



## A Systematic Review of Effect of Medicinal Plants on Treating Female Infertility

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### ABSTRACT

Infertility is the inability of a couple to achieve pregnancy over an average period of one year or 6 months despite adequate, regular unprotected sexual intercourse. In 2010, an estimated 48.5 million couples worldwide were infertile. Herbal remedies and naturally occurring compounds have gained popularity in recent times for the treatment of various health conditions due to their reduced side effect and affordability. Present study reviews the effectiveness of medicinal plants on treating female infertility. Through this review, we have explored 20 medicinal plants traditionally and scientifically recognized for their role in enhancing female reproductive health. These plants exhibit various fertility enhancing properties including hormonal regulation, antioxidant activity, estrogenic activity and improvement in ovarian function and proves its traditional use.

**Keywords:** Medicinal plants, Female infertility, Fertility enhancement, estrous cycle.

### INTRODUCTION

Infertility is the inability of a couple to achieve pregnancy over an average period of one year or 6 months despite adequate, regular unprotected sexual intercourse. Causes of female infertility are environmental factors, weight changes, lifestyle, hormonal imbalance, hyperprolactinemia, ovarian functional problem, tubal factors, uterine factors, thyroid disease, sexually transmitted disease, pelvic inflammatory disease, oxidative stress and PCOD.[1]

There are several infertility treatment such as Intra-uterine Insemination (IUI), *In-Vitro* Fertilization (IVF), Zygote Intra-fallopian Transfer (ZIFT) and Gamete Intra-fallopian, Transfer (GIFT), Intracytoplasmic Sperm Injection (ICSI), Assisted Hatching, Donor Eggs and Sperms, Gestational Carrier but these are very expensive. [2]

Commonly used Allopathic medicines are clomiphene citrate, letrozole, metformin, cabergoline, gonadotropin. The most significant drawbacks of allopathy are its adverse effects. In order to avoid side effect and to minimize cost, medicinal plants are investigated for fertility enhancing activity.

### MEDICINAL PLANTS USED TO TREAT FEMALE INFERTILITY

#### *Anthocleista vogelii*

The study investigates the *Anthocleista vogelii* enhances female fertility by analyzing its effects on biochemical and hematological markers in female albino rats. Ethanolic extracts of the plant were administered for 14 days after inducing temporary infertility using Micronor (norethisterone) or N-acetylcysteine (NAC). Hematological analysis showed an increase in absolute middle cells (basophils, eosinophils, monocytes), suggesting immune-modulating effects. The plant extract may help create a favorable reproductive environment by regulating cholesterol and fat levels. The results align with traditional beliefs that the plant enhances fertility.[3]

#### *Brillantaisia patula*

The study investigates the fertility-enhancing properties of *Brillantaisia patula* leaf extract against cyclophosphamide-induced ovarian damage in female Wistar rats. The extract significantly restored antioxidant markers, reduced inflammation and improved



reproductive hormone levels (estrogen, LH, FSH). It also enhanced implantation rates and reduced fetal resorption, indicating improved fertility outcomes. Histological analysis showed the extract reversed ovarian and uterine structures, counteracting cyclophosphamide-induced damage. These results highlight its potential as a natural fertility-preserving agent, especially for cancer patients undergoing chemotherapy.[4]

#### ***Byrsocarpus coccineus***

The study investigates the antioxidant and fertility-enhancing effects of *Byrsocarpus coccineus* in female rats. The ethanolic extract exhibited strong invitro antioxidant activity and In-vivo studies showed significant reduction in catalase (CAT) and superoxide dismutase (SOD) activity along with decreased lipid peroxidation, indicating oxidative stress modulation. Histological analysis confirmed its protective effects on reproductive organs. The findings suggest that *Byrsocarpus coccineus* enhance female fertility by combating oxidative stress and improving antioxidant defenses. [5]

#### ***Coccinia cordifolia L.***

The study investigates the fertility-inducing effects of *Coccinia cordifolia* L. in female rats. Traditionally it is used in India (West Bengal) for treating infertility, the plant was tested for its effects on different infertility models including hyperprolactinemia-induced, endometriosis-induced, and androgen-induced infertility. The aqueous extract of *Coccinia cordifolia* was administered in two doses (500 mg/kg and 1000 mg/kg), increased uterine implants and estrogen levels in hyperprolactinemic rats but was ineffective in androgen-induced infertility. It also reduced the weight of endometrial implants but did not restore fertility in endometriosis models.[6]

#### ***Cordia retusa***

The study evaluates the fertility-enhancing effect of *Cordia retusa* in female albino rats, traditionally used for treating reproductive disorders. The ethanolic extract of *cordia retusa* was administered on an ethinyl estradiol-induced anovulatory infertility model at doses of 125 mg/kg and 250 mg/kg. The results showed significant improvements in estrous cycle regulation, follicle-stimulating hormone (FSH) and estrogen levels with the high-dose group exhibiting the best outcomes. The fertility index( measured by the number of new borns) was significantly higher in plant extract-treated rats. The study concludes that *Cordia retusa* extract can enhance fertility in cases of hormonal imbalance supporting its traditional use and suggesting further research for identifying active constituents.[7]

#### ***Curculigo orchioides***

The study investigates the estrogenic activity of *Curculigo orchioides* rhizome extract in bilaterally ovariectomized albino rats. The extract was administered at doses of 300, 600, and 1200 mg/kg and compared with the standard estrogenic drug diethylstilbestrol (DES). Key parameters includes uterine weight, glycogen content, vaginal cornification and histological changes. The extract showed a dose-dependent increase in these parameters with the highest dose (1200 mg/kg) demonstrating estrogenic effects similar to DES. The findings suggest that *Curculigo orchioides* has potential in managing estrogen-deficient conditions like menopause and infertility.[8]

#### ***Plukenetia conophora***

This study investigates the effects of *Plukenetia conophora* extracts on female infertility. The study induced temporary infertility in female albino rats using Postinor, followed by oral administration of the extracts for 30 days. The ellagic acid extract showed higher total antioxidant capacity (TAC) inhibition compared to the aqueous ethanolic extract. Both extracts increased testosterone levels in the rats. Ellagic acid extract reduced catalase activities in the rats. Significant increase was observed in triglyceride and cholesterol level of both the induced infertile group and ellagic acid group as compared with the control group. The research concludes that *Plukenetia conophora* leaves possess antioxidant activity and may used as a female fertility agent.[9]

#### ***Ficus platyphylla***

This study investigates the effect of *Ficus platyphylla* to promote fertility in female rats. Researchers administered aqueous extracts of the plant at different doses to two groups of rats: one treated before mating and the other treated continuously until delivery. The study found that *Ficus platyphylla* reduced post-implantation loss in both treatment groups compared to control. The group treated continuously with 400 mg/kg of the extract showed an increase in litter size similar to that of the clomiphene group (fertility drug). The study concludes that *Ficus platyphylla* reduce post-implantation loss and increase litter size in rats and promotes fertility.[10]



### *Zingiber officinale*

This study investigates the effects of *Zingiber Officinale* on ovarian folliculogenesis and implantation in rats, examining vascular endothelial growth factor (VEGF) and endothelial nitric oxide synthase (eNOS) levels. The 5-day treatment with 100mg ginger showed a significant increase in antral follicle count and ovarian stromal VEGF compared to the control group. The 10-day treatment with 100mg ginger resulted in higher endometrial VEGF and ovarian stromal eNOS levels. The 200mg dose ginger did not show significant differences in either treatment group. The study suggests that low-dose (100mg) ginger may positively affect folliculogenesis in the short term. In Addition, low-dose ginger enhance implantation in the long term. The rise in antral follicle count and ovarian stromal VEGF suggests beneficial impacts on folliculogenesis. Its antioxidant and anti-inflammatory properties may contribute to improved ovarian function.[11]

### *Nigella sativa*

The study investigates the potential of *Nigella sativa* (black cumin) seed extract to enhance female fertility in rats. The extract exhibited estrogenic and LH-like activities, by increasing serum levels of Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Estrogen (E2) and Progesterone (P4) hormone. Molecular docking showed strong interactions with Er $\beta$  (Estrogen beta), GnRH (gonadotropin-releasing hormone), LH and P4 receptors. It induced morphological changes similar to Pregnant mare's serum gonadotropin (PMSG) treatment [control group] with wider uterine horns and a higher number of ovarian follicles. The *Nigella sativa* seed extract exhibited strong estrogenic and LH-like activities with weak FSH-like activity. [12]

### *Symplocos racemosa*

This research explores the impact of aqueous extract from *Symplocos racemosa* (SR) on the levels of Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) in immature female rats. This study identified that the oral administration of the aqueous extract increased serum levels of FSH and LH. Histopathological analyses revealed the improved folliculogenesis, the occurrence of mature follicles, and released oocytes, attributed to elevated levels of FSH and LH. The rise in ovary weight in the treated animals was linked to the FSH surge. These results supports the traditional use of *Symplocos racemosa* for female disorders.[13]

### *Justicia insularis*

The study investigates the effect of *Justicia insularis* aqueous extract on ovarian folliculogenesis and fertility in immature female rats. The results showed that the extract induced early vaginal opening and increased the number of hemorrhagic points, corpus luteum, implantation sites, ovarian weight, and uterine and ovarian proteins. Ovarian cholesterol levels decreased with the lowest dose. The extract also increased pre- and post-implantation losses and decreased the litter weight, suggesting toxicological effects on pregnancy. These findings indicate that *Justicia insularis* induces ovarian folliculogenesis, which supports its use in traditional medicine for fertility enhancement.[14]

### *Trigonella foenum-graecum*

This study investigates the estrogenic activity of fenugreek seeds in ovariectomized rats, analyzing morphological, histological, biochemical, and molecular endpoints. The results demonstrate that fenugreek seeds have estrogenic effects, as evidenced by a slight increase in uterine weight, thickening of the uterine stroma and epithelium and development of endometrial glands. In the vagina, fenugreek promotes an increase in epidermal cell number and a tendency towards keratinization leading to vaginal opening. The study also found overexpression of progesterone receptors in uterine tissues, suggesting interactions between phytoestrogens in fenugreek and estrogen receptors. These findings support the traditional use of fenugreek seeds for fertility and menopause-related disorders indicating that its phytoestrogens may activate estradiol-mediated cell signaling pathways. [15]

### *Turraeanthus africanus* In Combination With *Lepidium meyenii*

The study investigates the effects of *Turraeanthus africanus* (TA) alone and in combination with *Lepidium meyenii* (Black maca, BM) on fertility and estrogenic activity in female mice. The mice were treated with BM+TA, TA alone and a control vehicle at a dose of 1 g/kg BW for 30 days. The results showed that the BM+TA treatment significantly shortened the estrous cycle compared to the control group. Estradiol levels were significantly increased in the proestrous stage for both TA and BM+TA treated animals and in the estrous stage for BM+TA treated animals. The uterine weight of ovariectomized mice treated with TA was significantly higher than the control, while no change was observed in the BM+TA group. The number of fetuses in the uterus after BM+TA treatment was significantly higher than in the TA alone and control groups. The study concludes that TA can affect embryo implantation and uterine weight and this effect is enhanced when combined with BM, which could regulate the estrous cycle.[16]



### *Crocus sativus*

The study involved 50 adult female Sprague dawley rats divided into five groups: control, sham (group who received 1 ml distilled water that was injected) and three experimental groups. The experimental groups received intraperitoneal injections of 1, 2 and 4 dg/kg *Crocus sativus* extract over a ten-day period. Blood samples were taken to measure serum levels of luteinizing hormone, follicle-stimulating hormone, estradiol, and progesterone hormones. Ovaries were examined and analyzed. Results showed a significant increase in FSH and estradiol levels in the experimental groups compared to the control group. The administration of 2 and 4 dg/kg extracts also significantly affected ovarian weight with histological studies showing enhanced folliculogenesis and increased secondary follicle numbers.[17]

### *Fagonia arabica*

This study assessed the ability of an ethanolic extract of *Fagonia arabica* aerial parts to enhance fertility. 12 male and 24 female virgin Wistar rats were chosen. For 23 days, the dose was administered daily. They were cohabitated for mating after 23 days. The dosage was maintained for an additional five days. Sperm counting was carried out on the fifth day of mating by looking at a vaginal smear under a microscope, which revealed increased male fertility. Until delivery, females were housed apart. Compared to the control, the number of newborns increased female fertility. Result showed that the orally administered dose of *Fagonia arabica* possess highly significant fertility enhancing activity in male and female rats after observing improvement in the sperm count and number of newborns as compared to control.[18]

### *Myrianthus arboreus*

Through a 30-day oral administration of aqueous and methanol extracts of leaves at doses of 20, 110, and 200 g/kg/day, the effects of *Myrianthus arboreus* on the sexual maturation parameters (vaginal opening, ovarian relative weight and follicle maturation, gonadotropins and ovarian hormones serum levels) and fertility index have been assessed using immature female Wistar rats. Aqueous extract stimulated the development of ovarian follicles and raised serum levels of progesterone, gonadotropins and ovarian relative weight. In addition, the methanol extract caused uterine development, early vaginal opening and elevated serum levels of oestradiol. After treatments, the fertility index typically increased while the gestation rate remained unchanged with the exception of the highest dose of *Myrianthus arboreus* extracts where the lowest values were observed. *Myrianthus arboreus* increased fertility and caused an early onset of puberty confirming at least some of its traditional uses to treat female infertility.[19]

### *Psidium guajava*

The current study examined the pro-fertility effects of a hydroalcoholic extract of *Psidium guajava* (HEPG) leaves in female Wistar rats. The average weight of the placenta, ovary and foetus increased significantly in the treated groups in comparison to the control group. When the test groups are compared to the control group, there is a progressive increase in the number of pregnant rats, number of rats exhibiting implantation, number of live foetuses, mean corpus luteum number (CLN) per female, foetal crown-rump length (FCRL), percentage of a pregnant female in each group (PPF) and fertility index (FI). The findings suggest that HEPG leaves may have beneficial effects on female reproductive systems.[20]

### *Urtica pilulifera*

The purpose of this study was to assess the positive effects of *Urtica Pilulifera* on a Balb/c mouse model of decreased ovarian reserve (DOR) caused by cyclophosphamide.

In the DOR model, it was found that the *Urtica Pilulifera* extract increased superoxide dismutases activity in the ovaries in a dose-dependent manner while decreasing malondialdehyde levels and apoptosis. Additionally, it modulated steroidal hormones such oestradiol, luteinizing hormone, and follicle-stimulating hormone. The histopathological analysis revealed the therapeutic potential of the *Urtica Pilulifera* extract. This potential corresponds to the observed positive effects of fatty acids on fertility improvement and reduction of oxidative stress, modulation of apoptosis and regulation of steroidal hormones.[21]

### *Senecio bialfrae*

This study assessed the effect of an aqueous extract of *Senecio bialfrae* to enhance fertility. All *Senecio bialfrae* treated animals showed a significant increase in serum levels of proteins and estrogen as well as a significant increase in uterine weight. There was no noticeable change in the ovarian weight or follicle counts. In conclusion, its aqueous extract greatly enhanced the various biochemical and physiological parameters it offered, providing some of its traditional uses.[22]



S.NO	PLANT	PARTS USED	EXTRACT	DOSE	ANIMAL MODEL	PARAMETERS	AUTHOR
1.	<i>Anthocleista vogelii</i>	Leaves	Ethanolic extract	100mg/kg	Female albino wistar rats	Biochemical evaluation	Olooto <i>et al.</i> , 2012
2.	<i>Britallantaisia patula</i>	Leaves	Aqueous extract	200mg/kg	Female albino wistar rats	Estrous cycle evaluation, antioxidant markers, hormonal assay, histopathological study	Olalekan bukunmi ogunro <i>et al.</i> , 2024
3.	<i>Byrsocarpus coccineus</i>	Leaves	Ethanolic extract	100mg/kg 200mg/kg	Female albino wistar rats	Invitro and invivo enzymatic antioxidant activity	Oladimeji OS <i>et al.</i> , 2014
4.	<i>Coccinia cordifolia</i>	Aerial parts	Aqueous extract	500mg/kg 1000mg/kg	Female albino wistar rats	Estrogen level and corpus luteum count, endometrial implant weight, uterine implants	Urmilesh Jha <i>et al.</i> , 2009
5.	<i>Cordia retusa</i>	Aerial parts	Ethanolic extract	125mg/kg 250mg/kg	Female albino wistar rats	Estrous cycle evaluation, Fertility index, FSH and estrogen level	Murugesan Amudha <i>et al.</i> , 2020
6.	<i>Curculigo orchoides</i>	Rhizomes	Ethanolic extract	300mg/kg 600mg/kg 1200mg/kg	Female Sprague dawley rats	Estrogenic activity	Vijayarayana <i>et al.</i> ,
7.	<i>Plukenetia Conophora</i>	Leaves	Aqueous extract, Ethanolic extract	100mg/kg 1ml	Female albino wistar rats	Testosterone determination, biochemical assay, invitro and invivo antioxidant activity	Oladimeji SO <i>et al.</i> , 2020
8.	<i>Ficus platyphylla</i>	Stem bark , leaves and seeds	Aqueous extract	100mg/kg 200mg/kg 400mg/kg	Female rattus norvegicus wistar strain	Implantation sites, reproductive index, gestation length, deformity	Chinenye J Ugwah-Oguejiofor <i>et al.</i> , 2011
9.	<i>Zingiber officinale</i>	Roots	Powder	100mg/kg 200mg/kg	Female albino wistar rats	Estrous cycle evaluation, histopathological evaluation , immune histochemical assessment	Nafiye yilmaz <i>et al.</i> , 2017
10.	<i>Nigella sativa</i>	Seeds	Ethanolic extract	100mg/kg 200mg/kg 400mg/kg	Female albino wistar rats	Molecular docking , morphological and histopathological evaluation, estrogenic activity, FSH and LH level	Nagy AM <i>et al.</i> , 2024
11.	<i>Symplocos racemosa</i>	Stem bark	Aqueous extract	500mg/kg 1000mg/kg 2000mg/kg	Female Sprague dawley rats	Morphological and histopathological evaluation, FSH and LH level	Kamlesh kumar bhutani <i>et al.</i> , 2004
12.	<i>Justicia insularis</i>	Leaves	Aqueous extract	50mg/kg 100mg/kg	Female albino wistar rats	Puberty onset and fertility assay , biochemical analysis, gestational parameters and morphological evaluation	Phelix Bruno <i>et al.</i> , 2019
13.	<i>Trigonella foenum graecum</i>	Seeds	Aqueous extract	450mg/kg 900mg/kg	Female albino wistar rats	Vaginal opening measurement , histopathological evaluation	Hind brogi <i>et al.</i> , 2019
14.	<i>Turraeanthus africanus</i> in combination with <i>lepidium meyenii</i>	Stem and bark	Aqueous extract	1g/kg	Female mice	Estrogenic activity, estrous cycle evaluation, embryo implantation and fertility index	Dieudonne Massoma Lembe <i>et al.</i> , 2012





15.	<i>Crocus sativus</i>	Red dried stigma of flower	Hydro-alcoholic extract	1dg/kg 2dg/kg 4dg/kg	Female Sprague dawley rats	LH, FSH , progesterone , estradiol level , histopathological evaluation	Mokhtar Mokhtari <i>et al.</i> , 2010
16.	<i>Fagonia arabica</i>	Aerial parts	Ethanolic extract	50mg/kg	Male and Female albino wistar rats	Estrous cycle monitoring, sperm count , number of newborns	Nudrat Fatima <i>et al.</i> , 2022
17.	<i>Myrianthus arboreus</i>	Leaves	Aqueous extract and methanol extract	20mg/kg 110mg/kg 200mg/kg	Female albino wistar rats	Vaginal opening measurement, histopathological evaluation, serum and ovarian total cholesterol level, hormone levels, fertility index, gestational rate	Charline florence awounfack <i>et al.</i> , 2018
18.	<i>Psidium guajava</i>	Leaves	Hydro-alcoholic extract	100mg/kg 200mg/kg 400mg/kg	Female albino wistar rats	Number of pregnant rats , implantation , live foetus, CLN(mean corpus luteum number), FCRL(Foetal crown rump length), fertility index	Saganuma alhaji saganuwan <i>et al.</i> , 2021
19.	<i>Urtica pilulifera</i>	Seed	Ethanolic extract	50mg/kg 100mg/kg 200mg/kg	Female balb/c mice	FSH, LH and estradiol level, histopathological evaluation, malondialdehyde(MDA),super oxide Dismutases(SOD) assay	Hekmat <i>et al.</i> , 2024
20.	<i>Senecio biafrae</i>	Leaves and stems	Aqueous extract	8mg/kg 32mg/kg 64mg/kg 128mg/kg	Female albino wistar rats	Proteins and cholesterol level , sexual hormones amounts, follicle count	Lienou LL <i>et al.</i> , 2014

## CONCLUSION

The use of medicinal plants in treating female infertility has gained significant attention due to their natural origin, minimal side effects and cost-effectiveness. Through this review, we have explored 20 medicinal plants traditionally and scientifically recognized for their role in enhancing female reproductive health. These plants exhibit various fertility enhancing properties including hormonal regulation, antioxidant activity and improvement in ovarian function.

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