Use of Medicinal Plants as Contraceptive

Mehwish David[1*], Sarwat Jahan[1], Qurat-ul-Ain[2]

[1]Reproductive Physiology Laboratory, Department of Zoology, Quaid-i-Azam University, Islamabad, Pakistan
[2]Department of Zoology, Government College Women University, Sialkot, Pakistan
[*]Corresponding author: mdavid@bs.qau.edu.pk; mehwish28david@gmail.com

SUMMARY

According to current statistics, the world's population has risen to 7 billion people. It grows by 80 million people every year and is expected to reach 9-10 billion by 2050. Population expansion as such is a pivotal cause of resource deprivation and human distress from malnutrition and scarcity. To control overpopulation, birth control methods have been used since ancient times however, availability of safe and reliable methods has been ensured only in recent years, which include the use of physical, barrier, hormonal and behavioral methods. Family planning has also been introduced among couples through awareness to several approaches of contraception, such as use of contraceptive drugs, devices (Copper-T), Tubectomy, Condoms, Diaphragm, and coitus interrupts. In some cases, these methods are reliable however, in other cases, they may exert their detrimental effects by causing long term hormonal imbalances and endocrine disruptions in males and menstrual irregularities in females. Hence, medicinal plants have grabbed the minds of researchers as a major source of naturally present fertility regulating agents prior to their safe use and minimum side effects. A large number of medicinal herbs have been assessed for their antifertility ability. Studies have been conducted to identify medicinal plants to develop effective and safe contraceptives for men and women. Various plants containing terpenes, flavonoids, quinines, diterpenoid lactones and tannins have been described to induce male antifertility properties by mechanisms, such as, they exert spermicidal, anti-spermatogenic, and spermatotoxic effects, may lower sperm quality by reducing sperms mobility and viability; disrupt testicular morphology, induce hormonal alteration, and may modify antioxidant defense mechanism. More than 50 plants have been reported in literature to contain anti-fertility causing agents. Similarly, medicinal plants that act as infertility agent in females works either by interfering with hormonal profile or by inhibiting implantation. Based on their mode of action, plants can be categorized to have anti-ovulatory, anti-implantation, abortifacients and antifertility potential. Multiple researchers have reported novel medicinal plants from all over the world that can be used as contraceptives, which serves as cheap, safe and having reversible effects. However, more comprehensive studies on the isolation and purification of bioactive compounds from different parts of these plants should be planned, so that the most active compound responsible for their antifertility activity can be discovered, and its pharmacokinetic and pharmacodynamic properties can be determined for the development of oral formulations.

INTRODUCTION

Population growth is an essential contributor to environmental degradation and suffering among people across the world. According to current statistics, the population of the world has risen to 7 billion people. It grows by 80million people every year and is expected to extend 9-10 billion by 2050 (Segal & Segal, 2004). Unattended and unwanted pregnancies are a key contributor to overpopulation. Several epidemiological researchers have reported that one of the cause of overpopulation is the increased ratio of unwanted (41%) births, abortions (20%), and 47000 maternal deaths worldwide, underlining the need for more knowledge and improved contraceptive methods (David et al., 2022). Previously, according to Millennium Development Goals (MDG) regarding worldwide approach to reproductive health emphasizes on the use of contraceptives, and providence of reproductive health service such as safe abortion and reduced maternal mortality. Fertility control, through use of contraceptives and targeting problems associated with infertility serves as a fundamental part of reproductive health for men and women (Allag & Rangari, 2002). Because of the abundance of proof, scientists have started to address this serious issue by developing active contraceptive techniques (Unny et al., 2003). There is a need of hour to develop contraceptive techniques that are safe, inexpensive, effective, and reversible, and that are available to individuals of all religions, races, and cultures.

CONTRACEPTION

Contraception is the actual prevention of conception, but it is commonly understood to indicate the avoidance of pregnancy. Contraception methods such as contraceptive pills, Copper-intrauterine devices (IUD), tubectomy, diaphragms,

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condoms, and coitus interrupters have been used to aid in family planning. These techniques are mostly oriented toward women. The use of contraceptive pills has been proven to be an effective method of contraception and is still in use, however, recent research has concluded that as contraceptive pills are hormone treatments (hormones such as estrogen, progesterone, or their derivatives, either alone or in combination), therefore, they may bring long term disturbances in reproductive cyclicity of women (Pradhan et al., 2013). The use of physical barrier methods such as use of condoms and diaphragms are also effective in many cases. However, with the introduction and extensive use of copper-intrauterine devices (IUD), it has been considered as a highly effective nonhormonal reversible method (Teal & Edelman, 2021). Cu-IUDs have low pregnancy rates and very low ectopic pregnancy rates (Bahamondes et al., 2020). The effectiveness of coitus interrupters through withdrawal and fertility awareness depends on patient's education status, cycle regularity, and his response pertaining to its aftereffects, and his ability to avoid ejaculation during the time of peak fertility (Bahamondes et al., 2020). The literature review suggests that female sterilization through use of long-acting hormonal contraceptives and implants is the most effective method of contraception among other hormonal and nonhormonal methods of contraception (Mansour et al., 2010).

History

A scattering of historical sources on contraceptive techniques and abortion procedures survives from the extant literature of Latin, Egyptian, and Greek (Sultana, 2019). The history of use of birth control began with the correlation of coitus and conception. Some of the most common and ancient means of contraception include lactation, coitus interruptus, use of some barrier techniques, and traditional herbal methods. Coitus interruptus involves the abstraction of the penis from the vagina just before ejaculation. There are historical reports of Egyptian women employing a pessary (consisting of different acidic chemicals) greased with honey or oil to kill sperms, which may have partial effect. Use of oiled paper among Asian women as a cervical cap, while use of beeswax among Europeans was common practice (Tatman et al., 2018). In the last 50 years, there has been significant advancement in the field of fertility control. In the 1960s, the 1st oral contraceptive (OC) pill was developed, along with the development of other physical tools such as contraceptive vaginal ring (CVR) and transdermal patches. Later, in 1970, with the establishment of the "International Committee for Contraception Research (ICCR)", new avenues of study for the development of novel contraceptive techniques were introduced. ICCR and Population Council collaborated with the industrial sector to develop and manufacture various tools (Sitruk-Ware et al., 2013). Throughout human history, several abortifacients have been used to end unwanted pregnancy. Some were effective, while others were not; those that were most effective also had significant adverse effects.

Male contraception

While advances in the development of reliable, advanced, and efficient contraceptive drugs for women have been accomplished, male advancement has lagged far behind. Male contraceptive options now available result in either unplanned pregnancy or utter infertility. As a result, the development of male contraceptives that are safe, reversible, and physiologically active is critical, and can deliver significant public and community health advantages (Ain et al., 2022). Modern, more potent, less harmful drugs that are self-administered, cheap, and reversible and easy to use are typically the focus of new developments in this sector (Yadav et al., 2022). In patriarchal societies, the use of male contraceptives is not common and therefore, most of the commercially available contraceptives are women based. However, ensuring the safe use of herbal contraceptives among men is quite a task, as males feel reluctant to its use. Proper awareness on the reproductive system function should be delivered in family planning setups, so that male partners can be convinced to use contraceptives.

Female contraception

For a long time, several successful treatments for fertility control, including hormonal and pharmacological approaches, have been investigated (Gupta, 2006). In recent years, the idea of permanent contraception has gained attention among females as well (Fang et al., 2022). The most effective birth control methods revolve around three ways of population control, namely abortion, sterilization, and contraception. Contraceptive devices have also been classified into three types: physiological (physical methods), mechanical (barrier methods), and surgical (Azamthulla & Balasubramanian, 2015).

BIRTH CONTROL METHODS

Physical methods

Physical methods can hold conception through different mechanisms, which may prevent the sperm to access the female reproductive tract, inhibit ovulation through hormonal means, create an unfavorable environment for sperm in the woman's reproductive tract, or induce sterility through surgical alterations to the male or female reproductive organ (Azamthulla & Balasubramanian, 2015). Some methods combine multiple mechanisms. These approaches differ in terms of simplicity, convenience, and effectiveness.

Barrier methods

Sperm migration into the female reproductive system is physically impeded by barrier methods. The use of male condoms (made up of latex or polyurethane sheath) wrapped over the penis, is the most often utilized barrier method (Azamthulla & Balasubramanian, 2015). The female condoms (made of polyurethane) are also available in the market nowadays. Apart from condoms, cervical barrier devices such as cervical caps are also used that are completely contained within the vaginal canal. A depression in the contraceptive sponge, positions it above the cervix. The diaphragm is another type of barrier device that is placed beneath the woman's pubic bone and is made up of a strong yet flexible ring that allows it to push against the vaginal walls (Aliyu & Onwuchekwa, 2018). For creating a chemical barrier before intercourse, spermicide can be injected into the vagina, which can be used alone or in combination with another physical barrier.

HORMONES FORMULATIONS

Large number of hormonal formulations and therapies have been developed over the past few years to control overpopulation and induce contraception. The development of oral hormonal contraceptive drugs dates back to 1951, when Carl Djerassi, Mexican Luis E. Miramontes, and Hungarian George Rosenkranz worked to invent oral drugs. Norethindrone, a progestin analogue, was synthesized and used in the first effective oral contraceptive, the combined oral contraceptive pill (COCP) (Azamthulla & Balasubramanian, 2015). Recent researchers have suggested that although the use of hormonal contraceptives is a globally used method among premenopausal women, however, the risk of venous and arterial cardiovascular events is associated with the use of contraceptive pills with hormonal formulations (Williams & MacDonald, 2021).

Progestins

The progestin (a synthetic progestogen) molecule is responsible for the majority of the contraceptive action in hormonal treatments. Progestins are classified into three types: estranes, gonanes, and pregnanes. Norethindrone, ethynodiol diacetate, norethindrone acetate, and lynestrenol are examples of estranes. Nor estimate, desogestrel, and gestodene are examples of gonanes (Azamthulla & Balasubramanian, 2015). The half-lives of gonanes and estranes are different, as are their estrogenic and antiestrogenic effects. The prenames have been developed and are being used as injectables.

Progestin only contraceptives

Progestin-only contraceptives pills, commonly known as 'minipills,' are used in the same way as mixed OCs. It contains a progestin dosage that is quite close to the contraceptive effectiveness threshold (Azamthulla & Balasubramanian, 2015). This technique of contraception is mostly suggested among women who are breastfeeding; nonetheless, most women are eligible for it. Menstrual cycle irregularity is the most common negative effect linked with progestin-only tablets. The most common anomalies include amenorrhea, breakthrough bleeding, and shorter menstrual periods. According to a randomized, double-blind research conducted by World Health Organization (WHO), it was reported that users of this hormonal therapy experience frequent bleeding (53%), protracted bleeding (22%), irregular bleeding (13%), and amenorrhea (6%) within 3 months of treatment commencement (Azamthulla & Balasubramanian, 2015). Another recent case-control study involving cardiovascular disease and progestin-only tablet usage showed no notable rise in the risk of cardiac arrest, stroke, or venous thromboembolism. So far, it appears that progestin-only tablets have a negligible impact on metabolic health variables. However, recent research has shown that use of progestin only contraceptives are associated with impairment of female sexual function (Shahin et al., 2021).

Progestin only injectables

These include Depot-medroxyprogesterone acetate (DMPA), which is a 12-week deep intramuscular injection of 150 mg medroxyprogesterone acetate (MPA), whose active levels (>0.5mg/ml) are attained within 24hrs following its administration; the serum concentration of MPA remain 1.0ng/ml for next three months following dosing. By the 5^{th} month, serum levels fall to 0.2mg/ml (Azamthulla & Balasubramanian, 2015). The primary mode of action of DMPA is through ovulation suppression. The most often reported adverse effects of DMPA include irregularities in menstrual cycles, weight gain, and mood swings. Over half of DMPA users have amenorrhea after three months, while others experience irregular bleeding (Azamthulla & Balasubramanian, 2015).

Progestin only vaginal rings: These rings either contain 100 mg MPA, or norethindrone, that act to inhibit ovulation. To create a withdrawal bleed, these rings are adjusted on day 5 of the menstrual cycle, followed by their removal after 21 days of usage. The use of norethindrone containing rings has been associated with irregular bleeding and disturbed ovulation (Azamthulla & Balasubramanian, 2015).

Estrogens

In hormonal contraception, only two estrogenic chemicals are used, as opposed to a wide range of progestin formulations: mestranol and ethinyl estradiol (EE). Ethinyl estradiol remains active pharmacologically, however, mestranol is activated only when it is transformed into EE (Azamthulla & Balasubramanian, 2015). Commercially available contraceptives usually contain 35 mg or less of estrogen in them. EE is known to be readily absorbed and undergoes significant hepatic first pass metabolism. The half-life of EE in plasma is between 10-27 hours and is prolonged in endometrial tissues.

Intrauterine methods

Intrauterine methods (IUDs) include use of contraception devices, implanted into the uterus. They are often designed in a "T" shaped manner, with the arms of the "T" holding the device in place and blocking the sperm entry into the fallopian tubes. Two types of intrauterine devices have been devised so far: the one containing copper (responsible for spermicidal effect) and others releasing progestogen (Azamthulla & Balasubramanian, 2015). Copper ion release changes the uterine fluid in the uterus cavity, impairing sperm motility, viability and hence inhibiting conception.

Sterilization

Surgical sterilization is administered via tubal ligation in females and through vasectomy in males. Tubal ligation includes the processes where fallopian tubes are either tied, cut, or obstructed surgically. This prevents the sperm from reaching and fertilizing an egg. Sterilization induces permanent shutting of conception. Although tubal ligation is known to induce permanent changes, recently, tubal ligation reversal procedures have been under construction, to ensure conception again (Azamthulla & Balasubramanian, 2015). This depends on the number of factors that may affect reproductive outcomes such as the kind of tubal ligation procedure that was previously performed, tubal condition and woman's age.

Behavioral methods

Controlling the timing or style of intercourse is one behavioral technique of preventing sperm from entering the female reproductive system, either totally or while an egg is present (Azamthulla & Balasubramanian, 2015). Studies have proposed that use of contraceptive methods among females tend to reduce female sexual function index, however, it does not affect the quality of life (Gürbüz et al., 2020). Although a large number of barrier methods are in use, practicing permanent contraception in recent years ensures safe and healthy sexual intercourse with minimum mental and physical pressure on both the partners.

Birth control mechanisms

The primary mode of action of hormonal contraceptives is the suppression of ovulation/steroidogenesis (Fig 1). Pregestational effects include:

- Luteinizing hormone (LH) suppression inhibits ovulation.
- Cervical mucus thickening, restricting sperm movement.
- Sperm capacitation may be inhibited.
- Impaired implantation due to decidualized endometrium with depleted and atrophic glands.
- Ovulation is partially inhibited depending on the dosage via reduction of LH and follicle-stimulating hormone (FSH).
- Alterations in endometrial secretions and cellular structures within the uterus (Rajandeep et al., 2011).

THERAPEUTIC PLANTS

One of the most fascinating ideas of the therapeutic sciences and pharmacology is the search for novel medications with minimal side effects, lower costs, and reversibility. Plants have captured the interest of many scientists due to their low toxicity as a vital source of naturally present fertility regulating compounds. The WHO believes that owing to scarcity and lack of access to modern medication, 80% of the world's population relies mostly on herbs for their primary healthcare in underdeveloped nations (Payyappallimana, 2010). Herbs utilized in traditional medicinal systems such as folklore and herbalism are included in ethnobotanical awareness. The history of human civilization demonstrates man's reliance on plants and their derived products for nutrition, shelter, and relief from physical problems. Plant products have been used against a variety of diseases since olden times due to their better level of compatibility with the human body, religious and cultural tolerance, and reduced side effects. Herbal therapy expertise were passed down orally from generation to generation initially, however, later, documented records have been developed with the expansion of civilizations for the future (D'Cruz et al., 2010). Details of medicinal plants with the potential to cause infertility in males or females have been presented in Table 1.

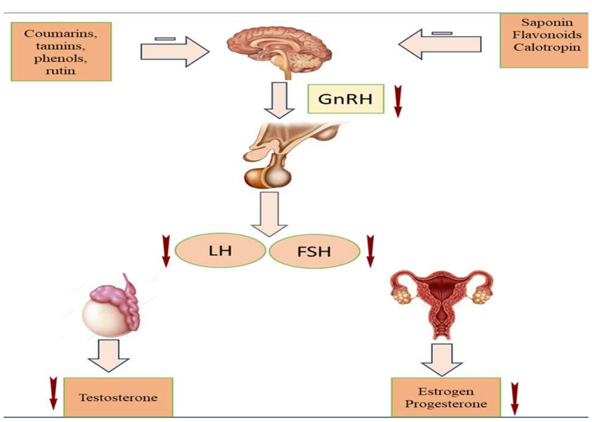

Fig 1. Effect of phytoconstituents isolated from plants effect on steroid production in males and females

Phyto-constituents

Phyto-constituents are present in abundance among different parts of medicinal plants. They have an inhibitory and suppressive impact on male fertility. Many plants containing tannins, flavonoids, quinines, terpenes, and diterpenoid lactones have been shown to elicit male antifertility characteristics via various mechanisms as shown in Fig 2 (Joshi et al., 2011). Various medications have been produced from plants, either directly or indirectly, in recent years for the identification of novel pharmacological molecules (Li, 2010).

Herbal female contraceptives

Various plants have been used in female contraception. Herbs such as, silphium and asafoetida, were recognized by ancient women because of their contraceptive and abortifacient effects. Some herbs have gained increased popularity due to their effectiveness in preventing undesired pregnancy, including silphium, which has remained high in demand in ancient Greece. *Pippalayadi Vati* seeds have been employed as an antifertility medicine since ancient times (Shweta et al., 2011). Likewise, in 1963, asafetida (*Ferula assa-foetida*) resin was shown to be effective as a contraceptive and for producing early abortion in humans. Hippocrates, also known as the "Father of Medicine," advised the use of seeds of Queen Anne's lace (wild carrot), that prevent and terminate pregnancy. Wild yam and neem are other two contraceptive plants that need to be used on a daily basis for the cumulative antifertility effects of the plant extract. Wild yam is an efficient and traditionally used herbal contraceptive whose fertility reducing effects are strengthened with its daily use. Each of the contraceptive plants exerts a unique effect on the body. Herbs can be used in a variety of ways to affect fertility. Some herbal medicines have qualities that impact the ovary, while others impress on the uterine or occasionally impede and even disrupt hormone synthesis (Shweta et al., 2011).

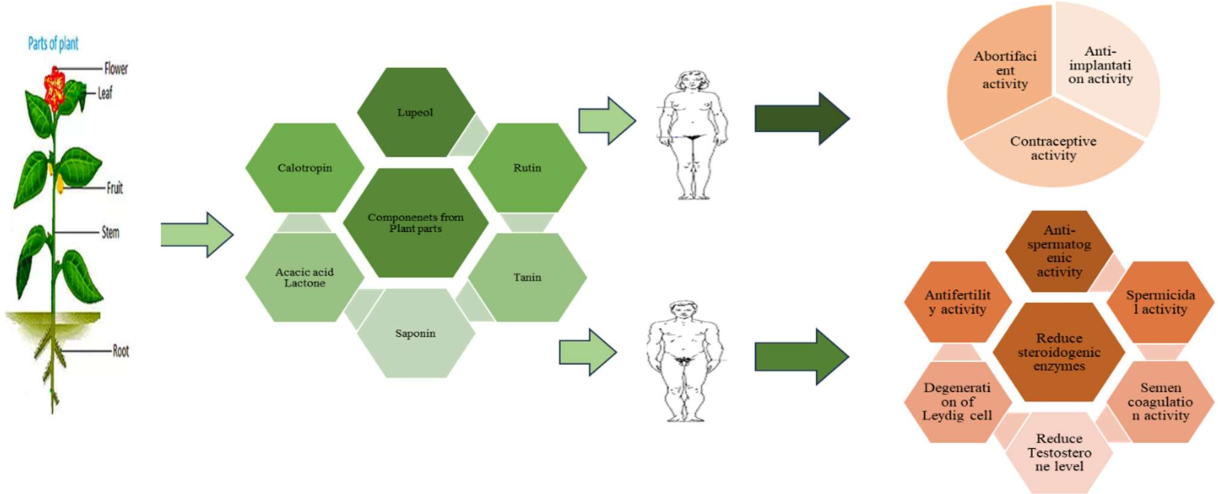

Fig 2. Phytoconstituents isolated from plants and their effects on the reproductive functions of males and females

Table 1. List of therapeutic plants that act as antifertility agent among male and female reproductive systems

Name of plant	Family	Part used	Active component	Dose	Subject	Mechanism of action	References
Acacia auriculiformis Benth.	Fabaceae	Seeds	Acacia acid lactone	0.35 mg/ ml	Human sperm	Sperm plasma membrane disintegration and immobilization	Prakash et al., 1991
Aegle marmelos (L.) Corrêa	Rutaceae	Leaves	Coumarins, tannins, phenols, rutin	200 and 300 mg/ kg	Rat	Suppress gonadotropic hormone	Chauhan & Agarwal, 2008
Albizia lebbeck (L.) Benth	Fabaceae	Pods	Labbekanin-E, saponins	100 mg/ kg B.W.	Rat	Decrease sperm density and motility, as well as testicular and prostrate size	Singh et al., 2011
Allium sativum L.	Liliaceae	Bulb	Allitridum	0.25 and 0.5 g/ml	Human sperm	Disrupt membrane architecture	Chakrabarti et al., 2003
Asplenium dalhousiae	Aspleniaceae	Leaf	Kaempferol 3-glucuronide, Kaempferol 3-digalactoside, Flavanone	0, 50, 100, 150 mg/kg	Rat	Lowered gonadotropin levels, Disrupts testicular architecture	David et al., 2019
Cananga odorata (Lam.) Hook. f. & Thomson	Annonaceae	Root bark	52-kd protein	1 g/kg B.W./day	Rat	Reduce androgen synthesis while promoting 3-hydroxy-3-methylglutaryl-CoA (HMG CoA) reductase activity	Pankajakshy & Madambath, 2009
Cestrum parqui (Lam.) L'Hér.	Solanaceae	Leaves	Saponin	40, 62.5, 100, 150, and 250 µg/ ml	Human semen	Disrupt sperm plasma membrane sterol	Souad et al., 2007
Chenopodium album L.	Chenopodiaceae	Fruits	Oleanolic acid, glucuronic acid	2 mg/m	Rat/ rabbit	Disintegrate plasma membrane of the sperm, dissolution of acrosomal cap, resulting in sperm death.	Sharma et al., 2007
Chenopodium ambrosioides Hook	Chenopodiaceae	Leaf		50, 100 and 150 mg/kg	Rat	Reducd concentrations of plasma testosterone, FSH and LH	Ain et al., 2018
Chromolaena odoratum (L.)	Compositae	Leaves	-	250 and 500 mg/ kg	Rat	Reduce the concentration of biomolecules and disturb the seminiferous tubules	Yakubu et al., 2007

Colebrookea oppositifolia	Lamiaceae	Leaves	5,6,7,4′-tetramethoxy flavones 5,7, 4′-trihydroxy flavones 3-oglucoside, 5,6,7-trimethoxy flavones,	100mg/kg 200 mg/ kg	Rat	Decrease the amount of ascorbic acid, fructose, and sialic acid.	Gupta et al., 2001
Juniperus phoenica (L.)	Cupressaceae	Ripe red cone	α-Pinene, δ-3-carone, βphellandrene	400 and 800 mg/ kg	Rat	LH and gonadotropin-releasing hormone inhibition	Shkukani et al., 2008
Mollugo pentaphylla L.	Molluginaceae	Aerial part	Mollugogenol-A (saponin)	10, 30,100, and300 µg/ m	Human sperm	Plasma membrane-losing osmoregulatory properties and improve4superoxide ion production and lipid peroxidation	Rajasekaran et al., 1993
Quassia amara L.	Simaraubaceae	Stem wood	Quassin, 2-methoxycanthin-6- one	0.1, 1.0, and 2 mg/kg	Rat	Reduce serum levels of LH, FSH and testosterone	Raji & Bolarinwa, 1997
Sapindus mukorossi Gaertn.	Sapindaceae	Stem wood	Saponins, digitonin	0.05%, 0.1%, 1.25%, and 5%	Human semen	Disruption and erosion of membrane	Pakrashi et al., 1991
Sapindus trifoliatus L	Sapindaceae	fruit pulp	Saponin	20mg	Rats	Antiestrogenic effects	Bhargava, 1988
Terminalia chebula Retz.	Combretaceae	Dry fruits	Anthraquinones, gallic acid, ellagitamic acid, ellagic acid, 4,2,4-chebulyl-β-Dglucopyranose	50 and 100 mg/ kg/day	Rat	Acrosomal enzyme and sperm hyaluronidase enzyme inhibition	Srivastav et al., 2010
Tinospora cordifolia (Willd)	Menispermaceae	Stem	-	100 mg/ rat/day	Rat	Decrease testosterone levels in the plasma and prevent glycolysis in spermatozoa.	Gupta, 2006
Ziziphus mauritiana Lam.	Rhamnaceae	Barks	Saponin	0.1 and 0.5 mg/ ml	Human semen	Disrupt lipid within sperm membrane	Dubey & Dubey, 2011
Phytoconstituents with anti-spermatogenic activity							
Bacopa monnieri (L.) Wettst.	Scrophulariaceae	All part	-	250 mg/ kg	Mice	Decrease fructose level and inhibit spermatogenesis	Singh & Singh, 2009
Barleria prionitis L.	Acanthaceae	Root	Apigenin-7-o-glucoside barlerin, acetyl barlerin,	100 mg/ kg	Rat	Decrease protein, sialic acid, and glycogen concentration, as well as components of germinal and Leydig cells.	Verma et al., 2005
Cannabis sativa L.	*Cannabinaceae*	Seeds	Cannabinoids	20 mg/kg	Rat	Act on cannabinoids receptors	Sailani & Moeini, 2007
Chrysophyllum albidum G. Don	*Compodeoidea*	Root bark	Alkaloids, tannin, saponin, phenol, flavonoids	100 and 200 mg/ kg	Rat	Decrease the levels of gonadotropins (FSH and LH) and hinder spermatogenesis	Mehra & Thakur, 2010; Ofoego et al., 2013
Citrullus colocynthis (L.) Schrad.	Cucurbitaceae	Root	1,2,6-hexa-cosanediol, Hentriacontane, n-octacosanol,	50, 100, and 200 mg/kg	Rat	Decrease sialic acid and protein levels by inhibiting pituitary gonadotropin release.	Mali et al., 2001
Crotalaria juncea L.	Papilionaceae	Seeds	-	25 mg/ 100 g/ day	Mice	Decrease the amount of seminiferous tubular fluid and the levels of protein, FSH, and LH.	Vijaykumar et al., 2004
Cuminum cyminumin L.	Apiaceae	Seeds	-	100 mg/	Rats	Sloughing or destruction of epithelial cells, as well as a reduction in glycogen content.	Muthu & Krishnamoorthy, 2011

Curcuma longa L.	Zingiberaceae	Rhizome	-	600 mg/ kg day	Mice	suppressing gonadotropin production and lowering serum levels	Mishra & Singh, 2009
Fadogia agrestis Schweinf. ex Hiern	Rubiaceae	Stem	Alkaloids, anthraquinones, flavonoids, saponin	18, 50, and 100 mg/kg	Rat	Elevate cholesterol levels while decreasing glycogen content	Yakubu et al., 2008
Hibiscus rosasinensis L.	Malvaceae	Flower	-	150 and 300 mg/ kg	Mice	Decrease androgen synthesis and reduce spermatogenic element	Jana et al., 2013
Lepidium meyenii Walp.	Brassicaceae	Roots	-	66.7 mg/ ml	Rat	Increase epididymal weight while decreasing seminiferous epithelium stages I-VI.	Gonzales et al., 2001
Leptadenia hastata	Asclepediaceae	Leaves and stem	-	100, 200, 400, and 800 mg/ kg	Rat	Lower Leydig cell and hormonal imbalances in testosterone LH and prolactin blood level	Bayala et al., 2011
Momordica charantia L.	Cucurbitaceae	Seed	-	25 mg/ 100 g B.W.	Rat	Reduce gonadotrophins (FSH) while increasing sudanophilic lipids and cholesterol.	Naseem et al., 1998
Mentha longifolia L	*Lamiaceae*	Leaf	-	50, 75, and 100 mg/kg/day	Rat	Decreases in spermatogonial populations, mature spermatids, seminiferous tubule diameter, lumen diameter, and epithelial height	David et al., 2022
Mondia whitei (Hook.f.) Skeels	Periplocaceae	Roots	Steroids, triterpenes	500 and 1000 mg/kg	Rat	Reduce intratesticular concentration of cholesterol	Watcho et al., 2005
Morinda lucida Benth.	Rubiaceae	Leaves	Anthraquinones, anthraquinols	400 mg/ kg/day	Rat	Decrease serum concentrations of testosterone and acetylcholinesterase inhibition.	Raji & Bolarinwa, 1997
Mucuna urens L.	Cannabaceae	Seed	Flavonoids, anthranoid, anthraquinones, polyphenols	70, 140, and 210 mg/kg B.W.	Rat	Inhibit endogenous gonadotrophic activity	Etta et al., 2009
Ocimum gratissimum L.	Lamiaceae	Leaves	Citral, Eugenol, charvicol, linalol, gerianol thymol	11–88 mg/kg	Mice	Decrease the number of Leydig and Sertoli cells and damage the cell membrane.	Obianime et al., 2010
Parkinsonia aculeate L.	Caesalpiniaceae	Stem bark	β-amyrin acetate α-Amyrin acetate, 6-hydroxytritriacontan-3-one 6-hydroxypentacosylpentanoate ethynoma decanoate,	50, 100, and 200 mg/day	Rat	Reduce testosterone levels, as well as Leydig cell and seminiferous tube diameters.	Gupta et al., 2007
Piper nigrum L.	Piperaceae	Fruits	Piperine	25 and 100 mg/kg	Mice	Decrease sialic acid level and reduce fructose concentration n seminal vesicle	Mishra & Singh, 2009
Ruta graveolens L.	Rutaceae	Leaves	-	500 mg/ kg.	Rat	Decrease serum testosterone levels and Leydig cell degeneration	Khouri et al., 2005
Semecarpus anacardium	Anacardiaceae	Fruits	-	100, 200, and 300 mg/kg	Rat	Reduce sialic acid levels and androgen synthesis (LH)	Sharma et al., 2003

Terminalia bellirica (Gaertn.) Roxb.	Combretaceae	Fruits	Triphal	10 and 25 mg/ 100 g	Rat	Lower testosterone levels while elevating cholesterol levels.	Patil & Patil, 2024
Thevetia peruviana	Apocynaceae	Stem bark	α-amyrin, α-Amyrin acetate β-amyrin, lupeol, thevetigenin, lupeol acetate	100 mg/day	Rat	Deform and damage the Leydig cell while decreasing androgen concentration.	Gupta et al., 2011
Phytoconstituents that act through Sertoli cells							
Azadirachta indica A. Juss.	Meliaceae	Leaves		100 mg/ day	Rat	Degenerate germ cells	Aladakatti & Ahamed, 2005
Dendrophthoe falcate (L.f.) Ettingsh.	Loranthaceae	Stem	Quercitrin (quercetin-3-orhamnoside), kaempferol, rutin	100 mg/ kg	Rat	Reduce the production of seminiferous tubular fluid, as well as androgen synthesis and sialic acid.	Gupta et al., 2008
Thespesia populnea (L.) Sol. ex Corrêa	Malvaceae	Leaves		400 mg/ kg	Mice	Elongate seminiferous tubules	Krishnamoorthy & Vaithinathan, 2003
Tripterygium wilfordi Hook. f	Celastraceae	Roots		100 mg/ kg/day	Rat	Degenerative alterations in the seminiferous epithelium, as well as a reduction in reproductive cells in the testes	Zi-Jian et al., 1992
Phytoconstituents interact with Leydig cells							
Berberis chitria Buch. -Ham. ex Lindl.	Berberidaceae	Root	Palmitine hydroxide	30 mg/ kg/day	Dog	Reduce post meiotic germ cells and androgen binding of Sertoli cells via FSH	Gupta & Dixit, 1989
Calotropis procera	Asclepiadaceae	Roots	Calotropin	25 mg/kg	Gerbil/rabbit	Reduce androgenic parameters to suppress testicular function.	Gupta et al., 1990
Garcinia cambogia	Cluciaceae	Seed	Biflavonoid, xanthone	100 and 200 mg/ kg	Rats	Increase interstitial spaces while decreasing Leydig cells and contraction of seminiferous tubule	Kayode et al., 2007
Malvaviscus conzattii Greenm.	Malvaceae	Flower	-	800 mg/ kg	Rats	Decrease germ cells and inhibits epididymites' function	Chakraborty & Pakrashi, 1991
Martynia annua L.	Martyniaceae	Root	-	50, 100, and 200 mg/kg	Rats	Decrease the amount of LH and testosterone in the bloodstream	Mali et al., 2002
Ocimum sanctum L.	Lamiaceae	Fresh Leaves	-	2g/day	Rabbit	Decrease pH, mucoprotein, and alkaline phosphatase levels, resulting in non-viable spermatozoa.	Sethi et al., 2010
Phytoconstituents with antimotility activity							
Carica papaya L.	Caricaceae	Seeds	-	50 mg/ kg	Monkey	Increases sperm movement, resulting in ejaculation, and alters the composition of epididymal fluid and the enzymes on spermatozoa.	Lohiya et al., 2008

Echinops echinatus Roxb.	Asteraceae	Roots	Echinopsine, echinopsidine, echinozolinone	50, 100, and 200 mg/kg	Rat	Reduce the protein concentration in the cauda epididymis and testicular glycogen levels, as well as the adrenal gland's ascorbic acid content.	Chaturvedi et al., 1995
Gossypum herbaceum	Malvaceae	Fruit	Gossypol acetic acid	20 mg/ day	Rabbit	-	Coutinho, 2002
Lagenaria breviflora (Benth.) Roberty	Cucurbitaceae	Whole fruit		1000, 2000, 4000, and 8000 mg/kg	Rat	Degenerate seminiferous tubules	Saba et al., 2009
Phytoconstituents that target and disturb hormone balance							
Abelmoschus esculentus (L.) Moench	Malvaceae	Fruit	Flavonoids, saponins	70 mg/ kg B.W./ day	Rat	Reduce serum testosterone level and spermatogenesis	Olatunji-Bello et al., 2009
Abrus precatorius L.	Leguminosae	Seed	Abridine	250 mg/ kg	Rat	Damage sperm plasma membrane function, inhibit oxidative/energy metabolism, and decrease motility of sperm.	Sinha, 1990
Bulbine natalensis Baker	Asphodelaceae	Stem	Alkaloids, tannin, anthraquinones	25, 50, and 100 mg/kg B.W.	Rat	Reduce serum testosterone and progesterone levels	Yakubu & Afolayan, 2009
Curcuma longa L.	Zingiberaceae	Rhizome s		500 mg/ kg/day	Rat	Reduce androgen production, Leydig cell nucleus diameter, and Leydig cell function.	Ashok & Meenakshi, 2004
Psoralea corylifolia L	Leguminosae	Seeds	Corylin, bavachin, psoralen, isopsoralen, psoralidin	10 g/kg B.W.	Rat	Reduce blood testosterone and FSH levels by suppressing the pituitary-testicular axis.	Takizawa et al., 2004
						testicular axis	
Stevia rebaudiana	Asteraceae	Leaves	Stevioside	2 ml/rat	Rat	Decrease androgen level	Melis, 1999
Syzygium aromaticum (L.) Merr. & L.M. Perry	Myrtaceae	Flower buds	Eugenol, β-caryophyllene	15, 30, and 60 mg/kg B.W.	Mice	Destroy germ cells and inhibit spermatogonia	Mishra & Singh, 2008
Phytoconstituents from plants with antifertility potential in female							
Abrus pricatorius Linn	Fabaceae	Seed	Abridine	1 mg/anima l	Rat	Anti-implantation activity	Okoko et al., 2010
Achyranthes bidentata	Amaranthaceae	Root	Saponins	218mg/kg	Mice	Anti-implantation activity	Kaluwa Kaingu et al., 2016
Adiantum capillus	Adiantaceae	PL	Isoadiantone	218 mg/kg	Rat	Anti-implantation activity	Ibraheim et al., 2011
Ananas comosus Merr.	Bromeliaceae	Leaf	5-stigmastane-3,5,6-triol 3-mon	40 mg/kg	Mice	Anti-implantation activity	Pakrashi & Chakrabarty, 1979
			Sitosterol	30 mg/kg			
			Ergosterol peroxide	30 mg/kg			
Aristolochia indica Linn.	Aristolochiacea e	Root	Aristolochic acid	100 mg/kg	Mice	Anti-implantation activity	Pakrashi & Chakrabarty, 1978
			p-Coumaric acid	50 mg/kg	Mice	Anti-implantation activity	
Butea monosperma (Lamb) Kuntz	Fabaceae	Seed	Butin	20 mg/kg	Rat	Anti-implantation activity	Sindhia & Bairwa, 2010
Centella asiatica	Apiaceae	Leaf	Isothankuniside and BK Compound [methyl-5-	20 mg/kg	Mice	Anti-implantation activity	Dutta & Basu, 1968

			hydroxy-3,6-diketo-23(or 24)-norurs-12-en-28-oat]				
Datura quercifolia	Solanaceae	Leaf	Daturalactone (DQ1)	100 mg/kg	Mice	Anti-implantation activity	Chandhoke, 1978
Dictamnus albus	Rutaceae	Root bark	Fraxinellone	100 mg/kg	Rat	Anti-implantation activity	Woo et al., 1987
Embelia ribes Burm.f.	Myrsinaceae	Barks	Embelin	100 mg/kg	Rat	Anti-implantation activity	Wankhade et al., 2021
Foeniculum vulgare	Apiaceae	Seed	Anethole	500 mg/kg	Rat	Anti-implantation activity	Jain & Bharathi, 2011
Heliotropium indicum	Boraginaceae	Seed	n-hexacosanol, sitosterol, stigmasterol, chalinasterol, campesterol	500 mg/kg	Rat	Anti-implantation activity	Kumar et al., 2012
Marsdenia koi	Apocynaceae	Whole plant	Marsdekoside A and B	500 mg/kg	Rat	Anti-implantation activity	Jin-Ian et al., 1991
Murraya paniculata	Rutaceae	Root	Yuehchukene	3 mg/kg	Rat	Anti-implantation activity	Kong et al., 1985
Piper longum Linn.	Piperaceae	Root	Piperine	150 mg/kg	Rat	Anti-implantation activity	Kholkute et al., 1979
Plumbago zeylanica Linn.	Plumbaginaceae	Whole plant	Plumbagin	20	Rat	Anti-implantation activity	Premakumari et al., 1977
Randia dumetorum Lamk.	Rubiaceae	Seed	Oleanolic acid-3-glucoside	100	Rat	Anti-implantation activity	Bhatt & Deshpande, 2021
Ruta graveolens Linn.	Rutaceae	Root and Leaf	Chalepensin	36 mg/kg	Rat	Anti-implantation activity	Kong et al., 1989
Striga lutea	Orobanchaceae	Whole plant	Acacetin, Luteolin	25 mg/kg	Rat, Mice	Anti-implantation activity	Hiremath & Rao, 1990
Vicoa indica (L.)	Asteraceae	Whole plant	Vicolide B		Rat	Anti-implantation activity	Kaluwa Kaingu et al., 2016
			Vicolide D	200 mg/kg	Rat	Anti-implantation activity	Alam et al., 1992
Vitex negundo Linn.	Verbenaceae	Seed	5,7,3 -trihydroxy-6,8,4 -trimethoxy flavones	100 mg/kg	Mice	Anti-implantation activity	Wankhade et al., 2021
Aristolochia indica Linn.	Aristolochiaceae	Root	Methyl aristolate	60 mg/kg	Rat	Abortifacient activity	Ren-Sheng & Yi-Sheng, 1986
Daphne genkwa	Thymelaeaceae	Root	Yuanhuacine	70-80 µg	Woman	Abortifacient activity	Ren-Sheng & Yi-Sheng, 1986
Momordica charantia Linn.	Cucurbitaceae	Seed	Momorcharins	70-80 µg	Mice	Abortifacient activity	Yeung et al., 1987
Momordica cochinchinensis	Cucurbitaceae	Root	Momorcochin	70-80 µg	Mice	Abortifacient activity	Yeung et al., 1987
Piper sp.	Piperaceae	Root	Piperine	70-80 µg	Mice	Abortifacient activity	Piyachaturawat et al., 1982
Plumbago zeylanica Linn.	Plumbaginaceae	Leaf extract	Plumbagin	200, 400 mg/kg	Rat	Antifertility activity	Edwin et al., 2009
Aehonychon purpurea		Whole plant	Lithospermic acid	50 mg/kg	Rats	Contraceptive activity	Unny et al., 2003
Androsace septentrionalis	Primulaceae	Whole plant	Triterpene glycoside	100 mg/kg	Mice, Rats	Contraceptive activity	Mats & Savchenko, 1986
Citrus aurantium	Rutaceae	Peel	Cirantine	0.75 mg/kg	Rabbit	Contraceptive activity	Ghosh et al., 1955
Ferula jaeschkeana	Apiaceae	Plant without root	Ferujol	0.6mg/kg	Rats	Contraceptive activity	Prakash et al., 1991

Herbal male contraceptive

Studies have reported a number of plants having contraceptive potential that can be used in men. Products obtained from plants having spermicidal activity are now the current interest of the day (Khillare & Shrivastav, 2003; Souad et al., 2007). Many studies have been conducted to explore the antifertility effect of medicinal plants in male animal models (Coutinho, 2002; Lohiya et al., 2000). The list of plants accessible for antifertility activity is provided below, along with the components employed and a method of action to help comprehend this activity.

CONCLUSION

Since olden times, traditional methods of contraception are being used in men and women that include use pf physical, surgical and hormonal methods. With the success of these methods in controlling conception and overpopulation, various side effects have become prominent with the excessive use of these methods. Therefore, scientists have shifted their research focus in the development of safe, cheap and easy to use methods of contraception. Since the use of therapeutic drugs has been in practice by folklore and ancient civilization, modern research is now focused on the discovery of plants having antifertility actions, isolation of fertility regulating compounds, and formulation of compounds using pharmacokinetic and pharmacodynamic approaches.

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