A Critical Review and Scientific Prospective on Contraceptive Therapeutics from Ayurveda and Allied Ancient Knowledge

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Commonly used synthetic or prescribed hormonal drugs are known to interfere with the endocrine system and may have adverse reproductive, neurological, developmental, and metabolic effects in the body. These may also produce adverse effects such as polycystic ovarian disorder, endometriosis, early puberty, infertility or toxicity to gonads, testicular germ cell cancer, breast or prostate cancer, brain developmental problems, and even birth defects. Globally, the emergence of renewed interest in natural products for reproductive health is on the rise, which offers opportunities for new contraceptive developments. The search for alternate, safer contraceptive products or agents of natural origin is of scientific interest. Ayurvedic classical texts offer knowledge and information about the reproductive function and therapeutics including those for enhancement and limiting male and female fertility. Review of ancient, medieval, and recent—including texts on erotica that provide information on approaches and large numbers of formulations and drugs of plant, mineral or animal origin—claimed to have sterilizing, contraceptive, abortifacient, and related properties is presented. Few among these are known to be toxic and few are not so common. However, most of the formulations, ingredients, or modes of administration have remained unattended to, due to issues related to consumer compliance and limitations of standardization and lack of appropriate validation modalities. Several of these ingredients have been studied for their phytoconstituents and for the variety of pharmacological activities. Efforts to standardize several classical dosage forms and attempts to adapt to modern technologies have been made. List of formulations, ingredients, and their properties linked with known constituents, pharmacological, biological, and toxicity studies have been provided in a series of tables. The possible effectiveness and safety of selected formulations and ingredients have been examined. Suggestions based on new drug delivery systems integrated with advances in biotechnology, to provide prospects for new therapeutics for contraception, have been considered. Ayurveda is built on a holistic paradigm of biological entity rather than limited gonadal functions. Graphic presentation of a few carefully chosen possibilities has been depicted. New approaches to standardization and ethnopharmacological validation of natural contraceptive therapeutics may offer novel mechanisms and modalities and therapeutic opportunities to satisfy unmet needs of contraception.

Keywords: natural contraceptive, herbal contraceptive, ayurved contraceptive, reproductive health and traditional medicine, contraceptive traditions
INTRODUCTION

The world population is expected to reach more than 11 billion by 2050 (Census of India, 2011). Population in the world is currently (2020) growing at a rate of around 1.05% per year. The current average population increase is estimated at 81 million people per year and current world population is 7.9 billion as of March 2021 (World Population Clock, 2021). This burgeoning population particularly in developing countries is a matter of concern for social, economic, and environmental reasons in terms of providing food, shelter, and life. The challenge of dealing with an ever-increasing population has been dealt with largely by conventional medicine using different methods of contraception such as oral contraceptive pills, intrauterine contraceptive devices, and barrier devices. These devices, techniques, and drugs seem to have been efficiently practiced for contraception but with many reported adverse effects as well as failure resulting in unwanted pregnancy. (Dutta, 2013).

BIRTH CONTROL HISTORY

Technically, birth control can be defined as the methods, procedures, or practices that are implemented to prevent conception leading to pregnancy in women. The term can be associated with contraception and family planning where knowledge about birth control is equally important.

The Egyptian Ebers Papyrus from 1550 BCE and the Kahun Papyrus from 1850 BCE have some of the earliest documented descriptions of birth control: the use of honey, acacia leaves, and lint to be placed in the vagina to block sperm. (Lipsey et al., 2005; Cuomo, 2010).

In medieval Europe, any effort to halt pregnancy was deemed immoral by the Catholic Church, (Cuomo, 2010), although it is believed that women of the time still used a number of birth control measures such as coitus interrupts and inserting lily root and rue into the vagina. Women in the middle ages were also persuaded to tie weasel—a small wild animal—testicles around their thighs during sex to prevent pregnancy. The oldest condoms discovered to date were recovered in the ruins of Dudley Castle in England and date back to 1640. They were made of animal gut and were most likely used to prevent the spread of sexually transmitted diseases during the English Civil War (Jon, 2012). Casanova, living in 18th-century Italy, described the use of a lambskin covering to prevent pregnancy; however, condoms only became widely available in the 20th century (Cuomo, 2010).

Modern Methods to Control Fertility (World Health Organization, 2020)

Several methods currently used to curb for contraception are presented (Figure 1).

ADVERSE EFFECTS

Commonly used synthetic or prescribed hormonal drugs are known to interfere with the endocrine system and may have adverse reproductive, neurological, developmental, and metabolic effects in the body. These may cause polycystic ovarian disorder, endometriosis, early puberty, infertility, toxicity to gonads, testicular germ cell cancer, breast or prostate cancer, brain developmental problems, and even birth defects. The search for alternate and safer means/drugs to prevent

![FIGURE 1](Frontiers in Pharmacology | www.frontiersin.org June 2021 | Volume 12 | Article 629591)

Bhatt and Deshpande Prospective Contraceptives from Ayurveda and Natural Ingredients
birth is an open-ended area of scientific research. It is always an appealing idea to further research to develop contraceptive drugs of natural origin that have high efficacy without any adverse effects on the reproductive system.

**UNMET NEEDS**

According to a recent report from the Guttmacher Institute, 214 million women of reproductive age in the developing world who want to avoid pregnancy are not using a modern contraceptive method. These women are considered to have an "unmet need" for modern contraception, with 59 million relying on traditional methods such as abstinence and withdrawal and 155 million simply using no contraception at all. (Elizabeth et al., 2020).

India’s total fertility rate (TFR) may have declined significantly over the years, but there remain significant challenges in family planning according to new research. In an Economic and Political Weekly article, Purushottam M. Kulkarni of Jawaharlal Nehru University suggested that there is a significant unmet need for contraception in India. Data from National Family Health Surveys (NFHS) have shown that while there was a decline in the unmet need for contraceptive services from 1992-93 (NFHS-1) through to 2005-06 (NFHS-3), and between 2005-06 and 2015-16 (NFHS-4), there has not been any significant improvement in access to contraception. (Mint, 2020).

**SIGNIFICANCE OF REVIEW**

Despite obvious success, the rise in population continues to remain a medical challenge due to reasons of social, economic, personal, and biological consequences. Though well-established contraceptive drugs and measures have been utilized, the long term and excessive use of hormonal contraceptives are of serious concerns due to their probable adverse effects. There is need to explore the alternative or new possibilities.

The search for an effective and safe contraceptive agent remains a challenge. Contraceptive drugs of natural origin are of all-time research interests. Traditional systems of medicine like Ayurveda address all issues related to health and illnesses based on the principle of equilibrium between the biosphere and cosmosphere, which include reproductive phenomenon. Ayurvedic pharmacopoeia has formulations and ingredients that are attributed to affect coitus, spermatogenesis, and ovulation, uterine, fetal, and placental activities. These include emmenagogues, ecobic drugs, contraceptives, uterine sedatives for females, and depurate or drugs that hamper male sexual and reproductive capabilities, affect fluidity or motility of the seminal fluid, destroy sperms, or impede libido.

A large number of drugs are known to have sterilizing, contraceptive, and abortifacients properties. However, these indigenous means and drugs were extensively used even in rural or tribal cultures until the 20th century, when there has been no noteworthy systematic or scientific efforts to study these aspects except for a few intermittent studies. While the list of such ingredients is quite big, unusually small scientific data are available about the nature of their active components and about their mechanisms of action.

As biomedical advances open up new vistas in biomedical research, it will be of interest to examine the subject of contraception once again, as in Ayurveda, in the light of present-day pharmacology for future possibilities.

A thoughtful attempt has been made here to explore Ayurvedic and scientific aspects of formulations and ingredients as described in multiplicity of classical texts covering different facets of contraception.

**METHODOLOGY**

Ancient classical texts, medieval compendia, and other pertinent texts were assessed for enlisting different methods used for contraception and to enlist formulations and ingredients used for a variety of activities that could be pharmacologically linked to contraception. Specific search was undertaken for any existing review that could add to information on the subject. A systematic review of published articles on the subjects related to contraception was undertaken. The description of methods used in the experimental animal models, and the antifertility effect of active ingredients, their doses, safety, and toxicity were examined. Ninety-four plants and six minerals are reported in this review having a variety of contraceptive activities.

Flowchart of the systematic review process to search for contraceptive plants is presented. (Figure 2).

**CONTRACEPTIVES IN AYURVEDA AND MEDIEVAL SANSKRIT LITERATURE**

Ayurvedic literature is rife with thousands of formulations and has about 1100 ingredients attributed with well-defined therapeutic approaches including reproduction. There are references to temporary or permanent sterilization. Search for contraception from traditional knowledge of Ayurveda has been of interest to the Central Drug Research Institute, Council of Scientific and Industrial Research under Ministry of Science and Technology, and the Central Council for Research in Ayurvedic Sciences under Ministry of Health (now Ministry of AYUSH), bodies under the Government of India. Several other private and industry organizations had undertaken studies in the past. However, there is a need to revive research interest in Ayurveda in reproductive biology for safe, low-cost, user-friendly, and reliable therapeutic solutions to satisfy different contraception requirements.

**Vedic Period (1500-500 BCE)**

Regulated sexual life or abstinence from sex was considered the ideal method of contraception in Vedic times. The emphasis was more on propensity of the right, healthy progeny. Indirect references to contraception can be found in the Atharva Veda.

The use of drugs leading to impotence as punishment meted out to a person committing social sins or to an enemy or infliction
of injury to two cords situated near the scrotum or the scrotum itself, to put an end to one's desire for progeny were in practice. These can be considered as references for use of drugs to prevent conception, vasectomy, and castration, respectively (Satvalekar, 1958a). A mechanical device made of stone to obstruct multiple channels of Yoni—the vaginal cavity to prevent conception has been mentioned. This could be considered as the earliest form of an intrauterine contraceptive device. Similarly, artificially induced changes to make the vaginal cavity rough or dry, besides its mechanical obstruction for futile coitus have been mentioned (Satvalekar, 1958b). This reference reflects some chemical changes to be produced artificially, probably in the cervical mucus obstructing the entry of sperms, or in the endometrium influencing the implantation of the zygote and a mechanical barrier in the vaginal canal. (Tewari and Chaturvedi, 1981). In Brhadaranyaka Upanishad, a breath exercise is advised during coitus to avoid conception (Dash and Basu, 1968).

**Samhita Period: (300-500 BCE)**

Though Charak Samhita, Sushrut Samhita, and Ashtang Sangraha–Bruhatryee, the three ancient most Ayurveda treatises, have elaborated the subject of reproduction extensively, there are no direct references to contraception. Kshetra—the female reproductive system as the field, ambu—the nutrient fluids, bija—the sperm or ovum as the seed, rutukal—the ideal ovulatory period, marga—the female canal, Vayu—the neural system, and hrid—the psychological status are considered the essential factors for conception. Any or more of these factors if influenced artificially can lead to a failure of conception. The shukravaha srotas and aartavavaha srotas representing seminal and menstrual flows, respectively, are among the 13th intrinsic and interdependent biological pathways or channels (that could be explained based on now prevalent means of system biology). This early knowledge could pave the way for the development of different kinds of contraceptive methods prevailing in the present scenario, and all of them influence one or the other factors that have been explained in the ancient classics (Vagbhatt, 2000; Sushrut, 2002).

Contraceptive activities in the context of Ayurvedic principle of fertility are explained in Figure 3.

**Medieval Period (1000 AD to 1900 AD)**

Rajamartanda written in the 11th century is probably one of the earliest texts to mention a specific prescription for contraceptives. Compendia texts like Bhava Prakash, Yoga Ratnakara, Bhaiṣajya Ratnavali, Gadanigrah, and several others prescribe many herbal and herbo-mineral contraceptive preparations for local and oral use by men and women.

By the 11th century, the oriental connectivity that had sociocultural effects also brought in practices to prevent conception or induce abortion. References to oral and local contraceptives are found in Bruhad Yoga Tarangini and RatiRahasya [AD800], RasaPrakashSudhakar [AD1300], Panchasayaka, Smaradeepika and RasaRatnaSamuccchay [AD1400], RatiManjiri [AD1500], Kandarpchudamani [AD1577], AnnangaRang, Bhavprakash and YogaRatnakar [AD1600], YogaRatnaSamuccchaya [AD 1800], and Brihan Nighantu Ratnakar and BhaiṣajyaRatnavali i! [AD 1900].

The subject of contraceptives in ancient times dealt not only with medieval medicine but also with art and the literary works of poets, playwrights, and philosophers. Like Kama Sutra, the famous text on erotica, a large number of books in the 19th century contain various recipes for contraception and for inducing abortions and diverse birth control practices.

Some of the most prescribed practices and recipes for preventing conception are as follows.

1. **Local Contraceptives for Females**

   Vaginal fumigation or application before coitus with (1) moistened Saindhava lavana (Rock salt) with Til (Sesame) oil. (Jugnu and Sharma, 2011), (2) wood of Neem (Azadirachta indica).
indica A. Juss.) before coitus (Tripathi, 1969), and (3) powdered root of Dhatura (Datura metel L.) plucked on the 14th day (dark night) of the lunar month [Indradev, 1998] or tying the waist with roots (Lakmipatishashtri, 1983).

2. Oral Contraceptives
- Powder of Pippali (Piper longum L.) and Vidanga (Embelia ribes Burm.f.) with Tankana (Borax) taken in equal quantity in fertile phase with milk (Lakmipatishashtri, 1983).
- Flowers of Japa (Hibiscus rosa-sinensis L.): immediately after the delivery of a child (Bhavamisra, 1961; Lakmipatishashtri, 1983) or with Kanji (fermented drink) along with 48 grams of old jaggery to be taken for 3 days in the fertile phase. (Lakmipatishashtri, 1983).
- Root of Tanduliyaka (Amaranthus spinosus L.) with Tandulodaka (rice water) to be taken after menstruation for 3 days. (Lakmipatishashtri, 1983).
- Powders of Talisa patra (Abies spectabilis (D.Don) Mirb.) and Gairika (Red Ochre, Fe₂O₃) in equal parts to be consumed on the 4th day of menstruation with water. (Lakmipatishashtri, 1983).
- Aqueous extract of Rasanjana (Extract of Berberis aristata DC.), Hemavati (Sweta – Vacha) (Iris × germanica L.), and Vayastha (Terminalia chebula Retz.) with cold water. (Rajeshwaradatta, 2001).
- Powders of Amla (Phyllanthus emblica L.), Arjuna (Terminalia arjuna (Roxb. ex DC)), and Abhaya (Terminalia chebula Retz.) with water. (Rajeshwaradatta, 2001).
- Paste made of the root of Chitraka (Plumbago zeylanica L.) mixed with Nigundi (Vitex negundo L.) juice given orally in the dose of one 12 gm with honey. (Lakmipatishashtri, 1983).
- Powder of seeds of Sarshapa (Brassica rapa L.) with Tanduliyam (Amaranthus spinosus L.) and Sarkara (Sugar candy) pounded with Tandulodaka (rice water) given with milk. (Jugnu and Sharma, 2011).
- Ashes of Sehund stem (Euphorbia neriifolia L.), 12 g daily. (Kuchimara, 2007).
- Rhizome of Haridra (Curcuma longa L.) daily during the 3 days of menstruation followed by an additional 3 days (Kuchimara, 2007).
- Powders of Krishna Jeeraka (Carum carvi L.), Karchooram (Hedychium spicatum Sm.), Nagakesara (Mesua ferrea L.), Haritaki (Terminalia chebula Retz.), Kalonji (Nigella sativa L.), and Kayaphala (Myrica nagi Thunb.) made into pills in the size of ziziphus fruit for 7 days. (Kuchimara, 2007).

3. Abortifacient
- Root of Sweta Aparajita (Clitoria ternatea L.), Kakadani (Sarngesta) (Cardiospermum halicacabum L.) or Punarnava (Boerhavia diffusa L.)—Patradanda (stem of leaf) to be inserted in the vagina (Rajamartanda), 1966; Tripathi, 1969; Lakmipatishashtri, 1983.
- Seeds of Grnjana (Carrot) (Daucus carota L.) with roots of Tuvari (Cajanus cajan (L.) Huth) and Sindura (lead oxide).
- Ghotipurisa (feces of mare) mixed with Kanji, filtered, and mixed with rock salt, Ugra (Apium graveolens L.), and Asuri Taila (Oil of Brassica juncea (L.) Czern.) with Visha (Aconitum chasmanthum Stapf ex Holmes) (Lakmipatishashtri, 1983).

Plant and mineral drugs mentioned as contraceptives in the Ayurvedic classical texts are given in Table 1.

It is observed that 79 plant drugs and six mineral drugs are used as abortifacients, oral contraceptives, or as local applications.
### TABLE 1: List of plant and metal drugs as contraceptives in Ayurveda classics. Vertical column numbers indicate AaartavJanan—Emmenagogue (1), Aparapatan—placental expulsion (2), Garbhanuloman/Garbhapatkar—Abortifacient or Garbhastravakar—expel Fetus (3), Garbhanirodhak Contraceptives (4), Garbhashayasancochak—Ecbolic (5), Shandhyakar/Pumstvopadhatin—drugs that hamper male sexual or reproductive capability (6), and Shukrashodhan—Depurates (7).

| Sr. No. | Sanskrit name | Botanical name | (1) | (2) | (3) | (4) | (5) | (6) | (7) |
|--------|---------------|----------------|-----|-----|-----|-----|-----|-----|-----|
| 1      | Aguru         | Aquilaria malaccensis Lam. | ✓   |     |     |     |     |     |     |
| 2      | Ahiphen       | Papaver somniferum L. |     | ✓   |     |     |     |     |     |
| 3      | Amalaki       | Phyllanthus emblica L. | ✓   |     |     |     |     |     |     |
| 4      | Ashok         | Saraca asoca (Roxb.) J.J.de Wilde | ✓   |     | ✓   |     |     |     |     |
| 5      | Asuri         | Brassica juncea (L.) Czern |     | ✓   |     |     |     |     |     |
| 6      | Arjuna        | Terminalia arjuna (Roxb. ex DC.) Wight &Am. | ✓ |     |     | ✓   |     |     |     |
| 7      | Bhanga        | Cannabis sativa L. |     |     | ✓   |     |     |     |     |
| 8      | Bhujapatra    | Betula utilis D. Don | ✓   | ✓   |     |     |     |     |     |
| 9      | Chandan       | Santalum album L. |     |     | ✓   |     |     |     |     |
| 10     | Chavya        | Piper retrofractum Vahl | ✓ |     |     |     |     |     |     |
| 11     | Chirilva      | Holostelea integrifolia (Roxb.) Planch. |     | ✓   |     |     |     |     |     |
| 12     | Chitraka      | Plumbago zeylanica L. | ✓   | ✓   | ✓   | ✓   | ✓   | ✓   | ✓   |
| 13     | Chuka         | Rumex acetosa L. |     | ✓   |     |     |     |     |     |
| 14     | Devdaru       | Cedrus deodara (Roxb. ex D. Don) G. Don | ✓ | ✓ |     |     |     |     |     |
| 15     | Dhanyak       | Coriandrum sativum L. |     | ✓   |     |     |     |     |     |
| 16     | Dhattura      | Datura metel L. |     |     | ✓   |     |     |     |     |
| 17     | Ela           | Elettaria cardamomum (L.) Maton |     | ✓   | ✓   |     |     |     |     |
| 18     | Eranda        | Ricinus communis L. |     | ✓   |     |     |     |     |     |
| 19     | Eshvari       | Aristolochia indica L. | ✓   |     | ✓   |     |     |     |     |
| 20     | Ginja         | Daucus carota L. |     |     | ✓   |     |     |     |     |
| 21     | Haridra       | Curcuma longa L. |     |     |     | ✓   |     |     |     |
| 22     | Haritaki      | Terminalia chebula Retz. |     |     | ✓   |     |     |     |     |
| 23     | Harmal        | Peganum harmala L. |     |     |     | ✓   |     |     |     |
| 24     | Hemavati      | Iris germanica L. |     |     |     | ✓   |     |     |     |
| 25     | Hingu         | Ferula asa-toetica L. |     |     |     | ✓   |     |     |     |
| 26     | Hirabol       | Commiphora myrrha (Nees) Engl. |     |     |     | ✓   |     |     |     |
| 27     | Japa          | Hibiscus rosa-sinensis L. |     |     | ✓   |     |     |     |     |
| 28     | Karchuram     | Hedychium spicatum Sm. |     |     |     | ✓   |     |     |     |
| 29     | Kadamb        | Neolamarckia cadamba (Roxb.) Bosser |     |     |     |     | ✓   |     |     |
| 30     | Kakadani (Saarsteya) | Cardiospermum halicacabum L. |     |     |     |     | ✔   |     |     |
| 31     | Kakamachi     | Solanum nigrum L. |     |     |     |     |     |     | ✔   |
| 32     | Karipas       | Gossypium herbaceum L. |     |     |     |     | ✔   |     |     |
| 33     | Karpur        | Cinnamomum camphora (L.) J. Presl |     |     |     |     |     | ✔   |     |
| 34     | Kasani        | Cichorium intybus L. |     |     |     |     |     | ✔   |     |
| 35     | Kayaphala     | Myrica nagi Thunb. |     |     |     |     |     | ✔   |     |
| 36     | Ketaki        | Pandanus tectorius Parkinson ex Du Roi |     |     |     |     |     |     | ✔   |
| 37     | Krishna Jeeraka | Carum carvi L. |     |     |     |     | ✔   |     |     |
| 38     | Kulaththa     | Vigna unguiculata (L.) Walp. |     |     |     |     | ✔   |     |     |
| 39     | Kushitha      | Aucklandia costus Falc |     |     |     |     |     | ✔   |     |
| 40     | Langalai      | Gloriosa superba L. |     |     |     |     |     | ✔   |     |
| 41     | Lodhara       | Symplocos racemosa Roxb. |     |     |     |     |     | ✔   |     |
| 42     | Mandukpamni   | Centella asiatica (L.) Urb. |     |     |     |     |     |     | ✔   |
| 43     | Muchas        | Bombax ceiba L. |     |     |     |     | ✔   |     |     |
| 44     | Nagakesara    | Mesua ferrea L. |     |     |     |     |     | ✔   |     |
| 45     | Nagdamani     | Artemisia nilagirica (C. B. Clarke) Pamp, |     |     |     |     |     | ✔   |     |
| 46     | Neem           | Azadirachta indica A. Juss. |     |     |     |     |     | ✔   |     |
| 47     | Nimbu         | Citrus × aurantium L. |     |     |     |     |     | ✔   |     |
| 48     | Nilophar      | Nymphaea alba L. |     |     |     |     |     | ✔   |     |
| 49     | Nirgundi       | Vitisnegundo L. |     |     |     |     |     | ✔   |     |
| 50     | Pippali       | Piper longum L. |     |     |     |     |     |     | ✔   |
| 51     | Punarnava      | Boerhavia diffusa L. |     |     |     |     | ✔   |     |     |
| 52     | Rasanjana      | Berberis aristata DC. |     |     |     |     |     | ✔   |     |
| 53     | Rason          | Allum cepa L. |     |     |     |     | ✔   |     |     |
| 54     | Sarshapa       | Brassica rapa L. |     |     |     |     |     | ✔   |     |
| 55     | Sehund         | Euphorbia neololia L. |     |     |     |     |     | ✔   |     |
| 56     | Shal-sarjarasa | Shorea robusta Gaertn. |     |     |     |     |     | ✔   |     |
| 57     | Shallaki       | Boswellia serrata Roxb. |     |     |     |     |     | ✔   |     |
| 58     | Shan           | Dioscorea polystachya Turcz. |     |     |     |     |     | ✔   |     |
| 59     | Shigru         | Morinda oleifera Lam. |     |     |     |     |     | ✔   |     |
| 60     | Shishapaha     | Dalbergia sssoco Roxb. ex DC. |     |     |     |     |     |     | ✔   |
| 61     | Shyronak       | Oroxyllum indicum (L.) Kurz |     |     |     |     |     |     | ✔   |

(Continued on following page)
along with Kanji (fermented drink), Tandulodaka (rice water), Sarkara (sugar candy), milk, and honey.

**POTENTIAL INGREDIENTS HAVING ANTIFERTILITY OR CONTRACEPTIVE PROPERTIES**

This literature survey revealed that there are about more than 94 indigenous medicinal plants having scientific evidence of acting as contraceptives. Some of the remarkable plant drugs with parts used, their chemical constituents, and pharmacological activities are described in Table 2. This compiled information will provide useful reference for new drug designing models, acting either as male or female contraceptives.

Pharmacologically, there are about 67 medicinal plants which possess antifertility activity in females and 56 medicinal plants in males. Several plants have shown to help contraception from the female and male perspectives.

In various experimental animal models, these herbal extracts have shown minimal side effects in comparison to the chemically synthesized contraceptives, which usually contain various combinations of hormones. These plant extracts have active phytoconstituents, which are responsible for the antifertility effects such as antiovulation, anti-implantation, and others.

**CLINICAL STUDIES**

Some of the plants that have demonstrated interesting antifertility activity in clinical trials are as follows.

**Embelia ribes Burm.f.**

Single drug was administered in a dose of 2 g for 5 days followed by 1 g daily for another 10 days. After observing the effect on 2051 cycles in 45 women over 4 years, it was reported that the plant protected 95% of women from pregnancy (Tewari et al., 1976).

**Hibiscus rosa-sinensis L.**

Red petals of the plant Rudrarpushpaka collected between October and December. The extract was administered to 30 sexually active women at a dose of 750 mg/day from day 7 to day 22 of the reproductive cycle. It was observed that no one had became pregnant (Tewari, 1974).

**Neem oil**

A study was conducted on neem seed oil as local application for the reproductive female [246 women in the fertile age-group, 4 dropped out] as a method of family planning for a period of 12–36 cycles. In nine cases, there was conception due to drug failure and in four cases, there was conception due to drug omission. Neem seed oil may be used as an external barrier as
TABLE 2 | Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortification, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatogenic, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|----------------------|---------|--------------------------------------|-----------|
| 1       | Abies spectabilis (D. Don) Mirb. Pinaceae Talisa Patra, leaf | Flavonoids, bioflavonoids, glycosides, phytosterols | Benzene, alcoholic | Anti-implantation activity | Anonymous (1996) |
| 2       | Abroma augusta (L.) L.f. Malvaceae Pishach karpas, roots | L-rhamnose, L-arabinose, D-xylene, D-mannose, D-galactose, D-glucose, D-galacturonic acid, and D-glucuronic acid | Alcoholic | Anti-implantation | Maurya et al. (2004), Pokharkar et al. (2010), Kalla et al. (2011) |
| 3       | Adhatoda vasica Nees synonym of Justicia adhatoda L. Acanthaceae Vasa, leaves | Alkaloids, tannins, saponins, and phenolics flavonoids | Aqueous | Anti-implantation | Pokharkar et al. (2010), Kaur et al. (2011), Raj et al. (2011) |
| 4       | Ailanthus excelsa Roxb Simaroubaceae Maharukha, leaves | Sitosterol, quassinoids, and altanic acid | Ethanolic | Anti-implantation decreased of implant sites | Priya et al. (2012), Tamboli and Konadawar (2013) |
| 5       | Allium cepa L. Amaryllidaceae Palandu, onion, bulb | Kampferol, β-sitosterol, ferulic acid, and myricic acid | Ethanol | Anti-implantation inhibition of implant sites | Thakare et al. (2009), Ola-Mudathir et al. (2008) |
| 6       | Aloe barbadensis Mill. Synonym of aloe vera (L.) Burm.f. Asphodelaceae Kumari, leaves | Water, polysaccharides, pectin, cellulose, hemicellulose, and glucomannan | Ethanol and aqueous | Anti-implantation | Shah et al. (2017), Shah et al. (2016) |
| 7       | Arecaceae catechu L. Areaceae Poogaphala, Nuts | Alkaloids—pilocarpine, arecadine, and arecoline | Petroleum ether, alcoholic, and aqueous | Anti-implantation | Garg and Garg (1970), Garg and Garg (1971) |
| 8       | Cassia fistula L. Fabaceae Aragavitha, fruits, bark | Alkaloid | Aqueous | Anti-implantation, decreased glycogen content in uterus, and antifertility | Yadav and Jain (2009) |
| 9       | Canis papaya L. Caricaceae, Papaya unripe fruit pulp, seeds, latex | Papain, caricacin, carpasemine, and oleanolic glycoside | Pet ether, alcohol, and aqueous ethanol | 60 % anti-implantation activity, abortifacient in abino rats | Garg and Garg (1970), Garg and Garg (1971), Das (1980), Sinha and Nathawat (1989), Chauganmala and Lakshman (2013) |
| 10      | Centratherum anthelminticum (L.) Gamble Asteraceae Vanya Jeeraka, seeds | Glycosides, carbohydrates, phenolic compounds, tannins, flavonoids, proteins, saponins, and sterols | Ethanol | Postcoital anti-implantation activity | Sharma et al. (1994) |
| 11      | Citrus x aurantium L Rutaceae Bijuara, seeds | Citroflavanoids, glucosides, and triterpenoids | Petroleum ether | Anti-implantation, antiovulatory, abortifacients increased ovarian weight, decreased Graafian follicles, and irregular estrous cycle | Patil and Patil (2013) |
| 12      | Embelia ribes Burm.f. Primulaceae Vidang, berries | Embelin, volatile oil, and fixed oil | Isolated embelin | Anti-implantation and postcoital antifertility activity | Prakash (1981), Nand (1981), Dixit and Joshi (1983) |

(Continued on following page)
TABLE 2 | Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortifacient, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatogenic, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|-----------------------------------------------|----------------------|---------|----------------------------------------|-----------|
| 13.     | Gloriosa superba L. Colchicaceae Lungi Root  | Colchicine (superbine) | Hydroalcoholic extract at two different doses | Antifertility, anti-implantation activity in postcoital study, abortifacient activity | Latha et al. (2013) |
| 14.     | Grewia asiatica L. Malvaceae, seeds Japa Flowers | Potassium, calcium, phosphorus, copper, zinc, and magnesium | Aqueous | Anti-implantation and abortifacient activity | Kamboj and Dhawan (1982) |
| 15.     | Hibiscus rosa-sinensis L. Malvaceae Japa Flowers | Cyclopeptide alkaloid | Ethanol and benzene extract | Anti-implantation, antiovulatory, increased uterine weight, secretion of estrogen by atretic follicles, postcoital antifertility | Neeru and Sharma (2008); Vasudeva and Sharma (2008); Hadimur et al. (2014); Pal et al. (1985) |
| 16.     | Mesua ferrea L. Calophyllaceae Nagakeshara, flowers | Mesul, mammegin, mesuaferronea, and mammeuisin | Aqueous | Anti-implantation activity | Seshadri and Pillai (1981); Munshi et al. (1977) |
| 17.     | Michelia champaca L. Magnoliaceae Champa, Anters | Essential oil | Benzene and hydroalcoholic extract | Postcoital anti-implantation activity | Sharma et al. (1994); Taprial et al. (2013) |
| 18.     | Momordica charantia L. Cucurbitaceae Karwetaka roots, leaves | Glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins, and steroids | Aqueous | Uterine stimulant activity, Antifertility, estrogenic activity | Jamwal and Anand (1962); Saksena (1971) |
| 19.     | Plumbago zeylanica L. Plumbaginaceae Chitrak, root | Plumbagin | Plumbagin-free alcohol | Anti-implantation and abortifacient activity | Gupta et al. (2011) |
| 20.     | Ricinus communis L. Euphorbiaceae Erand, castor bean Seed | Rcinine and isouquinoline | Aqueous | Anti-implantation, increase in diameter of the uterus, and decrease in uterine hormones | Makonnen et al. (1999) |
| 21.     | Rubia cordifolia L. Rubiaceae Manjishtha Root | Munjistin, purpurin, and pseudopurpurin | Ethanolic extract | Anti-implantation | Maurya et al. (2004) |
| 22.     | Sapindus trifoliatus L. Sapindaceae Anhthak Fruits, pulp, and seeds | Essential oil | Butanol | Antizygotic, blastocytotoxic, or anti-implantation activity | Pal et al. (2013); Bodhankar et al. (1974) |
| 23.     | Sesbania sesban (L.) Merr. Fabaceae Sesban | Alkaloids, flavonoids, glycosides, tannin, anthraquinone, steroid, pholobatannins, and terpenoids | Extract and powder | Inhibit the ovarian function, change the uterine structure, and prevent the implantation | Singh (1990a); Samajdar and Ghosh (2017) |

B Abortifacient activity

1. Abroma augusta (L.) L.f. Malvaceae Pishach karpas, roots | L-rhamnose, L-arabinose, D-xylene, D-mannose, D-galactose, D-glucose, D-galacturonic acid, and D-glucuronic acid | Alcoholic | Abortifacient activity | Pokharkar et al. (2010); Kalita et al. (2011) |

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TABLE 2 | (Continued) Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortifacient, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatogenic, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|--------------------------------------------|----------------------|---------|--------------------------------------|-----------|
| 2.      | Abrus precatorius L. Papilionaceae Gunja, Seeds | Abrin, abrasine, precasine, and precol | Aqueous | Abortifacient activity or antifertility agent with a risk of DNA damage | Sarwat et al. (2009); Kaur et al. (2011); Shrivastava et al. (2007); Azmeera et al. (2012); Priya et al. (2012) |
| 3.      | Achyranthes aspera L. Acanthaceae Gunja, Seeds | Fatty acids, oleic acid, bisdesmosidic, triterpenoid alkaloids, D-glucuronic, betaine, and achyranthine | Benzene, ethanolic, and chloroform | Abortifacient activity in rabbits | Raj et al. (2011); Vasudeva and Sharma (2008) |
| 4.      | Adhatoda vasica Nees synonym of Justicia adhatoda L. Acanthaceae, Vasa, Leaves, Stem bark, Root, Whole plant | Alkaloids, tannins, saponins, phenolics, and flavonoids | Aqueous | Abortifacient activity | Pokharkar et al. (2010); Kaur et al. (2011); Raj et al. (2011) |
| 5.      | Aegle marmelos (L.) Corrêa, Bilva, whole plant, leaves | Marmelosin, luvangetin, psoralen, tannins, and marmarin | Aqueous extract | Abortifacient activity in albino rats | Gangadhar and Lallakhumari (1995); Sathiyaraj et al. (2010) |
| 6.      | Annona squamosa L. Annonaceae Custard apple, Seeds, leaves, and bark | Atropine alkaloids, and anonaine | Ethyl acetate extract | Abortifacient induces early abortion | Jain and Dixit (1992) |
| 7.      | Areca catechu L. Arecaaceae, Poogaphala, nuts | Alkaloids—pilocarpine, arecaidine, and arecoline | Petroleum ether, alcoholic, and aqueous | Abortifacient activity in albino rats and antifertility activity | Garg and Garg (1970); Garg and Garg (1971); Shrestha et al. (2010) |
| 8.      | Barbieria prioritits L. Acanthaceae Saireyak, Roots | Acbarlerin, barlierin, 8-sitosterol, flavanol glycoside, and iridoids | Methanol extract | Abortifacient | Gupta et al. (2000) |
| 9.      | Carica papaya L. Caricaceae Papaya unripe fruit pulp, seeds, and latex | Papain, caricacin, carpasemine, and oleanolic glycoside, | Pet ether, alcohol, and aqueous ethanol | Abortifacient in albino rats and antifertility | Garg and Garg (1970), Garg and Garg (1971); Das (1980); Sinha and Nathawat (1989); Changamma and Lakshman (2013) |
| 10.     | Citrus × aurantium L Rutaceae Bijaura, Seeds | Citroflavonoids, glucosides, and triterpenoids | Petroleum ether | Abortifacient, increased ovarian weight, decreased Graafian follicles, and irregular estrous cycle | Patil and Patil (2013) |
| 11.     | Daucus carota L. Apiaceae Gnijanak, seed | Essential oil | Petroleum, ether, benzene, alcohol, and water | Abortifacient activity | Garg (1975); Jansen and Wolhmutm (2014); Shah and Varute (1980) |
| 12.     | Gloriosa superba L. Colchicaceae Langi, Root | Carbohydrates, flavonoids, steroids, alkaloids, tannins, and glycosides | Ether, chloroform, and ethyl alcohol extracts | Abortifacient activity and significant reduction in number of implants and number of pups born | Malpani and Mahurkar (2018) |
| 13.     | Grewia asiatica L. Malvaceae, seeds | Potassium, calcium, phosphorus, copper, zinc, and magnesium | Aqueous | Abortifaction activity | Kamboj and Dhawan (1982) |
| 14.     | Lepidium sativum L. Brassicaceae Chandrasur Mature explants | Lepidine | Methanolic | Abortifacient and antiovulatory | Pande et al. (2002) |

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TABLE 2 (Continued) Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortification, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatic activity, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|----------------------|---------|----------------------------------------|-----------|
| 15.     | Ricinus communis L. Euphorbiaceae Erand, Castor bean Seed | Ricinine and isoquinoline | Aqueous extract | Abortifacient | Makonnen et al. (1999), Sandhyakumary et al. (2003) |
| 16.     | Woodfordia fruticosa (L.) Kurz Lythraceae Dhataki, flowers | Tannins, flavonoids, anthraquinone glycosides, and polyphenols | Aqueous and ethanol | Abortifacient | Pathak et al. (2005) |
| C Antifertility activity 1. Abrus precatorius L. Papilionaceae Gunja, Seeds | Abrin, abrasine, precasine, and precoll | Aqueous | Antifertility agent with a risk of DNA damage | Sarwat et al. (2009); Kaur et al. (2011); Shrivastava et al. (2007); Azmeera et al. (2012); Priya et al. (2012) |
| 2.     | Acacia leucophloea (Forsk.) Willd. Leguminosae—Fabaceae Shwet babul, roots | N-hexacosanol, beta-amyrin, beta-sitosterol, and tannin | Alcoholic | Antifertility activity | Dheeraj (2011) |
| 3.     | Annona squamosa L. Annonaceae Custard apple Seeds, leaves, and bark Aroca catechu L. Anacaceae Poogaphala, Nuts | Atropine alkaloids and anonaine | Ethyl acetate extract | Abortifacient—induces early abortion | Jain and Dixit (1992) |
| 4.     | Areca catechu L. Arecaceae | Alkaloids—pilocarpine, arecainde, and arecicol | Nut oil Ethanolic extract | Antifertility activity in female albino rats, antiovulatory, and ovarian weight decreased due to imbalance in gonadotrophins | Garg et al. (1974); Shrestha et al. (2010) |
| 5.     | Azadirachta indica A. Juss Meliaceae Nimbta Leaves, flower, and seed | Azadirachtin, nimbinolin, nimbin, nimbidin, nimbidol, sodium niminate, and gedunin | Female albino rabbits Seed oil | Antifertility and functional sterility | Vyas and Purohit (2018) |
| 6.     | Carica papaya L. Caricaceae Papaya amrue fruit pulp, seeds, and latex | Papain, caricacin, carpassemine, and oleanolic glycoside | Pet ether, alcohol, aqueous, and ethanol | Antifertility | Garg and Garg (1970); Garg and Garg (1971); Das (1980); Sinha and Nathawat (1989); Changammai and Lakshman (2013) |
| 7.     | Cissampelos pareira L. Menispermaceae, Patha Leaves and stem | Berberine | Leaf extract | Altered the estrous cycle pattern in female mice, Antifertility | Ganguly et al. (2007); Samatha et al. (2011) |
| 8.     | Cuminum cyminum L. Apiaceae Jeerak, seeds | Cuminal and cuminic alcohol | Extract | Antifertility effect in female albino rat | Priya et al. (2012); Sharma J et al. (2001) |
| 9.     | Crateva nurvala Buch-Ham. Capparaceae Varuna Dried stem bark | Alkaloids, triterpene, tannins, saponins, flavonoids, sterols, glucosylamine, lupeol, and diosgenin | Ethanol, aqueous | Antifertility effects estrogenic activity | Bhaskar et al. (2009) |
| 10.    | Curcuma longa L. Zingiberaceae Haldi, rhizome | Curcumin and flavonoids | Ethanol, aqueous | Propylene glycol solution, antifertility, antiovulatory—suppression of GnRH | Ghosh et al. (2011); Bhagat and Purohit (1986) |

(Continued on following page)
Table 2 | Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortifacient, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatogenic, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|----------------------|---------|--------------------------------------|-----------|
| 11.     | Daucus carota L. Apioaceae, Grinjanak, Seed | Essential oil        | Petroleum, ether, benzene, alcohol, and water | Antifertility activity | Garg (1975); Jansen and Wolhlmuth (2014); Shah and Varute (1980); Pilai et al. (1982) |
| 12.     | Desmosium gangeticum (L.) DC. Fabaceae, Shalpami, Root | Lavenoid glycosides, pterocarpanoids, lipids, glycolipids, and alkaloids | Gangeticum | Antifertility effect | Prakash (1981b) |
| 13.     | Embelia ribes Burm. f. Primulaceae, Vridhan, Berries | Embelin, volatile oil, fixed oil, resin, tannin, chrestimbine (alkaloid), and phenolic acids | Isolated embelin | Anti-implantation and postcoital antifertility activity | Pathak et al. (1995) |
| 14.     | Ferula jaeschkeana Vatke Apioaceae, Heenugupati, Dried leaves | Flavonoids, alkaloids, terpenoids, cardiac glycosides, saponins, and phenolics | Hexane | Duration-dependent luteolytic changes in the corpora lutea | Pathak et al. (1995) |
| 15.     | Gloriosa superba L. Colchicaceae, Langi, Root | Colchicine (superbine) | Hydroalcoholic extract at two different doses 30 and 60 mg/kg | Antifertility, anti-implantation activity in postcoital study | Latha et al. (2013) |
| 16.     | Hibiscus rosa-sinensis L. Malvaceae, Japa Flowers | Cyclopeptide alkaloid | Ethanol and benzene extract | Anti-implantation, antiovulatory, secretion of estrogenic by atretic follicles, and postcoital antifertility | Neeru and Sharma (2008) |
| 17.     | Lawsonia inermis L. Lythraceae, Madayantika Leaves | Lawsone, esculetin, fraxetin, isoplumbagin, scopoletin, betulin, betulinic acid, hennadiol, lupeol, lacoumarin, quinone, and naphthaquinone | Powder | Preventing pregnancy in 60% of the animals tested | Munshi et al. (1977) |
| 18.     | Lepidium sativum L. Brassicaceae, Chandrasur Mature explants | Lepidine | Methanolic | Abortifacient and antiovulatory | Pande et al. (2002) |
| 19.     | Melia azedarach L. Meliaceae, Malai’vembu seed and leaves | Triterpenoids | Seed extract | Antifertility effect, increased preimplantation, postimplantation, and total prenatal mortalities | Mandal and Dharwal (2007) |
| 20.     | Momordica charantia L. Cucurbiteae, Karwella, Roots and leaves | Glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins, and steroids | Aqueous | Uterine stimulant activity, antifertility, and estrogenic activity | Jamwal and Anand (1962); Saksena (1971) |
| 21.     | Nigella sativa L. Ranuncucaee, Krishna jeerak, Seeds | Fixed oil, volatile oil, and alkaloids | Hexane | Antifertility activity in rats, postcoital contraceptive | Keshri et al. (1995) |
| 22.     | Piper betle L. Piperaceae, Betel leaf, Pan Petiol | Eugenol, eugenol acetate, piper betol, piperol, and methyl eugenol phytol | Alcoholic | Antifertility, antiestrogenic effects in female rats | Sharma et al. (2007) |
| 23.     | Piper longum L. Piperaceae, Pippali, Root and nuts | Piperine | Powder, hexane fraction, and benzene | Antifertility activity—prolonged the length of the estrous cycle, drastic reduction in the number of implantation sites, marked suppression in the ovarian cytokines and nitric acid level | Laxmi et al. (2006); Khokute et al. (1979) |

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| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|----------------------|---------|---------------------------------------|-----------|
| 24.     | **Trichosanthes cucumerina** L. **Cucurbitaceae** Snake gourd, **Fruit** | Cucurbitacin B, cucurbitacin E, isocucurbitacin B, E, sterols 2 β-sitosteryl stigmasteryl | Aqueous | Affected the normal estrous cycle, significantly reduced the number of healthy follicles, corpora lutea, and increased the number of regressing follicles. Reduced serum FSH and LH levels | Devendra et al. (2009) |
| 25.     | **Zingiber officinale** Roscoe **Zingiberaceae** Sunthi Rhizome | Monocyclic, phenols, sesquiterpenes, sesquiterpenoids, oleoresins, and proteolytic enzymes | Aqueous, ethanol extracts | Anti-implantation activity | Pathak et al. (2005) |

D Antiovulatory activity

1. **Achyranthes aspera** L. **Amaranthaceae** Aparnargal Whole plant, Stem bark, **Root** | Fatty acids, oleic acid, bisdesmosidic, triterpenoid alkaloids, D-glucuronic, betaine, and achyranthine | Benzene, ethanolic, chloroform | Antiadulatory, anti-implantation, hormonal disturbance in uterus, and expulsion of ovary | Shibeshi et al. (2006); Vasudeva and Sharma (2006) |

2. **Areca catechu** L. **Arecaceae** Poogaphala, Nuts | Alkaloids—pilocarpine, arecaidine, and arecoline | Ethanolic extract | Antiovulatory, ovarian weight decreased due to imbalance in gonadotrophins | Shrestha et al. (2010) |

3. **Azadirachta indica** A. Juss. **Meliaceae** Nimba Leaves, flower, and seed | Azadirachtin, nimbinolin, nimbin, nimbidin, nimbidol, sodium niminate, and gedunin | Alcoholic extract, flower in Sprague-Dawley rats | Disrupted the estrous cycle and caused a partial block in ovulation | Gbotolorun et al. (2003); Vyas and Purohit (2018) |

4. **Butea monosperma** (Lam.) Kuntze **Fabaceae** Patash, bark, and flowers | Kino-tannic acid, gallic acid, and pyrocatechin | Aqueous extract | Inhibit ovulation | Shrivastava et al. (2007), Sinha and Nathawat (1989) |

5. **Calotropis procera** (Alton) W.T. **Apocynaceae** Arka, **Root** | Steroidal alkaloid | Calotropin, aqueous ethanol | Antiovulatory prolonged di-estrous stage with temporary inhibition of ovulation | Gupta et al. (1990); Abdelgader and Elsheikh (2018); Sharma and Jacob (2001a); Pokharkar et al. (2010) |

6. **Catunaregam spinosa** (Thunb.) Tirveng. **Rubiaceae** Madanphal, **Seeds** | Saponins, valeric acid resin, wax, and coloring matter | Ethanolic extract, isolated oleic acid | Antiovulatory effect in rabbits, antimplantation activity in albino rats | Mali and Trivedi (1972); Pillai et al. (1977) |

7. **Citrus × aurantium** L. **Rutaceae** Bijaura, **Seeds** | Citroflavanoids, glucosides, and triterpenoids | Petroleum ether | Anti-implantation, antiovulatory, abortifacient, increased ovarian weight, decreased Graafian follicles, irregular estrous cycle | Patil and Patil (2013) |

8. **Curcuma longa** L. **Zingiberaceae** Harit, rhizome | Curcumin and flavanoids | Ethanol, aqueous | Propylene glycol solution antifertility, antiovulatory, decreased ovarian weight, suppression of GnRH | Ghosh et al. (2011) |

9. **Hibiscus rosa-sinensis** L. **Malvaceae** Japa, **Flowers** | Cyclopeptide alkaloid | Ethanol, benzene extract | Anti-implantation, antiovulatory, increased uterine weight, secretion of estrogen by atretic follicles, postcoital antifertility | Neeru and Sharma (2008) |

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TABLE 2 | Medicinal plants and their phytocomponents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortificient, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatic activity, (2G) spermicidal, and (2H) antandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|----------------------|--------|---------------------------------------|-----------|
| 10.     | Musa paradisiaca L., Musaceae, Banana, stem | Alkaloids and flavonoids | Ethanolic | Antiovulatory suppressed ovulation due to inhibition in secretion of GnRH | Soni et al. (2013) |
| 11.     | Papaver somniferum L., Papaveraceae, Aniphen, Latex | Noscapine alkaloid | Alcoholic extract | Antiovulatory decreased production of gonadotrophin | Kumar and Sachin (2013) |
| 12.     | Plumbago rosea L., Plumbaginaceae, Raktachitrak, Leaves | Plumbagin, sitosterol glycoside, tannins, and fatty alcohol | Acetone, ethanolic | Antiovulatory inhibition of ovulation with irregular estrous cycle | Sheeja et al. (2011) |
| 13.     | Semecarpus anacardium L.f., Anacardiaceae, Bhalitak | Alkaloids | Aqueous and ethanolic | Reversible antiovulatory activity | Sushma et al. (2016) |
| 14.     | Taxus baccata L., Taxaceae, Talishpatra Common Yew Leaves | Pseudo alkaloids | Leaf extract | Antiovulatory, inhibited secretion of ovarian hormones | Priya et al. (2012); Kaur et al. (2011) |
| 15.     | Vitex negundo L., Lamiaceae, Nirgundi, roots, and seeds | Casticin, isoorientin, chrysophanol D, luteolin, p-hydroxybenzoic acid, and D-fructose | Aqueous | Antiovulatory activity | Lai et al. (1992) |

E Antiestrogenic activity

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|----------------------|--------|---------------------------------------|-----------|
| 1.      | Allium sativum L., Amaryllidaceae, Rason, Bulb | Sulfur-containing compounds | Alcohol | Ecobolic in mice and rats, estrogenic activity in female albino rats | Tewari et al. (1971); Ola-Mudathir et al. (2008) |
| 2.      | Cyperus rotundus L., Cyperaceae, Musta, Rhizome | Cyperene, humulen, selinine, zierone, campholenicopaene, and limonene | Aqueous | Antiestrogenic property | Gediya et al. (2011) |
| 3.      | Glycyrrhiza glabra L., Fabaceae, Yashtimadhu, Roots | Triterpene glycyrrhizin acid and glycoside | Water | Estrogenic activity | Ahmad et al. (2011) |
| 4.      | Guilandina bonduc (L.) sy. Caesalpinia bonduc (L.) Roxb., Leguminosae, Karanja, seeds | Phytosterin, β-sitosterol, flavonoids, bonducellin, aspartic acid, arginine, and citrulline β-carotene | Aqueous | Antiestrogenic activity | Salunke et al. (2011) |
| 5.      | Nelumbio nucifera Gaertn., Nelumbonaceae, Kamala, Lotus Seeds | Hydrocarbons | Ethanolic extract | Antiestrogenic, decreased ovarian weight, estrogens inhibition | Mutreja et al. (2008) |
| 6.      | Sesamum indicum L., Pedalaceae, Tila, seeds | Oil, protein, and carbohydrate | Extract | Estrogenic effect in female albino rats | Priya et al. (2012) |
| 7.      | Vitex negundo L., Lamiaceae, Nirgundi, roots and seeds | Casticin, isoorientin, chrysophanol D, luteolin, p-hydroxybenzoic acid, and D-fructose | Aqueous | Antiovulatory activity | Lai et al. (1992) |

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TABLE 2 | (Continued) Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortifacient, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatogenic, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|---------------------|--------|---------------------------------------|-----------|
| 1       | Abrus precatorius L. Papilionaceae Gunja, seeds | Abrin, abrasine, precasine, and precol | Aqueous | Reduced sperm motility, density, antispermatogenic effect, reduced activity of testicular enzyme, post-testicular antifertility effect | Bajaj et al. (1981); Dixit et al. (1987); Kulshreshtha and Mathur (1990); Sinha (1990) |
| 2       | Aegle marmelos (L.) Corfi. Rutaceae Bilva, whole plant and leaves | Marmelosin, luangetin, psoralen, tannins, and marmin | Aqueous extract | Inhibit spermatogenesis and sperm motility, male rat reproduction, affecting the sexual behavior and epididymal sperm concentration | Sur et al. (1999); Sur et al. (2002) |
| 3       | Albizia lebbeck (L.) Benth. Fabaceae Shirish, Pods | Melacacidin, D-catechin, β-sitosterol, abiziahexoside, betulinic acid, and echinocystic acid glycosides | Methanolic extract | Spermatogenic arrest in male albino rats | Gupta et al. (2004); Gupta et al. (2005a) |
| 4       | Andrographis paniculata (Burm.f.) Nees Acanthaceae Kirattikta, leaves | Andrographolide, Andrographidoids A, B, C, D, E, diterpenoid, and lactone | Water extract | Antispermatogenic | Akbarsha et al. (1990); Akbarsha and Murugaian (2000) |
| 5       | Ananas comosus (L.) Merr. Bromeliaceae Custard apple, seeds | Atropine alkaloids and anonaine | Water | Antispermatogenic activity | Satyawati (1983) |
| 6       | Annona squamosa L. Annonaceae Custard apple | Atropine alkaloids and anonaine | Ethyl acetate extract | Antispermatogenic activity | Jain and Dixit (1992) |
| 7       | Areca catechu L. Arecaaceae Poongphala, Nuts | Alkaloids—pilocarpinearecadine, arecoline | Water | No abnormality in Leydig cell and interstitial tissue | Ave Olvia et al. (2020) |
| 8       | Aristolochia indica L. Aristolochiaceae Ishwari, roots | Aristolochic acid, ceryl alcohol, β-sitosterol, stigmast-4-en-3-one, friedelin, and cycloeucalenol | Aristolochic acid | Antispermatogenic | Gupta et al. (1996) |
| 9       | Azadirachta indica A. Juss. Meliaceae Nimba Leaves, flower, and seed | Azadirachtin, nimbolinin, nimbin, nimbidin, nimbol, sodium nimbinate, and gedunin | Aqueous, alcoholic | Decrease in the weight of seminal vesicles, ventral prostate, reduction in epithelial height, nuclear diameter, and the secretory materials in the lumens | Gediya et al. (2011) |
| 10      | Bacopa monnieri (L.) Wettst. Plantaginaceae Brahmi, whole plant | Bacosides and saponins | Aqueous extract | Reversible suppression of spermatogenesis and fertility, without producing apparent toxic effects | Singh et al. (2013) |
| 11      | Balanites roxburghii Blan. Zygophyllaceae Ingudi, Fruit pulp | Saponin, furanocoumarin, and flavonoid | Methanol, palmistine hydroxide | Antispermatogenic activity | Dixit et al. (1981), Agarwal and Dixit (1982) |
| 12      | Berberis aristata DC. Berberidaceae Danurhardtia, Roots | Berberine and berbamine | Palmistine hydroxide | Antispermatogenic action | Gupta and Dixit (1989) |

(Continued on following page)
| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|--------|---------------------------------------------|----------------------|---------|---------------------------------------|-----------|
| 13.    | *Butea monosperma* (Lam.) KuntzeFabaceaePalash, bark, and flowers | Kino-tannic acid, gallic acid, and pyrocatechin | Aqueous extract | Antispermatogenic effect | Wati and Verute (1988) |
| 14.    | *Calotropis procera* (Aiton) W.T. AitonApocynaceaeArka, root | Steroidal alkaloid | Calotropin, aqueous ethanol | Antispermatogenic, antiandrogenic activities, and/or endocrine disrupting effects, functional alteration in genital organs | Gupta et al. (1990); Abdelgader and Elsheikh (2018); Sharma and Jacob (2001b); Pokharkar et al. (2010) |
| 15.    | *Canca papaya* L. CaricaceaePapaya, unripe fruit pulp, seeds, latex | Papain, caricacin, carpasemine, oleanolic glycoside | Pet ether, Alcohol, aqueous Ethanol | Antispermatogenic activity reduced spermatogenesis, inhibition in steroid hormones | Changamma and Lakshman (2013) |
| 16.    | *Celastrus paniculatus* Wild. CelastraceaeJyotishmati, seeds | Alkaloids, tannins, saponins, steroid, terpenoid, flavonoids, phlobatannin, cardiac, and glycoside | Seed | Antispermatogenic activity | Bidwai et al. (1990) |
| 17.    | *Cichorium intybus* L. Asteraceae, ChicoryWhole plant | Inulin, sesquiterpene lactones, vitamins, minerals, fat, and mannitol | Aqueous | Antispermatogenic activity | Roy and Venkatakrisinha (1983) |
| 18.    | *Cinnamomum camphora* (L.) J.PreslLauraceaeKarpurCamphor, leaves and resin | Essential oil—camphor, linalool, and cineole | Leaf | Inhibition of spermatogenesis | Singh (1990b) |
| 19.    | *Cuminum cyminum* L. ApiaceaeJeerkak, seeds | Cuminal and cuminic alcohol | Extract | Antispermatogenic effect | Priya et al. (2012); Sharma J et al. (2001) |
| 20.    | *Embelia ribes* Burm.f. PrimulaceaeVidang, berries | Embelin, volatile oil, and fixed oil | Isolated embelin | Inhibition of spermatozoa motility | Prakash (1981); Nand (1981); Dixit et al. (1983); Gupta et al. (1989) |
| 21.    | *Euphorbia neriifolia* L. EuphorbiaceaeLatex, Whole plant | β-amyrin acetate, lupenone, 3-acetoxy-20-lupanol, cycloart-25-en-3β,24ζ,2ζ-diol, and cycloart | Ethanol | Antispermatogenic effect | Mali (1999) |
| 22.    | *Hibiscus rosa-sinensis* L. MalvaceaeJapa Flowers | Cyclopeptide alkaloid | Ethanol, benzene extract | Spermatogenic elements of testis and epididymal sperm count, androgenic activity | Reddy et al. (1997); Gupta et al. (1985) |
| 23.    | *Momordica charantia* L. CucurbitaceaeKarela, leaves | Glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins, and steroids | Aqueous | Antispermatogenic, antisteroidogenic activity | Naseem et al. (1998) |
| 24.    | *Ocimum sanctum* L. Lamiaceae, Tulsi, leaves | Carvacrol, sesquiterpene, hydrocarbon, and caryophyllene | Benzene extract | Decreased sperm count, weight of testis, and sperm motility | Pandey and Madhuri (2010) |

(Continued on following page)
**TABLE 2** (Continued) Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortifacient, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatogenic, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|-----------------------------------------------|----------------------|---------|---------------------------------------|-----------|
| 25.     | *Piper betle* L. *Piperaceae* Betel leaf, Pan Petiole | Eugenol, eugenol acetate, piper betol, piperol, methyl eugenol, and phytol | Alcoholic extract | Reduced sperm motility | Adhikary et al. (1989); Sarkar et al. (2000) |
| 26.     | *Piper nigrum* L. *Piperaceae* Marich, Black pepper Fruit | Piperine | Fruit powder—suspended in sterile distilled water containing milk powder | Alterations in the male reproductive organs, reversible after cessation of treatment | Mishra and Singh (2009), Malivi et al. (1999) |
| 27.     | *Plumbago zeylanica* L. *Plumbaginaceae* Chitrak, Root Part | Plumbagin | Ethanol | Antispermaticogenic | Purohit et al. (2008) |
| 28.     | *Plumbago zeylanica* L. *Plumbaginaceae* Chitrak, Root Part | Santalin A, B, savinin, calocedrin, pterolinus K, L, and pterostibenes | Water | Semen coagulating activity | Purohit et al. (2008) |
| 29.     | *Plumbago zeylanica* L. *Plumbaginaceae* Chitrak, Root Part | Puerarin, genistein, and daidzein | Methanol | Inhibition of spermatogenesis | Gupta et al. (2004), Gupta et al. (2005b) |
| 30.     | *Semecarpus anacardium* L.f. *Anacardiaceae* Anacardiales Hallisatk, Marking nut, Seeds | Shilawansol, phenolic compounds, biflavonoids, and sterol glycosides | Ethanol | Reduction in the number of primary spermatocytes, secondary spermatocytes, and spermatozoa | Gupta et al. (2013); Sharma et al. (2003) |
| 31.     | *Terminalia arjuna* (Roxb. ex DC.) Wight &Arn. *Combretaceae* Arjuna, Bark | Tannins, triterpenoid saponins, flavonoids, gallic acid, ellagic acid, and phytosterols | Crude form | Inhibition of spermatogenesis | Jha and Dixit (1986), Lal and Udupa (1993) |
| 32.     | *Tylophora asthmatica* (L. f.) Wight &Arn. *Apocynaceaee* Khadki Rasna, Leaf and stem | Aempferol, quercetin, tylonide, cetyl-alcohol, tannins, glucose, calcium salts, and potassium chloride | Pure alkaloid | Antispermatogenic activity | Dikshith et al. (1990) |

G Spermicidal activity

| 1. | *Acacia concinna* (Willd.) DC. *Leguminosae-Mimosoidae* Shikakai, stem bark | Hexacosanol, spinasterone, oxalic, tartaric, citric, succinic, ascorbic acid, alkaloids calyctomine, and nicotine | Alcoholic | Spermicidal and semen coagulating activity | Kamboj and Dhawan (1982) |
| 2. | *Achyranthes aspera* L. *Amaranthaceae* Apamarga Whole plant, Stem bark, Root | Fatty acids, dicarboxylic acid, bisdesmosidic, triterpenoid alkaloids, D-glucuronic, betaine, and achyrantheine | Benzene, ethanolic, and chloroform | Spermicidal | Raj et al. (2011); Shibeshi et al. (2006); Vasuveda and Sharma (2006) |
| 3. | *Aristolochia scholaris* (L.) R.Br. *Apocynaceaee* Saptaparna, stem bark | Erythrodiol, uvaol, betulin,oleanolic acid usric acid, and β-amyrin | Water extract | Decline germ cell population | Gupta et al. (2003, 2004) |
| 4. | *Azadirachta indica* A. Juss. *Meliaceae* Nimba | Azadiracthin, nimbinol, nimbin, nimbidin, nimbidol, sodium nimbinate, and gedunin | Aqueous and Alcoholic | Spermicidal effect on number of spermatozoa and level of fructose | Gediya et al. (2011), Kasturi et al. (1997) |
| 5. | *Bambusa bambos* (L.) Voss *Poaceae, Vanshara* Leaves, flower, and seed | Balarenone, barkerin, barlerinosideverbascoside, acetylbarlerin, and lupulinoside | Ethanol | Reduced sperm motility | Vanithakumar et al. (1989) |

(Continued on following page)
TABLE 2 | Medicinal plants and their phytoconstituents validated for various female/male contraceptive activities. Different contraceptive activities studied on medicinal plants could be categorized as follows. Female contraceptive activities: (2A) anti-implantation activity, (2B) abortifacient, (2C) antifertility, (2D) antiovulatory, and (2E) antiestrogenic activity. Male contraceptive activities: (2F) antispermatogenic, (2G) spermicidal, and (2H) antiandrogenic activity.

| Sr. No. | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|---------|---------------------------------------------|----------------------|---------|---------------------------------------|-----------|
| 6.      | Cannabis sativa L., Cannabaceae, Bhanga, leaves | Cannabinoids, terpenes, and sesquiterpenes | Butin | Testicular lesions | Dixit and Joshi (1982) |
| 7.      | Citrullus colocynthis (L.) Schrad. Cucurbitaceae Indrawaruni Bitter apple, fruits | Carbohydrate, protein, amino acid, tannins, saponins, phenolics, and cardiglycoloids | Ethanol | Impairment of sperm | Chaturvedi and Dixit (1997) |
| 8.      | Daucus carota L., Apiaceae Ginjaanak, Seed | Essential oil | Petroleum, ether, benzene, alcohol, and water | Spermicidal activity | Garg (1975); Jansen and Wohlhmut (2014); Shah and Varute (1980) |
| 9.      | Embelia ribes Burm.f., Primulaceae Vitang, Berries | Embelin | Embelin in 50 and 100 mg/kg doses | Reversable contraception like activity in male dogs | Nand (1981); Dixit and Bhagava (1983) |
| 10.     | Mentha arevensis L., Lamiaceae Pudina, leaves | Alkaloids, steroids, and glycosides | Petroleum ether | Spermicidal Decreased weight of testis, sperm motility, and viability | Sharma and Jacob (2001a) |
| 11.     | Myristica fragrans Houtt Myristicaceae Nutmeg, Jatiphal, seeds | Myristicin, elemicin, myristic acid, alpha-pinene, terpenes, beta-pinene, and trimyristin | Ethanol | Premature ejaculation | Mishra and Shukla (1980) |
| 12.     | Strychnos potatorum L.f., Loganiaceae Nimai, Seeds | Strychnine | Seed extract | suppressive effects on male fertility | Gupta et al. (2006) |
| 13.     | Terminalia bellirica (Gaertn.), Roxb. Combretaceae Bibhitaak Fruits | Phenolic acids, saponins, lignans, triterpenoids, resveratrol glycosides, arjunigenin, β-sitosterol, and stigmasterol | Aqueous | Spermicidal activity in rat semen, human semen | Kaur et al. (2011) |
| 14.     | Tinospora cordifolia (Wild.), Hook.f., & Thomson Menispermaeae Amrita Giloe Stems | Berberine, palmatine D, cholrine D, diterpene, terpenoids alkaldoids, and steroids | Aqueous | Spermicidal Reduced weight of testis, sperm count | Gupta and Sharma (2003) |
| 15.     | Trigonella foenum-graecum L., Fabaceae Methika, Seeds | Water, carbohydrates, protein, fat, and calcium | Aqueous | Spermicidal activity in human and rat semen | Priya et al. (2012) |
| 16.     | Withania somnifera (L.) Dunal Solanaceae Ashwagandha Stem and root | Withanolides | Stem, ethanolic | Reversable spermicidal and infertilizing effect | Singh et al. (2013); Mali (1999) |

H Antiandrogenic activity

1. Aloe barbadensis Mill. Synonym of Aloe vera (L.) Burm.f. Asphodelaceae Kumari, leaves | Water, polysaccharides, peclin, cellulose, hemicellulose, and glucomannan | Extract | Antiandrogenic activity on monkeys | Dixit et al. (1983) |

(Continued on following page)
| Sr. No | Botanical name, family, Sanskrit name, parts | Chemical composition | Extract | Mode of action in experimental studies | Reference |
|--------|---------------------------------------------|----------------------|---------|---------------------------------------|-----------|
| 2.     | *Aristolochia indica* L. Aristolochiaceae Ishwari, roots | Aristolochic acid, ceryl alcohol, β-sitosterol, stigmast-4-en-3-one, friedelin, and cycloeucalen | Aristolochic acid | Antiandrogenic effects on langur monkey | Gupta et al. (1996) |
| 3.     | *Andrographis paniculata* (Burm.f.) Nees Acanthaceae Kirtakta, leaves | Andrographolide, andrographidoids A, B, C, D, E, diterpenoid, and lactone | Water extract | Antiandrogenic | Akbarsha et al. (1990); Akbarsha and Murugaian (2000) |
| 4.     | *Azadirachta indica* A. Juss., Meliaceae Nimba Leaves, flower, and seed | Azadirachtin, nimbinolin, nimbin, nimbidin, nimbidol, sodium niminate, and gedunin | Seed oil | Antiandrogenic | Sharma et al. (1987); Sinha et al. (1984); Roop et al. (2005) |
| 5.     | *Cuscuta reflexa* Roxb Convolvulaceae Amarwela, whole plants | Alkaloids | Methanolic | Antiandrogenic | Gupta et al. (2003) |
| 6.     | *Curcuma longa* L. Zingiberaceae Haldi, rhizome | Curcum and flavanoids | Ethanol, aqueous | Antiandrogenic | Bhagat and Purohit (1986) |
| 7.     | *Foeniculum vulgare* Mill Apiaceae Common fennel, seeds | Anethole, alpha pinene, beta myrcene—pinene, bitter fenchone, camphene, and estragole | Alcoholic | Antiandrogenic | Farooq et al. (1997) |
| 8.     | *Hibiscus rosa-sinensis* L. Malvaceae Japa, Flowers | Cyclopeptide alkaloid | Ethanol and Benzene extract | Spermatogenic elements of testis and epididymal sperm count, androgenic activity | Reddy et al. (1997); Gupta et al. (1985) |
| 9.     | *Mucuna urens* (L.) Medik. Fabaceae Horase been, Kapikacchu Seeds | L-DOPA, with trace amounts of serotonin, nicotine, and bufotenine | Water | Effect on gonads and sex accessory glands | Udoh and Expenyong (2001) |
| 10.    | *Nicotiana tabacum* L. Solanaceae Tobacco, leaves | Lipid constituents, free fatty acids, triglycerides, and sterol esters free sterols | Nicotine | Antiandrogenic | Londonkar et al. (1998) |
| 11.    | *Plumbago zeylanica* L. Plumbaginaceae Chitrak, root | Plumbagin | Plumbagin-free alcohol | Antiandrogenic | Bhargava (1984) |
| 12.    | *Ruta graveolens* L. Rutaceae, Rue, leaves | Volatile oil | Aqueous extracts | Adverse effects on territorial aggression and sexual behavior in male albino rats | Khouri and Akawi (2005) |
| 13.    | *Semecarpus anacardium* L.f. Anacardiaceae Bhallatak, Marking nut, Seeds | Shihwanols, phenolic compounds, biflavonoids, and sterols glycosides | Aqueous extracts | Antiandrogenic | Singh (1985) |
a cost-effective herbal contraceptive for its spermicidal property and is considered safe for regular use. (Achintya, 2018).

**Ricinus communis L.**
The seeds of *Ricinus communis* Linn RICOM-1013-J, administered as a single oral dose of 2.3–2.5g once/12 months acted as protection against pregnancy in 50 women volunteers. The study revealed very minimal side effects. The antifertility and contraceptive efficacy of RICOM-1013-J is due to hormonal mechanisms (Isichei et al., 2000). Goncin et al. (2010) stated that one seed of *Ricinus communis* L. taken orally can prevent ovulation in humans and the anticonceptive effect may be due in part to the prevention of ovulation.

**Compound Formulation**
A study was conducted on a combination of Ashoka (*Saraca indica* L.), Vidanga (*Embelia ribes* Burm.f.), Laksha (lac), and Kramuk (*Areca nut*) on 834 young, healthy patients in active reproductive age below 40 years. The drug was administered from the 5th day of LMP for a period of 15 days in a daily dose schedule of 1gm (2 tablets) at bedtime with milk. Results suggested that the failure rate of treatment 1.19/HWY is comparable to both steroidal oral contraceptive pills and intrauterine device. It does not affect the hypothalamo-pituitary axis and did not have any other adverse effects. It can be a good alternative for lactating women (Palep and Jukar, 2003).

Central Council for Research in Ayurveda and Siddha had taken up a number of studies to evaluate the efficacy of Ayurvedic formulations like K Capsule, Ayush AC-IV, Pippalyadi yoga (in three different doses), Ayush AC-II, Talisadi yoga, Vidangadi yoga, etc., which were proved as safe and effective in different clinical studies. Besides this, the council also tried the efficacy of neem oil—as a local contraceptive and found encouraging results (Galib et al., 2008).

**TERATOGENIC EFFECT**
Ayurveda classical texts have references to congenital birth disorders as per the etiopathology and clinical presentation. Some congenital malformations in the fetus may occur but the mechanism is still not clear.

Teratogen is an agent or factor that causes malformation in the embryo. One of the causes of malformation may be toxic substances such as drugs and environmental toxins in pregnancy.

Herbal drugs with appropriate dose and duration may not cause teratogenic effect but in the case of excess dose with improper mode of administration, for a longer duration than therapeutically advised, teratogenic effect may be seen. Scientific validation of their safe use in pregnancy is hardly documented. Teratogenic effects of some of the medicinal plans have been mentioned in Table 3.

It is observed that drugs having contraceptive and abortifacient action have potent teratogenic effect in experimental models. There are several studies of teratogenicity on other herbal drugs which are not showing teratogenic effects in low doses and may cause teratogenic effects in high doses, for example, Ashwagandha (*Withania somnifera* L.) Dunal), Punarnava (*Boerhavia diffusa* L.), Narangi (*Citrus aurantium* L.), Nimba (*Azadirachta indica* A. Juss.), Jatamansi (*Nardostachys jatamansi* (D.Don) DC.), (Bala *Abutilon indicum* L.) Sweet), and Yastimadhu (*Glycyrrhiza glabra* L.) (Jati, 2018).

Different contraceptive activities in the abovementioned 94 plant ingredients are categorized in Table 4.

**DISCUSSION**
Presently, scientifically established methods of contraception and contraceptive drugs are used extensively. The synthetic contraceptive drugs known to interfere with the endocrine system and natural hormones may produce reproductive, neurological, developmental, and metabolic adverse effects that are serious at times. Search for safer drugs and preference for natural origin contraceptive drugs and methods are of research interests. Necessarily, the objectives for research of novel contraceptives from nature would be the assurance regarding effectiveness, safety, and user compliance. There are many plants known to have antifertility activity both in male and female. Some of these plants had spermicidal and altered hormone levels.

The classical Ayurvedic texts offer substantial knowledge on reproductive biology for healthy progeny and medieval Ayurvedic and specific Sanskrit texts provide information about methods and a broad range of therapeutics and ingredients that are described for use in contraception. These include local and oral contraceptives, abortifacients, and other methods of antifertility and birth control. These formulations and ingredients are a valuable source for extended research in the field of contraception.

In this study, 94 indigenous medicinal plants have been reviewed. Chemotaxonomically, it is of interest to note that the maximal number of plants having abortifacient and contraceptives are from Fabaceae, Acanthaceae, Euphorbiaceae, and Liliaceae families.

**Ingredients, Phytoconstituents, and Contraceptive Activities**
Certain alkaloids, glycosides, saponins, tannins, terpenoids, and other phytoconstituents are known to disrupt ovarian functions and estrous cyclicity through interplay of ovarian and extra ovarian hormones. Alkaloids are a major group of secondary metabolites bitter in taste that stimulate the central nervous system or directly work on the human brain. These are antiparasitic, antiplasmodial, anticorrosive, antioxidative, antibacterial, anti-HIV, and have insecticidal activities. In a review, it has been suggested that maximum alkaloids containing plant drugs have been reported to have an antifertility, anti-implantation, abortifacient effect on animals (Choudhury and Jadhav, 2013).

A majority of these medicinal ingredients used either in formulations or singly over centuries have also been studied for a variety of pharmacological, biological, and therapeutic activities.
**Achyranthes aspera L.**
A plant known to have antimicrobial, hypolipidemic, and has antifertility qualities is also used to treat asthma and cough.

**Fruits of Annona squamosa L.**
A known insecticidal, antiovulatory, and abortifacient plant that is hematinic, cooling, a sedative, stimulant, expectorant, and tonic. Its seeds are abortifacient and insecticidal and are used to destroy lice in the hair.

**Calotropis gigantea L.**
*Calotropis gigantea* L. having certain antifertility glycosides and cardenolides is used for colic pain, flatulence, asthma, cough, and whooping cough and has wound healing, anticancer, and hypoglycaemic effects. *Calotropis Madar* root bark is used for abortive purposes and in India is used as an antidote and in the treatment of elephantiasis, leprosy, and chronic eczema.

**Camphor**
Camphor, the well-known aromatic, has hormone-modulating, contraceptive, abortifacient, and lactation-inhibiting properties in women. It has a dose-dependent effect in human sperm motility and viability. Camphor can pass the placental barrier and affect embryo development. Camphor-containing compounds have shown uterotrophic antitussive, anticonvulsant, nicotinic receptor blocking, anti-implantation, antiestrogenic, as well as estrogenic activities and can reduce serum triglyceride and thyroid hormone.

**Flowers of Hibiscus rosa-sinensis L.** containing quercetin-7-O-galactoside, polyphenolic compounds, and kaempferol, having antispermatogetic compounds, is prescribed for contraception.

| Sr. No. | Name of plants Phytoconstituent | Dose and duration | Teratogenic effect |
|---------|----------------------------------|-------------------|-------------------|
| 1       | Asparagus racemosus Wild. Shatavarin, Racemosol Root | 1000 mg/kg/body weight for 60-day Charles foster rat pups Methanolic extract | Prenatal study—increased resorption of fetus, gross malformation i.e., swelling in legs, IUGR with small placental size. Postnatal study—decreased number of pups per litter and increased mortality of pups and delayed developmental parameters Goel et al. (2006) |
| 2       | Datura metel L. Leaves Atropine alkaloids | 500 mg/body kg wt rats, ethanolic extract | Teratogenic in the late stage of pregnancy Azeez and Philip (2013) Antifertility activity scarcely produced abnormal embryos. Induce high percentage of abnormalities. Bachvak (2011) |
| 3       | Gloriosa superba L. Tuber Colchicine | 1-3 ppm and 4-5 ppm Hydroalcoholic extract | 90% embryo, more extra ribs anencephaly, exencephaly, skeletal abnormalities, height and weight loss in embryos Lobat (2015) |
| 4       | Lawsonia inermis L. Rauvoboid and phenolic compounds | 100 mg/kg body wt. BALB/c mice between 8-12 wk hydroalcoholic extract | 90% embryo, more extra ribs anencephaly, exencephaly, skeletal abnormalities, height and weight loss in embryos Lobat (2015) |
| 5       | Luffa operculata (L.) Cogn. Tea, decoction Glycosides, saponins, resin, free sterols, aliphatic esters, quinones | After ingestion of a variable amount of tea made with dried fruit, decoction | Abortion/reduction in birth rate Barilli et al. (2005) |
| 6       | Plumbago zeylanica L. Plumbagin | 100 mg/kg body wt orally with 0.5% milk of distilled water in mice | Stunted growth, subcutaneous, and deep hemorrhage, kinking of tail, protrusion of back of head Srivastava (2017) |
| 7       | Ruta graveolens L. Essential oil | 5, 10, and 20% w/v or plain water (control) orally for 4 days | Changes in the blastocyst formation, reducing the number, and delaying the development of embryos Gutierrez-Pajares et al. (2003) |
| 8       | Sena (Senna) alexandrina Mill- Fabaceae Sennosides Extract | Orally at 0, 250, 500, 1000, or 2000 mg/kg bw/day—five groups | Embryotoxic effect De Fretas et al. (2005) Increase blood flow to the uterus and its attachments, increasing the risk of fetal loss, and may pass spasms in the infant Schulz et al. (2002) |
| 9       | Zingiber officinale Rosco Root Carbohydrates (50–70%), lipids (3–8%), terpenes, and phenolic compounds | Orally at 0, 250, 500, 1000, or 2000 mg/kg bw/day—five groups | High dose significantly reduced the number of live fetuses, increased fetal death, and resorption. Recla et al. (2018) |
| 10      | Pipalyadi gutika Piperine | 5 times to one and five times to the other than the recommended dose for humans Rats | Fetus—LBW, smaller in length, developmental defects of soft tissues, skeletal herniation of intestines into umbilical cord, Mother—less weight gain during gestation Chaudhury et al. (2001) |
| 11      | Vishamustivati [VV] & Shuddha Tankana [ST] | 175 mg/kg of aqueous solutions of Visamustivati, 300 mg/kg aqueous solutions of SuddhaTankana, orally from day 1 to day 7 of post mating period | VV and ST shows positive Teratological effect on new-borns, gross remarkable external morphological and skeletal defects Jati (2018) |
TABLE 4 | List of medicinal plants with one or more contraceptive activities.

| Sr. No | Plant name | Anti-implantation | Abortification | Antifertility | Antioestrogenic activity | Antispermatogenic Spermicidal | Antiandrogenic activity |
|--------|------------|-------------------|----------------|--------------|--------------------------|-----------------------------|------------------------|
| 1      | Abies spectabilis (D.Don) Mirb. | ✓          |               |              |                          |                             |                        |
| 2      | Abroma augusta (L.) L.f. | ✓          | ✓             |              |                          |                             |                        |
| 3      | Abrus precatorius L. | ✓          | ✓             |              |                          |                             |                        |
| 4      | Acacia concinna (Wild.) DC. | ✓          |              |              |                          |                             |                        |
| 5      | Acacia leucophloea (Roxb.) Wild. | ✓          |              |              |                          | ✓                           | ✓                      |
| 6      | Achyranthes aspera L. | ✓          | ✓             |              |                          |                             | ✓                      |
| 7      | Adhatoda vasica Nees | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 8      | Aegle marmelos (L.) Corria | ✓          | ✓             |              |                          |                             | ✓                      |
| 9      | Allium cepa L. | ✓          |              |              |                          |                             | ✓                      |
| 10     | Allium sativum L. | ✓          |              |              |                          |                             | ✓                      |
| 11     | Aloe barbadensis Mill. | ✓          | ✓             |              |                          |                             | ✓                      |
|        | Synonym of Aloe vera (L.) Burm.f. | ✓          |              |              |                          |                             |                        |
| 12     | Alstonia scholaris (L.) R.Br. | ✓          |               |              |                          |                             | ✓                      |
| 13     | Andrographis paniculata (Burm.f.) Nees | ✓          | ✓             |              |                          |                             | ✓                      |
| 14     | Annona squamosa L. | ✓          |               |              |                          |                             | ✓                      |
| 15     | Annona squamosa L. | ✓          |               |              |                          | ✓                           | ✓                      |
| 16     | Ailanthus excelsa Roxb | ✓          |               |              |                          |                             |                        |
| 17     | Ailanthus excelsa Roxb | ✓          |               |              |                          | ✓                           | ✓                      |
| 18     | Areca catechu L. | ✓          | ✓             |              |                          |                             | ✓                      |
| 19     | Aristolochia indica L. | ✓          | ✓             |              |                          |                             | ✓                      |
| 20     | Azadirachta indica A. Juss. | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 21     | Bacopa monnieri (L.) Wettst. | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 22     | Balanites roxburghii Planch. | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 23     | Barbodes bambos (L.) Voss | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 24     | Barleria prionitis L. | ✓          |               |              |                          |                             |                        |
| 25     | Berberis aristata DC | ✓          |               |              |                          |                             |                        |
| 26     | Butea monosperma (Lam.) Kuntze | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 27     | Calotropis procera (Alston) Dryand. | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 28     | Cannabis sativa L. | ✓          |               |              |                          |                             | ✓                      |
| 29     | Carica papaya L. | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 30     | Cassia fistula L. | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 31     | Catunaregam spinosa (Thunb.) Tirveng. | ✓          |              |              |                          |                             | ✓                      |
| 32     | Celastrus paniculatus Wild. | ✓          |               |              |                          |                             |                        |
| 33     | Centratherum artemisianum (L.) Gamble | ✓          |               |              |                          |                             | ✓                      |
| 34     | Cichorium intybus L. | ✓          |               |              |                          |                             | ✓                      |
| 35     | Cinnamomum camphora (L.) J. Presl | ✓          |               |              |                          |                             | ✓                      |
| 36     | Cissampelos pareira L. | ✓          |               |              |                          |                             |                        |
| 37     | Citrus colocynthis (L.) Schrad. | ✓          |               |              |                          |                             |                        |
| 38     | Citrus × aurantium L | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 39     | Crateva unualba Buch. -Ham | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 40     | Cuminum cyminum L. | ✓          |               |              |                          | ✓                           | ✓                      |
| 41     | Cuscuta reflexa Roxb | ✓          |               |              |                          | ✓                           | ✓                      |
| 42     | Curcuma longa L. | ✓          |               |              |                          | ✓                           | ✓                      |
| 43     | Cyperus rotundus L. | ✓          |               |              |                          | ✓                           | ✓                      |
| 44     | Daucus carota L. | ✓          |               |              |                          | ✓                           | ✓                      |
| 45     | Desmodium gangeticum (L.) DC. | ✓          | ✓             |              |                          |                             | ✓                      |
| 46     | Embelia ribes Burm.f. | ✓          | ✓             |              |                          | ✓                           | ✓                      |
| 47     | Euphorbia nerifolia L. | ✓          | ✓             |              |                          | ✓                           | ✓                      |

(Continued on following page)
| Sr. No | Plant name | Anti-implantation | Abortification | Antifertility | Antiovulatory activity | Antiestrogenic activity | Antispermatogenic activity | Spermicidal activity | Antiandrogenic activity |
|--------|------------|-------------------|---------------|--------------|-----------------------|------------------------|--------------------------|----------------------|-----------------------|
| 48     | Ferula jaeschkeana Vatke |             |               | √            |                       |                       |                          |                      |                       |
| 49     | Foeniculum vulgare Mill |               |               |             |                       |                       |                          |                      |                       |
| 50     | Gloriosa superba L.      | √             |               | √            |                       |                       |                          |                      |                       |
| 51     | Glycyrrhiza glabra L.    |             |               |             |                       | √                      |                          |                      |                       |
| 52     | Grewia asiatica L.       | √             |               |             |                       | √                      |                          |                      |                       |
| 53     | Gulandina bonduc L.      |               |               |             |                       | √                      |                          |                      |                       |
| 54     | Sy. Caesalpinia bonducella (L.) Fleming | √              |               |             |                       | √                      |                          |                      |                       |
| 55     | Hibiscus rosa-sinensis L. | √              |               | √            | √                     | √                      | √                        |                      | √                    |
| 56     | Lawsonia inermis L.      |               |               |             | √                     |                       |                          |                      |                       |
| 57     | Lepidium sativum L.      | √             |               |             | √                     |                       |                          |                      |                       |
| 58     | Melia azedarach L.       |               |               |             |                       | √                      |                          |                      |                       |
| 59     | Mentha arvensis L.       | √             |               |             |                       | √                      |                          |                      |                       |
| 60     | Mesua ferrea L.          |               |               |             |                       | √                      |                          |                      |                       |
| 61     | Michelia champaca L.     |               |               |             |                       | √                      |                          |                      |                       |
| 62     | Morinda charantia L.     | √             |               |             | √                     |                       |                          |                      | √                    |
| 63     | Mucuna urens (L.) Medik. |               |               |             |                       | √                      |                          |                      |                       |
| 64     | Nigella sativa L.        | √             |               |             |                       | √                      |                          |                      |                       |
| 65     | Ocimum sanctum L.        |               |               |             |                       | √                      |                          |                      | √                    |
| 66     | Ocimum sanctum L.        |               |               |             | √                     | √                      |                          |                      | √                    |
| 67     | Plumbago zeylanica L.    | √             |               |             |                       | √                      |                          |                      | √                    |
| 68     | Pterocarpus santalinus L.f. |               |               |             |                       | √                      |                          |                      | √                    |
| 69     | Ricinus communis L.      |               |               |             |                       | √                      |                          |                      | √                    |
| 70     | Ruta graveolens L.       | √             |               |             |                       | √                      |                          |                      | √                    |
| 71     | Sapindus trifoliatus L.  |               |               |             |                       | √                      |                          |                      | √                    |
| 72     | Semecarpus anacardium L.f. |               |               |             |                       | √                      |                          |                      | √                    |
| 73     | Sesbania sesban (L.) Merr |               |               |             |                       | √                      |                          |                      | √                    |
| 74     | Taxus baccata L.         |               |               |             |                       | √                      |                          |                      | √                    |
| 75     | Terminalia arjuna (Roxb. ex DC.) Wight & Arn |               |               |             |                       | √                      |                          |                      | √                    |
| 76     | Terminalia bellirica (Gaertn.) Roxb |               |               |             |                       | √                      |                          |                      | √                    |
| 77     | Tylophora asthmatica (L. f.) Wight & Arn |               |               |             |                       | √                      |                          |                      | √                    |
| 78     | Withania somnifera (L.) Dunal |               |               |             |                       | √                      |                          |                      | √                    |
| 79     | Woodfordia fruticosa (L.) Kurz |               |               |             |                       | √                      |                          |                      | √                    |
| 80     | Zingiber officinale Roscoe |               |               |             |                       | √                      |                          |                      | √                    |
and is used to treat bacterial infection, hyperlipidemia, and depression and act as an antioxidant.

Two of the most bitter stimulant plants, *Momordica charantia* L. and *Azadirachta indica* A. Juss., produce an irregular pattern of estrous cycle with prolonged diestrus phase. Steroids, triterpenoids, reducing sugars, alkaloids, phenolic compounds, flavonoids, and tannins in the plant cause reduction in the number of normal follicles because of atresia which occur due to disruption of the process of follicle selection. *Azadirachta* arrests spermatogenesis and androgen depletion.

Roots of *Plumbago zeylanicum* L. have been used as an abortifacient, internally or as an irritant to the uterus. This acrid and stimulant root increases appetite helps indigestion and is used for dyspepsia, piles, and skin diseases. It induces sweating, its powder is occasionally taken as snuff to relieve headache, and it helps in the adhesion of tissues in the body and is antidiarrheal.

*Tinospora cordifolia* (Willd.) Hook.f. and Thomson, an immunomodulator plant used to treat tuberculosis, fever, and wounds, has antifertility qualities. It is used for antioxidant, hypoglycaemic, and cardioprotective activities.

Excessive use of substances having pungent, bitter, and astringent tastes is contraindicated for sexual functions. Excess consumption of bitter taste leads to loss of strength and energy, astringent taste affects the sperm count, and can even reduce the sex drive while strongly pungent ingredients like pepper exhibit spermicidal or abortifacients effects. Prolonged consumption of these tastes may lead to emaciation of the body.

**Mechanism of Action**

**Female Contraceptives**

Medicinal plants may induce infertility in distinct ways. They may affect the ovarian, uterine, and hormone production functions and interfere with implantation or sperm production. These drugs are of natural origin, hydrophilic, and lipophilic; can traverse paracellularly through the vaginal mucosa; and exhibit its efficacy as contraceptive, by altering the vaginal pH. These drugs may variably act locally to bring changes in the cervical mucus and alter decidual embedding and thereby act as anti-implantation agents, or may inhibit propulsion of sperm in the fallopian tubes by altering tubal mechanism or may act on hormones as antiovulation agents. They may act through rapid expulsion of the fertilized ova from the fallopian tube or inhibit implantation due to disturbance of the estrogen progesterone balance or induce fetal abortion by inhibition of nutrition to the uterus and the embryo.

Moreover, plants with estrogenic property can directly influence pituitary action by peripheral modulation of luteinizing hormone (LH) and follicle stimulating hormone (FSH), decreasing their secretions and blocking ovulation (Brinker, 1997). Plants with antiestrogenic activities intercept in the process of development of ovum and endometrium and on the other hand, plants have abortifacient effects (Gark et al., 1978; Prakash et al., 1985).
The site of action of antifertility agents in females comprises the hypothalamus, the anterior pituitary, the ovary, the oviduct, the uterus, and the vagina. The mammalian uterus is the main site of antifertility effects (Williamson et al., 1996). Typical estrogenic compounds possess the ability to increase the uterine wet weight and induce cornification and opening of vagina in immature rats, which results in anti-implantation effects (Turner, 1971).

Antifertility plants prevent fertilization; these drugs obstruct the formation of gametes and interfere with the process of fertilization. Anti-implantation plants prevent the attachment or penetration of fertilized ovum into the uterus. Butea monosperma (Lam.) Kuntze, Ocimum sanctum L., Calotropis procera (Aiton) W.T. Aiton, Mentha arvensis, and Lawsonia inermis L.—all have anti-implantation activity. Abortifacient plants cause early expulsion of the fetus. These act during the first five weeks of pregnancy as they block the action of progesterone so that the uterus sloughs off the embryo. Abrus precatorius L., Annona squamosa L., Calotropis procera (Aiton) W.T. Aiton, Carica papaya L., Dhatura metel L., Momordica charantia L., and Carunagam spinosa (Thunb.) Tirveng are medicinal plant drugs which can be used as abortifacients. Stimulant, irritant, and bulk forming characteristics of these drugs facilitate abortion along with hormonal regulation and modulation of genital functioning. These ingredients are considered stimulants and are hot in nature and hence should be used for a short duration.

It observed that large numbers of antifertility plant extracts are known to exhibit estrogenic activity in rats (Dahanukar et al., 2000). Estrogenic substance may cause the expulsion of ova from the tube, disruption of luteotropic activity of the blastocyst, and disrupt the functional equilibrium between the endogenous estrogen and progesterone, which may result in failure in fertility. Increase in the wet weight of uterus of substance-treated ovariectomized immature rats may indicate that the substance has an estrogenic effect (Mukherjee, 2002).

The hypothalamus has threshold requirement for estrogen to cause a massive release of LH by the pituitary gland. This surge of LH is the trigger, which initiates the rupture of the follicle (ovulation) (Bullock et al., 1995). It is known that an increase in the serum progesterone level prevents pregnancy through inhibition of ovulation and alteration of cervical mucus. Most of the plants possess inhibition of implantation or reduction of estrogen level and increment of progesterone level as the possible mechanism of antifertility effect. The anti-implantation effect may be due to the disturbance of endocrine–endometrial synchrony that is dependent on estrogen and progesterone balance. Factors other than the hormones such as histamine, prostaglandins, proteolytic enzyme NOS, alkaline phosphatase, interleukins, and leukemia-inhibitory factors, which are important for implantation, may also be affected by the various plant extracts (Gupta, 1994; Garg et al., 1978; Novaro et al., 1997; Prakash et al., 1989; Dimitriadis et al., 2003; Yang et al., 1994)

**Male Contraceptives**

Male contraceptive drugs may inhibit spermatogenesis or act on male hormones when used orally or may be spermistatic or spermicidal when used intravaginally. Male contraceptives might work to suppress sperm production by antispermatic or prevent maturation of sperm or prevent the flow of sperm through the vas deferens or deposition of the sperm (Soni et al., 2015).
Plant extracts have also shown promising antifertility effects when administered to male rats. The various effects on male reproductive system to induce antifertility action shown by plants includes antispermatogenic effect, post-testicular antifertility effect, spermicidal effect, sperm-immobilizing effect, antiandrogenic effect, etc.

Antispermatogenic activity indicates interference in the steroidogenesis when the cholesterol level rises and sudanophilic lipid accumulates (Mandal et al., 2010). Some of the plant extracts kill the viability and work on Sertoli cells and have various effects on spermatogenesis, such as reducing the nuclear and cytoplasmic volume and vacuolizing Sertoli cells (Sharma RS et al., 2001) or acts through Leydig cells (Dufau et al., 1984). Some plant extracts act by unbalancing the hormones or through their antimotility activity (Verma and Yadav, 2021).

Spermicides are contraceptive substances that destroy the sperm when inserted vaginally prior to intercourse. The spermicidal agents consist of a surfactant that destroys the sperm cell membrane. Lipid peroxidation may play an important role in disrupting the sperm membrane physiology that may or may not be accompanied with a detrimental effect on the defense system of the human spermatozoa against the ROS.

Antiandrogens, also known as androgen antagonists or testosterone blockers, prevent androgens like testosterone and dihydrotestosterone (DHT) from mediating their biological effects in the body. *Andrographis paniculata* (Burn.f.) Nees, *Azadirachta indica* A. Juss., *Curcuma longa* L., *Hibiscus rosa-sinensis* L., and *Plumbago zeylanica* L. act by blocking the androgen receptor (AR) and/or inhibiting or suppressing androgen production. They can be considered as the functional opposites of AR agonists, for instance, androgens and anabolic steroids (AAS) like testosterone, DHT, and nandrolone and selective androgen receptor modulators (SARMs) like enobosarm.

Figures 4, 5 provide group of these plants 3 (a) and 4 (a) with probable female and male contraceptive activities 3 (b) and 4 (b), respectively.

Limitations/Challenges

A major limitation is the contradictory reports or non-reproducibility of published data, which can provide useful leads. At times, failure of reproducibility of contraceptive activity of a plant or its constituent is observed. This could be due to the multiple factors at different levels that are known to affect the reproductive process. The other reason could be the variable effect of the herbal contraceptive/s in animals as against when used in humans.

The contraceptives of natural origin are not used much in practice, the main factor being the lack of standardization and reliable validation studies. The information has thus remained fragmented. Studies have consequently been scarce. Interest has weaned due to the complexity and enormity of the large and long-term study requirements covering multiple variables.

Analytical methods, information on phytoconstituents, availability of markers, and their activities have now provided new standardization approaches to herbal products that assure higher safety and stability.

The solution to this is to investigate the efficacy of these herbs in humans themselves, after ascertaining their safety in animal models. There is also a need to record the conditions under which the plants are used by indigenous people, including the time and place of collection, proper botanical authentication, and schedule of administration. Advances in biology offer adaptable and promising experimental models to examine the effectiveness of natural products for altering reproductive functions and contraception.

CONCEPTION AND NEW TECHNOLOGIES FOR NATURAL PRODUCTS

There is a need to use new contraceptive methods to minimize the side effects. The following technological advances are relevant in the context of this review for discovery and development of novel contraceptives of natural origin.

- Ayurveda recommends fumigation as a method and as a therapeutic procedure to treat various diseases, including microbial infections. Ayurvedic methods of sterilization with fumigation can be alternated as a modern contraceptive with the help of nanotechnology. Natural novel bioactive compound drugs could be developed with novel drug-delivery systems.
- A team in the University of Washington has developed an electrically spun cloth with nanometer-sized fibers that get dissolved to release drugs, thus providing a platform for cheap, discrete, and reversible protection ("Drug-Eluting Fibers for HIV-1 Inhibition and Contraception").
- Pharmacy on a chip is one of the most exciting parts of the drug-delivery system. It is a chip implanted into the body which releases drugs at set intervals. It would release the hormones estrogen and progesterone over a specific period to stop the release of eggs from the ovaries and thus prevent pregnancy.
- Nanotechnology-based condom systems have the potential to prevent the spread of HIV and STIs.
- Transdermal drug delivery (TDD) is an alternative method of drug administration for drugs whose delivery by conventional oral, topical, intravenous, and intramuscular methods is of limited efficacy. Recent advances in TDD involve the use of nanoparticles (NPs), which exhibit great potential to enhance drug permeation across the skin.
- Skin patches containing microneedles is a painless and minimally invasive method of TDD in which micron-sized pores are created in the epidermis to allow delivery of drugs to the blood vessels present in the dermal layer of the skin.
- Researchers report on a technique for administering contraceptive hormones through special backings on jewelry such as earrings, wristwatches, rings, or necklaces. The contraceptive hormones are contained in patches applied to portions of the jewelry in contact with the skin, allowing the drugs to be absorbed into the body (Georgia Institute of Technology, 2019).
Possibilities for new means of drug development

- Developing newer biotechnology-based cellular or molecular models that could better replicate reproductive processes.
- Methods that act after ovulation and interfere with sperm delivery or function in the male or in the female genital tract or both ought to be adopted.
- Design of nonhormonal contraceptive agents—as an alternative option to hormonal formulations—with the help of herbs.
- New delivery mechanisms that can act both short and long term; the possibilities are to develop herbal pessary, jelly, patches, and condoms, or mechanical devices with natural ingredients to optimize the effects.
- Methods which limit the side effects associated with systemic exposure should be developed in lower dosage forms to ensure efficacy.
- Technologies that markedly improve the cost, acceptability, and deliverability of contraceptives.
- Personalized contraception-human genome could minimize the side effects while maximizing health benefits at the individual level.

CONCLUSION

Fertility and contraception are continued subjects of biomedical research and innovation. Alternatives to unmet needs for safer contraception methods and drugs are searched for. Many Ayurvedic medicinal ingredients and compound formulations are claimed to inhibit male and female fertility as mentioned in classical literature. Several of these validated drugs possess spermicidal, antispermatogenic, antiovulatory, anti-implantation, antiestrogenic, and abortifacient activity. The Indian system of medicine, Ayurveda, offers highly promising opportunities when analytical, biological, technological, and clinical advances are collectively integrated with therapeutic rationale based on Ayurvedic principles. A plethora of available data, information, and knowledge on these ingredients could be the subject of newer research interests.

These medicinal ingredients need further reexamination and critical evaluation to explore their lesser known or unknown pharmacological and biological activity/activities and effects. Present-day biotechnological methods could be usefully utilized to evaluate their contraceptive efficacies. There is a need to revive and stimulate new research programs and projects that will not only benefit the need of contraception but will also throw new light on reproductive biology.

AUTHOR CONTRIBUTIONS

The corresponding author Dr. NB contributed to the concept, initial compilation, structure of the review, and final editing of the text and figures. Co-author Dr. MD contributed to compiling and comparing pharmacological data and the preparation of tables and figures.

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**Conflict of Interest:** Author NB is Owner / Director of the company CRIA Consultants Pvt. Ltd., Mumbai (India).

The remaining author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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