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Medicinal Plants with Male Antifertility Potential and their Impact on Male Reproductive Health: Mechanisms and Evidence

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Abstract

Background: Although there are limitations and potential side effects with current methods of contraception, male contraception is an important field of reproductive health research. The medicinal plants have inherent bio-active phytochemical constituents and biological activities which have captured the scientific interest as potential natural male anti-fertility agents. **Aim:** The current research will compile and assess medicinal plants that have been reported to have male antifertility activity in a systematic manner. **Methods:** Electronic databases like PubMed, Scopus, ScienceDirect, Google Scholar, and INFLIBNET were used to conduct a comprehensive literature review. The inclusion criteria were relevant studies that were published between 1980 and 2025. **Results and Discussion:** A total of 233 medicinal plant species with reported antifertility activity were identified, of which 100 plants exhibiting experimentally validated male antifertility effects were selected for detailed evaluation. It was found that antifertility effects of medicinal plants occur in various ways, such as inhibition of spermatogenesis, hormonal effects, antiandrogenic effects, etc. Families of plants including *Fabaceae, Asteraceae, Apocynaceae* and *Lamiaceae* were highly represented. Plant parts that were most used were seeds, roots, and leaves, meaning that concentrations of bioactive phytoconstituents were high. One of the greatest limitations found was the absence of clinical literature and standardisation of plant extracts. **Conclusion:** Medicinal plants are a potentially rich and untapped source of male contraceptive agents. Nevertheless, additional studies that entail isolation of active compounds, mechanistic validation, safety assessment, and clinical trials are necessary to ensure their successful translation into viable contraceptive solutions.

Major Findings: A total of 233 species were identified as medicinal plants and 100 plants with experimentally reported male antifertility activity were investigated in detail. The main mechanisms involved were inhibition of spermatogenesis, hormonal modulation, antiandrogenic effect, decreased sperm motility, and testicular changes. The limited clinical evidence, lack of standardised plant extracts, and uncertainty about safety and reversibility underscore the need for more mechanistic studies and clinical trials to be conducted.

Keywords: Antiandrogenic, Herbal Contraception, Male Antifertility, Medicinal Plants, Phytoconstituents, Spermatogenesis

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1 Introduction

The rapid population growth and the increasing cases of unwanted pregnancies remain significant social health issues on the global front. The family planning programs have long been inclined to female-oriented contraceptive measures such as hormonal pills, intrauterine devices, and surgical sterilisation. Conversely, male contraceptives are confined to condoms and vasectomy. Condoms are also very common, but they need frequent and proper use and vasectomy, though very effective, is usually deemed permanent and is not easily accepted. This discrepancy highlights the pressing requirement to come up with new, safe, reversible and user-friendly male contraceptive measures[1].

Existing male contraceptive methods have several significant drawbacks. Though cheap and effective usage of condoms leads to high typical use failure rates. Although extremely effective, vasectomy is considered to be a permanent contraceptive procedure, but its reversibility is not certain; the procedure for reversing vasectomy is costly, and restoration of fertility is not always achievable. Clinical trials in recent years have demonstrated promising contraceptive efficacy of hormonal male contraceptive regimens using combinations of testosterone and progestins. However, they have been scarcely used in the clinic due to side effects including mood disorders, acne, weight gain, changes in lipid metabolism, endogenous testosterone suppression, the need for frequent injections or implants and high inter-individual variability in the degree of spermatogenesis suppression. Furthermore, none of the hormonal male contraceptives has been broadly approved by the regulators for routine use. All these restrictions highlight the necessity of finding alternative safe, effective, reversible, economical and non-hormonal male contraceptive agents and medicinal plants are a promising source of novel male contraceptive agents.

In this respect, more focus has been laid on natural products, especially medicinal plants, as a possible source of antifertility agents. Traditional medicine Systems of medicine like *Ayurveda*, *Unani*, *Siddha* and Traditional Chinese Medicine have been using medicinal plants for centuries to regulate fertility and control reproductive health. A variety of bioactive phytoconstituents such as alkaloids, flavonoids, glycosides, saponins, tannins, and terpenoids are abundant in these plants and have been reported to have many pharmacological effects. Most of these compounds have also proven capable of affecting the reproductive processes in males; hence, they make good candidates in the development of contraceptives[2].

The experimental research has indicated that plant-based compounds can influence male fertility in a variety of mechanisms. The inhibition of spermatogenesis, which is the production of sperm in the testes is one of the main mechanisms. Failure in this process may lead to low sperm count, abnormal sperm morphology and loss of fertility. Also, other medicinal plants were reported to reduce sperm motility, which is a necessary condition of fertilisation. Other processes involve antiandrogenic impacts, in which plant compounds disrupt the production, release, or the activity of androgens, including testosterone, which influences male reproduction. Other plants also prevent the production of steroids by acting on key hormone biosynthesis-related enzymes.

Moreover, some extracts of plants have a direct spermicidal effect and destroy the sperm membrane or weaken its functional integrity, causing the immobilisation or death of sperm cells. Medicinal plants have been observed to cause structural and functional alteration of reproductive organs in other cases, such as the testes, epididymis and the accessory sex glands[3]. A major benefit of the plant-based antifertility agents is that they may be reversible, a favourable trait of a contraceptive. A number of studies have indicated that normal fertility has been restored following the termination of the treatment, implying that the agents can be used as a safer alternative to permanent treatment. Nevertheless, not all the compounds of plant origin lack adverse effects. Others have been linked to testicular toxicity, oxidative stress, and permanent destruction of reproductive tissues, and it is essential to consider the safety profiles closely.

Although this has undergone a lot of preclinical research, little has been done to translate plant-based male contraceptives into clinical application. Among the key challenges are the absence of standardisation of plant extracts, the variability of the phytochemical composition due to geographical and environmental conditions, the lack of identification of active constituents, and the lack of well-designed clinical

trials in humans. There are also problems with dosage, formulation, long-term safety, and regulatory approval that should be addressed.

Based on these, there is an evident necessity to organise the existing data on medicinal plants reported to have male antifertility effects in a systematic manner and to critically analyse the available information. This will not only increase knowledge on their mechanisms of action but also help in coming up with good candidates for research and development. Thus, this review paper will aim to review in a comprehensive way medicinal plants that have male antifertility activity, their mechanisms, experimental models, and their potential to be developed into safe and effective male contraceptive agents.

2. Classification of Male Antifertility Agents

Antifertility agents in males can be classified into broad categories depending on the mechanism of action, source, and duration of action.

2.1 Hormonal Antifertility Agents

Hormonal agents are the ones that disrupt the hypothalamic-pituitary-gonadal (HPG) axis, which controls male reproductive activity. The main effects of these agents are the inhibition of gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion that decrease testosterone synthesis and prevent spermatogenesis. Hypothalamus and pituitary gland negative feedback can be established by exogenous administration of androgens, progestins, or both. This leads to a reduction in the endogenous levels of testosterone in the testes, which eventually suppresses the production of sperm. Despite the encouraging outcomes of approaches in clinical trials, they are commonly linked to such side effects as mood changes, weight gain, altered lipid profile, and cardiovascular risk. In addition, some individuals are not always completely suppressed in spermatogenesis[4].

2.2 Non-hormonal Antifertility Agents

Non-hormonal agents do not change the systemic hormone levels but act directly on the reproductive system. These agents affect certain processes in the production, maturation, motility, or activity of the sperm. Antifertility mechanisms act in several pathways, all of which interfere with male reproductive functioning. These involve suppression of spermatogenesis at different stages, thus lowering the yield of viable sperm. Also, some of them cause structural and morphological defects in sperm, which affect their fertilising ability. Reduced sperm motility also reduces the fertilisation of the ovum by the sperm. Other compounds also directly affect spermicidal action, which results in the death or inactivation of sperm cells. In addition, epididymal dysfunction disrupts sperm maturation, storage and transportation, thereby leading to impaired fertility. This category is characterised by a large number of medicinal plants, which include bioactive compounds that have a local effect on the reproductive tissues. The use of non-hormonal agents is deemed to have benefits against systemic side effects and targeted action. Nevertheless, their efficacy, reversibility and safety need additional validation.

2.3 Natural Antifertility Agents

Natural agents are plants, animals or microorganisms, and medicinal plants are the most thoroughly studied. These agents are known to have phytoconstituents like alkaloids, flavonoids, saponins and terpenoids that are reported to have effects on male fertility. Antifertility agents made of plants can have several effects: antispermatogenic, antiandrogenic, and spermicidal. They are commonly applied in conventional medicine and are mostly seen as less harmful and less expensive than synthetic medicines. Moreover, several natural agents have reversible antifertility effects, and therefore, they can be considered in the development of contraceptives. The issues with natural agents, however, are variability in composition, not being standardised, inconsistent dose, and limited clinical evidence.

2.4 Synthetic Antifertility Agents

Synthetic agents are those that are chemically designed compounds that have been developed using modern pharmaceutical methods. These comprise contraceptives, chemical spermicides, as well as compounds with targeted effects on spermatogenesis or sperm activity. Controlled formulation and dosage make synthetic agents more predictable and consistent in their results. Nevertheless, they can be poorly tolerated due to side effects such as hormonal

disruption, systemic toxicity and chronic health risks. In addition, the issues of acceptability and compliance may arise, particularly when it is used on a long-term basis.

2.5 Temporary (Reversible) Antifertility Agents

Temporary contraceptives offer reversible contraception, which is temporary and normal fertility is restored once the contraceptive is stopped. The agents are very desirable since they are flexible and controllable in family planning. The processes are usually based on a temporary blockage of spermatogenesis, which entails a temporary decrease in sperm production without permanent damage. This is normally supplemented by reversible regulation, in which any changes in the concentration or activity of reproductive hormones are controlled to produce controlled testicular functioning. Also, there can be short-term impairments in the functioning of sperm (that is, changes in their motility and fertilising capabilities), but such effects are usually reversible when the agent is stopped, and normal sperm functioning is regained. A lot of plant-based and a few other agents belong to this category. Their effects are reversible, and this is why they are the best candidates to be used in manufacturing male contraceptives. It is, however, possible that the time taken to recover fertility may depend on the agent and period of use.

2.6 Permanent (Irreversible) Antifertility Agents

Long-term or permanent antifertility procedures lead to permanent or irreversible infertility. The most widespread one is vasectomy, which is a surgical operation that obstructs the passing of the vas deferens to avoid the sperm transport.

There are also certain chemical or plant-based agents that can result in irreversible damage to the testes or reproductive tissues that cause permanent infertility. Although these are effective, they are not so popular because they are irreversible and may cause long-term complications.

3. Mechanisms of Male Antifertility Action

Male antifertility actions of medicinal plants have multiple biological pathways that overlap with each other, and they target the hypothalamic-pituitary-gonadal (HPG)-axis, testicular action, sperm maturation and sperm viability. Knowledge of these mechanisms is important when discovering possible targets on which safe and effective male contraceptive agents can be developed[5].

3.1 Antispermatogenic Activity

The critical process of spermatogenesis in the seminiferous tubules of the testes is interrupted or inhibited, and this can be referred to as antispermatogenic activity. The process of spermatogenesis is highly coordinated, and the differentiation of the spermatogonia to mature spermatozoa and their development is controlled by the Sertoli cells and testosterone.

Substances of plant origin can interfere with the physiological differentiation of spermatogenesis by causing several cellular and structural changes in the testes. These include degeneration of the germinal epithelium, which is highly involved in the production of sperm, and disruption of the functionality of the Sertoli cells, thus disrupting the nourishment and support that is needed to develop the germ cells. Moreover, these materials have the potential to arrest sperm cells in different stages of development, like spermatogonia, spermatocytes and spermatids and eventually prevent their maturation. Besides, they can trigger apoptosis of germ cells, which are cells that undergo programmed cell death, causing a resulting decrease in the number of sperm and the fertility rates, as generally depicted in Figure 1.

The decrease in seminiferous tubules diameter, the loss of the germ cells and the disorganisation of the spermatogenic layers are frequently proved with the support of histopathological analysis. It is also among the most frequently reported antifertility measures that are usually reversible on withdrawal of the treatment, depending on the level of the damage[6].

3.2 Spermicidal Activity

The Spermicidal activity is based on the direct killing or freezing of spermatozoa. This especially applies to the agents to be used as topical contraception. Phytoconstituents like saponins, alkaloids, and essential oils can mediate this effect and have a direct effect on the sperm. These compounds have the ability to change the

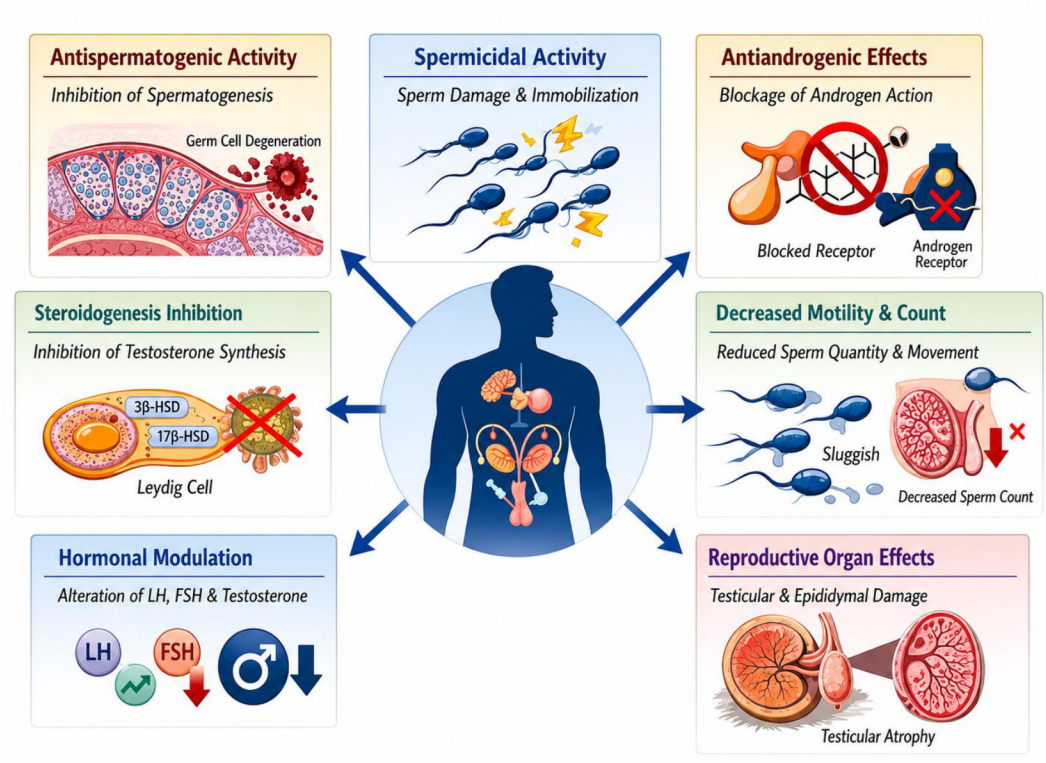


Figure 1. Schematic representation of mechanisms underlying male antifertility activity of medicinal plants.

integrity of the sperm plasma membrane and change its permeability, causing functional disturbances. In others, they can cause sperm to immobilise temporarily, thus halting their development. They may also cause the intracellular enzymes and ions to leak out, which interrupts the necessary metabolic activities in the sperm. The important parameters, including sperm viability, motility, and membrane integrity, are consequently altered and are typically assessed *in vitro* to establish spermicidal activity. Potent spermicidal agents are generally quick-acting and can be used as a good candidate to be included in contraceptive preparations such as gels and creams[7].

3.3 Antiandrogenic Effects

Antiandrogenic activity can be described as the interference in the production, release or the response of the androgens, particularly the testosterone required to facilitate the functionality of the male reproductive mechanism. Antiandrogenic effects of plant extracts can be achieved in various ways which disrupt androgen action and signalling. These effects include blocking of androgen receptors, hence preventing the binding and activity of androgens at the target site. Moreover, these extracts can suppress the synthesis of testosterone by the Leydig cells, which would result in a decrease in circulating concentrations of this important hormone. Moreover, they may interfere with the conversion of testosterone to more active metabolites and, as a result, reduce its biological activity and general androgenic effect on reproductive processes. Spermatogenesis impairment, libido, and accessory sex organs regression (prostate and seminal vesicles) are caused by the androgen decreases. The antiandrogenic activities are usually associated with the decrease in weights of the reproductive organs and histological structure[8].

3.4 Inhibition of Steroidogenesis

Steroidogenesis is the biochemical process of converting cholesterol to steroid hormones (like testosterone) in the testes. It is a multi-enzyme process which involves 3 beta-hydroxysteroid dehydrogenase (3 beta-HSD) and 17 beta-hydroxysteroid dehydrogenase (17 beta-HSD). Some phytochemicals have antifertility effects through inhibition of major enzymes in the production of testosterone biosynthesis, thus leading to lower synthesis of this vital androgen. This enzyme block may cause maladaptive Leydig cell functioning,

which is the major testosterone producer. This interference therefore causes disharmony which distorts the endocrine regulation required to maintain normal spermatogenesis and eventually affects male reproductive ability. The steroidogenesis inhibition has a direct influence on the intratesticular testosterone, which is crucial in the development of spermatogenesis. This procedure normally supplements antiandrogenic effects and assists the generation of an overall antifertility effect[9].

3.5 Decrease in Sperm Motility and Count

The fertility of males relies on the count and sperm motility. A number of medicinal plants have been mentioned to decrease these two parameters by a significant margin. The mechanisms that are involved are the mitochondrial dysfunction, which results in the decrease of the ATP production as well as the general drop in energy required to support the normal sperm activity. Moreover, a higher level of oxidative stress may lead to lipid peroxidation of sperm membranes, undermining their integrity and functionality. Changes in the activity of ion channels and flagellar motility further worsen sperm motility and fertilising potential. Additionally, interference with the epididymal environment in the development of sperm obstructs sperm development, storage, and functional competence, which contributes to infertility. The loss of the number of the sperm might be caused by a defect in the spermatogenesis or a greater degradation of the sperm but the reason of reduced motility has an impact on the capacity of the sperm to approach and fertilize ovum. They are usually dose-effective, and they can be reversible[10].

3.6 Hormonal Modulation (LH, FSH, Testosterone)

The HPG axis is involved in the strict control of male reproductive activity, in cooperation with LH, FSH, and testosterone. Through their action on major regulators of the hypothalamic-pituitary-gonadal axis, these processes can be altered by medicinal plants. These are plant-based compounds which can suppress the secretion of luteinising hormone (LH) and thus lower the secretion of testosterone by the Leydig cells. Moreover, they can inhibit follicle-stimulating hormone (FSH), which is key in the regulation of Sertoli cells and the stimulation of spermatogenesis. The combined effects of these actions are capable of modulating the balance and disrupting normal sperm production and maturation with medicinal plants. Disrupted spermatogenesis and infertility are caused by hormone imbalance. Depending on the properties of the bioactive compounds, antifertility mechanisms can be hormone-dependent[11].

3.7 Reproductive Organ Effects

Along with the biochemical and cellular ones, most of the antifertility agents induce structural and functional alterations in male reproductive organs, such as testes, epididymis, vas deferens, and accessory glands. The effects observed are degeneration of the seminiferous tubules followed by testicular atrophy, which to a great extent affects the production of sperm. This is usually coupled with weakness or diminished functional ability of the testes and accessory sex organs. As well, failure to store and mature sperm in the epididymis also compromises fertility. There are also histopathological changes such as necrosis of cells, vacuolisation, and disorganisation of the tissue structure, which are responsible for the general deterioration of reproductive health and function. The mutations will impact on the production, maturation and transportation of the sperm that will lead to decreased fertility. The high doses or long-term effects may be permanently harmful despite the fact that some of the effects are reversible.

4. Materials and Methods

4.1 Study Design

The present systematic review was done following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) for the identification, screening, eligibility assessment and inclusion of relevant studies in the systematic review.

4.2 Literature Search Strategy

An extensive literature review was carried out for studies reporting male antifertility activity of medicinal plants using the electronic databases PubMed, Scopus, ScienceDirect, Google Scholar, Web of Science and INFLIBNET. The search period was from January 1980 to March 2025.

4.2.1 Keywords and Search Terms

The following keywords and Boolean operators were used: Male infertility OR male contraception OR male antifertility OR male reproductive toxicity AND medicinal plants OR herbal medicine OR phytotherapy OR plant extract AND antifertility activity OR spermatogenesis inhibition OR spermaticidal activity OR antiandrogenic activity OR fertility regulation. The reference lists of relevant review articles and eligible studies were manually searched for additional publications as well.

4.3 Eligibility and Inclusion Criteria

4.3.1 Inclusion Criteria

Original experimental research papers from 1980 to 2025. Experimental animal or *in vitro* studies assessing the anti-fertility activity of medicinal plants in male animals. Research on reproductive parameters like sperm count, sperm motility, sperm morphology, hormonal changes, testicular histopathology, fertility index or reproductive organ changes. Articles published in English.

4.3.2 Exclusion Criteria

The exclusion criteria are as follows:

- Female antifertility studies.
- Review articles, editorials, conference abstracts, letters, book chapters, and dissertations.
- Studies with inadequate experimental data.
- Research on synthetic products or non-plant products.
- Duplicate publications.

4.4 Study Selection

There were 233 records initially found in the database search. Duplicate records were removed, leaving 198 articles for title and abstract screening. After screening, 134 articles were excluded due to the lack of experimental data, review articles, and female reproductive studies, and 17 were excluded because they were not related to male antifertility. The remaining 64 full-text articles were assessed for eligibility. After full-text evaluation, 31 studies were deemed to be ineligible due to not meeting inclusion criteria or insufficient outcome data. Figure 2 outlines the PRISMA 2020 selection process for the systematic review. Finally, 33 eligible studies describing 100 medicinal plant species were included in the qualitative synthesis. Several studies investigated multiple medicinal plant species, so, despite the fact that only 33 studies met the eligibility criteria, they were able to report the experimental findings on 100 different medicinal plants included in Table 1.

4.5 Extraction and Compilation of Data

Based on the obtained literature, useful data were identified and tabulated. Overall, 233 species of medicinal plants that were reported to contain antifertility activity were identified and discussed. The following information was recorded and summarised for each plant species: botanical name, plant family, part of the plant used, extract type, experimental model (animal or *in vitro* model), and antifertility mechanism reported. The information obtained was also tabulated to provide a clear and detailed picture of medicinal plants that had potential antifertility activity.

5. Medicinal Plants with Male Antifertility Activity

Table 1 gives a comprehensive list of medicinal plants that have male antifertility effects. The sample comprises 95 species of plants which represent a great variety of botanical families, indicating the enormous diversity of natural resources with possible contraceptive properties. Table 1 is a systematic compilation of important parameters including botanical name, family, part of plant used, experimental model, mechanism of action, and references to support past studies in this field, hence giving a systematic representation of research done so far on this area[12].

Table 1 analysis shows that most commonly, plants of the families *Fabaceae, Asteraceae, Apocynaceae, Cucurbitaceae, Euphorbiaceae*, and *Lamiaceae* have been reported to have antifertility activity. Of them, the proportions of *Fabaceae* and *Asteraceae* are high, indicating that these families can be important sources of bioactive compounds affecting male reproductive activity.

Regarding parts utilised in plants, seeds, roots, leaves, bark, fruits, and whole plants have been researched. The most widely used parts are seeds and roots, probably because they contain the greatest concentration of secondary metabolites like alkaloids,

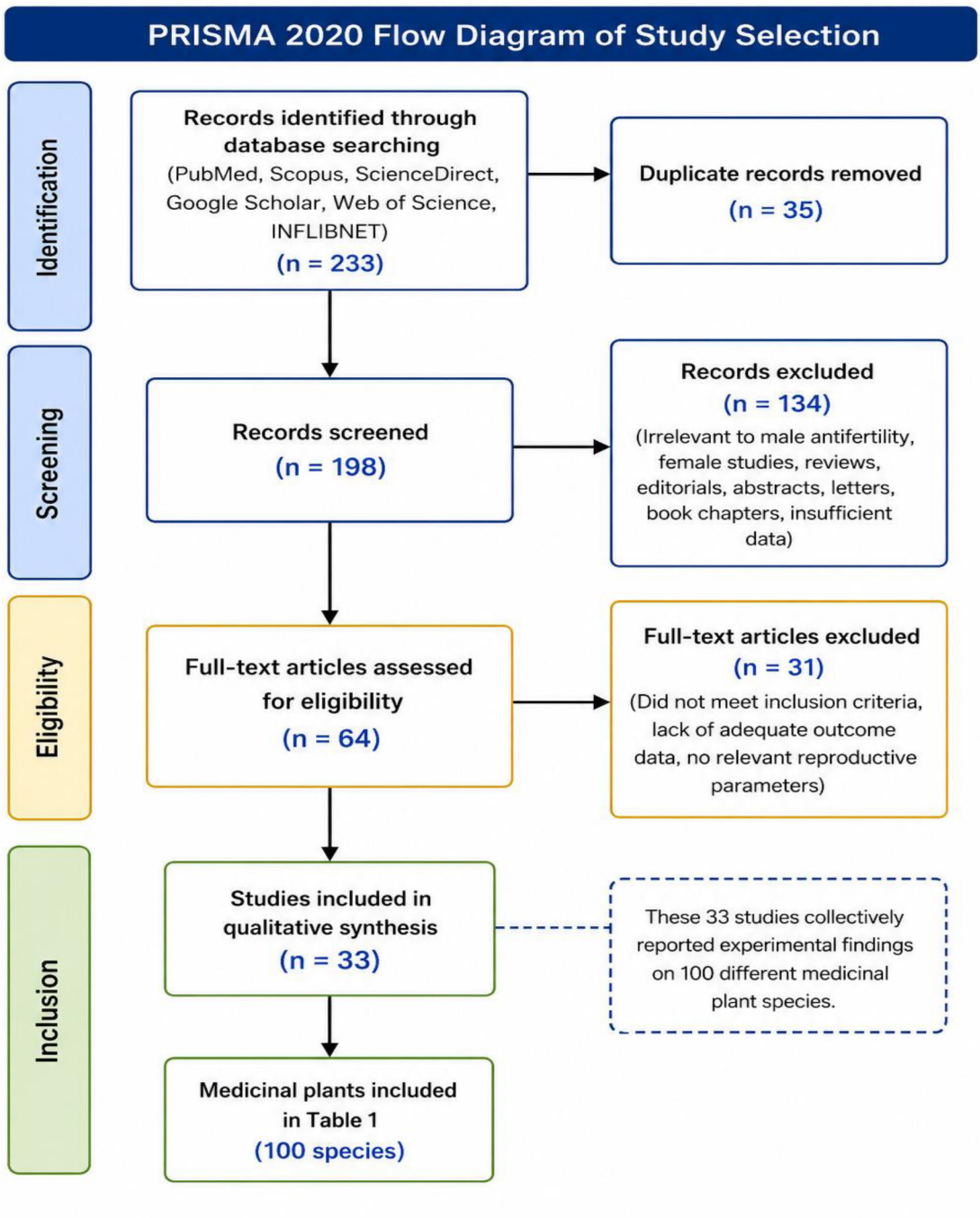


Figure 2. PRISMA 2020 study selection process for the systematic review.

saponins and flavonoids. More than one part of the plant of a particular species has been tested in other instances, which suggests the distribution of antifertility-active constituents throughout the plant.

The animal-based experimental models used in the studies are mostly of the rat type; the next most frequent models used are rats, mice, dogs, rabbits, and primates. There are fewer studies that have used higher animal models and humans, which represents a clinical translation gap.

6. Family-wise Classification

The analysis of the family-wise distribution of antifertility activity indicates that some families of plants are concentrated in the pattern of antifertility

activity. There are also examples of plant families that have been linked to antifertility effects, which indicates that they can be used for drug discovery. The *Fabaceae* family comprises *Abrus precatorius, Acacia concinna, Albizia procera*, and *Butea monosperma*, all of which are usually associated with spermicidal and antispermatogenic effects.

In the same way, the *Asteraceae* family which includes plants such as *Achillea millefolium, Echinops echinatus*, and *Wedelia trilobata* have all shown significant antifertility activity which is mainly by inhibiting spermatogenesis. Antiandrogenic and antispermatogenic activities are observed in species of the *Apocynaceae* family such as *Calotropis procera* and *Mondia whiteii*. *Citrullus colocynthis* and *Momordica charantia* are members of the family *Cucurbitaceae* and are characterised by reversible antifertility effects alongside interference with spermatogenesis. Also, the *Lamiaceae* family, including *Ocimum sanctum* and *Clerodendrum serratum*, is known to have antiandrogenic and spermicidal effects. On balance, such classification emphasises the fact that certain plant families could be used as potential sources of the creation of new antifertility agents depicted Figure 3[13].

7. Mechanism-wise Classification

The medicinal plants with antifertility potential can be systematically grouped into various functional categories depending on the way they disrupt male reproductive physiology. Another significant group is antispermatogenic agents, in which plants like *Carica papaya, Andrographis paniculata*, and *Cichorium intybus* are used by blocking spermatogenesis at various stages. These plants can inhibit the proliferation, meiosis or differentiation of the germ cells, resulting in low sperm production. This repression can be direct by cytotoxic action on germinal epithelium or indirect by disequilibrium, which eventually leads to oligospermia or azoospermia depending on the degree of repression.

Plants like *Acacia concinna, Anacardium occidentale* and *Cananga odorata* are spermicidal agents with direct toxic action against sperm cells. These agents disrupt the integrity of the sperm plasma membrane, causing a rise in permeability, loss of intracellular contents and ultimately the death of the cell. They are also quick to paralyse sperm; hence, they are especially applicable in the potential development of topical contraceptives like gels or creams, as they are fast-acting. The antiandrogenic plants like *Azadirachta indica, Ocimum sanctum* and *Nicotiana tabacum* disrupt the androgen signalling pathways. These plants can either block androgen receptors, inhibit testosterone production by Leydig cells or inhibit testosterone from being converted to its more active metabolites. These activities interfere with the hormonal control of the male reproductive system, causing a disruption of spermatogenesis and libido or reproductive capacity[14].

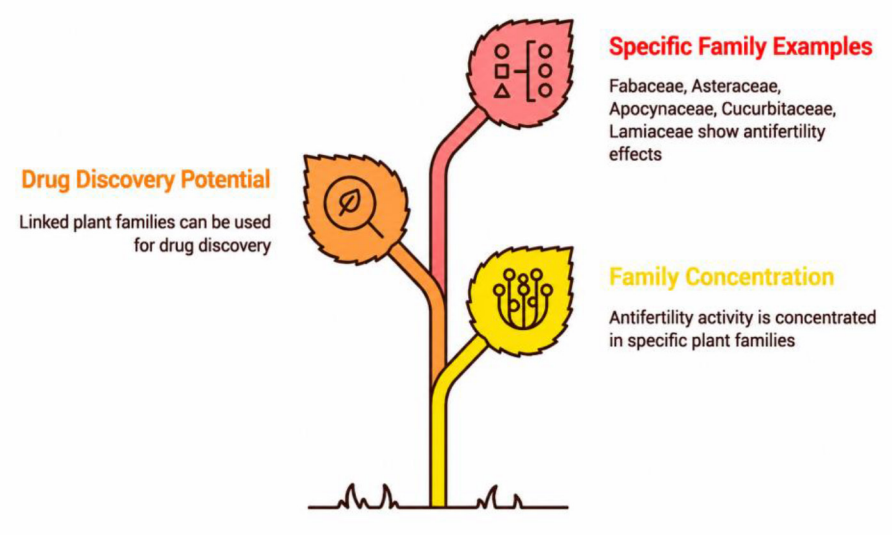


Figure 3. Representation of the underexplored plant families in antifertility drug discovery.

Plants such as *Aegle marmelos, Bambusa arundinacea* and *Withania somnifera*, which have been reported to reduce sperm concentration and motility to a significant extent, are sperm count and motility reducers. These results could be due to oxidative stress, mitochondrial dysfunction, or changes in ion channels and flagellar movement, and eventually affect the process through which sperm reach and fertilise the ovum. Another type is hormonal modulators, in which some medicinal plants affect the endocrine axis, changing the concentration of luteinising hormone (LH), follicle-stimulating hormone (FSH), and testosterone. Such plants indirectly influence the activity of Sertoli and Leydig cells by influencing the activity of these important hormones, and thus affect spermatogenesis and general fertility. Such effects are usually reversible, based on the length and amount of exposure.

Lastly, testicular and reproductive toxicants include plants like *Balanites roxburghii* and *Cannabis sativa* that cause structural and functional impairment of reproductive organs. They can lead to degeneration of seminiferous tubules, testicular atrophy, and damage to Leydig cells, as well as histopathological alterations such as necrosis, vacuolisation, and disorganisation of the tissues. These toxic impacts can be very debilitating to reproductive capacity and, in a few instances, may result in infertility that is permanent or even irreversible. On the whole, this classification demonstrates the wide and complex nature of the mechanisms by which medicinal plants can affect male fertility, from reversible functional modulation to direct cellular toxicity, providing therapeutic prospects and warning of their use.

8. Results and Discussion

The literature search on the available literature was done thoroughly to identify medicinal plants with antifertility properties. The literature search has helped identify more than 300 peer-reviewed scientific articles that contained information on the traditional and ethnomedicinal use of plants in the regulation of fertility. These articles were acquired from different internationally recognised scientific databases and journals in order to achieve reliability and credibility of the information provided in this review.

The present systematic review showed that medicinal plants are a rich source of bioactive compounds with potential to regulate male reproductive functions. This study showed that there is no single botanical family or phytochemical class that is completely represented by plants with antifertility properties, but rather a widespread distribution of plants and their mechanism of action. However, most of the available evidence comes from experimental animal research and is therefore not directly applicable to humans.

The most important finding is that the antifertility effects of medicinal plants have several mechanisms. Mechanisms of inhibition in the most common cases were: Spermatogenesis inhibition, hormonal modulation, antiandrogenic activity, oxidative stress induction, and degeneration of testicular tissues. This polypharmacological function can render a higher contraceptive effect than that of the synthetic single-target ones, but also make the identification of the main active components and the actual molecular targets more difficult.

The distribution of anti-fertility activity of plant families showed that the highest number of medicinal plants belongs to the *Fabaceae* family, followed by *Apocynaceae, Lamiaceae, Malvaceae, Apiaceae, Asteraceae* and *Euphorbiaceae*. This imbalance could be a reflection of the quantity of pharmacologically active secondary metabolites in these families as well as the increased research interest in these families. The prevalence of plant families, however, suggests possible publication bias because a significant part of medicinal plants used traditionally for fertility regulation are not yet explored scientifically.

The review also showed that the most common parts of the plants studied were seeds, leaves and roots. The tissues contain abundant amounts of alkaloids, flavonoids, saponins, terpenoids, glycosides, and phenolic compounds, known to be involved in endocrine regulation, oxidative stress, germ cell apoptosis and inhibition of sperm maturation. However, few studies have succeeded in separating and identifying the bioactive molecules responsible for the anti-fertility action. Most investigations were conducted using simple extracts, and this hampered the determination of actual structure–activity relationships or the exact molecular targets.

One of the major drawbacks of the studies included here is the high degree of methodological variation across the studies. A variety of animal species were used, different methods for preparing extracts, different

Table 1. List of Medicinal plants reported to possess Male antifertility effects

Sr. No.	Botanical Name	Family	Part Used	Extract	Reported Activity	Mechanism of Action	Major Phytoconstituents	Reference
1	*Azadirachta indica* A. Juss.	*Meliaceae*	Leaves/ Seed	Ethanolic	Antispermatogenic	Inhibits spermatogenesis, ↓ testosterone	Azadirachtin, nimbin	[15,16]
2	*Carica papaya* L.	*Caricaceae*	Seeds	Aqueous	Spermicidal	Disrupts sperm membrane and motility	Carpaine, benzyl isothiocyanate	[17]
3	*Momordica charantia* L.	*Cucurbitaceae*	Fruit	Methanolic	↓ sperm count	Testicular degeneration	Charantin, momordicin	[18]
4	*Catharanthus roseus* (L.) G. Don	*Apocynaceae*	Leaves	Ethanolic	Testicular toxicity	Inhibits cell division in germ cells	Vincristine, vinblastine	[19]
5	*Hibiscus rosa-sinensis* L.	*Malvaceae*	Flowers	Ethanolic	Antispermatogenic	Alters androgen levels	Flavonoids, anthocyanins	[20]
6	*Ocimum tenuiflorum* L. (syn. *Ocimum sanctum* L.)	*Lamiaceae*	Leaves	Aqueous	↓ sperm motility	Oxidative stress induction	Eugenol, ursolic acid	[21]
7	*Andrographis paniculata* (Burm. f.) Nees	*Acanthaceae*	Whole plant	Ethanolic	Spermatogenic arrest	Suppresses LH and testosterone	Andrographolide	[22]
8	*Tinospora cordifolia* (Willd.) Hook. f. and Thomson	*Menispermaceae*	Stem	Ethanolic	Hormonal imbalance	Alters pituitary–gonadal axis	Tinosporin, berberine	[23]
9	*Calotropis procera* (Aiton) W.T. Aiton	*Apocynaceae*	Latex	Methanolic	Antiandrogenic	Blocks androgen receptors	Calotropin, uscharin	[24]
10	*Curcuma longa* L.	*Zingiberaceae*	Rhizome	Petroleum ether	Antifertility	Reduces spermatogenesis	Curcumin	[25]
11	*Aegle marmelos* (L.) Corrêa	*Rutaceae*	Leaves	Ethanolic	Spermicidal	Membrane disruption	Marmelosin	[26]
12	*Jatropha curcas* L.	*Euphorbiaceae*	Seeds	Ethanolic	Testicular degeneration	Induces apoptosis in germ cells	Phorbol esters	[27]
13	*Piper nigrum* L.	*Piperaceae*	Fruits	Ethanolic	↓ fertility index	Inhibits sperm maturation	Piperine	[28]
14	*Cannabis sativa* L.	*Cannabaceae*	Leaves	Ethanolic	Hormonal disruption	↓ testosterone synthesis	THC (tetra hydrocannabinol)	[29]
15	*Abrus precatorius* L.	*Fabaceae*	Seeds	Ethanolic	Spermicidal	Protein synthesis inhibition	Abrin	[30]
16	*Datura stramonium* L.	*Solanaceae*	Seeds	Methanolic	↓ spermatogenesis	Anticholinergic effects	Atropine, scopolamine	[31]
17	*Solanum xanthocarpum* Schrad. and H. Wendl.	*Solanaceae*	Whole plant	Ethanolic	Antiandrogenic	↓ androgen production	Solasodine	[32]

Table 1. Continued...

Sr. No.	Botanical Name	Family	Part Used	Extract	Reported Activity	Mechanism of Action	Major Phytoconstituents	Reference
18	*Albizia lebbeck (L.) Benth.*	*Fabaceae*	Bark	Methanolic	↓ sperm count	Testicular degeneration	Saponins, flavonoids	[33]
19	*Cuscuta reflexa* Roxb.	*Convolvulaceae*	Whole plant	Ethanolic	Antifertility	Hormonal imbalance	Cuscutin	[34]
20	*Lawsonia inermis* L.	*Lythraceae*	Leaves	Aqueous	Spermatogenic inhibition	Germ cell toxicity	Lawsone	[35]
21	*Plumbago zeylanica* L.	*Plumbaginaceae*	Roots	Alcoholic	Antispermatogenic	ROS-mediated damage	Plumbagin	[36]
22	*Terminalia chebula* Retz.	*Combretaceae*	Fruits	Ethanolic	↓ motility	Oxidative stress	Tannins, chebulagic acid	[37]
23	*Eclipta prostrata* (L.) L. (syn. *Eclipta alba*)	*Asteraceae*	Whole plant	Methanolic	Hormonal changes	Alters androgen/ estrogen ratio	Wedelolactone	[38]
24	*Ficus religiosa* L.	*Moraceae*	Bark	Aqueous	Spermicidal	Membrane disruption	Flavonoids, sterols	[39]
25	*Achyranthes aspera* L.	*Amaranthaceae*	Roots	Ethanolic	Antifertility	↓ spermatogenesis	Saponins	[40]
26	*Withania somnifera* (L.) Dunal	*Solanaceae*	Roots	Extract (Unspecified)	↓ sperm production	Hormonal suppression	Withanolides	[41]
27	*Ricinus communis* L.	*Euphorbiaceae*	Seeds	Oil	Antiandrogenic	Testicular toxicity	Ricin	[42]
28	*Allium sativum* L.	*Amaryllidaceae*	Bulb	Extract (Unspecified)	Testicular toxicity	ROS generation	Allicin	[43]
29	*Zingiber officinale* Roscoe	*Zingiberaceae*	Rhizome	Extract (Unspecified)	Hormonal alteration	↓ testosterone	Gingerol	[44]
30	*Butea monosperma* (Lam.) Taub.	*Fabaceae*	Flowers	Ethanolic	Spermicidal	Direct sperm immobilisation	Butrin	[45]
31	*Barleria prionitis* L.	*Acanthaceae*	Leaves	Ethanolic	Antifertility	↓ spermatogenesis	Iridoids	[46]
32	*Persicaria hydropiper* (L.) Delarbre (syn. *Polygonum hydropiper*)	*Polygonaceae*	Leaves	Extract (Unspecified)	Antifertility	Hormonal modulation	Polygodial	[47]
33	*Juniperus communis* L.	*Cupressaceae*	Fruits	Extract (Unspecified)	Antifertility	↓ sperm viability	Terpenes	[48]
34	*Citrus limon* (L.) Osbeck	*Rutaceae*	Peel	Extract (Unspecified)	↓ sperm viability	Acidic pH damage	Limonene	[49]
35	*Artemisia vulgaris* L.	*Asteraceae*	Leaves	Methanolic	Antifertility	Hormonal imbalance	Artemisinin	[50]
36	*Aloe vera* (L.) Burm. f.	*Asphodelaceae*	Gel	Aqueous	Spermicidal	Membrane lysis	Aloin	[51]
37	*Abutilon indicum* (L.) Sweet	*Malvaceae*	Leaves	Extract (Unspecified)	Antifertility	↓ spermatogenesis	Flavonoids	[52]

Table 1. Continued...

Sr. No.	Botanical Name	Family	Part Used	Extract	Reported Activity	Mechanism of Action	Major Phytoconstituents	Reference
38	*Rubia cordifolia* L.	*Rubiaceae*	Roots	Ethanolic	Antifertility	Hormonal imbalance	Anthraquinones	[53]
39	*Urtica dioica* L.	*Urticaceae*	Leaves	Extract (Unspecified)	Antifertility	↓ androgen activity	Lignans	[54]
40	*Dysphania ambrosioides* L.	*Amaranthaceae*	Leaves	Extract (Unspecified)	Spermatogenic suppression	Toxic metabolites	Ascaridole	[55]
41	*Leonotis ocymifolia* (Burm. f.) Iwarsson	*Lamiaceae*	Leaves	Extract (Unspecified)	↓ fertility	Hormonal imbalance	Diterpenes	[56]
42	*Melia azedarach* L.	*Meliaceae*	Leaves	Ethanolic	Antispermatogenic	↓ spermatogenesis	Meliatoxins	[57]
43	*Diospyros embryopteris* Pers.	*Ebenaceae*	Leaves	Extract (Unspecified)	Testicular damage	Cellular toxicity	Tannins	[58]
44	*Cordia dichotoma* G. Forst.	*Boraginaceae*	Leaves	Extract (Unspecified)	Antifertility	↓ sperm count	Alkaloids	[59]
45	*Millettia auriculata* Baker	*Fabaceae*	Leaves	Extract (Unspecified)	↓ sperm count	Testicular degeneration	Isoflavones	[60]
46	*Beaumontia grandiflora* Wall.	*Apocynaceae*	Leaves	Extract (Unspecified)	Antifertility	Hormonal imbalance	Alkaloids	[61]
47	*Striga orobanchioides* Benth.	*Orobanchaceae*	Whole plant	Extract (Unspecified)	Antifertility	Anti-implantation	Glycosides	[62]
48	*Cichorium intybus* L.	*Asteraceae*	Roots	Extract (Unspecified)	Antifertility	Hormonal modulation	Inulin, lactucin	[63]
49	*Abroma augusta* (L.) L.f.	*Malvaceae*	Leaves	Extract (Unspecified)	Antifertility	↓ spermatogenesis	Sterols	[64]
50	*Eleutherococcus senticosus* Rupr. and Maxim.	*Araliaceae*	Roots	Extract (Unspecified)	Hormonal modulation	Affects endocrine axis	Eleutherosides	[65]
51	*Acorus calamus* L.	*Acoraceae*	Rhizome	Ethanolic	Antifertility	Neuroendocrine disruption	β-asarone	[66,67]
52	*Adhatoda vasica* Nees	*Acanthaceae*	Leaves	Methanolic	↓ sperm count	Hormonal imbalance	Vasicine	[68]
53	*Aerva lanata* (L.) Juss. ex Schult.	*Amaranthaceae*	Whole plant	Extract (Unspecified)	Antifertility	↓ spermatogenesis	Flavonoids	[69]
54	*Alstonia scholaris* (L.) R.Br.	*Apocynaceae*	Bark	Ethanolic	Antispermatogenic	Testicular toxicity	Alkaloids	[70]
55	*Amaranthus spinosus* L.	*Amaranthaceae*	Roots	Extract (Unspecified)	Antifertility	Hormonal modulation	Saponins	[71]
56	*Anethum graveolens* L.	*Apiaceae*	Seeds	Extract (Unspecified)	↓ fertility	↓ testosterone	Carvone	[72]

Table 1. Continued...

Sr. No.	Botanical Name	Family	Part Used	Extract	Reported Activity	Mechanism of Action	Major Phytoconstituents	Reference
57	*Annona squamosa* L.	*Annonaceae*	Leaves	Extract (Unspecified)	Antispermatogenic	Germ cell apoptosis	Acetogenins	[73]
58	*Argemone mexicana* L.	*Papaveraceae*	Seeds	Methanolic	Antifertility	Cellular toxicity	Sanguinarine	[74]
59	*Asparagus racemosus* Willd.	*Asparagaceae*	Roots	Extract (Unspecified)	Hormonal imbalance	Estrogenic activity	Saponins	[75]
60	*Bacopa monnieri* (L.) Wettst.	*Plantaginaceae*	Whole plant	Extract (Unspecified)	Antifertility	↓ sperm motility	Bacosides	[76]
61	*Boerhavia diffusa* L.	*Nyctaginaceae*	Roots	Extract (Unspecified)	Antifertility	↓ spermatogenesis	Punarnavine	[77]
62	*Bombax ceiba* L.	*Malvaceae*	Bark	Extract (Unspecified)	↓ sperm count	Hormonal disruption	Flavonoids	[78]
63	*Brassica nigra* (L.) Koch	*Brassicaceae*	Seeds	Extract (Unspecified)	Spermicidal	Membrane damage	Allyl isothiocyanate	[79]
64	*Caesalpinia bonduc* (L.) Roxb.	*Fabaceae*	Seeds	Extract (Unspecified)	Antifertility	↓ testosterone	Bonducin	[80]
65	*Cassia fistula* L.	*Fabaceae*	Fruit pulp	Extract (Unspecified)	Antifertility	Hormonal imbalance	Anthraquinones	[81]
66	*Celastrus paniculatus* Willd.	*Celastraceae*	Seeds	Extract (Unspecified)	↓ fertility	Neuroendocrine effect	Celastrine	[82]
67	*Centella asiatica* (L.) Urb.	*Apiaceae*	Whole plant	Extract (Unspecified)	Antifertility	↓ spermatogenesis	Asiaticoside	[83]
68	*Cinnamomum verum* J. Presl	*Lauraceae*	Bark	Extract (Unspecified)	↓ sperm motility	Oxidative stress	Cinnamaldehyde	[84]
69	*Clerodendrum serratum* (L.) Moon	*Lamiaceae*	Roots	Extract (Unspecified)	Antifertility	Hormonal imbalance	Steroids	[85]
70	*Coriandrum sativum* L.	*Apiaceae*	Seeds	Ethanolic	↓ fertility	↓ testosterone	Linalool	[86]
71	*Croton tiglium* L.	*Euphorbiaceae*	Seeds	Ethanolic	Testicular toxicity	Inhibits protein synthesis, germ cell damage	Phorbol esters	[87]
72	*Cuminum cyminum* L.	*Apiaceae*	Seeds	Ethanolic	Antifertility	Hormonal alteration (↓ testosterone)	Cuminaldehyde	[88]
73	*Dalbergia sissoo* Roxb.	*Fabaceae*	Leaves	Ethanolic	↓ sperm count	Testicular degeneration	Flavonoids	[89]
74	*Desmodium gangeticum* (L.) DC.	*Fabaceae*	Roots	Ethanolic	Antifertility	↓ spermatogenesis	Alkaloids	[90,91]

Table 1. Continued...

Sr. No.	Botanical Name	Family	Part Used	Extract	Reported Activity	Mechanism of Action	Major Phytoconstituents	Reference
75	*Phyllanthus emblica* L.	*Phyllanthaceae*	Fruits	Ethanolic	Antifertility	Hormonal imbalance	Tannins, Vitamin C	[90,91]
76	*Erythrina variegata* L.	*Fabaceae*	Bark	Aqueous	↓ fertility	CNS-mediated reproductive suppression	Alkaloids	[92]
77	*Syzygium cumini* (L.) Skeels	*Myrtaceae*	Seeds	Extract	Antifertility	↓ sperm motility	Jamboline	[93]
78	*Ferula asafoetida* L.	*Apiaceae*	Resin	Ethanolic	Antifertility	Hormonal modulation	Ferulic acid	[94,95]
79	*Glycyrrhiza glabra* L.	*Fabaceae*	Roots	Ethanolic	↓ testosterone	Antiandrogenic activity	Glycyrrhizin	[94,95]
80	*Gossypium herbaceum* L.	*Malvaceae*	Seeds	Ethanolic	Antispermatogenic	Inhibits spermatogenesis	Gossypol	[96]
81	*Heliotropium indicum* L.	*Boraginaceae*	Leaves	Ethanolic	Antifertility	Toxic alkaloid-induced testicular damage	Pyrrolizidine alkaloids	[97]
82	*Holarrhena pubescens* Wall. ex G. Don	*Apocynaceae*	Bark	Methanolic	↓ fertility	Hormonal imbalance	Conessine	[98]
83	*Ipomoea carnea* Jacq.	*Convolvulaceae*	Leaves	Extract (Unspecified)	Antifertility	Neurotoxicity affecting reproductive axis	Swainsonine	[99]
84	*Lantana camara* L.	*Verbenaceae*	Leaves	Extract (Unspecified)	Antifertility	Testicular toxicity	Lantadene	[100]
85	*Leucas aspera* (Willd.) Link	*Lamiaceae*	Leaves	Extract (Unspecified)	↓ fertility	↓ spermatogenesis	Diterpenes	[101]
86	*Madhuca longifolia* (J. Koenig ex L.) J.F. Macbr.	*Sapotaceae*	Flowers	Extract (Unspecified)	Antifertility	Hormonal imbalance	Saponins	[102]
87	*Moringa oleifera* Lam.	*Moringaceae*	Leaves	Extract (Unspecified)	↓ sperm count	Hormonal suppression	Isothiocyanates	[103]
88	*Myristica fragrans* Houtt.	*Myristicaceae*	Seeds	Extract (Unspecified)	Antifertility	CNS-mediated reproductive suppression	Myristicin	[104]
89	*Nerium oleander* L.	*Apocynaceae*	Leaves	Extract (Unspecified)	Testicular toxicity	Cardiac glycoside-induced toxicity	Oleandrin	[105]
90	*Nigella sativa* L.	*Ranunculaceae*	Seeds	Extract (Unspecified)	↓ fertility	Hormonal imbalance	Thymoquinone	[106]
91	*Papaver somniferum* L.	*Papaveraceae*	Latex	Extract (Unspecified)	Antifertility	CNS suppression of reproductive hormones	Morphine, codeine	[107]
92	*Phyllanthus amarus* Schumach. and Thonn.	*Phyllanthaceae*	Whole plant	Extract (Unspecified)	Antifertility	↓ spermatogenesis	Lignans (phyllanthin)	[108]

Table 1. Continued...

Sr. No.	Botanical Name	Family	Part Used	Extract	Reported Activity	Mechanism of Action	Major Phytoconstituents	Reference
93	*Pongamia pinnata* (L.) Pierre	*Fabaceae*	Seeds	Extract (Unspecified)	↓ fertility	Hormonal imbalance	Karanjin, pongamol	[109]
94	*Prosopis juliflora* (Sw.) DC.	*Fabaceae*	Leaves	Extract (Unspecified)	Antifertility	Toxic metabolite-induced testicular damage	Alkaloids, flavonoids	[110]
95	*Rauvolfia serpentina* (L.) Benth. ex Kurz	*Apocynaceae*	Roots	Extract (Unspecified)	↓ fertility	CNS-mediated reproductive suppression	Reserpine	[111]
96	*Sida cordifolia* L.	*Malvaceae*	Leaves	Extract (Unspecified)	Antifertility	Hormonal modulation	Ephedrine, flavonoids	[101]
97	*Smilax china* L.	*Smilacaceae*	Roots	Extract (Unspecified)	Antifertility	↓ spermatogenesis	Saponins, diosgenin derivatives	[109]
98	*Strychnos nux-vomica* L.	*Loganiaceae*	Seeds	Extract (Unspecified)	Toxic antifertility	Neurotoxicity affecting reproductive axis	Strychnine, brucine	[110]
99	*Tephrosia purpurea* (L.) Pers.	*Fabaceae*	Whole plant	Extract (Unspecified)	Antifertility	Hormonal imbalance	Rotenoids, flavonoids	[108]
100	*Trigonella foenum-graecum* L.	*Fabaceae*	Seeds	Extract (Unspecified)	↓ fertility	↓ testosterone synthesis	Diosgenin, saponins	[111]

extraction solvents, different doses administered, different lengths of treatment, different endpoints measured, and different ways of measuring fertility. The methodological variation makes it difficult to make direct comparisons among studies and makes quantitative meta-analysis impossible. Moreover, several studies were not randomised, blinded, justified for sample size and did not provide a uniform reporting of experimental procedures, which introduced a risk of bias.

Reversibility of the fertility suppression was suggested for some of the medicinal plants after a period of treatment, but the available evidence is not conclusive. Numerous studies examined fertility recovery in relatively short time intervals, and extensive studies on long-term reproductive outcomes, offspring health and genetic safety were not done. Moreover, some plants exhibited considerable damage to the testicles in addition to their antifertility action, indicating that these effects could be due to general reproductive toxicity or to the action of other unknown mechanisms.

Another important point to note is that there are no well-designed clinical studies. Almost all existing evidence comes from *in vivo* animal studies or *in vitro* studies. Therefore, the safety, efficacy, pharmacokinetics, optimal dose, reversibility and long-term effects of these medicinal plants in human beings are not well known. Before the use of plant-derived anti-fertility agents can be incorporated in clinical practice, standardisation of plant materials, identification of active constituents, Good Manufacturing Practice (GMP) compliance and multi-centre randomised clinical trials are needed.

The evidence in general confirms the high potential of medicinal plants as potential sources of novel male contraceptive agents. Future research should focus on bioassay-guided separation of active compounds, understanding the molecular mechanisms, standardising toxicity testing, evaluating reversibility, and thorough clinical trials; however, these problems will be solved by creating a safe, effective, reversible, and evidence-based plant-based male contraceptive for use in worldwide family planning initiatives.

9. Comparative Scientific Study of Male Antifertility Plants

There was a lot of variation in the botanical origin, phytochemical composition and mode of action of male antifertility effects of medicinal plants used in this review. Ten species each had one or more members, with the greatest number from the *Fabaceae* family, followed by *Apocynaceae, Lamiaceae, Malvaceae, Apiaceae, Asteraceae,* and *Euphorbiaceae***.** This was probably due to the high prevalence of *Fabaceae,* which contain flavonoids, rotenoids, saponins and isoflavonoids that have been reported to interfere with the biosynthesis of testosterone, spermatogenesis and sperm maturation. Species of *Apocynaceae***,** however, showed mostly reproductive toxicity due to the presence of steroidal glycosides and alkaloids, which caused degeneration of seminiferous tubules and affected androgen functions. While antioxidant imbalance and hormonal modulation were frequently involved in the production of mild reproductive effects in *Lamiaceae* species, diterpenes and phorbol esters were commonly involved in the production of severe testicular toxicity in *Euphorbiaceae* plants. Based on the observations made, it is concluded that there is significant variation in the antifertility activity among different plant families and that their characteristic phytochemical constituents are more important than botanical classification.

Based on this literature review, the different mechanisms of male antifertility action can be divided into two categories: one is hormonal, and the other is non-hormonal. The hormonal mechanisms include suppression of the HPT axis, antiandrogenic effects, inhibition of the synthesis of testosterone, and reduction in levels of the hormone's releasing factors, Luteinising Hormone (LH) and Follicle-Stimulating Hormone (FSH). These mechanisms mostly affect the production of sperm by affecting the endocrine regulation of the testes. Non-hormonal mechanisms, on the other hand, have a direct effect on the reproductive tissues and/or sperm by possessing spermicidal activity, inhibiting sperm maturation and motility, inducing oxidative stress, apoptosis of germ cells, mitochondrial dysfunction, and structural degeneration of the seminiferous epithelium. Hormonal mechanisms tend to produce gradual and reversible suppression of fertility, whereas non-hormonal mechanisms tend to have more rapid antifertility effects and, when coupled with high levels of cytotoxicity, may cause irreversible damage to reproductive tissues.

The difference between reversible and irreversible antifertility effects is an important one that was established in this review. Several medicinal plants showed that normalisation of sperm count, sperm motility and testosterone levels could be achieved after stopping treatment, which indicates that they may be used as a reversible male contraceptive. This is a reversible effect that is especially desirable since long-term reproductive capacity is preserved. In contrast, other plants caused permanent degeneration of seminiferous tubules, significant loss of germ cells, fibrosis or persistent dysfunction of the testicle, reflecting permanent reproductive toxicity. Although having significant antifertility activity, these irreversible changes limit the clinical potential of these plants as contraceptive agents. Hence, reversibility should be considered as one of the main parameters for the selection of phytoconstituents for the development of new contraceptives in the future.

The relationship between effectiveness and toxicity is another important factor to take into account. Several medicinal plants exhibited very strong anti-fertility activity by significantly reducing the sperm concentration, the percentage of viable sperm, the fertility index and the reproductive hormone levels. Usually, however, these beneficial contraceptive effects were associated with oxidative stress, histopathological changes, hepatotoxicity, nephrotoxicity, or reproductive toxicity in general. Therefore, the suitability for contraceptive development cannot be assumed from strong antifertility activity. Ideal candidate plants should be able to reduce fertility selectively and reversibly without causing irreversible damage to the reproductive organs or systemic toxicity. Therapeutic index, dose optimisation, long-term safety, reproductive recovery and pharmacokinetic characterisation should therefore be the focus of future investigations instead of only antifertility efficacy.

Medicinal plants have a great potential as sources of new male contraceptive drugs, but there is a large degree of heterogeneity in terms of mechanism, efficacy, reversibility and side effects. The relative activities of the different plant families illustrate the fact that the ability to suppress fertility is more related to the phytochemical composition than to taxonomy. The bioassay-guided isolation of bioactive compounds, identification of molecular targets, standardised extraction of the plants, extensive toxicity studies, and design of proper clinical studies deserve consideration in future research to discover compounds from plants that can safely and effectively render men infertile in a fully reversible manner.

10. Clinical Relevance and Translational Perspectives

The need for male contraceptive agents has increased due to the inadequacies of the existing male contraceptive agents, especially medicinal plant-based ones. While many medicinal plants exhibit marked antifertility activity in experimental systems, only a few show properties that would be desirable for clinical development. The ideal male contraceptive would consistently suppress fertility, be entirely reversible, have low systemic toxicity, leave sexual function and libido intact, and be readily accepted over the long term. Up to now, the majority of medicinal plants studied meet only partial of these requirements, which underscores the great potential difference between promising preclinical studies and clinical use.

Of the medicinal plants discussed, special emphasis should be given to those plants showing reversible antifertility effects. A number of experimental studies have shown recovery of sperm concentration, motility, testosterone level and fertility after cessation of treatment, suggesting temporal, not permanent, reproductive effects. This reversibility is one of the most desirable properties of potential male contraceptives. However, plants that cause irreversible degeneration of the seminiferous tubules, long-term suppression of spermatogenesis or permanent testicular fibrosis are not suitable, even though they are very potent in their antifertility activity. Future investigations should focus on plants which have been shown to have reversible reproductive effects and avoid plants that have contraceptive activity through irreversible toxicity of tissue.

A major hurdle to clinical translation is the lack of standardisation of herbal extracts. A variety of factors affecting the geographical origin, climatic conditions, harvesting season, plant age, cultivation, solvent used for extraction, extraction technique, storage and

manufacturing process influence the pharmacological activity of medicinal plants. This means that since each study uses distinct samples of the same plant species, there can be any number of inconsistencies in the plant's phytochemical makeup and subsequent biological activity. Furthermore, numerous investigations are based on crude extracts without quantitative standardisation and lack identification of marker compounds, which can lead to difficulties in repeatability. International standardisation of quality control is still a big hurdle in getting products approved and scaling up pharmaceutical development. For better consistency and reproducibility, standard procedures in extraction, phytochemical fingerprinting, quantitative marker analysis, and Good Manufacturing Practice (GMP) compliant production methods should be used in future studies.

Another important aspect that has been relatively less studied is the long-term toxicity. A number of studies showed a strong decrease in sperm count and fertility following short-term exposure, but few chronic exposure or post-treatment recovery studies have been conducted over long periods. For some medicinal plants, chronic oxidative stress, loss of the seminiferous tubules, apoptosis of germ cells, endocrine imbalance, and changes in the architecture of the epididymis have been documented, and it is quite possible that the reproductive function of these plants could be permanently impaired. In addition, systemic toxicities of the liver, kidney, cardiovascular system and endocrine organs were rarely assessed. Therefore, comprehensive chronic toxicity studies, reproductive recovery studies, multi-generational studies and detailed histopathological analysis must be conducted prior to the use of plant-derived anti-fertility agents in humans.

Evidence is also mounting that the antifertility effects of many medicinal plants involve oxidative stress. Multiple phytochemicals induce an overproduction of reactive oxygen species (ROS), leading to lipid peroxidation of sperm membranes and mitochondrial dysfunction, DNA damage and activation of apoptotic pathways in germ cells. Sperm are especially vulnerable to oxidative damage because they have low levels of their own antioxidant enzymes and contain a large amount of polyunsaturated fatty acids. An association between increased oxidative stress and lower sperm concentration, lower sperm motility, abnormal morphology, lower fertilising capacity, and disruption of testicular steroidogenesis has been found consistently. However, oxidative stress can be a direct mechanism of antifertility action, or it may be a secondary effect of the general toxicity of cells. In future mechanistic studies, validated oxidative stress biomarkers such as malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and glutathione peroxidase (GPx) should be added along with molecular analysis of the apoptotic and inflammatory pathways to further elucidate causality.

Although preclinical results are promising, there is very limited human clinical evidence available so far. Almost all data are available from rodent models, and only a handful of studies have gone beyond lab testing. While animal studies have yielded useful mechanistic insight, there are significant interspecies differences in reproductive physiology, endocrine regulation, metabolism, pharmacokinetics and fertility recovery that will restrict extrapolation to humans. In addition, efficacy, reversibility and optimal dose, long-term safety, acceptability and quality of life have been poorly assessed by randomised controlled clinical trials. Thus, there are no medicinal plants that have been approved as male contraceptives yet. Future translational research should focus on standardisation of herbal formulations, thorough toxicological assessment, pharmacokinetic studies, and multicenter, randomised controlled clinical trials, along with the process of regulatory compliance, to close the gap between scientific findings and clinical use.

On a general note, medicinal plants are an important source of bioactive compounds for non-hormonal male contraceptive development. But for successful implementation in clinical practice, a multidisciplinary approach has to be developed between pharmacognosy, phytochemistry, molecular pharmacology, reproductive toxicology, pharmaceutical formulation and clinical research. There may be a special focus on the identification of standardised phytochemicals with reversible contraceptive activities, low systemic toxicity and an unambiguous mode of action for the development of safe and effective plant-based male contraceptive agents that are clinically acceptable.

11. Toxicity and Safety Considerations

In experimental models, several medicinal plants reviewed in this paper have been reported to have potential toxicological effects, especially with increased dose and/or prolonged treatment. Many of these plants exhibit potential male antifertility properties by modulating hormones, inhibiting the development of germ cells, inducing oxidative stress and/or damaging germ cells, but their safety is still an important factor to consider. Some species, including *A. precatorius, R. communis, D. stramonium, N. oleander* and *S. nux-vomica*, have known toxic phytochemicals which can be neurotoxic, hepatotoxic or have systemic effects. Likewise, other plants with antifertility activity may cause interference with endocrine or reproductive systems, which may give rise to reversible or irreversible physiological changes if given at high doses for longer durations. It is worth emphasising that the majority of the reported studies are of a preclinical nature, and extensive clinical safety studies are limited. In addition, differences in type of extract, dosage, and experimental design between studies also result in varying toxicity outcomes.

Thus, medicinal plants are important sources of lead compounds for male antifertility drug development but, before being considered for their translational or therapeutic application, it is critical to undertake proper toxicological evaluation, dose standardisation, and safety profiling. This review highlights the importance of always considering the safety data when interpreting the efficacy in an antifertility study to ensure there is a balanced risk–benefit assessment.

12. Future Perspectives

Future studies for the plant-based male antifertility agents should aim to bridge the gap between promising preclinical studies and their use in clinical practice with scientific rigour. Isolation and structural characterisation of active phytoconstituents with antifertility activities and detailed mechanistic studies at molecular and cellular levels to establish the exact target involved in male reproductive regulation would be given priority. To reduce variability in phytochemical composition and biological activity, herbal extracts need to be standardised, and quality control and reproducibility studies must be performed. Full toxicological and pharmacokinetic studies are also necessary to define safety profiles, effective dose ranges, and the reversibility of anti-fertility effects. In addition, sophisticated research and development combining these omics technologies, computational biology and delivery via nanotechnology could yield better understanding and better therapeutic outcomes. Well-designed, large-scale preclinical and clinical trials are crucial to validate efficacy and safety in humans. Finally, a multi-disciplinary approach that incorporates pharmacognosy, reproductive biology, phytochemistry, toxicology and clinical studies will play an important role in bringing medicinal plants to the fore in the development of safe, effective, reversible and affordable male contraceptives for reproductive health management in the world.

13. Conclusion

The present systematic review gives a thorough review of the medicinal plants reported to have male antifertility activity from 1980 to 2025. This review systemically gathers data on 100 medicinal plant species and classifies them into their botanical families, parts of the plant used, phytochemical constituents and antifertility action mechanisms, and identifies research trends and gaps. This combined method is useful for researchers interested in the development of a male contraceptive using plants.

The results indicate that medicinal plants have a good source potential for novel male antifertility agents. Bioactive compounds found in plants can exert multiple effects on male reproductive function, such as inhibiting spermatogenesis, impacting hormones, acting as antiandrogens, being spermicidal, inducing oxidative stress and causing structural changes in the reproductive organs. These multi-targeted mechanisms are unique to many phytochemicals and help explain how they differ from a number of conventional synthetic contraceptive drugs, offering the potential for the creation of safer and more effective male contraceptive approaches.

It is also noted that the most frequently investigated plant families are *Fabaceae, Asteraceae, Apocynaceae* and *Lamiaceae*, and seeds, roots and leaves are the most common sources of bioactive compounds with

antifertility activity. The secondary metabolites, especially alkaloids, flavonoids, saponins, terpenoids and glycosides, are abundant in these parts of the plants, which have important roles in controlling the reproductive physiology and are potential targets for drug development.

Importantly, the evidence shows that several medicinal plants show a reversible anti-fertility effect, thus having potential for the development of reversible male contraceptives. However, there are some plant extracts reported to cause testicular toxicity and irreversible reproductive damage, highlighting the importance of thorough assessment of efficacy, safety, dosage, duration of exposure, and therapeutic window prior to clinical use.

Although there is promising preclinical data, there is a lack of translation of these into clinical practice. Some of the main problems are the lack of standardisation of herbal extracts, variability in phytochemical composition, not enough studies on the identification of bioactive principles, poor mechanistic studies, no pharmacokinetic or toxicological parameter studies, and very few well-designed clinical trials. It is important to overcome these drawbacks for successful regulatory approval and therapeutic development.

Medicinal plants are an under-explored but very promising source of male contraceptive agents. This review not only summarises the existing evidence, but it also highlights the key research areas for further investigations in this field, such as bioactive compound isolation, identification of molecular targets, mechanistic studies, standardisation of herbal preparations, extensive toxicity evaluation, and clinical validation. Multidisciplinary research involving pharmacognosy, phytochemistry, reproductive biology, toxicology and clinical pharmacology is needed in the future for the development of male contraceptive drugs derived from plants into safe, effective, and reversible products that can assist in global family planning and reproductive health.

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