (L) L.f. Gossipium herbacium* L., *Carica papaya* L., *Daucus carota* L., The vulgaris artemisia *Cichorium intybus, Striga orobanchioides, Rubia cordifolia*, Roxb.; *Cuscuta reflexa, Urtica diocia, Curcuma longa, Aloe barbadensis*, *Abutilon indicum*, and *Plumbago rosea*. These plants have active components that prevent fertilized eggs from adhering to the uterine endometrium and show anti-implantation activity.

**Table 3:** Medicinal plants showing abortifacient activity

| Common name | Scientific name | Family | Plant part used | Treatment/dose |
|---|---|---|---|---|
| Phalsa | *Grewia asiatica* L. | *Tiliaceae* | Seeds | Fresh extract |
| Champa | *Michelia Champaca* L. | *Magnoliaceae* | Bark | Infusions are taken |
| Reetha | *Sapindus trifoliatus* auct.non L. | *Sapindaceae* | Pulp, seeds | Fresh extract |
| Dhaitee | *Woodfordia fruticosa* (L) Kurz. | *Lythraceae* | Flowers | Infusions are taken |
| | *Moringa oleifera* | | Ethanol extract | Oral treatment |
| Persian hogweed | *Heracleum persicum* | *Umbelliferae* | Extracts *improve sperm motility* | Infusions are taken orally |
| Sathra | *Origanum vulgare* | *Lamiaceae* | *Essential oil reduced sperm mobility* | Infusions are taken orally |
| Satar | *Zataria multiflora* Boiss | *Lamiaceae* | *Essential oil reduced sperm mobility* | Oral treatment |
| sesame | *Sesamum indicum* | *Pedaliaceae* | Hot water extract | Oral treatment |
| Guggul or Indian Myrrh | *Commiphora myrrha* Human (clinical trial) | *Burseraceae* | Gum resin | Aqueous Extract |
| *Mountain tea* | *Stachys lavanduliflora* Lamiaceae | *Lamiaceae* | Powdered fruits | Aqueous Extract |
| Lahouri Harmal | *Peganum harmala* Mice | *Nitrariaceae* | seeds | Aqueous Extract |
| Sadab | *Ruta graveolens* L. | *Rutaceae* | powder from root | Edible extract |
| Saffron | *Crocus sativus* | *Iridaceae* | Buds | Edible aqueous extract |
| *Galbanum* | *Opoponax ferula galbanifulas* | *Apiaceae* | Leaves | Fresh juice |
| Hina | *Lawsonia inermis* | Lythraceae | Leaf | Aqueous-alcoholic Extract |
| Indian leadwort | *Plumbago rosea* | Plumbaginaceae | Root | Alcoholic extract |
| Savin juniper | *Juniperus sabina* L. | Cupressaceae | *the leaves and seeds* | Edible aqueous extract |
| Chamomile | *Matricaria chamomilla* L. | Asteraceae | Aqueous-alcoholic Extract | Abortive |
| Neem | Azadirachta indica A Juss | *Meliaceae* | Leaf/bark | Aqueous extract |
| Danti | *Jatropha curcas* | *Euphorbiaceae* | Fruit | Aqueous extract |
| Papita | *Carica papya* Linn | *Caricaceae* | Leaf/roots/bark | |
| Sausage Tree | *Kigelia Africana* (Lam.) Benth | Bignoniaceae | Bark/root | Aqueous extract |
| Tulsi or Basil | *Ocimum viride* Willd | Labiateae | Leaf | Aqueous extract |
| hog plum or amra | *Spondias mombin* Linn | *Anacardiaceae* | Leaf | Infusions are taken orally |
| *Ashanti pepper* | *Piper guineensis* Schum. and Thonn. | *Piperaceae* | Leaf/seed | Infusions are taken orally |
| Indian tree of heaven | *Ailanthus excels* | *Simaroubaceae* | Stem bark | Aqueous extract |
| Hopbush | *Dodonaea viscosa* | *Sapindaceae* | Aerial parts | Infusions are taken orally |
| Aagadha | *Achyranthes aspera* | *Amarnthaceae* | Root | Aqueous extract |
| Betel nut | *Areca catechu* | *Arecaeceae* | Nut | Aqueous extract |
| Pursley | *Portulaca oleracea* | *Portulaceae* | Aerial parts | Aqueous extract |
| Desert Horse Purslane | *Trianthema portulacastrum* | *Aizoaceae* | Stem leaf | Infusions are taken orally |
| Common rue | *Ruta graveolens* | *Rutaceae* | Aerial parts | Aqueous extract |
| Calliandra | *Derris brevipes* | *Papillionaceae* | Root | Infusions are taken orally |

**Table 3: *(Continued)***

| Common name | Scientific name | Family | Plant part used | Treatment/dose |
|---|---|---|---|---|
| Ashoka | *Saraca indica* | *Caesalpiniaceae* | Leaf and seed | *contraceptive, anti-fertility*, |
| Lodhra | *Symplocos racemosa* | *Symplocaceae* | Seed | *Antifertility* and contraceptive efficac |
| *Arjun* | *Terminalia arjuna* | *Combretaceae* | Bark | *Fresh extract* |
| Nut grass | *Cyperus rotundus* | *Cyperaceae* | Leaf | *Suppression* of cauda epididymis sperm count |
| Karingali | *Acacia catechu* (L.f.) Willd. | (*Fabaceae*) | Bark juice | *Antifertility* activity |
| Kannara | *Ananas comosus* (L.) Merr. | (*Bromeliaceae*) | Ripened fruit | Induce abortion |
| Seetha pazham | *Annona reticulata* L. | (*Annonaceae*) | Seed paste is given orally on empty stomach | Induce abortion |
| Rajamally | *Caesalpinia pulcherrima* (L.) Sw | (*Fabaceae*) | Bark juice (2 mL) | Orally on empty stomach |
| Kappalam | *Carica papaya* L. | *(Caricaceae*) | Raw fruit *the leaves and seeds* | Induce abortion |
| Kattumuthir | *Dolichos trilobus* L. | (*Fabaceae*) | Whole plant juice | |
| Pavakka | *Momordica charantia* L. | (*Cucurbitaceae*) | Raw Fruit juice | Orally twice a day |
| Koduveli | *Plumbago zeylanica* L. abortion. | (*Plumbaginaceae*) | 3–5 mL of root paste is taken orally | Root paste with warm water |
| Ramachempu | *Rhynchosia rufescens* (Willd.) DC. | (*Fabaceae*) | Leaf decoction | Two teaspoon in a day |
| Ana chunda | *Solanum torvum* Sw | (*Solanaceae*) | Leaf extract | Orally for 5 days. |
| Kunch Seed | *Abrus precatorius* | (*Fabaceae*) | Fresh seed powder | Fresh seed powder mixed with glass of luke warm water |
| Apang | *Achyranthus aspera* Linn | (*Amaranthaceae*) | Fresh root | Extract in luke warm water |
| Chaya | *Aerva lanata linn* | (*Amaranthaceae*) | Fresh root extract | terminating pregnancy |
| Jalsachi ara | *Alternanthera philoxeroides* | *Amaranthaceae* | Fresh pieces of whole plant | used to induce abortion |
| Nilappana | *Curculigo orchioides* Gaertn | *Hypoxidaceae* | Tuber paste of the tuber | Orally in empty stomach |
| Nona | *Annona reticulate* Linn Seeds | *Annonaceae* | Seed powder | Orally in empty stomach |
| Anaras Leaves | *Ananas cosmosus* Linn | *Bromeliacea* | leaves paste with black pepper seed powder | Orally in empty stomach |
| Iswarmul | *Aristolochia indica* Linn | *Aristolochiaaceae* | Fresh root | Aqueous mixture intake orally |
| Peyara ban Leaf | *Avicennia marina* | *Avicenniaceae* | Leaf | Extract is mixed with glass of luke warm goat milk and sugar |
| Krishna chura | *Caesalpinia pulcherrima* | *Caesalpiniaceae* | Dried leaf infusion | Empty stomach induce abortion. |
| Baramanda Stem | *Dendrophthoe falcate* Linn | *Loranthaceae* | Fresh stem and black pepper seeds paste | This paste is given in early morning in empty stomach |
| Ulat chandal | *Gloriosa superb* Linn | *Liliaceae* | Fresh roots | Fresh roots are used in paste along with black pepper seeds |

*(Contd...)*

**Table 3: *(Continued)***

| Common name | Scientific name | Family | Plant part used | Treatment/dose |
|---|---|---|---|---|
| *Gurhal* | *Hibiscus rosa sinensis* Linn | *Malvaceae* | Jaba Root bark Inner portion | Root bark is used into paste along with seeds of black pepper |
| *Lahsun* | *Allium sativum* Linn. | *Alliaceae* | Whole plant | Oral intake of pills |
| Bhela | *Semecarpus anacardium* Linn | *Anacardiaceae* | Root bark | Powder with fresh water |
| Ahnad ne muka | *Stephania japonica* | *Mensispermaceae* | Root Fresh | Root paste with water |
| Chakulia Plant | *Uraria lagopodioides* | *Fabaceae* | Leaf | Aqueous mixture intake orally |

Ethanolic root extract of *Asparagus africanus*[38] and *Calotropis gigantea showed* in strong anti- implantation activity in female rats.[39,40] This activity may be due to presence of active principles of glycosides, cardenolides, and calotropin. Similarly quercetin-7-O-galacto- side, polyphenolic compounds, kaempferol, and scutellarein found in *H. rosa-senensis* flowers exhibited strong anti-implantation and uterotropic activity in rats at a dose level of 400 mg/kg.[41] Similar activity is reported in *H. rosa-senensis* in benzene extract-related that imposes 80% lowering in implantation on the 10$^{th}$ day of pregnancy.[42] Similarly, *Andrographis paniculata* (Burm. f.) Wall. ex Nees: Possess contraceptive activity due to presence of ent-labdane diterpenoids, 30 flavonoids, eight quinic acids, four xanthones, and five rare noriridoids [Tables 2 and 3].[11]

According to Noh *et al*., Astragalus mongholicus extract and Angelica keiskei powder demonstrated anti-infertility effects in males and females, respectively.[42] However, it has acute toxicity and negative effects. Male and female fertility was reduced by tripterygium glycoside (Noh *et al*., 2020).[10] One of the plants that is widely used for its anti-fertility essential oil is Chromolaena odorata, also known as ylang-ylang (Cananga odorata Hook. F. and Thomson) [Tables 2 and 3].[43]

In female mice, an alcoholic extract from the flowers of Butea monosperma (Lam.) Taub exhibits potential antifertility.[44,45] At a dose of 300 mg/kg, its hot alcohol extract demonstrated anti-implantation.[46] Similarly, in test animals, an aqueous extract of Ocimum sanctum leaves demonstrated antizygotic, anti-implantation, and early abortifacient properties.[47] In male albino rabbits, it also dramatically reduced the number of sperm and reproductive hormones.[48] Ocimum sanctum leaves inhibit spermatogenesis in males by delaying the activity of sertoli cells.[49] Ursolic acid, which is present in Tulsi leaves, has been shown to have anti-fertility properties.[50] It also exhibits anti-estrogenic activity, stops male spermatogenesis, and inhibits female ovum implantation [Table 2].[49]

Anti-implantation activity has been reported for S. orobanchioides, Ricinus communis (80 mg/kg), fruits of Punica granatum (1.82 mg/kg), roots of Calotropis procera (30 mg/kg), roots of P. hydropiper (150 mg/kg), leaves of Mentha arvensis (100 mg/kg), Lawsonia inermis (134 mg/kg), seeds of Juniperus communis (200 mg/kg), roots of Hagenia abyssinica (120 mg/kg), seeds of Crotalaria juncea (300 mg/kg), and roots of Cicer arietinum (1900 mg/kg).

A. aspera Linn has been shown to exhibit comparable anti-fertility activity in fertile female albino rats when given an oral dose of 200 mg/kg.[30,51]

The active ingredients found in *C. limonum* (*Rutaceae*) include limonoid glycosides, limonene, geranial, neral, ichangin 4-beta-glucopyranoside, nomilinic acid, and limonene. Its seeds cause female albino mice to become less fertile.[52] Similarly, *Achyranthes aspera* L methanolic extract inhibited implantation in male rats primarily through antiestrogen, progesterogen, and uterotonic effects.[52] In female albino rats, PB has an antifertility effect.[17] *Mentha longifolia* L (ML) is used as a natural form of birth control. According to David *et al*., it results in a decline in adult male spermatogonial populations, mature spermatids, seminiferous tubule diameter, and lumen diameter.[53] Male mice from *A. indica*, *C. longa*, *Allamanda cathartica*, and *Bacopa monnieri* have also been shown to exhibit similar behavior[54] According to D'Cruz *et al*. these plant- and plant-based products demonstrated antispermatogenic and/or antisteroidogenic qualities.[55] They also had negative effects on a variety of target cells in the testis [Tables 2 and 3].

## ABORTIFACIENT ACTIVITY

Abortifacient substances are those which are used to terminate a premature pregnancy or assist in abortion. More precisely, a lot of herbal abortifacients pose a risk to the woman's health when used by women to end pregnancies. When taken orally, the active ingredients in following plant species cause abortions when taken at least 100 mg/kg of body weight [Table 2]. *Grewia asiatica* L., *Michelia Champaca* L, *Moringa oleifera*, *Origanum vulgare*, *Gloriosa superb* Linn, *H. rosa-senensis* Linn, *Allium sativum* Linn, *Semecarpus anacardium* Linn, *Stephania japonica*, *Uraria lagopodioides*, *Dendrophthoe falcate* Linn, *Caesalpinia*

*pulcherrima*, *Avicennia marina*, *Aristolochia indica* Linn, *Ananas cosmosus* Linn, *Annona reticulate* Linn Seeds, *Curculigo orchioides* Gaertn, *Alternanthera philoxeroides*, *Aerva lanata* linn, *A. aspera* linn, *Abrus precatorius*, *Stachys lavanduliflora Lamiaceae*, *Commiphora myrrha*, *Crocus sativu L. inermis Sesamum indicum*, *A. indica* A Juss, *A. aspera*. Flowers from *H. rosa-senensis* are also used to induce abortions in rats.[23] An overdose of it can also result in an abortion. The active ingredients in the leaves of *Spondias mombin* (*Anacardiaceae*) are flavonoids, quercetin, ellagic acid, and rutin, which have anti-fertility properties. According to Chukwuka and Uchendu a leaf extracts from *S. mombin* exhibits anticonceptive, abortifacient, and estrogenic properties.[56] Methotrexate is a synthetic drug used in abortion, but it can harm the mother's liver and kidneys, so it should be used with caution [Table 3].[57,58]

## INTERFERENCE AND SIDE EFFECTS IN ENDOCRINE SYSTEM

Most hormonal drugs prescribed for abortion interfere with the endocrine system and have negative effects on reproductive, neurological, developmental physiology, and metabolism in the body. These side effects occur in the form of polycystic ovarian disease, endometriosis, early puberty, and gonadal toxicity. These cause testicular germ cell necrosis and prostate cancer in men and breast cancer in women. These can also lead to birth defects.[2] The contraceptive effect is exerted primarily by inhibiting ovulation and secondly by changes in the cervical mucus, endometrial glands, ovaries, fallopian tubes, and uterine muscles. There are three categories of oral contraceptives; the first category affects the main target organs of the female reproductive tract (ovaries, myometrium, endometrium, cervix, vagina, breasts, and hypothalamus). These changes include temporary interstitial fibrosis in the ovaries, enlargement of fibromyomas, intermenstrual bleeding or amenorrhea, increased amount of cervical mucus, polypoid hyperplasia of the endocervical glands, breast tenderness, and changes in breastfeeding. They also affect general metabolism (serum protein, carbohydrate metabolism, lipid metabolism, water and electrolyte metabolism, body weight, tryptophan metabolism, vitamins, and minerals).

The second category affects the endocrine organs, while the third category affects the rest of the body, mainly organ systems (liver, central nervous system, skin, genitourinary tract, gastrointestinal tract, eyes, immune phenomena, and subsequent effects on fertilit).[59] They also affect the adrenal glands, hypothalamus, thyroid (increased thyroid-binding globulin), and pancreas (changes in glucose metabolism). Endogenous testosterone levels in humans vary depending on the season. Remarkably, normal cycling women have normal testosterone concentrations, with above-minimum levels in summer and above-maximum levels in winter.[60]

In Ayurvedic classical texts, large numbers of plant based preparations are available which are used to enhance and limit male and female fertility. These products showed antispermatogenic and/or antisteroidogenic properties and mainly target sperm-producing cells inside testis.[55] 300 mg St John's wort extract given twice daily (cycle A) or 3 times daily (cycle B) affect follicle maturation and serum oestradiol and progesterone concentrations. It results in intracyclic bleeding episodes.[61]

## REGULATION OF MALE FERTILITY

There are two important targeting points in male gamete production, if these are blocked the male fertility can be challenged. This proposed contraceptive method focused on suppressing spermatogenesis by exploiting the hypothalamic-pituitary-gonadal axis.[62] Few non-hormonal methods, such as compounds targeting sperm motility, theoretically guarantee specificity to the reproductive tract. Gene and protein array technologies continue to identify potential targets for this approach. There are two types of contraceptive methods used: Hormonal and non-hormonal.[63] First, it targets structural components of the testis, as well as enzymes, ion channels, and other proteins unique to sperm.[63] Such nonhormonal agents might be more effective, reversible, male contraceptive an option for family planning [Figure 2].[64]

## INHIBITION OF SPERMATOGENESIS

In the seminiferous tubules of the testes, a phase of cellular proliferation known as spermatogenesis occurs. Temperature, androgens, and gonadotrophins are the main factors that control it. The inhibition of gonadotropin secretion is how these steroid hormones impact spermatogenesis. Spermatogenesis is blocked by its synthetic anabolics. Additionally, a combination of gonadotropins and androgens inhibits the functions of the testicles. Nearly all anti-spermatogenic substances work by preventing spermatocyte growth, preventing spermatozoa from forming, maturing, and moving, and inhibiting mitosis through damage to Sertoli cells. All of these non-steroidal drugs have an impact on the maturation of the epididyma and impede both spermatogenesis and steroidogenesis. All of these non-steroidal spermatogenesis inhibitors; however, were discovered to be toxic. Certain chemicals inhibit the vigorous physical activity known as epididymal sperm motility, which is essential for fertilization through the vas deferens into the female vagina. For centuries, vaginal spermatozoa have been the focus of contraceptive research. Spermicides and immobilizers render sperm inactive as soon as they are deposited in the vagina, but they also increase the risk of infection [Table 4 and Figure 2].[65]

**Table 4:** Plants with anti-fertility and anti-spermatogenic effects

| Common name | Scientific name | Family | Plant part used | Use and effects |
|---|---|---|---|---|
| Behada | *Terminalia bellirica* | Alcoholic extracts | Intramuscular injections | Antifertility effect |
| *Bitterwood* | *Quassia amara* | Chloroform extracts | Intramuscular injections | Single daily intramuscular injections |
| Chota chirayata | *Enicostemma axillare* | Ethanolic extract | Intramuscular injections | Antispermatogenic |
| *White's ginger* | *Mondia whitei* Linn | Ethanolic extract | Intramuscular injections | Antispermatogenic |
| Haldi | *Curcuma longa* Linn | Alcoholic extract | Intramuscular injections | Antispermatogenic |
| Gulugunji | *Abrus precatorius* Linn | methanolic extract | Intramuscular injections | Antifertility |
| Bel | *Aegle marmelos* | Ethanolic extract | Intramuscular injections | Antifertility effect |
| Siris | *Albizzia lebbeck* | Methanolic extract | Intramuscular injections | Antifertility effect |
| *Brahmi* | *Bacopa monnieri* | Dry powder | Oral infusion | Antispermatogenic |
| *Marijuana,* | *Cannabis sativa* | Alcoholic extract | Intramuscular injections | Antispermatogenic |
| *Bara manda* | *Dendrophthoe falcata* | methanolic extract | Intramuscular injections | Antispermatogenic |
| *Swertia chirayita* | *Fadogia agrestis* | Aqueous extract | Intramuscular injections | Adverse effects on male rat testicular function |
| *Aaraar* | *Juniperus phoenica* | Ethanolic extract | Intraperitoneal injections of | Antifertility activity |
| *Akamongot* | *Leptadenia hastata* | Aqueous extract | Intramuscular injections | Antispermatogenic activity |
| Tulsi | *Ocimum sanctum* | Benzene extract | Intramuscular injections | Antifertility |
| *bitter-wood,* | *Quassia amara* | Chloroform extracts | Intramuscular injections | Antifertility effect |
| *Laung or clove* | *Syzygium aromaticum* | Hexane extract | Intramuscular injections | Degenerative changes in the seminiferous tubules |

## ANTISPERMATOGENIC ACTIVITY

*Annua martynia* Linn (*Martyniaceae*) fruits and seeds demonstrated anti-fertility effects when administered daily for 60 days at a dose of 200 mg/kg of aqueous. Spermatogenesis was stopped, and semi-niferous tubules have shrunk in size. In male rats, spermatocytes eventually degenerated at pachytene.[66] As active components, juniperin, volatile oil, glycosides, formic acid, acetic acid, diterpine acid, resin, and tannins are present in *J. communis* (*Cupressaceae*).[67] Plant exhibits anti-fertility and antiprostaglandin properties. *A. paniculata* is known to exhibit similar behavior, stopping the spermatogenesis of male albino rats. A good male contraceptive, andrographolide, is present in plants. Chlorohydrin a Alpha-chlorohydrin used orally results in anti-fertility, which is reversed upon withdrawal of the substance. Alpha-chlorhydrin dosages of high concentration display nephrotoxic and neurotoxic effects.[68] Furthermore, male rats administered *Quassia amara* extract showed an increase in the anterior pituitary gland and a decrease in the weight of the seminal vesicle, epididymis, and testis. *Quassia amara* plant extracts lower serum testosterone levels, luteinizing hormones (LH), follicle-stimulating hormones, and epididymal sperm counts [Table 4 and Figure 2].[69]

A few significant active ingredients have been extracted from *P. nigrum* Linn (*Piperaceae*) fruits, including thujon, piperettine, piperolin A, piperolin B, terpene, volatile oil, starch, piperine, calcium, phosphorus, iron, thiamine, riboflavin, nicotinic acid, Vitamin C, carotene, and piperidine. Together, these demonstrated the antispermatogenic and antifertility effects of oral doses of 25 mg/kg/d and 100 mg/kg/d for 20 and 90 days, respectively, in rats.[70] The seeds and leaves of *A. indica*, a member of the *Meliaceae* family, have active ingredients that include margosic acid, azadirachtin, polysaccharides, nimbine, nimbidinate, nimbidol, oil, and nimbidin.[71] In male rats, its oil exhibits anti-fertility primarily through spermicidal activity at a dose of 10 mg per day for a duration of 30 days.[72] Spermatogenesis is stopped by a 50% ethanol extract of *A. indica* applied subcutaneously for 30 days [Table 4].[72,73]

Worldwide, women can be freed from the burden of childbearing using the male contraceptive plant *R. communis* Linn.[74] This substance has strong anti-spermatogenic and anti-motility effects. Up to 6 weeks following treatment, spermatogenesis and sperm motility were inhibited by its seed extract. However, after 7 weeks of treatment, semen parameters returned to normal levels, indicating the presence of primary spermatocytes and spermatids in the seminiferous tubules.[74] *Enicostemma axillare*, *M. whitei* Linn, *C. longa* Linn, *Cannabis sativa*, *D. falcate*, *Leptadenia hastate*, and *P. zeylanica* roots and leaves have all been shown to exhibit presence of active principles are plumbagin, isoshinanolone, trans-cinnamic acid, vanillic acid, beta-sitosterol, 4-hydroxybenzaldehyde, and plumbagic acid. These effectively caused a reduction in immature and mature Leydig cells

at a dose of dose of 159 mg/kg extract that results in anti-fertility activity[75] It has decreased seminiferous tubules diameters and inhibited formation of spermatocytes and spermatids production. Multiglycoside extract of the plant *Tripterygium wilfordii* caused reductions in sperm motility and concentration in patients [Table 5].[76]

A diterpene triepoxide, triptolide functions as a post-testicular male contraceptive drug. It affects the pathophysiology of epididymal sperm and inhibits spermatogenesis and fertility. Both mature and maturing germ cells are impacted. It impairs spermatogenesis and has an impact on the viability of epididymal sperm.[49] It results in head-tail separation, early chromatin decondensation of sperm nuclei, total absence of the plasma membrane in the middle and major portions, disarray of the mitochondrial sheath, and aggregation of numerous sperm tails, among other structural abnormalities in sperm. The impacted seminiferous tubules displayed tubular atrophy, multinucleated giant cells, intraepithelial vacuoles of different sizes, and germ cell exfoliation.[49] In a similar vein, an antimicrobial substance exhibits spermicidal effects in the female reproductive tract without causing any harm. It prevents unintended pregnancies and STIs (sexually transmitted infections) when applied topically to the vagina [Table 4].[77]

## INHIBITION OF STEROIDOGENESIS

### Use of Antigonadotropin Steroids

The contraceptive effectiveness of testosterone drug-induced azoospermia and oligozoospermia, as well as combinations of androgen and gonadotropin-releasing hormone analogs, are examples of hormonal methods [Figure 3]. Antigonadotropin steroids prevent the release of gonadotropins, particularly LH, which in turn prevents spermatogenesis. Even though steroids and androgens contribute to the biosynthesis of testosterone, when taken in large enough quantities, they promote spermatogenesis. For male contraception, certain endogenous antispermatogenic substances are also utilized. These substances regulate germ cells; LH is the main inducer of testosterone secretion by Leydig cells, which are located between seminiferous tubules and Leydig cells.[78]

These cells may respond differently to LH depending on the direct effects of androgens and estrogens. In addition, men use reversible hormonal contraceptives, primarily gonadotropin inhibitors. According to Swerdloff *et al*.,[79] it is based on observations that men who are hypophysectomized and hypogonadotropicor men who lack LH and follicle-stimulating

**Table 5:** Medicinal plants with estrogenic activity

| Common name | Scientific name | Family | Plant part used | Use and effects |
|---|---|---|---|---|
| Desert date | *Balanites roxburghii* | *Zygophyllaceae* | Fruit | Antifertility activity |
| Lasura | *Cordia dichotoma* | *Boraginaceae* | Bark | antifertility effect |
| Jiwanti/Dodi | *Leptadenia reticulata* | *Asclepiadaceae* | Whole plant | antifertility effect |
| fenzl | *Momodica cymbalaria* | *Cucurbiatceae* | Root | *direct toxic to seminiferous tubules* |
| Callindra | *Derris brevipes* | *Papillionaceae* | Root | Powder or infusion taken orally |
| Ambushi | *Oxalis corniculata* | *Oxalidaceae* | Whole plant | *Antifertility* activity |
| *Ghritkumari* | *Aloe buttneri* | Liliaceae | Leaves | Stimulated uterine growth, increased ovarian weight |
| Patera | *Dicliptera verticillata* | *Acantahceae* | Leaves | Increased ovarian and uterine levels |
| *Gandarusa* | *Justicia insularis* | *Acanthaceae* | Leaves | Increased serum estradiol levels and decreased ovarian cholesterol |
| *Roselle* | *Hibiscus macranthus* | *Malvaceae* | Stem leaves | Stimulated uterine growth and vaginal epithelial proliferation. |
| *Indian Coral Tree* | *Erythrina lysistemon* | *Fabaceae* | Stem barks | Slightly stimulated uterine growth. |
| *Millettia* | *Millettia conrauii* | *Leguminoseae* | Stem barks Ethyl acetate extract | Increased uterine and vaginal epithelial |
| *Yoruba* | *Millettia drastica* | *Leguminoseae* | Stem barks Ethyl acetate extract | *Menopausal disorders* |
| *straggly tree* | *Bridellia ferruginea* | *Leguminoseae* | Leaves methanolic extract | Male anti-fertility |
| Lal Gurhal | *Hibiscus macranthus* | *Malvaceae* | Stem leaves | Male sexual fertility problems |
| Rorowo | *Senecio biafrae* | *Asteraceae* | Leaves Aqueous | Puberty onset and stimulation of folliculogenesis |
| *Indian Nettle* | *Acalypha indica* Linn | *Euphorbiaceae* | Ethanolic extract | Estrogenic activity |

hormone (FSH) are aznoospermic. Steroid hormones inhibit the production of spermatozoa and gonadotropin, which in turn inhibit testicular function.[79] Androgens affect the peritubular cells' ability to differentiate and contract. Before puberty, FSH is the main stimulant for Sertoli cell secretory function; however, androgens work in concert with FSH. Androgens by themselves are able to keep Sertoli cells functioning at their best after puberty [Figure 3].

Spermatogenesis is maintained by sertoli cells that are activated by androgens.[80] Consequently, gonadotropin deficiency is necessary to maintain male infertility. Therefore, infertility and disruption of testicular function arise from the pituitary's inability to secrete LH and FSH.[80] However, selective alteration of epididymal function by local androgen deprivation is necessary for the male to induce functional sterility. These substances reduce the motility of ejaculated spermatozoa and partially inhibit spermatogenesis.[81] Male fertility is dependent on normal plasma levels of LH, FSH, prolactin, testosterone (T), and 17-beta-estradiol (E2). Most azoospermic patients are infertile men, who have low levels of these hormones.[82] Testosterone ester androgen injections inhibit spermatogenesis; sperm counts decrease as treatment levels rise in relation to concentrations [Table 5 and Figure 3].[83]

## INTERFERENCE WITH SPERM MATURATION IN THE EPIDIDYMIS

Numerous chemical substances have been investigated for their ability to inhibit spermatogenesis and regulate male fertility in humans.[84] These progestational substances lower libido by interfering with the hypothalamo-hypophysial system, which inhibits spermatogenesis. It is necessary to investigate the possibility of modifying the minimal dosage of progestational compounds needed to cause spermatogenesis to be suppressed and plasma testosterone levels to be lowered to a level that is compatible with maintaining libido and potency at normal levels. In a novel approach to male contraception, progestational compounds are used to suppress spermatogenesis, while intramuscular injections of testosterone, or silastic capsule implants, are used to maintain libido and accessory sex gland function. Thus, control of male fertility can be greatly enhanced by selectively suppressing the synthesis and release of FSH by administering "Inhibin," or by selectively interfering with the action of FSH on the Sertoli cells through active or passive immunization. Men from different ethnic backgrounds have varying levels of contraceptive steroid efficacy. In addition, it is important to keep an eye on the acceptability and safety of hormonal treatments for men [Figure 3].[85]

There are currently improved and novel methods for stimulating and inhibiting the hypothalamic-pituitary-testicular axis is available. These impose azoospermia and severe oligozoo/azoospermia using a combination of GnRH antagonists and replacement doses of testosterone. In over 90% of Asian men, androgens and androgen-progestogen concentrations will cause azoospermia; in Caucasian ethnic groups, however, they will cause either severe oligospermia or azoospermia. To find out if giving women testosterone will be a more effective form of contraception than using condoms, field trials are currently underway. With GnRH analogs, gonadotropin secretion can be suppressed more successfully than in the past, resulting in true precocious puberty.

## ANTI-SPERM ANTIBODIES IN INFERTILITY

For contraceptive purposes, antisperm antibodies are also used.[86] The production of these anti-sperm antibodies is stimulated by the vaginal mucosal secretions. This immunological infertility can impose normozoospermia.[87] It is necessary to work on developing an immunocontraceptive vaccine for Arvicola terrestris scherman, which has been tested as a long-term substitute for chemical contraceptives.[88] It is predicated on protein antigens that could be involved in molecular processes that are critical to reproduction, like sperm motility, acrosomal reaction, or sperm-egg interaction.[88] Macaque sperm counts are significantly reduced by passive or active immunization against FSH for rapid anti-fertility control contraceptive vaccines. In a similar vein, research is underway to develop a synthetic vaginal contraceptive that works by blocking sperm motility in the vagina. Sperm motility in the vagina is inhibited by the cloned and over-expressed r-SIF gene, which could potentially be a powerful and secure vaginal contraceptive in the future.[89]

## CONTRACEPTIVE DEVICES

Although hormonal contraceptives are effective and available to women in a variety of forms, many are discouraged by concerns about side effects and perceptions of safety. Permanent sterilization, copper intrauterine devices (IUDs), chemical/physical barriers like spermicides and condoms, as well as conventional family planning techniques like withdrawal and the rhythm method, are examples of non-hormonal contraceptives currently in use. Long-acting, reversible contraceptives (LARCs) are the most effective and adherence-friendly method for individuals who want to maintain their fertility in the future. The only non-hormonal LARC is the copper IUD.[90] As a result, different biomaterials have been searched for long-acting reversible contraception through various delivery routes, including subcutaneous implant, transdermal patch, oral administration, vaginal ring, IUDs, fallopian tube occlusion, vas deferens contraception, and intravenous administration.[91] Blocking fertility is a time-based need of family planning, but it is emerging as long-acting reversible contraception. Both in intrauterine and ectopic pregnancies mainly bleeding and pain due to expulsion is highly problematic.[86]

## NON-HORMONAL CONTRACEPTIVES

There are agents which especially target different stages of spermatogenesis. These are retinoic acid inhibitors, sperm ion channels, Sertoli cell-germ cell interactions, and other small molecular targets, which are referred to as non-hormonal contraceptives. In, addition proteolysis targeting chimeras and CRISPR has advanced for obstruction of male fertility.[92] For the development of non-hormonal contraceptives, genes specific to the reproductive tract that are linked to male infertility have been explored. According to Salicioni *et al*., testis-specific serine kinases are known to be important in signaling events related to sperm differentiation and function.[93] In addition, these target genes are involved in the molecular pathways of sperm maturation, production, or function. These serve as targets for non-hormonal male contraception and to inhibit male fertility.[94] The blood-testis barrier is crucial for preventing nutrients from reaching seminiferous tubules and growing spermatocytes, as well as for supporting male reproductive health and contraception.[91]

## CONCLUSION

Medicinal plants undoubtedly have anti-fertility properties, but before using them, it is crucial to understand the dosage, potential side effects, and involved pathways. Understanding chemical structure, activity, and functional mechanisms is necessary for this purpose. Natural anti-fertility extracts, products, or drugs cause irreversible sterility by lowering the total spermatogenic count. While it is true that herbal products are widely used throughout the world to manage reproduction and treat issues related to reproductive health, their toxic effects make them unsuitable. More specifically, mode of actions or fertility action of so many plant natural products is lacking. Hence, to find and develop new safe non-hormonal contraceptives, both men and women negative side effects must be studied. To fully understand the bioactivity of active ingredients found in crude extracts and to take advantage of their potential as anti-fertility agents, more investigation is needed. In addition, new potential sources are being explored by using contemporary techniques and technology for development of novel and effective anti-fertility medications. More than the safety of any contraceptive product, young women are particularly vulnerable to higher rates of spontaneous abortion and severe bleeding.

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## REFERENCES

1. Jaradat N, Zaid AN. Herbal remedies used for the treatment of infertility in males and females by traditional healers in the rural areas of the West Bank/Palestine. BMC Complement Altern Med 2019;19:194.
2. Bhatt N, Deshpande M. A critical review and scientific prospective on contraceptive therapeutics from ayurveda and allied ancient knowledge. Front Pharmacol 2021;12:629591.
3. Jackson H, Schnieden H. Pharmacology of reproduction and fertility. Annu Rev Pharmacol 1968;8:467-90.
4. Browner CH. Plants used for reproductive health in Oaxaca, Mexico. Econ Bot 1985;39:482-504.
5. Dias TR, Alves MG, Oliveira PF, Silva BM. Natural products as modulators of spermatogenesis: The search for a male contraceptive. Curr Mol Pharmacol 2014;7:154-66.
6. Bourdy G, Walter A. Maternity and medicinal plants in Vanuatu. I. The cycle of reproduction. J Ethnopharmacol 1992;37:179-96.
7. Maurya R, Srivastava S, Kulshreshta DK, Gupta CM. Traditional remedies for fertility regulation. Curr Med Chem 2004;11:1431-50.
8. Korkhov VV, Mats MN. Kontratseptivnye preparaty rastitel'nogo proiskhozhdeniia Contraceptive preparations of plant origin. Akush Ginekol (Mosk) 1983;11:8-10.
9. Sabourian R, Karimpour-Razkenari E, Saeedi M, Bagheri MS, Khanavi M, Sadati N, *et al*. Medicinal plants used in Iranian traditional medicine (ITM) as contraceptive agents. Curr Pharm Biotechnol 2016;17:974-85.
10. Noh S, Go A, Kim DB, Park M, Jeon HW, Kim B. Role of antioxidant natural products in management of infertility: A review of their medicinal potential. Antioxidants (Basel) 2020;9:957.
11. Hossain MS, Urbi Z, Sule A, Hafizur Rahman KM. *Andrographis paniculata* (Burm. f.) Wall. ex Nees: A review of ethnobotany, phytochemistry, and pharmacology. ScientificWorldJournal 2014;2014:274905.
12. Kumar D, Kumar A, Prakash O. Potential antifertility agents from plants: A comprehensive review. J Ethnopharmacol 2012;140:1-32.
13. Zhao Y, Zhao K, Jiang K, Tao S, Li Y, Chen W, *et al*. A review of flavonoids from *Cassia* species and their biological activity. Curr Pharm Biotechnol 2016;17:1134-46.
14. Yadav R, Jain GC. Antifertility effect of aqueous extract of seeds of *Cassia fistula* in female rats. Adv Contracept 1999;15:293-301.
15. Bronson RA. Oral contraception: Mechanism of action. Clin Obstet Gynecol 1981;24:869-77.
16. Kapoor M, Garg SK, Mathur VS. Anthiovulatory activity of five indigenous plants in rabbits. Indian J Med Res 1974;62:1225-27.
17. Yegnanarayan R, Joglekar GV. Antifertility effect of non-steroidal anti-inflammatory, drugs. Jpn J Pharmacol 1978;28:909-17.
18. Kholkute SD, Udupa KN. Antiestrogenic activity of *Hibiscus rosa-sinensis* Linn. flowers. Indian J Exp Biol

1976;14:175-6.
19. Gbotolorun SC, Osinubi AA, Noronha CC, Okanlawon AO. Antifertility potential of neem flower extract on adult female Sprague-Dawley rats. Afr Health Sci 2008;8:168-73.
20. Biswal S. Lacunar infarction with oral contraceptives: An unusual case report. J Midlife Health 2013;4:188-90.
21. Kholkute SD, Chatterjee S, Srivastva DN, Udupa KN. Proceedings: Effect of *Hibiscus rosa sinensis* on the reproductive organs of male rats. J Reprod Fertil 1974;38:233-4.
22. Murthy DR, Reddy CM, Patil SB. Effect of benzene extract of *Hibiscus rosa sinensis* on the estrous cycle and ovarian activity in albino mice. Biol Pharm Bull 1997;20:756-8.
23. Tan CH. Is *Hibiscus rosa sinensis* Linn. a potential source of antifertility agents for males? Int J Fertil 1983;28:247-8.
24. Afiune LA, Leal-Silva T, Sinzato YK, Moraes-Souza RQ, Soares TS, Campos KE, *et al*. Beneficial effects of *Hibiscus rosa-sinensis* L. flower aqueous extract in pregnant rats with diabetes. PLoS One 2017;12:e0179785.
25. Pakrashi A, Bhattacharya K, Kabir SN, Pal AK. Flowers of *Hibiscus rosa-sinensis*, a potential source of contragestative agent. III: Interceptive effect of benzene extract in mouse. Contraception 1986;34:523-36.
26. Kholkute SD, Udupa KN. Effects of *Hibiscus rosa sinensis* on pregnancy of rats. Planta Med 1976;29:321-9.
27. Arullappan S, Zakaria Z, Basri DF. Preliminary screening of antibacterial activity using crude extracts of *Hibiscusrosa sinensis*. Trop Life Sci Res 2009;20:109-18.
28. Tiwari KC, Majumder R, Bhattacharjee S. Folklore information from Assam for family planning and birth control. Int J Crude Drug Res 1982;20:133-7.
29. Kabir SN, Bhattacharya K, Pal AK, Pakrashi A. Flowers of *Hibiscus rosa-sinensis*, a potential source of contragestative agent: I. effect of benzene extract on implantation of mouse. Contraception 1984;29:385-97.
30. Vasudeva N, Sharma SK. Post-coital antifertility activity of *Hibiscus rosa-sinensis* Linn. roots. Evid Based Complement Alternat Med 2008;5:91-4.
31. Farnsworth NR, Bingel AS, Cordell GA, Crane FA, Fong HH. Potential value of plants as sources of new antifertility agents I. J Pharm Sci 1975;64:535-98.
32. Ghogar A, Jiraungkoorskul W. Antifertility effect of *Bougainvillea spectabilis* or paper flower. Pharmacogn Rev 2017;11:19-22.
33. Shehab NG, Abu-Gharbieh E. Phenolic profiling and evaluation of contraceptive effect of the ethanolic extract of *Salsola imbricata* Forssk. in male albino rats. Evid Based Complement Alternat Med 2014;2014:695291.
34. Ghosh A, Pakhira BP, Tripathy A, Ghosh D. Male contraceptive efficacy of poly herbal formulation, contracept-TM, composed of aqueous extracts of *Terminalia chebula* fruit and *Musa balbisiana* seed in rat. Pharm Biol 2017;55:2035-42.
35. Lu Z, Wang L, Zhou R, Qiu Y, Yang L, Zhang C, *et al*. Evaluation of the spermicidal and contraceptive activity of Platycodin D, a Saponin from *Platycodon grandiflorum*. PLoS One 2013;8:e82068.
36. Alhaj WT, Moharram BA, Al-Maqtari T, Al-Mahbashi HM, Al-Doaiss AA. The potential of *Jatropha variegate* fruits as a natural contraceptive: Antifertility activity and phytochemical analysis. Evid Based Complement Alternat Med 2022;2022:1365526.
37. Kyarimpa C, Nagawa CB, Omara T, Odongo S, Ssebugere P, Lugasi SO, *et al*. Medicinal plants used in the management of sexual dysfunction, infertility and improving virility in the East African community: A systematic review. Evid Based Complement Alternat Med 2023;2023:6878852.
38. El-Ishaq A, Alshawsh MA, Mun KS, Chik Z. Phytochemical screening and anti-implantation activity of Asparagus africanus root extract in female Sprague-Dawley rats. Rev Bras Farmacogn 2019;26:621-30.
39. Srivastava SR, Keshri G, Bhargavan B, Singh C, Singh MM. Pregnancy interceptive activity of the roots of *Calotropis gigantea* Linn. in rats. Contraception 2007;4:318-22.
40. Kamath JV, Rana AC. Preliminary study on antifertility activity of *Calotropis procera* roots in female rats. Fitoterapia 2001;73:111-5.
41. Kirtikar K, Basu BD. Indian medicinal plants. Period Exp 1935;2:848-9.
42. Neeru V, Sharma SK. Post-coital antifertility activity of *Hibiscus rosa sinensis* Linn. roots. Evid Based Complement Alternat Med 2008;5:91-4.
43. Tan LT, Lee LH, Yin WF, Chan CK, Abdul Kadir H, Chan KG, *et al*. Traditional uses, phytochemistry, and bioactivities of *Cananga odorata* (Ylang-Ylang). Evid Based Complement Alternat Med 2015;2015:896314.
44. Parween S, Kausar H, Alam I, Nehar S. Antifertility effect of methanolic extract of Butea monosperma (Lam.) Taub. flower in male albino rats. Ayu 2021;42:57-66.
45. Dreisbach R. Effect of drugs on reproduction in mice. Indian J Physiol Pharmacol 1963;7:63-71.
46. Khanna U, Chaudhury R. Antifertility screening of plants, 3333 Part I. Investigation on *Butea monosperma* Lam. Kuntz. Indian J Med Res 1968;56:1577-80.
47. Vohora SB, Garg SK, Chaudhury RR. Anti-fertility screening of plants. III. Effects of six indigenous plants on early pregnancy in albino rats. Indian J Med Res 1969;51:893-9.
48. Sethi J, Yadav M, Sood S, Dahiya K, Singh V. Effect of tulsi (*Ocimum sanctum* Linn.) on sperm count and reproductive hormones in male albino rabbits. Int J Ayurveda Res 2010;1:208-10.
49. Gupta G, Jangir S, Sharma VL. Targeting post-ejaculation sperm for value-added contraception. Curr Mol Pharmacol 2014;7:167-74.
50. Prakash P, Gupta N. Therapeutic use of *Ocimum sanctum* Linn (Tulsi) with a note on eugenol and its pharmacological actions: A short review. Indian J

Physiol Pharmacol 2005;49:125-31.
51. Nadig P, Laxmi S. Study of anti-tussive activity of *Ocimum sanctum* Linn in guinea pigs. Indian J Physiol Pharmacol 2005;49:243-5.
52. Shibeshi W, Makonnen E, Zerihun L, Debella A. Effect of *Achyranthes aspera* L. on fetal abortion, uterine and pituitary weights, serum lipids and hormones. Afr Health Sci 2006;6:108-12.
53. Kulkarni TR, Kothekar MA, Mateenuddin M. Study of antifertility effect of lemon seeds (*Citrus limonum*) in female albino mice. Ind J Physiol Pharmacol 2005;49:305-12.
54. David M, Ain QU, Jahan S, Ahmad M, Shah Q, Afsar T, *et al*. Determination of possible contraceptive potential of methanolic leaf extract of *Mentha longifolia* L. in adult male rats: A biochemical and histological study. Toxicol Res (Camb) 2022;11:951-61.
55. Mishra RK, Singh S, Singh SK. Natural products in regulation of male fertility. Indian J Med Res 2018;148:S107-14.
56. D'Cruz SC, Vaithinathan S, Jubendradass R, Mathur PP. Effects of plants and plant products on the testis. Asian J Androl 2010;12:468-79.
57. Uchendu CN, Isek T. Antifertility activity of aqueous ethanolic leaf extract of *Spondias mombin* (*Anacardiaceae*) in rats. Afr Health Sci 2008;8:163-7.
58. *Romm A. Pregnancy and botanical medicine use and safety. In: Botanical Medicine for Women's Health. Ch. 11. United Kingdom: Churchill Livingstone; 2010. p. 321-4.*
59. *Anderson IB, Mullen WH, Meeker JE, Khojasteh-Bakht SC, Oishi S, Nelson SD, et al. Pennyroyal toxicity: Measurement of toxic metabolite levels in two cases and review of the literature. Ann Intern Med 1996;124:726-34.*
60. Wood RI, Stanton SJ. Testosterone and sport: Current perspectives. Horm Behav 2012;61:147-55.
61. Pfrunder A, Schiesser M, Gerber S, Haschke M, Bitzer J, Drewe J. Interaction of St John's wort with low-dose oral contraceptive therapy: A randomized controlled trial. Br J Clin Pharmacol 2003;56:683-90.
62. Khourdaji I, Zillioux J, Eisenfrats K, Foley D, Smith R. The future of male contraception: A fertile ground. Transl Androl Urol 2018;7:S220-35.
63. Payne C, Goldberg E. Male contraception: Past, present and future. Curr Mol Pharmacol 2014;7:175-81.
64. Page ST, Amory JK, Bremner WJ. Advances in male contraception. Endocr Rev 2008;29:465-93.
65. Palmeira-de-Oliveira R, Duarte P, Palmeira-de-Oliveira A, das Neves J, Amaral MH, Breitenfeld L, *et al*. What do Portuguese women prefer regarding vaginal products? Results from a cross-sectional web-based survey. Pharmaceutics 2014;6:543-56.
66. Mali PC, Ansari AS, Chaturvedi M. Antifertility effect of chronically administered *Martynia annua* root extract on male rats. J Ethnopharmacol 2002;82:61-7.
67. Pathak S, Tewari RK, Prakash AO. Hormonal properties of ethanolic extract of *Juniperus communis* Linn. Anc Sci Life 1990;10:106-13.
68. Jones AR. Antifertility actions of alpha-chlorohydrin in the male. Aust J Biol Sci 1983;36:333-50.
69. Raji Y, Bolarinwa AF. Antifertility activity of *Quassia amara* in male rats - *in vivo* study. Life Sci 1997;61:1067-74.
70. Mishra RK, Singh SK. Antispermatogenic and antifertility effects of fruits of *Piper nigrum* L. in mice. Indian J Exp Biol 2009;47:706-14.
71. Daniyal M, Akram M. Antifertility activity of medicinal plants. J Chin Med Assoc 2015;78:382-8.
72. Riar SS, Bardhan J, Thomas P, Kain AK, Parshad R. Mechanism of anti-fertility action of neem oil. Indian J Med Res 1988;88:339-42.
73. Upadhyay SN, Kaushic C, Talwar GP. Antifertility effects of neem (*Azadirachta indica*) oil by single intrauterine administration: A novel method for contraception. Proc Biol Sci 1990;242:175-9.
74. McNeil RT, Ekwere E. *Ricinus communis* Linn. (castor plant), male contraceptives and reproductive health of women. Afr J Reprod Health 2021;25:135-41.
75. Parohit A, Vyas SK, Vyas KB. Contraceptive efficacy of *Plumbago zeylanica* root extract (50% ETOH) in male albino rats with special emphasis on testicular cell population dynamics. Anc Sci Life 2008;27:31-5.
76. Qian SZ. *Tripterygium wilfordii*, a Chinese herb effective in male fertility regulation. Contraception 1987;36:335-45.
77. Tanphaichitr N, Srakaew N, Alonzi R, Kiattiburut W, Kongmanas K, Zhi R, *et al*. Potential use of antimicrobial peptides as vaginal spermicides/microbicides. Pharmaceuticals (Basel) 2016;9:13.
78. Ewing LL, Robaire B. Endogenous antispermatogenic agents: Prospects for male contraception. Annu Rev Pharmacol Toxicol 1978;18:167-87.
79. Swerdloff RS, Wang C, Bhasin S. Developments in the control of testicular function. Baillieres Clin Endocrinol Metab 1992;6:451-83.
80. Hansson V, Djoseland O, Torgersen O, Ritzen EM, French FS, Nayfeh SN. Hormones and hormonal target cells in the testis. Andrologia 1976;8:195-202.
81. Prasad MR, Rajalakshmi M. Target sites for suppressing fertility in the male. Adv Sex Horm Res 1976;2:263-87.
82. Pierrepoint CG, Jenkins BM, Wilson DW, Phillips MJ, Gow JG. An examination of blood steroid and gonadotropin concentrations in relation to fertility status and testicular function in men. Fertil Steril 1982;38:465-70.
83. de Kretser DM. Endocrinology of male infertility. Br Med Bull 1979;35:187-92.
84. Singh SP, Prasad MR. Changes in fructose & citric acid in accessory glands of reproduction of rats following long-term treatment with isomers of clomiphene citrate. Indian J Exp Biol 1973;11:23-6.
85. Waites GM. Male fertility regulation: The challenges for the year 2000. Br Med Bull 1993;49:210-21.

86. Mishell DR Jr., Lumkin M, Jackanicz T. Initial clinical studies of intravaginal rings containing norethindrone and norgestrel. Contraception 1975;12:253-60.
87. Vickram AS, Dhama K, Chakraborty S, Samad HA, Latheef SK, Sharun K, *et al*. Role of antisperm antibodies in infertility, pregnancy, and potential for contraceptive and antifertility vaccine designs: Research progress and pioneering vision. Vaccines (Basel) 2019;7:116.
88. Chorfa A, Goubely C, Henry-Berger J, Guiton R, Drevet JR, Saez F. Identification of *Arvicola terrestris* scherman sperm antigens for immune contraceptive purposes. Int J Mol Sci 2021;22:9965.
89. Answal M, Prabha V. *Escherichia coli* recombinant sperm immobilizing factor RecX as a potential vaginal contraceptive. Reprod Biol Endocrinol 2018;16:88.
90. Howard SA, Benhabbour SR. Non-hormonal contraception. J Clin Med 2023;12:4791.
91. Cheng CY, Mruk DD. The blood-testis barrier and its implications for male contraception. Pharmacol Rev 2012;64:16-64.
92. He Y, Khan S, Huo Z, Lv D, Zhang X, Liu X, *et al.* Proteolysis targeting chimeras (PROTACs) are emerging therapeutics for hematologic malignancies. J Hematol Oncol 2020;13:103.
93. Salicioni AM, Gervasi MG, Sosnik J, Tourzani DA, Nayyab S, Caraballo DA, *et al*. Testis-specific serine kinase protein family in male fertility and as targets for non-hormonal male contraception. Biol Reprod 2020;103:264-74.
94. Wisniewski A, Georg GI. BET proteins: Investigating BRDT as a potential target for male contraception. Bioorg Med Chem Lett 2020;30:126958.

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