

## **Review Article**

### **Medicinal plants affected reproductive systems (part 2) - plant based review**

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**Abstract:** In our previous paper, we reviewed the reproductive effects of many medicinal plants included *Achillea santolina*, *Ailanthus altissima*, *Alhagi maurorum*, *Allium cepa*, *Althaea rosea*, *Ammannia baccifera*, *Anthemis nobelis*, *Anethum graveolens*, *Arachis hypogaea*, *Arctium lappa*, *Asclepias curassavica*, *Asplenium trichomanes*, *Avena sativa*, *Bacopa monniera*, *Bryophyllum calycinum*, *Caesalpinia crista*, *Calendula officinalis*, *Calotropis procera*, *Carum carvi*, *Capsella bursa-pastoris*, *Carthamus tinctorius*, *Chenopodium album* and Date palm. This review represented a second part of medicinal plants affected the functions of reproductive systems in males and females.

**Keywords:** reproductive, male, female, medicinal plants, herbs, pharmacology, pharmacognosy.

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#### **Introduction:**

Many drugs could be beneficially or adversely affected the reproductive functions [1-22]. Furthermore a wide range of medicinal plants also exerted reproductive effects. In our previous review [23], we mentioned that many plants possessed reproductive effects on both males and females reproductive systems, these plants included *Achillea santolina*, *Ailanthus altissima*, *Alhagi maurorum*, *Allium cepa*, *Althaea rosea*, *Ammannia baccifera*, *Anthemis nobelis*, *Anethum graveolens*, *Arachis hypogaea*, *Arctium lappa*, *Asclepias curassavica*, *Asplenium trichomanes*, *Avena sativa*, *Bacopa monniera*, *Bryophyllum calycinum*, *Caesalpinia crista*, *Calendula officinalis*, *Calotropis procera*, *Carum carvi*, *Capsella bursa-pastoris*, *Carthamus tinctorius*, *Chenopodium album* and Date palm. This review represented a second part of medicinal plants affected the functions of reproductive systems in males and females.

#### **I-Plants affected male reproductive system:**

##### ***Achillea santolina***

The hydroalcoholic extract (300 mg/kg/day intraperitoneally, for 20 days) of *Achillea santolina* caused histological alterations in the seminiferous tubules included disorganized germ epithelium, exfoliation of immature germ cells, germ cell necrosis and increased number of metaphases in germinal epithelium of seminiferous tubules in mice. The authors concluded that *Achilleasantolina* exerted antispermatogenic effect [24-25].

##### ***Arctium lappa***

The aqueous extract of *Arctium lappa* L. roots enhanced sexual behavior in male rats. Oral administration of *Arctium lappa* L. roots extract at 600 and 1,200 mg/kg body weight significantly increased the frequencies of mount, intromission, and ejaculation frequency ( $p < 0.05$ ). Administration of the extract also reduced the post-ejaculatory interval [26-29].

##### ***Bacopa monniera***

*Bacopa monniera* extracts caused reversible suppression of spermatogenesis and fertility. The treatment caused reduction in motility and viability of the sperms and reduced the number of spermatozoa in caudaepididymidis and testis, and caused alterations in the somniferous tubules in mice [30-31].

##### ***Caesalpinia crista***

When *Caesalpinia crista* meal fed to mice and rats, it caused antifertility effect. This effect could be attributed to its contents of gossypol and cyclopropane fatty acids, which has been implicated as an antifertility compounds[32-33]. Electron microscopic examination showed that the graded doses of an alcoholic extract of *Caesalpinia crista* caused morphological changes in the sperm of albino rats including disturbance in the plasma membrane and acrosomal membrane. Considerable changes in the shape and size of the sperm head were observed, with the middle region of the sperm head being slightly constricted dorso-ventrally. Most sperm appeared morphologically abnormal in the head region showing the distortion at the anterior region and bulging of the

acrosomal membrane when compared with the control. The authors suggest that such effects might have resulted from general disturbance in proteins and alteration in the caudaepididymal milieu, probably due to an androgen deficiency consequent to the treatment with *Caesalpinia crista* [34].

#### ***Capsella bursa-pastoris***

*Capsella bursa-pastoris*, dried and ground, was added at rates of 20 and 40% to the stock diet of male and female mice, found that at the 40% level, both materials impeded ovulation and produced temporary infertility in males and females [35-36].

#### ***Carthamus tinctorius***

The effects of aqueous extract of *Carthamus tinctorius* was tested on mouse spermatogenesis. Histopathological criteria such as epithelial vacuolization, sloughing of germ and detachment were significantly decreased in *Carthamus tinctorius* L. treated mice ( $p < 0.001$ ). *Carthamus tinctorius* extract induced formation of multinucleated giant cells in the germinal epithelium. It also caused a significant decrease in seminiferous tubule diameter, seminiferous epithelium height and maturation arrest ( $p < 0.001$ ). Accordingly, *Carthamus tinctorius* extract has toxic effects on mouse testicular tissue, and it was recommended to be use with caution with reproductive problem[37-38].

#### ***Chenopodium album***

Ethanol extract of *Chenopodium album* at doses of 100, 250 and 500mg/kg bw orally, in male albino mice showed significant increase in the mount frequency, intromission frequency, intromission latency as well as aggregate of penile reflexes and significant reduction in the post ejaculatory interval. Moreover 500 mg/kg, orally, was found to be the most effective dose[39]. The ethanolic extract of seeds of *Chenopodium album* was evaluated for its effect on anabolic activity, sexual behavior and sperm count in male rats. Administration of ethanolic extract at a concentration of 200 mg/kg bw resulted in pronounced anabolic effect in treated animals as evidenced by an increased body weight as well as the weight of reproductive organs. Sexual behavior and performance were also markedly improved as reflected in reduction of mount, intromission and post ejaculatory latency. Furthermore, the extract also enhance sperm count [40]. However, on the other hand, the effect of *Chenopodium album* seed extract (CAE) induced sperm death, the effect which is due to (a) lipid peroxidation of the sperm cell membrane, oxidation of some critical cellular proteins and depletion of intracellular reduced glutathione, indicating production of ROS; (b) activation of Mn-SOD and inactivation of catalase favoring endogenous accumulation of H<sub>2</sub>O<sub>2</sub>; (c) generation of O<sub>2</sub><sup>-</sup> at an enhanced rate during oxidative stress as evidenced by increased Mn-SOD activity and protein expression; (d) accumulation of ROS in

spermatozoa and (e) increased production of O<sub>2</sub><sup>-</sup> and H<sub>2</sub>O<sub>2</sub> induced apoptosis-like death in sperm cells as observed by DNA ladder formation. Therefore, the sperm death caused by CAE is due to oxidative damage of cellular macromolecules by in situ generation of ROS [41]. Aqueous decoction of *Chenopodium album* seeds (CAD) was assessed for its sperm-immobilizing and contraceptive efficacy in laboratory mammals. The minimum effective concentration of CAD that induced instantaneous immobilization of rat spermatozoa *in vitro* was 2 mg/ml. The mechanism of CAD action involved disintegration of sperm plasma membrane and dissolution of acrosomal cap causing sperm death. Fertilization of oocytes and establishment of implantation were prevented in the uterine horn that was administered with CAD. In rabbit, intravaginal application of CAD significantly blocked the establishment of pregnancy. Accordingly, CAD possesses appreciable spermicidal potential, which may be explored as an effector constituent of vaginal contraceptive [42].

#### ***Cicer arietinum***

The potential aphrodisiac effect of seeds of methanolic extract of *Cicer arietinum* (MECA) was studied in sexually sluggish male albino rats. Sexual behavioral parameters like mount frequency (MF), intromission frequency (IF), ejaculation frequency (EF), ejaculation latency (EL), mount latency (ML) and intromission latencies (IL) were observed in male rats. The male serum cholesterol and testosterone concentrations were also estimated. Oral administration of MECA at 200 and 400 mg/kg body weight was significantly increased the MF, IF, EF and EL ( $P < 0.05$ ) in comparison to control groups, while, ML and IL were significantly decreased ( $p < 0.05$ ). The extract also significantly ( $p < 0.05$ ) increased the serum cholesterol and testosterone levels. From these effects, MECA possessed significant increase in the sexual activity in male rats. The authors postulated that the augmented sexual behavior in male rats might be due to the presence of alkaloids, saponins and flavonoids in MECA [43-44].

#### ***Cistanche tubulosa***

The effect of ethanol extract of *Cistanche tubulosa* (Schenk) R. Wight stem (CTE) was studied on hormone levels and testicular steroidogenic enzymes in rats. It appeared that the administration of CTE (0.4 and 0.8 g/kg) increased sperm count (2.3 and 2.7 folds) and sperm motility (1.3 and 1.4 folds) and decreased the abnormal sperm (0.76 and 0.6 folds) respectively. The serum level of progesterone and testosterone in rats was also increased by CTE administration ( $p < 0.05$ ). Results of immunohistochemistry and western blot analysis confirmed that the expression of CYP11A1, CYP17A1, and CYP3A4 was enhanced by CTE ( $p < 0.05$ ) [45].

The weights of seminal vesicle and prostate gland of castrated young rats were significantly increased by administration of alcohol soluble extract from the decoction of *Cistanche tubulosa*. The phagocytic function of intra-abdominal macrophage in mice was activated by the decoction of *Cistanche tubulosa* [46].

#### ***Citrullus colocynthis***

A crude 50% ethanol extract of *Citrullus colocynthis* Schrad was administered orally to male albino rats for evaluation of antifertility effects. The animals were divided into five groups: group A was a vehicle-treated control group; treatment groups B, C, and D received 100 mg/kg/day *Citrullus colocynthis* extract for periods of 20, 40, and 60 days, respectively, and group E animals received the extract at dose of 100 mg/kg/day for 60 days followed by 60 days of recovery. For androgenicity evaluation of the extract, the animals were divided into four groups: group F animals were castrated 30 days before the experiment to serve as controls, and group G, H, and I were subjected to castration 30 days before the experiments, followed by administration of fruit extract (100 mg/kg/day po), testosterone propionate (0.01 mg/rat/alternate day sc), and fruit extract along with testosterone propionate, respectively, for 30 days. Significant reduction of cauda epididymis sperm motility and density, number of pups, fertility, and circulatory levels of testosterone were observed in all treatment groups. The weights of testes, epididymis, seminal vesicle, and prostate were significantly decreased in groups B, C, and D. The weights of all organs in the different groups of the androgenicity study were markedly decreased in group F when compared with group A, in group G when compared with group F, and in group I when compared with group H, and increased in group H when compared with group F. The serum testosterone levels also showed a similar pattern. The concentration of testicular cholesterol was significantly elevated, while protein, sialic acid, acid and alkaline phosphatase concentrations were decreased. The histoarchitecture of the testes showed degenerative changes in the seminiferous epithelium, arrest of spermatogenesis at the secondary spermatocyte stage, cytolysis, and the lumen filled with eosinophilic material. Histometric parameters (except Sertoli cell) revealed that the nuclear area and the number of round spermatids were markedly altered. All altered parameters restored to normal in group E. No changes were observed in body weight, litter size, hematology, and serum biochemistry. The authors concluded that 50% ethanol extract of *Citrullus colocynthis* showed an antiandrogenic nature, thereby reduced infertility in male albino rats [47-48].

#### **Citrus species**

Studies have shown that lime juice destroys sperm cells, fifty percent of *Citrus aurantifolia* juice wiped out 2000 of sperm cells in 30 seconds. The high acidity of *Citrus aurantifolia* juice may probably

responsible for this destruction [73]. The effect of lime juice was studied on the fetal parameters of Sprague-Dawley rats. The estrous cycles of the female rats were studied for the first 16 days to establish cyclicity. The rats were mated with male SD rats of proven fertility on the estrous day (heat period) of estrous cycle. Rats in group I received 1ml of undiluted lime juice while rats in group II received distilled water by gastric gavage. The rats were sacrificed on the 20<sup>th</sup> day of gestation and fetal parameters were evaluated. There was a reduction in the number of fetus of treated pregnant rats when compared to the control. There was a significant reduction in the crown-rump length, weight and umbilical cord length of the fetus when compared with the control. Accordingly, lime juice showed abortifacient effect but no obvious teratogenic effect was observed [49].

The anti fertility effect of *Citrus limonum* seeds was studied on male rats. Male albino rats were orally treated with alcoholic extract and its fractions for 30 and 60 days. Testis and epididymis were removed and tested for sperm count, sperm motility, sperm morphology in addition to histopathological examination. sperm counts were also studied 90 days after discontinuation of the treatment to see reversibility of effect. 60 days treatment significantly decreased the sperm count. Size and weight of testis and epididymis were reduced indicating atrophic changes in testis and epididymis. It caused drastic effect on sperm motility and morphology which decreased fertility. Sperm counts returned to normal after 90 days [50].

#### ***Cressa cretica***

Oral administration of a methanolic extract of *Cressa cretica* (whole plant) at a dose level of 100 mg/kg/day for a period of 60 days led to a significant decrease in the weight of testis, epididymis, seminal vesicle, and ventral prostate. *Cressa cretica* reduced the fertility of male rats by 100%. There was a marked reduction in the number of primary spermatocytes, secondary spermatocyte, and spermatids. Sertoli cell counts were significantly decreased. Leydig cell nuclear area and the number of mature Leydig cells were also significantly decreased. The protein, sialic acid, glycogen, and cholesterol content of the testis, the fructose in the seminal vesicle, and protein and sialic acid in the epididymis were significantly decreased. Serum testosterone levels were also reduced after *Cressa cretica* treatment. The RBC and WBC counts, hemoglobin, hematocrit, blood sugar, serum cholesterol, phospholipids, triglyceride, and HDL-cholesterol were within the normal range [51].

The various fractions (FrI 75:25 CHCl<sub>3</sub>:CH<sub>3</sub>OH, FrII 50:50 CHCl<sub>3</sub>:CH<sub>3</sub>OH and FrIII 25:75 CHCl<sub>3</sub>:CH<sub>3</sub>OH) of the *Cressa cretica* whole plant methanol extract were isolated by column chromatography on silica gel. These fractions were used to evaluate their effects on the reproductive functions in

male albino rats. Oral administration of fractions I, II and III to male rats (50mg/rat/day) for a period of 60 days did not cause body weight loss, whereas the weight of testes and accessory sex organs were decreased significantly ( $P \leq 0.001$ ). Sperm counts of testes and cauda epididymis as well as cauda epididymal sperm motility was also declined significantly ( $P \leq 0.001$ ) in comparison to control rats. The serum testosterone production was reduced in treated male rats. The fertility was decreased by 90% in FrI, 100% in FrII and FrIII treated male rats. Total protein, sialic acid, glycogen content of testes and seminal vesicular fructose content were reduced significantly, whereas testicular cholesterol level was increased significantly. The seminiferous tubular diameter and Leydig cell nuclear area were reduced significantly. The population of spermatogenic cells (spermatogonia, preleptotene, pachytene, secondary spermatocytes and round spermatids) were also reduced significantly in comparison to controls [52].

*Cressa cretica* was evaluated for male contraceptive activity due to their rich amount of flavonoids (rutin and scopoletin). After 60 days oral administration of *Cressa* constituents, results showed 100% antifertility activity in male rats with the reduction in testosterone levels and spermatogenic elements [53-54].

#### ***Crocus sativus***

The aphrodisiac activities of *Crocus sativus* stigma aqueous extract and its constituents, safranal and crocin, were evaluated in male rats. The aqueous extract (80, 160 and 320 mg/kg bw), crocin (100, 200 and 400 mg/kg bw), safranal (0.1, 0.2 and 0.4 ml/kg), sildenafil (60 mg/kg bw, as a positive control) and saline were administered intraperitoneally to male rats. Mounting frequency (MF), intromission frequency (IF), erection frequency (EF), mount latency (ML), intromission latency (IL) and ejaculation latency (EL) were evaluated. Crocin, at all doses, and the extract, especially at doses 160 and 320mg/kg body wt., increased MF, IF and EF behaviors and reduced EL, IL and ML parameters. Safranal did not show aphrodisiac effects [55].

A randomized, parallel-group, double-blind, placebo-controlled trial was designed to investigate the effects of *Crocus sativus* gel on erectile dysfunction in diabetic men. Patients were randomly allocated to 2 equal groups (with 25 patients each). The intervention group was treated with topical saffron, and the control received a similar treatment with placebo. The 2 groups were assessed using the international index of erectile function questionnaire before the intervention and 1 month after the intervention. Compared to placebo, the prepared saffron gel significantly improved erectile dysfunction in diabetic patients ( $P < .001$ ) [56-57].

#### ***Crotalaria juncea***

The antifertility activity of various extracts of *Crotalaria juncea* seeds was studied in male mice. Adult male mice were gavaged the petroleum ether, benzene and ethanol extracts of *Crotalaria juncea* seeds, 25 mg/100mg/day for 30 days. On day 31 the animals were sacrificed by cervical dislocation and the testes, epididymis, vas deferens, seminal vesicles, prostate gland, bulbourethral gland and levator ani were dissected out and weighed. The organs were processed for biochemical and histological examination. In petroleum ether, benzene and ethanol extracts treated rats, there was a decrease in the weights of testis and accessory reproductive organs. The diameters of the testis and seminiferous tubules were decreased. Spermatogonia, spermatocytes and spermatids in the testis and the sperm count in cauda epididymis were also decreased. There was a significant reduction in the protein and glycogen contents and an increase in the cholesterol content in the testis, epididymis and vas deferens. Of the 3 extracts, the ethanol extract appeared to be the most potent antispermatogenic extract. When the ethanol extract was tested in immature male mice, it exerted antiandrogenic effect as the weights of accessory organs were reduced [58-59].

Petroleum ether, benzene and ethanolic extracts of *Crotalaria juncea* seeds were administered intraperitoneally at the dose level of 25 mg/100 g body weight to albino male mice for 30 days. The results showed decreased number of spermatogonia, spermatocytes and spermatids in testis along with reduced caudal spermatozoa. Biochemical observations indicated increased level of cholesterol and significant reduction in protein and glycogen content. The increased cholesterol content along with degeneration of Leydig cells indicated inhibition of steroidogenesis. The decrease in the weight of accessory reproductive organs further attributes lowered availability of androgens due likely to inhibition of steroidogenesis. Out of three extracts, ethanolic extract seems to be more potent in antispermatogenic and antisteroidogenic activities. When ethanolic extract was tested in immature mice for androgenic activity, it showed its antiandrogenic potency as the weight of accessory sex organs were reduced [60].

#### ***Cuminum cyminum***

The contraceptive efficacy of *Cuminum cyminum* isolated fractions (CcFr) was investigated in male albino rats. Oral dose of CcFr 50 mg/rat/day for 60 days revealed no significant changes in body weight, while marked abnormalities in spermatogenesis were observed with decreased counts ( $P \leq 0.001$ ) in round spermatids, preleptotene spermatocytes and secondary spermatocytes. Cross sectional surface area of Sertoli cells as well as number of mature Leydig cell were decreased significantly ( $p \leq 0.001$ ). Testicular as well as accessory sex organ biochemical parameters were significantly changed ( $p \leq 0.001$ ). Sperm motility,

density and morphology were resulted in 100% negative fertility. Testosterone levels were declined significantly. The authors concluded that *Cuminum cyminum* inhibited spermatogenesis in rats and can be acting as herbal male contraceptive [61-62].

#### ***Cydonia oblonga***

The effect of quince (*Cydonia oblonga* Miller) leaf decoction was evaluated in testicular injury and impaired spermatogenesis induced by hypercholesterolemia in rabbits. Mature New Zealand white male rabbits were randomly divided into three groups: group 1 (hypercholesterolemia), group 2 (hypercholesterolemia plus quince treatment), and group 3 (control). Groups 1 and 2 received a cholesterol-enriched diet for six weeks. Group 2 received *Cydonia oblonga* leaf decoction as drinking supplement as well. After six weeks, a normal diet was substituted in groups 1 and 2 for another six weeks. Group 3 (control group) was maintained throughout the study on a regular diet. At the end of the 12<sup>th</sup> week, the left testes of the animals were resected for light microscopic study for evaluation of the maturity of germ cells in seminiferous tubules using Johnsen's score. Increase in intertubular connective tissue and diameter of vessels, abundant spermatogonia and primary spermatocytes along the reduced germinal epithelium were noted in all rabbits of the group 1. The animals in groups 2 and 3 had no significant changes in their testicular sections. The mean Johnsen's score of group 1 ( $4.20 \pm 1.92$ ) was significantly lower than that of group 2 ( $7.33 \pm 0.52$ ) and group 3 ( $7.05 \pm 0.07$ ). ( $p=0.01$ ). According to the results, authors concluded that quince leaf decoction (*Cydonia oblonga*) protected rabbit testes and spermatogenesis from damage induced by hypercholesterolemia [63-64].

The aphrodisiac activity of the hydroalcoholic extract of the fruits of *Cydonia oblonga* was studied in Wistar rats. The extract was administered orally by gavage in the dose of 500 and 800 mg/kg bw per day as a single dose for 28 days. The results showed that after administration of the extract, mounting frequency and the mating performance of the rats increased highly significantly ( $p<0.01$ ). The extract also influenced the behaviour of treated animals in comparison to non-treated rats in a remarkable manner, making them more attracted to females [65].

#### **Phoenix dactylifera (Date palm)**

Pollen of Date palm (500 mg iq) and a combination of zinc sulphate & pollen of Date palm (500 mg iq) in infertile men significantly increased serum LH, FSH, & testosterone levels. It was also, increased significantly sperm count & motility. Sexual desire was also significantly increased. Wives of treated men got pregnancy during the treatment period [66-67].

## **II-Plants affected female reproductive system:**

#### ***Ailanthus altissima***

*Ailanthus altissima* was evaluated for progestogenic and anti-progestogenic properties. Extracts of the plant were analysed for progestogenic and antiprogestogenic activities by using progesterone response element-driven luciferase reporter gene bioassay. *Ailanthus altissima* was recognized to have anti-progestogenic like activities. It inhibited the 314.46 ng/ml progesterone activity in a dose-response manner [68-69].

#### ***Alhagi maurorum***

Adding of histamine in doses of 3 µg/ml bathing fluid to the isolated guinea-pig ureter induced continuous contractions. Adding of the ethanolic extract (EE) of *Alhagi maurorum* powdered roots in doses of 5 mg/ml bathing fluid completely suppressed histamine induced contractions. Addition of another dose of histamine did not reverse the inhibition. Glyceryl-n-tetracosan-17-ol-1-oate (a new aliphatic ester isolated from the root of the plant) induced relaxations to the guinea – pig ureter and suppressed histamine – induced spasms. It seemed to possess an anticolitic action and a ureter relaxing action that can enhance getting rid of renal stones and relieve of the accompanying pain (contraction of the ureter). Treatment of the ureter with two doses of 20 and 40 micrograms/ ml of solution surrounding the ureter for 5 min, reduced the ability of histamine to contract the ureter through 100 s by a percentage equal to 75% and 100%, respectively [70-71].

#### ***Allium cepa***

*Allium cepa* showed significant antifertility activity, female rats treated with ethanolic extract showed significant inhibition of number of implant sites at a dose of 300 mg/kg. There was no change in ovulation, hence the antifertility activity observed for *Allium cepa* was attributed largely to its antiimplantation activity [72]. Fresh bulb juice was enhanced uterine contraction in rats. The treatment was equivalent to 0.003 IU of oxytocin. Water extract of the bulb was also produced strong activity on pregnant mice and rats [73]. *Allium cepa* was investigated in renal failure in male rats which experimentally infected by *Toxoplasma gondii*. The study showed that *T. gondii* exerted significant effect on serum creatinine, albumin, blood urea nitrogen (BUN), malondialdehyde (MDA) and total antioxidant capacity (TAC), and fresh onion juice returned and treated these harmful effects [74-75].

#### ***Ammannia baccifera***

Ethanol (90%) extract of *Ammannia baccifera* (whole plant) was evaluated for antisteroidogenic activity in mature female mice ovaries. The ethanol extract at the doses of 100, 200 and 400 mg/kg body weight (ip) arrested the normal estrus cycle at dioestrus phase and significantly decreased weight of ovaries. The cholesterol and ascorbic acid

content in ovaries were significantly elevated in treated mice. The extract also significantly inhibited the activity of  $\Delta 5$ - $3\beta$ -hydroxy steroid dehydrogenase and Glucose-6-phosphate dehydrogenase, the two key enzymes involved in ovarian steroidogenesis. These results showed that the ethanol extract of whole plant of *Ammannia baccifera* induced antisteroidogenic activity [77-78]. The ethanol extract of *A. baccifera* whole plant induced antifertility effects in rat males. It was significantly reduced the weight of the testis, epididymis, sperm density and motility, content of fructose in the seminal vesicles,  $\Delta 5$ - $3\beta$ -hydroxy steroid dehydrogenase ( $\Delta 5$ - $3\beta$ -HSD) and glucose-6-phosphate dehydrogenase (G-6-PD) [79].

#### ***Anthemis nobelis***

The effectiveness of *Anthemis nobelis* aqueous-alcoholic extract was studied in polycystic ovary syndrome induced in rats by a single dose of estradiol valerate. Histological investigations revealed that the animal administered with dose of 50 mg/day showed small cysts and less inflammation, with decreasing of serum estrogen hormone ( $P < 0.029$ ) [80-81].

#### ***Anethum graveolens***

The effects of *Anethum graveolens* L. (dill) extracts on female reproductive system were studied in female rats. The experimental groups were fed 0.045 g/kg and 0.45 g/kg of aqueous extract and 0.5 g/kg and 5 g/kg of ethanol extract for 10 days. Treatment with high dose of the extract resulted in a significant increase in duration of the estrous cycle and diestrus phase. Smooth endoplasmic reticulum (SER), rough endoplasmic reticulum (RER) and mitochondria were increased in granulosa lutein cells in high dose groups. There were no significant statistical differences in amount of serum estradiole between experimental, control and sham groups but the serum progesterone concentration increased significantly in high dose treatment group compared with control and sham groups [82-83]. Dill seed possessed contractive effects on myometrium, enhanced releasing of oxytocin which is an effective hormone in uterus contractions. A dose of 6-7 gm of dill seed extract after delivery decreases postpartum hemorrhage due to its contractive characteristic. Limonene and anethole showed contractive effect on uterine myometrium [84-87]. Zagamil *et al.* carried out a clinical study to evaluate the effect of Dill seed on uterus contractions in active phase of labor. 40 women used *Dill* seed infusion (one tablespoon of whole dill seed steeped in a half or whole cup boiling water for 3-4 min before going to the hospital at the beginning of uterus contractions), and 60 women used nothing in the control group. Interpretable electronic fetal monitoring was obtained for half an hour at the beginning of the active phase. The Fall: Rise ratio was calculated by measuring the duration of time for a contraction to return to its baseline from its peak (fall) divided to the duration of its rise time to its peak

(rise). The number of contractions in the treated group was significantly more than the control group. The ratio of contraction's fall time to its rise time in the treated group was shorter than the control group. The study showed that dill seed shortens duration of the first stage of labor [88].

#### ***Arachis hypogaea***

Introduction of refined peanut oil to form 10% of the food ration of immature mice increases uterine weight [89-90]. Phytoestrogens are plant-derived compounds that structurally or functionally mimic mammalian estrogens and therefore are considered to play an important role in the prevention of cancers, heart disease, menopausal symptoms and osteoporosis. *Arachis hypogaea* showed high levels of phytoestrogens including isoflavones (formononetin and biochanin A, 729  $\mu\text{g/g}$  dry weight) [91-94].

#### ***Arctium lappa***

In Traditional Chinese Medicine, *Arctium lappa* L. root is recommended as an aphrodisiac agent, and used for the treatment of impotence and sterility, while Native Americans included the root in herbal preparations for women in labor [95]. *In vivo* *A. lappa* induced uterine stimulant activity [96].

#### ***Asplenium trichomanes***

Investigate the *in vitro* estrogenic activity of *Asplenium trichomanes* extracts ability to activate ER $\alpha$  and ER $\beta$ , MCF7/ERE $\text{Luc}$  cell line which expresses endogenous ER $\alpha$ , and SK-NBE cells transiently transfected with the estrogen receptors (ER $\alpha$  and ER $\beta$ ) were used for the estrogenic activity assays. Leaves infusion and methanolic extract were active in MCF7 model; selectivity for the ER $\beta$  receptor was observed in the SK-NBE test [97].

#### ***Avena sativa***

In an experimental study, oat straw stimulated the release of luteinizing hormone from the adenohypophysis of rats. *Avena sativa* contained oestrone which been shown to induce ovulation [98-101].

#### ***Bryophyllum calycinum***

The plant exerted relaxant effect *in vitro* on the contractility of human myometrium on oxytocin-stimulated contraction at a minimum concentration almost 100-fold lower than in the case of spontaneous contraction [102]. A prospective double-blind trial with orally applied *Bryophyllum* versus placebo was carried out. Thirty-two patients divided into two groups, 15 patients received *Bryophyllum* and 17 received the placebo. The time of delivery did not differ between the groups. In both groups the mean time of birth was in the 35 week of gestation. The mean birth weight was slightly higher in the placebo group (2192 g) compared to the *Bryophyllum* group (1948 g). A transition to the intensive care unit was slightly higher in the placebo

group (13) compared to the Bryophyllum group (11)[103-104].

#### ***Caesalpinia crista***

*Caesalpinia crista* alcoholic seed extract caused histological follicular degeneration in ovary, vacuolation and mild disorganization of uterus in rats treated with graded doses of alcohol seed extract of *Caesalpinia crista*. There was a significant decrease ( $p \leq 0.05$ ) in duration of estrous cycle and mean ovarian weight. However, there were no uniform variations in mean uterine weight, serum estradiol and progesterone level. The authors suggest that antiestrogenic effects of alcohol seed extract of *Caesalpinia crista* could be resulted from an inhibition of estrogen secretion [102].

The effect of oral administration of the ethanolic seed extract of *Caesalpinia bonducella* (100, 200 and 300 mg/kg) was studied on the reproductive system in Wistar female albino rat. The treatment prolonged the length of estrous cycle with significant increase in the duration of diestrus stage. The analysis of the principal hormones viz. LH, FSH, estradiol and progesterone showed significantly decreased levels in dose-dependent manner. Ovarian and uterine weight was significantly reduced as compared to that of the control group. Histoarchitectural observations revealed follicular atresia and degeneration of corpora lutea in ovary. Oviduct showed degeneration of mucosal folds and epithelium cells. Uterus showed evidence of degeneration of endometrial epithelium and endometrial glands. Lamina propria and muscularis layer of vagina were found slightly disorganized [103].

#### ***Calendula officinalis***

*Calendula officinalis* flowers extracts exerted estrogenic activity in ovariectomized animals [90-92].

#### ***Calotropis procera***

The effects of ethanolic and aqueous extracts of *Calotropis procera* roots were studied on the oestrouscycle regularity. Both extracts were found to interrupt the normal oestrous cycle in 60 % and 80 % of female rats respectively. The extracts had no oestrogenic activity when tested in immature female bilaterally ovariectomized rats[107]. The antifertility effect of the ethanolic extract of roots of *Calotropis procera* was investigated in female rats. A strong antiimplantation (inhibition 100%) and uterotonic activity was observed at the dose level of 250 mg/kg (1/4 of LD50) [94]. *Calotropis procera* was uterotonic drug, its aqueous extracts induced significant sustained increases in human myometrial smooth muscle cell contractility, with varying efficiencies, depending upon time of exposure and dose [108].

#### ***Carum carvi***

The effects of aqueous and ethanolic extract of the seeds of *Carum carvi* were investigated on hormone and reproductive parameter of female rat.

Aqueous and ethanolic extracts of the seeds of the plant were administered orally to female rat for 30 consecutive days. Estrous cycle, reproductive hormones (LH, FSH and estrogen) and weight of reproductive organ were studied. After oral administration of different doses of aqueous and ethanolic extracts of *Carum carvi*, a significant antifertility activity was recorded. FSH and LH levels were significantly decreased, while amount of estrogen in ethanolic extract was found to be increased. The estrus phase was blocked by treatment with aqueous and ethanolic extract. It also increase the weight of ovary, uterus and body weights, while uterine weight in immature rats increased in extract treated group. Accordingly, the study showed that *Carumcarvi* exerted a significant antifertility activity [109]. Caraway oil was effective in inhibiting tonic and phasic rhythmic contractions of isolated uterine preparations [110-111].

#### ***Capsella bursa-pastoris***

*Capsella bursa-pastoris*, dried and ground, was added at rates of 20 and 40% to the stock diet of male and female mice, found that at the 40% level, both materials impeded ovulation and produced temporary infertility in males and females [112].

#### ***Carthamus tinctorius***

In order to evaluate the safety of the flowers of *Carthamus tinctorius*, the teratogenic effects of carthamiflos on the central nervous system development in mice was investigated. Furthermore, its cytotoxic effect on the rat nervous cell culture was studied. The pregnant mice were treated with different dosage regimens of aqueous carthamiflos extract during 0-8 days of gestation. Embryos were then isolated at the 13th gestation day and evaluated for macroscopic, microscopic and morphometric characteristics. The results showed that in higher doses (1.6 and 2 mg/kg/day) the embryos were absorbed, whereas with lower dose (1.2 mg/kg/day) changes in external, internal and longitudinal diameters, open neuropore, changes in cellular orientation and cellular degeneration were observed [113]. The lignan glycoside, tracheloside, was tested as an anti-estrogenic principle against cultured Ishikawa cells. Tracheloside significantly decreased the activity of alkaline phosphatase (AP), an estrogen-inducible marker enzyme, with an IC50 value of 0.31 microg/ml, a level of inhibition comparable to that of tamoxifen (IC50=0.43 microg/ml) [114]. The decoction of *Carthamus tinctorius* exerted stimulating action on the uterus of mouse *in vitro*. The stimulating action of *Carthamus tinctorius* has been found related to the stimulating effects on H1-receptor and alpha-adrenergic receptor of uterus [115]. On the other hand, intraperitoneal administration of a hot aqueous extract of the *Carthamus tinctorius* flowers increased uterine contractions in pregnant female rats [116].

***Cicer arietinum***

Aqueous, alcoholic and chloroform extract of *Cicer arietinum* were tested for abortifacient activity in female albino rat, it was given from day 11 to 15 of pregnancy at the dose level of 100, 200 and 400 mg/kg body weight. The aqueous extract at a dose of 400mg/kg was found to be most effective abortifacient. Similarly it was also found to increase the reproductive organ weight and possess estrogenic activity when tested in immature ovariectomised female albino rats [117]. Isoflavones, the important chemical components of the seeds and sprouts of chickpea, have drawn attention due to their potential therapeutic use. The estrogenic activity of isoflavones extracted from chickpea *Cicer arietinum* L sprouts (ICS) was observed recently. MTT assay showed that ICS at the low concentration ranges ( $10^{-3}$  /mg/l) promoted MCF-7 cell growth, while at high concentrations, ( $>1$  mg/l) inhibited cell proliferation, indicating that ICS worked at a diphasic mechanism. Flow cytometric analysis further calculated the proliferation rate of ICS at low concentration (1 mg/l). ER $\alpha$ /Luc trans-activation assay and then semi-quantitative RT-PCR analysis indicated that ICS at low concentrations induced ER $\alpha$ -mediated luciferase activity in MCF-7 cells and promoted the ER downstream target gene pS2 and PR trans-activation. These effects were inhibited by ICI 182,780, a special antagonist of ER, indicating that an ER-mediating pathway was involved. Alkaline phosphatase (AP) expression in Ishikawa cells showed that ICS at low concentrations stimulated AP expression. Accordingly, ICS has significant estrogenic activity *in vitro*. ICS may be useful as a supplement to hormone replacement therapy and in dietary supplements [118].

Isoflavones extracted from chickpea sprouts (ICS) stimulated estrogen responsive element (ERE)-promoter activity in cells, and concurrent treatment with the nonselective estrogen receptor antagonist ICI 182,780 abolished the estrogenic activity induced by ICS [119].

The estrogenic activities of the isoflavones extracted from chickpea sprouts (ICS) was studied in ovariectomized rats (OVX). The rats were administered via intragastric gavage 3 different doses of ICS (20, 50, or 100 mg/kg/day) for 5 weeks. Their uterine weight and serum levels of 17 $\beta$ -estradiol (E2), follicle stimulating hormone (FSH) and luteinizing hormone (LH) were measured. The epithelial height, number of glands in the uterus, and number of osteoclasts in the femur were histologically quantified, and the expression of proliferating cell nuclear antigen (PCNA) was assessed immunohistochemically. Bone structural parameters, including bone mineral density (BMD), bone volume/tissue volume (BV/TV), trabecular thickness (Tb.Th) and trabecular separation (Tb.Sp) were measured using Micro-CT scanning. Treatments of OVX rats with ICS (50 or 100 mg/kg/day) produced significant estrogenic effects on the uteruses, including

the increases in uterine weight, epithelial height and gland number, as well as in the expression of the cell proliferation marker PCNA. The treatments changed the secretory profile of ovarian hormones and pituitary gonadotropins: (serum E2 level was significantly increased, while serum LH and FSH levels were decreased) compared with the vehicle-treated OVX rats. Furthermore, the treatments significantly attenuated the bone loss, increased BMD, BV/TV and Tb.Th and decreased Tb.Sp and the number of osteoclasts. Treatment of OVX rats with the positive estrogen control drug E2 (0.25 mg/kg/day) produced similar, but more prominent effects [120].

***Citrullus colocynthis***

The toxic effects of *Citrullus colocynthis* was studied on the female reproductive system. After administration of 400 mg/kg/body weight to female rats for two time periods 4 and 12 weeks, females were allowed mating with males after 10 days prior to the last administration dose. Then females were autopsied under light anesthesia and several parameters were determined including: number of pregnant rats, body and reproductive organ weight, number of implantation sites, viable fetuses and resorption sites. Exposure to *Citrullus colocynthis* for 4 weeks did not have much effect on fertility. Significant decrease in the relative ovarian weights and embryo weights in female rats exposed to *Citrullus colocynthis* were observed. Exposure to *Citrullus colocynthis* for a 12 weeks resulted in a reduction in the percentage of pregnancies and in the number of implantation sites when compared with controls in both treatment periods. Rats receiving 12 weeks treatment showed a decrease in ovarian weights and a decrease in viable fetus's number. These results indicate that long-term exposure of female rats to *Citrullus colocynthis* causes adverse effects on the reproductive system and fertility [121].

***Citrus species***

The petroleum ether, alcoholic and aqueous extracts of *Citrus limonum* seeds were investigated for anti-fertility effect in female albino mice. The extracts were administered orally for 7 days after insemination (i.e. post-ovulatory test). The control group received 4% gum acacia. The animals were examined for implantation sites on 10<sup>th</sup> day of pregnancy. The number of pups delivered at term was recorded for each group. The alcoholic extract showed significant anti-fertility effect as compared to petroleum ether and aqueous extracts. The alcoholic extract was subjected for fractionation and the fractions were again tested for their anti-fertility effect. The fraction of ethyl-acetate showed most encouraging anti-fertility activity. In second part of the study, the alcoholic extract and its ethyl-acetate fraction were subjected to evaluation of their mechanism of action and it was found that their principal mode of action is as an anti-zygotic agent.



Withdrawal of the treatment, resulted in complete restoration of fertility [122].

Estrogenic /anti-estrogenic activities of alcoholic extract of *Citrus limonum* seeds was studied in Albino rats. The standard drug estrogen was given sub-cutaneously and test drug, alcoholic extract of lemon seeds was given orally for 7 days from 8<sup>th</sup> to 14<sup>th</sup> days of ovariectomised rats. The extract treated rats exhibited estrogenic effect, which include vaginal epithelium cell cornification and increased in uterine weight. For further supporting the estrogenic activity of the extract, isolated rats uterus preparation was mounted, and it showed that alcoholic extract of lemon seeds produced the contraction as pretreatment with telbistrol [123].

Three extracts of the peels of *Citrus medica* including oil, ethanolic and chloroform extract were investigated for antifertility activity. The alcoholic extract at the dose of 2.5gm/kg and the chloroform extract at dose of 1.0 gm/kg on female wistar rats on days 1-7 post-coital, exhibited significant anti-implantation activity. While, the oil extract at the dose of 100mg/kg on days 1-7 didn't exhibit significant anti-implantation activity [124].

Petroleum ether extract of *Citrus medica* seeds, was administered orally (400 mg/kg body weight) for 30 days to study its effect on fertility in Wistar strain Albino rats. Animal were divided into 3 groups: Group I, received 400mg petroleum ether extract/kg in 0.2ml Tween-80 (1%) orally for 30 days. Group-II, received only 0.2ml Tween-80 (1%)/kg for 30 days and left untreated for another 30 days to served as control. Group-III: received 400mg petroleum ether extract/kg in 0.2ml Tween-80 (1%) for 30 days and left untreated for next 30 days to see the withdrawal effects. The results were analysed depending on gravimetric, histological, histometric and biochemical parameters. Histologically, ovary and uterus in extract treated rats showed reduced number of healthy follicles, regressing follicles and also elevation in corpora lutea in the Group I and II. For the study of withdrawal effects of this extract in Group III, the results indicated that the animals returned to normal and regained gonadotrophin secretion similar to that of control rats [125].

Petroleum ether, benzene and ethanol extracts of the seeds of *Citrus medica* were administered orally at the dose level of 200 and 400 mg/kg to adult female albino rats for 30 days. The estrous cycle of these rats was irregular with prolonged proestrus and estrous, reduced metestrus and diestrus phase during the experimental period. At autopsy on day 31<sup>st</sup>, petroleum ether extract treated rats showed reduced ovarian weight, benzene extract treated rats showed increased ovarian weight and ethanol extract treated rats showed non-significant change in the weight of ovary. Histological changes of the ovary indicated increases in

the number of atretic follicles but decreases in the number of healthy developing follicles, Graafian follicles and corpora lutea. The total cholesterol, activity of acid and alkaline phosphatase and ascorbic acid content of the ovary were increased, whereas, protein and glycogen content were decreased. The uterine weight and its micrometric measurements in the treated rats were increased significantly. However, petroleum ether extract of *Citrus medica* seeds was more effective in causing these changes comparing to other extracts [126].

Estrogenic/anti-oestrogenic activities of petroleum ether extract of *Citrus medica* seeds were studied in albino rats. The extract at the dose level of 200 and 400 mg/kg body weight was administered for seven days to immature ovariectomised rats, along with or without 1 µg ethinyl estradiol. The extract-treated rats exhibited estrogenic effects, which included increase in uterine weight and vaginal epithelial cell cornification. The micrometric measurements of the uterus and its components were increased and glands showed high secretory activity. When the extract was tested in 30-day-old immature rats, they exhibited opening of vagina on the fifth day and cornification of vaginal epithelial cells, which was about 10 days earlier compared to controls, which further supporting the estrogenic activity of the extract. Hence, these results strongly indicate the potent estrogenic nature of petroleum ether extract of *Citrus medica* seeds [127].

The estrogenic activity of petroleum ether extract of *Citrus medica* leaves was studied in immature female rats. The petroleum ether extract proved to retain high estrogenic activity in immature female rats. Oral administration of petroleum ether extract of *Citrus medica* in ovariectomized immature female Wistar rats for 7 days in a dose of 400 mg/kg resulted in significant increase in the uterine weight (g) ( $1.7 \pm 0.11$ ) when compared with ovariectomized control rats ( $1.3 \pm 0.07$ ) [128].

#### ***Coriandrum sativum***

Effect of the aqueous extract of fresh coriander (*Coriandrum sativum*) seeds has been studied on female fertility in rats including the effects on oestrus cycle, implantation, foetal loss, abortion, teratogenicity and serum progesterone levels on days 5, 12 and 20 of the pregnancy. The extract at doses of 250 and 500 mg/kg orally produced a dose-dependent significant anti-implantation effect, but did not produce complete infertility. Treatment of animals during day-8 to day-12 and day-12 to day-20 of the pregnancy did not produce any significant abortifacient activity. There was no significant change in the weight and length of the foetuses delivered by rats treated with the extract and no abnormalities were seen in the organs of the offsprings. The extracts produced a significant decrease in serum progesterone levels on day-5 of pregnancy

which may be responsible for its anti-implantation effect [129].

#### ***Crocus sativus***

The effects of different concentrations of saffron (*Crocus sativus*) aqueous extract (SAE), was evaluated in *in vitro* maturation (IVM) of immature mouse oocytes. Cumulus-oocyte complexes (COCs) were collected from 6-8 weeks old female mice ovaries. COCs were cultured in IVM medium supplemented with 0 (control), 5, 10, 20 and 40 µg/ml of (*Crocus sativus*) aqueous extract (SAE) in 5% CO<sub>2</sub> at 37°C. The rates of maturation, fertilization and development were recorded. The maturation rate was significantly higher in all groups treated with different concentrations of SAE compared with the control group ( $p < 0.05$ ). However, the lower concentrations of SAE (10 and 5 µg/ml in maturation medium) increased the fertilization rate of oocytes and *in vitro* developmental competence when compared with the control group ( $p < 0.05$ ). The authors conclude that addition of appropriate amounts of SAE to maturation medium improved oocyte maturation and embryo development [130].

The effects of different concentrations of saffron (*Crocus sativus*) aqueous extract (SAE) and its ingredient, crocin, were evaluated on the improvement of *in vitro* maturation (IVM) and subsequent *in vitro* fertilization (IVF) and embryo development of mouse oocytes. Cumulus oocyte complexes were collected from ovaries, and germinal vesicle oocytes were cultured in the presence of SAE and crocin. SAE was added at dosages of 5, 10, and 40 µg/ml and crocin 50, 100, and 400 µg/ml. All dosages were added to maturation medium and a group without SAE or crocin was considered as the control group. Both SAE and crocin improved the rate of IVM, IVF, and *in vitro* culture. Addition of 40 µg/ml SAE to maturation medium significantly increased the rate of IVM, IVF, and *in vitro* culture ( $p < 0.05$ ). Furthermore 100 µg/ml crocin significantly increased the IVM rate compared to the control group ( $p < 0.05$ ) [131].

A double-blind and placebo-controlled trial was designed to investigate the effect of saffron (stigma of *Crocus sativus*) on the symptoms of premenstrual syndrome. The study was carried out on women aged 20–45 years with regular menstrual cycles and experience of PMS symptoms for at least 6 months. Women were randomly assigned to receive capsule saffron 30 mg/day (15 mg twice a day; morning and evening) or capsule placebo (twice a day) for two menstrual cycles. The primary outcome measure was the daily symptom report, and secondary outcome measure was the Hamilton depression rating scale. The trial showed that saffron was effective in relieving symptoms of PMS. A significant difference was observed in efficacy of saffron in the total premenstrual daily symptoms and Hamilton depression rating scale [132].

#### ***Crotalaria juncea***

Petroleum ether, benzene and alcohol extracts of seeds of *Crotalaria juncea* administered orally at the dose level of 25mg/100g bw to adult female mice for 30 days, resulted in irregular estrous cycle with prolonged estrus and metaestrus and reduced diestrus and proestrus during the experimental period. Histological studies of the ovary indicated increases in the number of atretic follicles but decreases in the number of developing follicles, Graafian follicles and corpora lutea. The total cholesterol content of the ovary was increased, whereas ascorbic acid content is decreased. The weight of the uterus and its micrometric measurement in all experimental mice were increased significantly. The alcoholic extracts showed estrogenic activity in immature mice by early opening of the vagina, premature cornification of the vaginal epithelium and increases in uterine weight. However, alcohol extract of seeds of *Crotalaria juncea* was more effective in causing these changes compared to other extracts [133].

The ethanol extract of *Crotalaria juncea* seeds which showed promising antioviulatory activity in female albino rats was examined for the isolation of its active fractions. Two fractions were obtained using thin layer chromatography (TLC). Both fractions were subjected for testing their anti-ovulation activity and the effect on estrous cycle in rats. After preliminary trials, the fraction I (200mg/kg body weights) showed maximum antioviulatory activity when administered orally to the rats for 30 days. Decreased number of healthy follicles (Class I – Class VI) and corpora lutea and increased number of regressing follicles (Stage IA, Stage IB, Stage IIA, Stage IIB) were observed in the ovary after 30 days treatment. The treatment caused an increase in the cholesterol level and acid/alkaline phosphatase activity and a decrease in protein and glycogen contents of the ovary. Estrous cycle was affected as a significant increase in estrus and metaestrus phases with a decrease in diestrus and proestrus phases in the treated groups during experimental period of 30 days [134].

Petroleum ether, benzene and alcohol extracts of the seeds of *Crotalaria juncea* were tested for antiimplantation and pregnancy interruption activities in female albino rats. Of these three extracts, the alcohol extract was found to be the most effective in causing antiimplantation and pregnancy interruption activities. These adverse effects on fertility were reversible upon withdrawal of the extract treatments. The alcohol extract was found to possess estrogenic activity [135].

#### ***Cynodon dactylon***

The effect of administration of aqueous extract of entire plant of *Cynodon dactylon* for thirty days on reproductive hormones and reproductive organ weight of female, was studied in Wistar rats. Administration of the extract produced significant

increase ( $p < 0.001$ ) in the serum estradiol concentration whereas, follicle stimulating and luteinizing hormones were significantly ( $p < 0.001$ ) reduced. Furthermore, a significant increase ( $p < 0.001$ ) in the weight of the uterus and significant decrease in the weight of the ovaries ( $p < 0.001$ ) was observed in the treated group when compared to the control group. In addition, the estrous cycle was found to be irregular and disturbed [136-137].

#### *Cyperus rotundus*

The anti-dysmenorrhea effect of the essential oil of the rhizome of *Cyperus rotundus* (EOC) was investigated in mice. Mice were divided into four groups: Group 1 served as control and group 2, group 3, group 4 were given low, middle and high dosage (0.01g/kg, 0.02g/kg, 0.1g/kg) of EOC respectively. The animals were first given diethylstilbestrol for 12 consecutive days (2mg/kg/day) by intragastric administration to create dysmenorrhea animal model. Different dosage of EOC and equivalent saline were given to animals in each group during the last three days. 30 mins after the last drug administration, the mice were injected intraperitoneally with 0.1ml oxytocin injection and distortions were observed and recorded in 15 mins and 30 mins. EOC obtained from rhizome of *Cyperus rotundus* was subjected to column chromatography for fractionation, six fractions were obtained, namely F1-F6. EOC and its fractions F2 - F6 significantly reduced distortion times in 15 mins, 30mins after ip oxytocin injection; F4 performing the best among the fractions, it was contained spathulenol as well as  $\beta$ -caryophyllene oxide and isoaromadendrene oxide according to GC-MS analysis. Accordingly, EOC and its fractions F2 - F6 showed significant anti-dysmenorrhea. More than one components were attributed to anti-dysmenorrhea effect according to the GC-MS analysis of EOC and its fractions F2 - F6 [138].

#### Conclusion:

The paper reviewed the effects of the medicinal plants on the functions of reproductive systems in males and females, to be utilize in medical applications as a result of effectiveness and safety.

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