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Anti-androgenic effect of *Symplocos racemosa* Roxb. against letrozole induced polycystic ovary using rat model

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PEER REVIEW

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Comments

This study contributes to the understanding of effect of *S. racemosa* Roxb. on the reproductive tract of females. The hypothesis of the authors was ascertained and the results provided a good evidence to support its use in the reproductive medicine in the treatment of PCOS.
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ABSTRACT

Objective: To investigate the anti-androgenic properties of *Symplocos racemosa* Roxb. (*S. racemosa*) in the treatment of hyperandrogenemia associated polycystic ovary syndrome (PCOS) in a letrozole induced PCOS rat model.

Methods: The testosterone levels were used to evaluate the anti-androgenic effect of *S. racemosa* in letrozole induced PCOS rats for 21 d. The low (250 mg/kg), mid (500 mg/kg) and high dose (1 000 mg/kg) of *S. racemosa* was given to the PCOS induced rats for 15 d post letrozole induction to determine the effective dose of *S. racemosa* in the treatment of hyperandrogenemia associated PCOS. The hormones such as estrogen and progesterone were also assayed along with testosterone to determine the fluctuations in sex steroid levels in PCOS rats induced by letrozole.

Results: *S. racemosa* treatment significantly decreased testosterone levels which were found to be elevated in PCOS rats induced by letrozole. *S. racemosa* significantly restored other blood biochemical parameters such as estrogen, progesterone and cholesterol levels. It also restored the histology of ovarian tissue. The ovarian weights and uterine weights were also significantly recovered after the *S. racemosa* treatment.

Conclusions: The mid dose (500 mg/kg) and high dose (1 000 mg/kg) of *S. racemosa* were found to be effective in the treatment of hyperandrogenemia in PCOS. This effect of *S. racemosa* was found to be comparable with clomiphene citrate. Clomiphene citrate which was being used as the major medicine in the treatment of PCOS could now be replaced with *S. racemosa* in the management of PCOS.

KEYWORDS

Symplocos racemosa Roxb., Letrozole, Polycystic ovary syndrome, Clomiphene citrate

1. Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder of unknown etiology affecting 5%-10% of women of reproductive age[1,2]. It is a disorder that affects the reproductive, endocrine and metabolic systems and it is the most common cause of anovulatory fertility[3,4]. Hyperinsulinemia and hyperandrogenemia are the chief culprits responsible for oligo/amenorrhoea, hirsutism, obesity and enlarged ovaries with small multiple cysts resulting in anovulation[5,6]. Although the etiology of PCOS is still not known, it is generally agreed that hyperandrogenemia is the heart of PCOS. The excess androgen levels are the root cause of PCOS producing the characteristic signs and symptoms which are then exacerbated by a propagation of excess ovarian androgen production from multiple small follicles, anovulation and insulin resistance in the reproductive life span, thus

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setting up a vicious perpetual circle of androgen excess[7,8]. Thus androgen excess is the key element in PCOS and androgen levels are one of the most predictable markers of patients with PCOS[9]. While modern medicines such as hormonal therapies, anti-androgens, insulin sensitizers and clomiphene citrate address these concerns, often with undesirable adverse effects, the herbal medicines offer an option for women as a natural approach to reduce menstrual cycle discomforts[10]. Due to the lesser or no side effects, some of the herbal medicinal plants have been used for the treatment of various ailments related to different parts of the body and also disorders caused by hormonal imbalances related to the female reproductive system[11,12]. Herbal medicines have been recognized as a valuable and readily available resource for primary health care and WHO has endorsed their safe and effective use[13].

Symplocos racemosa Roxb. (*S. racemosa*) from the family Symplocaceae, is an evergreen tree or shrub found in the plains and lower hills throughout North and East India, ascending in the Himalayas up to an elevation of 1 400 m[14]. *S. racemosa* is a widely used Ayurvedic remedy mainly for gynecological disorders. It is also known as Lodhra and is used in Indian System of Medicine as single drug or in multicomponent preparations (*viz. Lodhrasava*). Traditionally bark is given in menorrhagia and other female reproductive dysfunctions which are some of the symptoms of PCOS[15]. The heterogeneity of PCOS is reflected by the existence of several animal models. Since the etiological factors are still unclear, it is challenging to create a single animal model that expresses all the PCOS characteristics[14]. Therefore the aim of this study was to investigate anti-androgenic properties of *S. racemosa* in the treatment of PCOS induced by chemical agent, letrozole in the rat model.

2. Materials and methods

2.1. Animals

Six-week-old female albino Wistar rats (mean body weight, 180 g) with 4 d regular estrus cycles were procured from Haffkine Biopharmaceuticals Limited, Parel, Mumbai. They are maintained at (25±2) °C and 45%-55% of humidity in 12 h light/12 h dark cycle. Animals were given free access to standard laboratory food (supplied by Amrut Feed) and water *ad libitum*[10,16]. Approval for carrying out the experiments was obtained from Institutional Animal Ethics Committee (CPCSEA/315).

2.2. Plant material of S. racemosa

The stem barks of *S. racemosa* were collected from their natural habitat from Mahabaleshwar, Maharashtra state of India. The plant species were taxonomically verified from Agharkar Research Institute, Pune. The voucher specimen number ARI 10-75 of 24/12/2010 was deposited in Herbal Research Laboratory of Ramnarain Ruia College, Matunga, Mumbai. The plant materials were washed thoroughly and dried at (37±5) °C before preparation of aqueous extract. The plant material was then powdered and stored in airtight bottles until use. The aqueous slurry of plant material was prepared in 2.0 mL of water before dosing.

2.3. Experimental design

The study was conducted on 42 female albino Wistar rats divided into seven groups of six rats each, including a control group that received vehicle only (1% aqueous solution of carboxymethyl cellulose once daily *p.o.* The six treatment groups rats were administered with letrozole (Femara® Manufactured by Novartis Pharma Stein AG, Stein, Switzerland) at concentrations of 1.0 mg/kg *p.o.* dissolved in 1% carboxymethyl cellulose (2.0 mL/kg) once daily. The treatment period was 21 d[16]. Along with normal control group, letrozole induced PCOS rats were divided into six treatment groups. The first PCOS group was left for natural recovery for 15 d post letrozole treatment. The second PCOS group was given repetitive dose of 1.0 mg/kg daily clomiphene citrate (Fertomid-50 Manufactured by Cipla Ltd., Kumrek, Rangpo Sikkim, 737132, India), a well known modern drug for the treatment of PCOS[10]. One of the PCOS groups was sacrificed after 21 d of letrozole treatment. The other three PCOS groups were given repetitive doses of 250 mg/kg (low dose), 500 mg/kg (mid dose) and 1 000 mg/kg (high dose) of aqueous extract of *S. racemosa* once daily *p.o.* for 15 d post letrozole induction. Ovarian and uterine weight changes and hormonal assay were carried out in PCOS rats and the results were compared with that of the group treated with clomiphene citrate.

2.4. Blood sampling

At 24 h post the last dose of treatment and after 18 h fasting period, the rats were weighed and blood samples were collected by retino orbital puncture into different eppendorf tubes containing heparin sodium as an anticoagulant. The blood samples were centrifuged at 3 000 r/min for 15 min and plasma was separated for hormonal assay. The plasma was stored in a freezer at -20 °C till further analysis.

2.5. Biochemical analysis

Plasma testosterone and estradiol were assayed by competitive chemiluminescent immunoassay using automated instrument ADVIA Centaur, Bayer Diagnostics Europe Limited, Ireland. The testosterone was estimated using ADVIA Centaur TSTO kit and estrogen was estimated using ADVIA Centaur E2-6 kit[17]. The plasma progesterone was assayed by microparticle enzyme immunoassay using AxSYM analyzer-Abbott AxSYM® System, Abbott Japan[18]. The plasma cholesterol levels were assayed by using method of Wybenga and Pileggi using Biolab Diagnostics Kit. The

plasma testosterone levels, estrogen levels, progesterone levels and cholesterol levels were recorded after letrozole induction of 21 d (*i.e.* on Day 22 of study period) and after plant treatment for 15 d (*i.e.* on Day 37 of study period).

2.6. Tissue sampling

After blood sampling, the animals were sacrificed, ovaries and uterus were excised, cleaned off fat and weighed.

2.7. Histopathological examinations

The excised ovaries were fixed in Bouin's fixative. Histopathological examinations of the ovaries were carried out using standardized histological methods. Sections of the ovary were cut from paraffin-embedded blocks. Histological examinations were carried out on hematoxylin-eosin stained sections using light microscopy.

2.8. Statistical analysis

Statistical analysis was performed using ANOVA followed by Dunnett's test as a multiple comparison test. $P<0.001$, $P<0.01$ and $P<0.05$ were considered significant[19]. Values were expresses as mean±SD.

3. Results

3.1. S. racemosa decreases testosterone levels

The plasma testosterone level in normal control group was observed to be around (235.82±14.98) ng/dL on Day 22 and is maintained consistently up to (245.33±13.84) ng/dL on Day 37 indicating the stable condition. After the animals were treated with letrozole for the induction of PCOS, the mean testosterone level in letrozole control group was significantly increased up to (795.20±24.10) ng/dL ($P<0.001$). Clomiphene citrate treatment led to a significant decrease in testosterone level from (716.37 ±28.86) ng/dL to (255.42±17.43) ng/dL. Significant fall of (279.95 ±21.30) ng/dL and (273.62±23.07) ng/dL ($P<0.001$) was recorded when PCOS induced rats were treated with mid and high dose of *S. racemosa* respectively. Decrease in testosterone level with low dose of *S. racemosa* was found to be (608.33±164.86) ng/dL (Table 1).

3.2. S. racemosa increases estrogen levels

Estrogen level increased significantly from (29.88±3.64) pg/mL to (48.00±5.48) pg/mL ($P<0.001$) in PCOS induced rats after clomiphene citrate treatment. Estrogen levels increased up to (43.83±3.19) pg/mL and (43.67±2.94) pg/mL ($P<0.01$) after repetitive administration of mid and high dose of *S. racemosa* respectively. No significant effect was recorded after the treatment with low dose of *S. racemosa* (Table 1).

3.3. S. racemosa increases progesterone levels

Progesterone level, which significantly decreased in PCOS rats from (8.81±0.81) ng/mL to (2.16±0.82) ng/mL ($P<0.001$) increased significantly to (7.02±0.77) ng/mL ($P<0.001$) due to clomiphene citrate treatment. *S. racemosa* treatment also elevated progesterone levels to (5.58±0.68) ng/mL with mid dose and (5.54±0.61) ng/mL with high dose ($P<0.001$). The decrease in progesterone level was found to be 4.63±2.37 ($P<0.01$) after the treatment with low dose of *S. racemosa* (Table 1).

3.4. S. racemosa decreases cholesterol levels

The cholesterol levels were found to be elevated significantly from (54.83±4.54) mg/dL to (92.83±9.54) mg/dL ($P<0.001$) in PCOS induced rats. A decrease in cholesterol levels to (49.00±4.65) mg/dL ($P<0.01$) was observed after clomiphene citrate treatment. A repetitive administration of mid and high dose of *S. racemosa* decreased cholesterol levels significantly to (72.83±4.88) mg/dL and (70.00±6.90) mg/dL ($P<0.01$) respectively. Low dose of *S. racemosa* did not show any significant effect in restoring cholesterol levels (Table 1).

3.5. S. racemosa decreases ovarian weights

There was a significant decrease in ovarian weight from (0.21±0.02) mg to (0.13±0.04) mg ($P<0.001$) after the treatment of PCOS induced rats with clomiphene citrate. When the PCOS induced rats were administered with low, mid and high dose of *S. racemosa*, the significant decrease to (0.16±0.01) mg and (0.15±0.01) mg ($P<0.01$) was recorded with mid and high dose of *S. racemosa* respectively. *S. racemosa* treatment with low dose did not show any significant effect on ovarian weights (Table 2).

Table 1

Effect of various treatments on plasma testosterone level, estrogen level, progesterone level and cholesterol level in letrozole induced PCOS rats (Mean±SD, n=6).

Groups	Testosterone (ng/dL)		Estrogen (pg/mL)		Progesterone (ng/mL)		Cholesterol (mg/dL)	
	22nd day	37th day	22nd day	37th day	22nd day	37th day	22nd day	37th day
Normal control	235.82±14.98	245.33±13.84	56.17±3.66	55.83±5.19	8.57±0.71	8.81±0.81	58.00±7.43	54.83±4.54
Letrozole control	795.20±24.10^{b****}	–	29.88±3.64^{b****}	–	2.16±0.82^{b****}	–	92.83±9.54^{b****}	–
Natural recovery	781.10±18.83^{b****}	759.73±55.39^{a*}	34.67±4.03^{b****}	31.17±7.94^{a*}	3.42±0.97^{b****}	3.01±0.57^{a*}	96.00±5.55^{b****}	87.33±12.04^{a*}
Clomiphene citrate	716.37±28.86^{b****}	255.42±17.43^{a****}	27.33±3.56^{b****}	48.00±5.48^{a****}	3.45±0.87^{b****}	7.02±0.77^{a****}	96.83±6.01^{b****}	49.00±4.65^{a***}
SR 250 mg/kg	785.47±27.80^{b****}	608.33±164.86^{a****}	27.83±3.43^{b****}	47.80±14.13^{a*}	2.31±0.37^{b****}	4.63±2.37^{a***}	95.17±3.49^{b****}	85.17±17.70^{a*}
SR 500 mg/kg	755.23±16.26^{b****}	279.95±21.30$^{a****, c*}$	30.00±3.69^{b****}	43.83±3.19$^{a****, c*}$	2.80±0.26^{b****}	5.58±0.68$^{a****, c*}$	92.50±6.72^{b****}	72.83±4.88^{a***}
SR 1000 mg/kg	792.13±20.30^{b****}	273.62±23.07$^{a****, c*}$	26.00±2.19^{b****}	43.67±2.94$^{a****, c*}$	2.30±0.61^{b****}	5.54±0.61$^{a****, c*}$	95.33±1.86^{b****}	70.00±6.90^{a***}

SR: *S. racemosa*; ^{a*}: NS, ^{a**}: $P<0.05$, ^{a***}: $P<0.01$, ^{a****}: $P<0.001$ compared with letrozole control group; ^{b*}: NS, ^{b**}: $P<0.05$, ^{b***}: $P<0.01$, ^{b****}: $P<0.001$ compared with normal control group; ^{c*}: NS, ^{c**}: $P<0.05$, ^{c***}: $P<0.01$, ^{c****}: $P<0.001$ compared with modern drug group.

3.6. S. racemosa increases uterine weights

The uterine weights which decreased from (1.71±0.28) mg to (0.57±0.09) mg (P<0.001) in PCOS induced rats, increased significantly to (1.15±0.18) mg (P< 0.001) after clomiphene citrate treatment. The repetitive administration of mid and high dose of *S. racemosa* also led to a significant increase in uterine weights to (1.69±0.24) mg and (1.58±0.21) mg (P<0.001) respectively (Table 2).

Table 2

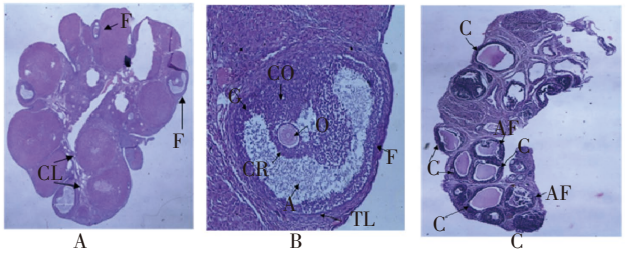
Effect of various treatments on ovarian and uterine weights (mg) in letrozole induced PCOS rats (mean±SD, n=6).

Groups	Ovarian weights	Uterine weights
Normal control	0.14±0.03	1.71±0.28
Letrozole control	$0.21\pm0.02^{b****}$	$0.57\pm0.09^{b****}$
Natural recovery	$0.20\pm0.02^{a*}$	$0.70\pm0.15^{a*}$
Clomiphene citrate	$0.13\pm0.04^{a****}$	$1.15\pm0.28^{a****}$
SR 250 mg/kg	$0.19\pm0.03^{a*}$	$0.78\pm0.37^{a*, c**}$
SR 500 mg/kg	$0.16\pm0.01^{a***, c*}$	$1.69\pm0.24^{a****, c***}$
SR 1000 mg/kg	$0.15\pm0.01^{a***, c*}$	$1.58\pm0.21^{a****, c**}$

SR: *S. racemosa*; ^{a*}: NS, ^{a**}: P<0.05, ^{a***}: P<0.01, ^{a****}: P<0.001 compared with letrozole control group; ^{b*}: NS, ^{b**}: P<0.05, ^{b***}: P<0.01, ^{b****}: P<0.001 compared with normal control group; ^{c*}: NS, ^{c**}: P<0.05, ^{c***}: P<0.01, ^{c****}: P<0.001 compared with modern drug group.

3.7. S. racemosa improves ovarian histology in PCOS rats

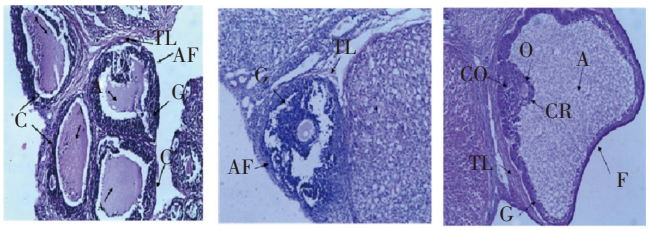
The significant number of atretic follicles were found in the cortex of ovary from letrozole induced PCOS rats. Atretic secondary follicles were randomly interspread among normal follicles. In addition to marked atresia, descruption of the granulosa layer was also seen. Many cysts were found. Theca layer was found to be delineating, dying cells and the debris was collected in the antrum (Figure 1C and Figure 2A). When rats with PCOS were left for natural recovery, the recovery was not to its potential as compared to plant and clomiphene citrate treatment as many cysts and atretic follicles were still found (Figure 2B). *S. racemosa* treatment with mid and high dose resulted in the ovarian tissue to show marked recovery of follicle with intact structure of granulosa layer and thecal layer. The ovary showed presence of well developed antral follicle with oocyte and antrum which appeared to be clear without any cell debris (Figure 2C and Figure 3).



A B C

Figure 1. Ovarian histology in rats.

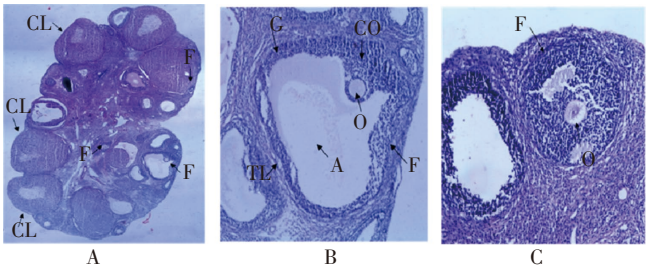
a: Section of ovary from normal rat showing the presence of antral follicles (F) and corpus luteum (CL) (H&E, ×4). b: Section of ovary from normal rat showing the presence of antral follicle (F) with antral cavity (A), oocyte (O) surrounded by granulosa cells (G), corona radiata (CR), cumulus oophorus (CO) and thecal layer (TL) (H&E, ×10). c: Section of ovary from PCOS rat exhibiting many cystic degenerating follicles (C) with thin granulosa layer (H&E, ×4).



A B C

Figure 2. Ovarian histology in PCOS rats.

a: Section of ovary from PCOS rat with cystic degenerating follicle (C) with thin granulosa layer and atretic follicle (AF) with degenerated granulosa layer (G), delineated thecal layer (TL) and the antrum (A) filled with the cell debris and dying cells (H&E, ×10). b: Section of ovary from PCOS rat left for natural recovery exhibiting atretic follicle (AF) with degenerating granulosa layer (G) and delineated thecal layer (TL) (H&E, ×10). c: Section of ovary from PCOS rat treated with clomiphene citrate showing marked recovery with the presence of antral follicle (F) with intact thecal layer (TL), granulosa layer (G) and oocyte (O) with corona radiata (CR) and cumulus oophorus (CO) (H&E, ×10).



A B C

Figure 3. Ovarian histology in PCOS rats treated with *S. racemosa*.

a: Section of ovary from PCOS rat treated with *S. racemosa* 500 mg/kg showing the presence of developing follicles (F) and corpus luteum (CL) in the ovarian cortex (H&E, ×4). b: Section of ovary from PCOS rat treated with *S. racemosa* 500 mg/kg showing the presence of normal antral follicle (F) with clear antrum (A), and oocyte (O) surrounded by cumulus oophorus (CO), granulosa layer (G) and thecal layer (TL) (H&E, ×10). c: Section of ovary from PCOS rat treated with *S. racemosa* 1 000 mg/kg showing the presence of normal developing follicle (F) with oocyte (O) (H&E, ×10).

4. Discussion

Polycystic ovaries may be created *de novo* as a result of exogenous androgen administration or secondarily to endogenous androgen excess[20]. Abnormal follicular maturation or acceleration of follicular atresia was reported in presence of elevated intraovarian androgen levels. Therefore, intraovarian androgen excess resulting from either circulating hyperandrogenemia or abnormal steroidogenesis may result in abnormal follicular development and polycystic ovary. Testosterone and androstenedione were converted into estradiol and estrone, respectively, by P450 aromatase, which was expressed in ovary. A decrease in activity of this enzyme could be expected to result in increased ovarian androgen production and development of PCOS[16]. In the present study, the animal model with PCOS was developed

using non-steroidal aromatase inhibitor letrozole in rat which showed many histologic and biochemical findings consistent with human PCOS. In polycystic ovary syndrome, the testosterone levels increase in humans[12,16,21-23]. The similar results were obtained in the present research work. In the present research work, when the rats were induced with PCOS by letrozole, the testosterone levels were found to be significantly increased when compared with normal rats. PCOS induced rats treated with *S. racemosa* showed reduced levels of testosterone.

Earlier findings, have reported that being a non-steroidal aromatase inhibitor letrozole blocks the conversion of testosterone to estradiol. This leads to the reduction in estrogen production[12,16,24-26]. The similar effect was seen in the present research work. The PCOS induced rats showed decreased levels of estrogen. Repetitive administration of *S. racemosa* led to a significant increase in estrogen levels. The plasma progesterone levels decreased significantly after induction of PCOS with Letrozole. This is in accordance with the earlier observations[12,16,22,24]. Increased progesterone levels were observed when the PCOS induced rats were repetitively administered with mid and high dose of *S. racemosa*.

Women with PCOS are hyperandrogenemic which is associated with alterations in circulating lipids and lipoprotein levels resulting in dyslipidemia. Characteristically PCOS patients have elevated cholesterol levels[23,27]. The patients with PCOS tend to be obese, probably due to high lipid and cholesterol content. The similar effect was seen in the current research work after the induction of PCOS. The PCOS induced rats showed elevated cholesterol levels which decreased significantly when the PCOS induced rats were treated with *S. racemosa*.

Ovarian weight in PCOS induced rats was more than the normal rats which is in accordance with the earlier findings[12,16,23-26]. The treatment with *S. racemosa* prevented further increase in ovarian weight. In the present research work, the uterine weight was found to be decreased in PCOS induced rats. This coincides with the earlier findings[16]. The uterine weights were returned to the normalcy when the treatment of *S. racemosa* was given to the PCOS induced rats.

The biochemical results are also supported by histopathological observations of light microscopy. It is reported that the histopathological study of PCOS induced rats show the formation of cysts in the ovary[16,22,24]. The ovarian cortex shows the presence of atretic follicles and the formation of more than two cysts in the ovary. The cysts show the attenuated layer of granulosa cells and hyperplasia of thecal layer[16,24,28]. Atretic follicles exhibit massive degeneration and sloughing-off of the central granulosa layer into the antrum. Thus the follicles become atretic with the presence of dying cells and debris in the antrum. In PCOS condition the corpora lutea do not form or the number of corpora lutea are diminished indicating anovulation and the frequency of estrus cycle is almost nil in PCOS rats[10,24,28]. In PCOS high local androgen concentrations are responsible for anovulation by direct effect on the ovary. Androgen-induced follicular atresia is thought to occur by entry of androgens into the granulosa layer of pre-antral follicles, where they bind to the cell receptors and cause the cell death. Androgens cause deterioration of follicles by increasing the number of pycnotic granulosa cells and degenerating oocytes[29]. The similar observations were seen in the current research work when the rats were induced with PCOS by Letrozole. The histopathological observations of the *S. racemosa* treated group showed marked recovery of the ovarian tissue with the presence of normalized structure of antral follicle. The light microscopic observations also revealed the presence of many well defined antral follicles in the process of normalizing. The follicles showed normal granulosa and defined thecal layers. The follicles also showed the presence of a clear antrum free of any cell debris. The presence of corpora lutea was also seen after plant treatment suggesting that treatment with *S. racemosa* restored estrous cyclicity back to normal. The ovarian cortex showed the presence of many follicles in the various stages of development.

The effect of *S. racemosa* treatment with mid and high dose was found to be comparable with that of clomiphene citrate alone while no significant changes were observed with low dose of *S. racemosa* treatment in the normalization of various parameters in the PCOS induced rats.

S. racemosa treatment exhibited significant recovery of testosterone, estrogen, progesterone levels and ovarian tissues. *S. racemosa* showed good anti-androgen effect by reducing increased androgen levels and prevented ovarian cell dysfunction in PCOS to improve fertility. The observed recovery of ovarian tissue as well as anti-androgen potential of *S. racemosa* may be responsible for its efficacy in the management of PCOS. This might be helpful to understand the role of *S. racemosa* in the management of PCOS. Findings of the current study can provide a baseline data for designing further investigations on the therapeutic benefits of *S. racemosa* as an adjunct therapy along with modern drug in the management of PCOS so as to reduce the side effects of modern drug without compromising the therapeutic activity.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

S. racemosa Roxb. commonly known as Lodhra is widely used as a traditional medicine in the treatment of gynecological disorders. Due to the undesirable adverse effects of modern medicines, herbal medicines can be used to treat disorders caused by hormonal imbalances related to the female reproductive system. Since the increased androgen levels are characteristic clinical features of PCOS, the anti-androgenic properties of *S. racemosa* Roxb. were evaluated in the treatment of PCOS using *in vivo* animal model.

Research frontiers

The study was performed by using letrozole induced PCOS rat model to determine the effective dose of *S. racemosa* Roxb. in the treatment of PCOS.

Related Reports

No work has been reported on the use of *S. racemosa* Roxb. as a herbal remedy in the treatment of PCOS and the findings of the study were in accordance with the earlier findings reported for the other plants.

Innovations and breakthroughs

S. racemosa Roxb. possesses anti-androgenic properties in the treatment of hyperandrogenism associated with PCOS.

Applications

Due to the potential anti-androgen effect of *S. racemosa* Roxb., the modern drug therapy for PCOS can now be replaced with *S. racemosa* Roxb. as an alternative therapy so as to reduces the side effects of modern drug.

Peer review

This study contributes to the understanding of effect of *S. racemosa* Roxb. on upon the reproductive tract of females. The hypothesis of the authors was ascertained and the results provided the good evidence to support its use in the reproductive medicine in the treatment of PCOS.

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