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Medicinal plants with endocrine modulating effects

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Abstract

Nowadays endocrine disorders have become a more prevalent complex global health problem which increases the economic burden on governments worldwide due to treatments and their serious complications. Extensive attention has been focused on natural therapies for the treatment of different endocrine disorders because of their availability, effectiveness and safety. This review attempts to discuss the latest reports on the medicinal plants possessed various endocrine and hormonal effects as an alternative treatment.

Keywords: Medicinal plants; Hormonal; Endocrine; Modulation; Thyroid; Reproduction

1. Introduction

Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives. World Health Organization reports that 70% – 80% of the world population confide in traditional medicine for primary health care. Medicinal plants contained phytohormones which possessed hormonal effects, many natural compounds might act as endocrine modulators by mimicking, stimulating, or inhibiting the actions of different hormones, such as thyroid, sex and steroidal hormones. These potentials might be effectively employed in clinical practice as novel alternative therapies [1-5]. This review attempts to discuss the latest reports on the medicinal plants possessed hormonal effects and plants which possessed an endocrine modulating effect.

2. Medicinal plants with endocrine modulating effects

2.1. *Althaea officinalis*

Scopoletin (7-hydroxy-6-methoxy coumarin) is therapeutically evaluated in rats for hyperthyroidism, lipid peroxidation and hyperglycemia. Scopoletin (1.00 mg/kg, po) administered daily for 7 days decreased the levels of serum thyroid hormones and glucose as well as hepatic glucose-6-phosphatase activity. Scopoletin also mimic hepatic lipid peroxidation and promote antioxidants activity, superoxide dismutase and catalase. It indicated that scopoletin produce anti-thyroid activity and hyperglycemia without hepatotoxicity [6].

2.2. *Althaea rosea*

Althaea rosea flowers were regarded as an emmenagogue. Literature data have proved that the infusion and methanolic extract of *Althea rosea* influence hormonal activity and affected the morphology of the sexual organs of the rats. It exerted estrogenic activity , but exact component of this plant responsible for this activity was not determined . The *in vivo* test proved that *p*-hydroxybenzoic acid was estrogenic. Dudek *et al* proved that this compound present in different parts of *Althea rosea* and could be responsible for its estrogenic activity [7-8].

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2.3. *Anchusa italica*

Oral administration of Abnormal Savda Munsiq (ASMq) which contained *Anchusa italica*, also found to exert a memory-enhancing effect in the chronic stressed mice induced by electric foot-shock. The memory improvement of the stressed mice was shown by an increase of the latency time in the step-through test and the decrease of the latency time in the Y-maze test. Treatment with ASMq induced significant decrease the serum levels of adrenocorticotropic hormone, corticosterone and *β*-endorphin as well as the brain and serum level of norepinephrine. Furthermore, ASMq was able to significantly reverse the chronic stress by decreasing the brain and serum levels of the monoamine neurotransmitters dopamine , 5-hydroxytryptamine and 3,4-dihydroxyphenylalanine [9-10].

2.4. *Anethum graveolens*

Dill seed possessed contractive effects on myometer, 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 [11-14].

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 seeped 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 [15-16].

2.5. *Anthemis nobilis*

The effectiveness of *Anthemis nobilis* 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($P<0.029$) [17-18].

2.6. *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 [19-23].

2.7. *Bacopa monniera*

Bacopa extract (200 mg/kg orally) increased the thyroid hormone, T4, by 41% in mice. T3 was not stimulated, suggesting that the extract may directly stimulate synthesis and/or release of T4 at the glandular level, while not affecting conversion of T4 to T3[24].

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 cauda epididymidis and testis, and caused alterations in the somniferous tubules in mice [25-26].

2.8. *Bellis perennis*

Bellis perennis was used as skin lightening drug (Belides ™ , *Bellis perennis* flower extract). It affected the metabolic pathways involved in melanin synthesis. It inhibited tyrosinase, transcriptional control of tyrosinase expression , reduced pro-melanogenic mediators endothelin , and α MSH (melanin stimulating hormone) , as well as reducing melanosome transfere keratinocyte[27-28].

2.9. *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 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 *Carum carvi* exerted a significant antifertility activity [29].

Carum carvi elevated TSH level, high TSH levels was recorded in few patients with thyroid cancer who receiving *Carum carvi* despite being on suppressive dose of levothyroxin. TSH level returned to normal after discontinuation of the *Carum carvi* [31-32].

2.10. *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[28]. 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). ERα/Luc trans-activation assay and then semi-quantitative RT-PCR analysis indicated that ICS at low concentrations induced ERα-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[33].

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[34].

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 17β-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[35-36].

2.11. *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) respectivily. 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 ($p<0.05$)[37-38].

2.12. *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[39].

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[40-41].

2.13. *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[42-44].

2.14. *Ficus carica*

Ficus carica was evaluated for its ameliorative effect in the regulation of thyroidism in rat model. Male albino rats were treated orally with doses of 500, 250 and 125 mg/ Kg of ethanolic extract of *Ficus carica* leaf. Propylthiouracil (PTU) (10 mg/kg, sc) and Thyroxine (T4) (0.5 mg/kg, ip) were used as standards for anti thyroid and thyroid drug. The treatments were given between 9.00 and 10.00 h of the day to avoid circadian variation and continued for 21 days. T4 administration (0.5 mg/kg/d for 21 days, ip) increased the levels of serum T3 and T4, However, simultaneous administration of the *Ficus carica* leaf extract showed a potential in the regulation of thyroidism as estimated by relative potency of plant extract calculated in terms of percent increase or decreases in thyroid hormones. Phytochemical analyses revealed the presence of tyrosine in the leaf extract which was the precursor of T3 and T4 hormones[45-46].

2.15. *Fumaria parviflora*

The ethanolic extract of the plant as well as the isolated alkaloid protopine exhibit a stimulatory effect on rat's uterus at various stages of sex cycle in vitro. The extract shows in vivo an oestrogen-like effects as evidenced by vaginal smear and uterine weight tests. In contrast, it failed to produce progesterone or testosterone-like activities[22].

2.16. *Galium verum*

The effect of *Galium verum* extract (25 mg extract/100 g bw) on the hypothalamic- pituitary- adrenal axis was evaluated under anakinetic stress conditions, in rats. It appeared that administration of extract , in conditions of exposure to stress, resulted in an enhancement of neurosecretory activity of the hypothalamic paraventricular nucleus - associated with a possible stimulation of CRH release, a possible activation of adenohipophyseal hormones, as well as stimulation of adrenal steroid hormones. Histological results of the study proved that the administration of *Galium verum* vegetal extract in condition of anakinetic stress exposure induced important morphological changes at the all constitutive assembly of hypothalamo-hypophyseal-adrenal axis. These results justify the stimulation of secretory activity of the axis[49].

The protective potential of the 1:1 *Galium verum* hydro-alcoholic extract, on the thyroid and ovarian morphological parameters was studied in rats under anakinetic conditions. The 15 days subchronic anakinetic stress induced by immobilization and darkness caused an inhibition of the thyroid and ovarian functions observable in the histological aspects, while, the administration of the *Galium verum* vegetal extract in a dose of 25 mg/100 g bw caused a stimulation of the thyroid and ovarian activity in rats subjected to a anakinetic stress of 3 hours/day and darkness for 15 days[50-51].

2.17. *Glycyrrhiza glabra*

The aphrodisiac activity of aqueous extract of G. glabra roots & rhizomes was investigated. 150 mg/kg & 300 mg/kg body wt/day were administered orally by gavage for 28 days. Mount latency , intromission latency, mounting frequency, intromission frequency observed before and during the study at day 0, 7, 10, 14, 21, and 28. The extract reduced significantly mount latency and intromission latency. The extract also increased significantly mounting frequency and intromission frequency[52].

Licorise showed mineralocorticoid properties due to the presence of glycyrrhizin and its metabolite 18β-glycyrrhetinic acid, which was an inhibitor of cortisol metabolism. It was suggest the mineralocorticoid properties of liquorice, agonist of mineralocorticoid receptors and mild inhibitor of androgen synthesis, can reduce the prevalence of side effects related to the diuretic activity of spironolactone in patients with PCOS (Polycystic Ovarian Syndrome)[53-54].

18β-glycyrrhetinic acid, was a potent competitive inhibitor of 11β-HSD (11β-hydroxysteroid dehydrogenase). Lowered 11β-HSD activity resulted in higher peripheral and intrarenal concentrations of corticosterone in experimental animals and cortisol in humans, which interacted with mineralocorticoid receptors and promote Na^+ re-absorption. acute pretreatment of adrenalectomized male rats with the the water-soluble succinate derivative of 18β-glycyrrhetinic acid (carbenoxolone sodium) caused both cortisol and corticosterone to display significant mineralocorticoid-like activity, particularly Na^+ retention[55-56].

Glycyrrhiza glabra (25 mg alcoholic extract) showed high estrogenic activity reflected by uterine response and vaginal opening. Based upon the mouse uterine weight method, three doses of 25 mg of the alcoholic extract showed an estrogenic activity 1:4716980 of estradiol monobenzoate[57].

Six *Glycyrrhiza* phenols showed binding affinities for the bovine uterine estrogen receptor. The affinity of a dihydrostilbene with two 3-methyl-2-butenyl (prenyl) groups, gancaonin R, was higher than those of isoflavone phytoestrogens (genistein and daidzein) in dietary foods. The affinities of the other five phenols, a flavanone (liquiritigenin), two prenylflavanones (isobavachin and sigmoidin B), a prenylated coumestan (glycyrol), and a pyranoisoflav-3-ene (glabrene), were similar to that of the dietary isoflavone, genistein or daidzein[58].

Licorice with glycyrrhizin may cause serious side effects. Too much glycyrrhizin causes a condition called pseudoaldosteronism, which can cause a person to become overly sensitive to a hormone in the adrenal cortex. This condition can lead to headaches, fatigue, high blood pressure, and even heart attacks. It may also cause water retention, which can lead to leg swelling and other problems. Although the dangerous effects mostly happen with high doses of licorice or glycyrrhizin, smaller amounts of licorice may cause side effects. Some people have muscle pain or numbness in the arms and legs[59-60].

2.18. *Helianthus annuus*

In studying the effects of the ethanol extract of the leaves of *Helianthus annuus* on the histology of the testes, blood level of some reproductive hormones and epididymal sperm properties in Wistar rats, It appeared that the extract possessed some anti-fertility effects[61-62].

2.19. *Heliotropium europaeum*

The effect of ethanol extracts of Heliotropium europaeum (orally at 3 dose levels, 100, 200 and 400 mg/kg for a period of 7 weeks) on reproductive organs and fertility was studied in male rats. Sperm motility, count, viability and morphology and serum levels of testosterone, follicle stimulating hormone (FSH), leutinizing hormone (LH) and prolactin were assessed. Percentage of mating and fertility success and fertility index were also calculated. The testes, liver and kidney were processed for histological examination. The effect on biochemical parameters like aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, and creatinine were estimated. Hematological profiles such as red blood cell (RBC) count, total leucocyte count (TLC), hemoglobin (Hb) concentration and packed cell volume (PCV) were quantified. The results showed that the ethanol extract of H. europaeum possesses potential fertility lowering effects without altering general body metabolism(63-64).

2.20. *Hibiscus sabdariffa*

The effects of *H. sabdariffa* UKMR-2 (HSE) variety (100 mg/kg/bw orally for 28 consecutive days) on sperm functioning of streptozotocin-induced diabetic was studied in rats. Administration of HSE significantly lowered the level of fasting blood glucose and increased plasma insulin level in group as. Sperm quality was improved with significantly higher

sperm concentrations ($p<0.05$) and sperm motility ($p<0.001$) as well as lower percentage of sperm abnormality ($p<0.05$) as compared to the diabetic group. Plasma follicle-stimulating hormone (FSH) level was significantly elevated ($p<0.05$) in HSE group than in diabetic group while no significant alteration in plasma testosterone and luteinizing hormone (LH) level were seen between groups[65].

The effects of different concentrations of aqueous extracts of H. sabdariffa calyces (10%, 15% and 20%) in drinking water for 10 consecutive weeks, and its anthocyanins (50, 100, 200 mg/kg for 5 days, orally) were investigated in male and female rats, on the weight and histology of the testis, and on some biochemical constituents in testicular homogenates, as well as on plasma concentrations of testosterone, luteinizing hormone and estradiol. The possible presence of an estrogenic effect of the extract and anthocyanins on the uteri of immature female rats was also tested. Neither the *H. sabdariffa* extract nor the anthocyanins significantly altered either testicular weight and histology, or uterus weight. Plasma concentrations of the three hormones, the testicular concentrations of protein, reduced glutathione and total cholesterol, and superoxide dismutase activity were all insignificantly affected by either the extract or the anthocyanins[66-67].

Hibiscus sabdariffa consumption caused delayed puberty of the offspring either the mothers consumed it during pregnancy or during lactation periods[68-70].

2.21. *Juniperus communis*

The antifertility mode of action of *Juniperus communis* various extracts were investigated for estrogenic, antiestrogenic, progestagenic and antiprogestagenic properties in laboratory animals. Investigations reveal that the extract possessed only antiprogestational activity which accounts for its antifertility effect[71].

Extract of *juniperus communis* fruits in 50 % ethanol was screened for antifertility activity in female rats. 300 mg and 500 mg per kg bw of the extract was administered orally from day 1 to 7 of pregnancy. The extract possessed dose dependent antiimplantation activity, it also showed abortifacient activity at both dose levels when administered on days 14, 15 and 16 of pregnancy. No evidence of teratogenicity was observed[72-73].

2.22. *Lepidium sativum*

The effect of *Lepidium sativum* aqueous extract on the fertility criteria in males was studied in mice. The aqueous extract was given alone for 2 weeks, or after sulpiride for 6 weeks and then with the aqueous extract for 2 weeks. The results showed that the weight does not change over the first three weeks, but there was a significant increase in body weight at the fourth week. The group treated with both, sulpiride and *Lepidium sativum* aqueous extract showed the higher level of LH, while the group which was treated with *Lepidium sativum* aqueous extract only showed the higher level of FSH. Prolactin showed its lowest level in the group treated only with *Lepidium sativum* aqueous extract. Testosterone showed the higher level in the group treated only with *Lepidium sativum* aqueous extract. Histological sections for the testes in the group treated with *Lepidium sativum* aqueous extract only showed normal appearance of seminiferous tubule with presence of high number of sperms, sulpiride hyperprolactinemic mice testis showed partial degeneration and damage of dispersed spermatogonia cells with still presence of sperms inside the lumen with certain morphological abnormality in the shape of the sperms. Sections of treated mice testis showed a look like normal shape and structure of seminiferous tubules with the presence of normal morphology shape sperms in the lumen[74].

However, the effects of aqueous extract of *Lepidium sativum* seed on the development and magnitude of surge releases of GnRH, LH, FSH, testosterone secretion and spermatogenesis were studied in rat. Rats that received *Lepidium sativum* extract showed no changes in hormonal status and reproductive organs histology. The author concluded that there was no conclusive data for the aphrodisiac claims. There is a paucity of information on of *Lepidium sativum* seed effects on female reproductive function. *Lepidium sativum* seed has been shown in females to act as a galactagogue, abortifacient and contraceptive[75].

The effect of methanolic extract (200 and 400 mg/kg for 21 days) of seeds of *Lepidium sativum* was studied on proceptive and receptive behaviors of ovariectomized female Wistar rats. On 11th and 21st day, each female was tested in estrous phase for their sexual behavior in copulatory test. Behavioral estrus was induced by subcutaneous administration of 25 μg estradiol benzoate 48 h prior to behavioral testing and 500 μg of progesterone 5 h before testing. As a measure of proceptivity, the number of hops, darts, ear wiggling and solicitations made by methanolic extract treated female rats were significantly increased when compared against control estrous females. Lordosis quotient, as a measure of receptivity was unaffected by doses of methanolic extract[76].

However, the effects of dietary supplementation of *Lepidium sativum* seed powder (0%, 5%, 7% and 10% w/w) on growth performance and gonadotropins secretion were studied in ovariectomized, estradiol implanted rabbits. Feed intake was significantly ($p< 0.05$) increased in *Lepidium sativum* seed powder supplemented group, but its didn't increase body weight gain. *Lepidium sativum* seed powder supplementation significantly ($p< 0.001$) increased mean plasma LH, dose-dependently from the low- to the mid- *Lepidium sativum* seed powder level and then decreased LH at the high- *Lepidium sativum* seed powder level. *Lepidium sativum* seed powder supplementation increased ($p< 0.001$) plasma FSH secretion[77-78].

2.23. *Linum usitatissimum*

The effects of administration of *Linum usitatissimum* (flax seed) hydro alcoholic extract on brain weight and plasma sex hormone levels were studied in young and aged mice. The results showed that the hydroalcoholic extract of *Linum usitatissimum* for 3 weeks didn't change the brain weight of mice significantly, but the sex hormone levels increased significantly ($p< 0.05$) in comparison with the control groups[79].

Effects of aqueous methanolic extract of Flax seeds (*Linum usitatissimum*) (500 mg/kg for 14 days) on serum estradiol, progesterone and some biochemical metabolites were studied in immature female rats. Thirty six immature female rats were divided into 3 equal groups. Body weight of rats given flax seeds extract was higher ($p< 0.05$) compared to control rats and those given estradiol. Serum estradiol, progesterone, total proteins and total cholesterol contents were higher ($p< 0.05$) in rats given flax seeds extract and estradiol compared to controls. The ovarian cholesterol contents were reduced in rats of both treatment groups ($p< 0.05$). Serum ALT and AST activities were higher in flax seeds treated rats compared to control, while it was not so in estradiol treated group. There was no difference in serum urea concentrations among rats of the three groups[80].

The aqueous methanol extract of flax seeds (200 or 300 mg/kg for 25 days) significantly increased the body weight, uterine weight and the ovarian weight of mice, which could be attributed to the phytoestrogenic activity of the flax seeds[81-82].

The reproductive effects of feeding flaxseed were studied in rats during a hormone-sensitive period. Rat dams were fed a basal diet or the basal diet supplemented with 10% flaxseed, 5% flaxseed or SDG at the level in 5% flaxseed during pregnancy and lactation. Flaxseed had no effect on pregnancy outcome except that the 10% flaxseed diet lowered birth weight ($p< 0.05$), compared with other treatments. The female offspring had shortened anogenital distance, greater uterine and ovarian relative weights, earlier age and lighter body weight at puberty, lengthened estrous cycle and persistent estrus ($p< 0.05$), whereas the males had reduced postnatal weight gain and, at postnatal day 132, greater sex gland and prostate relative weights ($p< 0.05$), which suggested estrogenic effects. 5% flaxseed reduced immature ovarian relative weight by 29% ($p< 0.05$), delayed puberty by approximately 5 days ($p< 0.05$) and tended to lengthen diestrus, indicating an antiestrogenic effect. The SDG produced results similar to those of 5% flaxseed, suggesting that lignans were responsible for the observed effects. Lignans were transferred to the offspring via rat dam's milk as indicated by the recovery of radioactivity in the offspring of lactating dams given ^{3}H-SDG[83].

The effect of the ingestion of flax seed powder, which produce high concentrations of urinary lignans, on the menstrual cycle was studied in 18 normally cycling women, using a balanced randomized cross-over design. Each subject consumed her usual omnivorous, low fiber (control) diet for 3 cycles and her usual diet supplemented with flax seed for another 3 cycles. The second and third flax cycles were compared to the second and third control cycles. Three anovulatory cycles occurred during the 36 control cycles, compared to none during the 36 flax seed cycles. Compared to the ovulatory control cycles, the ovulatory flax cycles were consistently associated with longer luteal phase lengths (12.6 ± 0.4 vs. 11.4 ± 0.4 days, $p= 0.002$). There were no significant differences between flax and control cycles for concentrations of either estradiol or estrone during the early follicular phase, midfollicular phase, or luteal phase. Flax seed ingestion had no significant effect on luteal phase progesterone concentrations, but the luteal phase progesterone/estradiol ratios were significantly higher during the flax cycles. Midfollicular phase testosterone concentrations were slightly higher during flax cycles[84].

A placebo, controlled trial was conducted to evaluate the efficacy of flaxseed (providing 410 mg of lignans for 6 weeks versus a placebo) in reducing hot flashes. The mean hot flash score was reduced 4.9 in the flaxseed group and 3.5 in the placebo group ($p= 0.29$). In both groups, slightly more than a third of the women showed 50% reduction in their hot flash score[134].

A double-blind, placebo-controlled, randomized clinical trial was performed to study the therapeutic effects of daily intake of bread produced with partially defatted ground flaxseed [2 slices of bread containing 25 g of flaxseed (46 mg

lignans), or wheat bran (<1 mg lignans) every day for 12 consecutive weeks] in the climacteric symptoms and endometrial thickness of postmenopausal women. Both treatments showed significant, but similar, reductions in hot flashes and Kupperman Menopausal Index (KMI), after 3 months of treatment. Moreover, endometrial thickness was not affected in either group. Accordingly, although flaxseed was safe, but its consumption at this level (46 mg lignans/day) was not more effective than placebo for reducing hot flashes and KMI[85].

The efficacy of flaxseed meal and flaxseed extract was tested for reducing climacteric symptoms of menopausal women. Both the flaxseed extract (P=.007) and the flaxseed meal (p=0.005) were effective in reducing the menopausal symptoms when compared with the placebo control (p=0.082) [86].

A randomized, double-blind study was performed to study the effects of flaxseed incorporation in the diet of healthy menopausal women. Flaxseed reduced serum total cholesterol concentrations (-0.20 ± 0.51 mmol/liter, p= 0.012) and high-density lipoprotein cholesterol concentrations (-0.08 ±0.24 mmol/liter, p= 0.031) compared with wheat germ placebo. BMD did not differ significantly between the two groups (flaxseed and wheat germ) . Both flaxseed and wheat germ reduced (p< 0.0001) the severity scores of menopausal symptoms, but no statistical difference was found between the two groups[87-88] .

2.24. *Lithospermum officinale*

Water extracts from the above ground portion of *Lithospermum officinale* at doses of 50 mg/kg exhibited contraceptive effects in 27% of the rats. Water extracts from above ground parts of *Lithospermum officinale* depressed ovarian compensatory regeneration at a dose of 50 mg/kg bw. *Lithospermum officinale* also block the action and releasing of anterior pituitary hormones[89-95].

Saline extracts of the aerial parts and roots, administered to experimental animals by injection, inhibit oestrus and the functions of ovaries and testes, the activity of the thyroid gland was also reduced. The active principle was formed from phenolic precursors like caffeic, chlorogenic, rosmarinic acid as well as luteolin-7- beta-glucuronide by an oxidation[96].

In vitro, the effects of thyroid hormone was abolished by dry leaf extracts from *Lithospermum officinale*. *In vivo*, the same extracts in rats cause thyroid immobilization and suppression of oestrus[97].

The antithyrotropic activity of freeze-dried-extracts of *Lithospermum officinale* was investigated in the rat. When freeze-dried-extract was administered together with TSH, it blocked the TSH-induced increase in endocytotic activity of the thyroid glands followed by a strong decline of thyroid hormone levels. When the extract was injected alone, the endogenous TSH-levels, thyroidal secretion and thyroid hormone levels were declined. The efficacy of the extract in blocking thyroid secretion was compared to that of potassium iodide with faster onset and longer duration[98].

The antithyroid properties of *Lithospermum officinale* were investigated in the rat. The effect of *Lithospermum officinale* on serum levels of thyroxine and triiodothyronine and the secretion rate (endocytosis) were studied. *Lithospermum officinale* freeze dried extract decreased T4 and T3 level. However, *Lithospermum officinale* cold water freeze dried extracts significantly lowered thyroid hormone content in the serum whereas an inactivated extract exhibited a considerable loss of biological activity. The efficacy of different plant extracts greatly depended on the extraction procedure: extraction of powdered leaves with boiling water or ethanol yielded extracts without thyroid hormone-lowering capacity. The chemical oxidation of a hot-water (100°C) extract by $KMnO_4$ served to reintroduce the antihormonal effectiveness. In goiter suppression test, the chronic administration of *Lithospermum officinale* freeze-dried-extract greatly suppressed TSH-levels and consequently goiter weight. The antithyrotropic and antithyroidal activity of a variety of plant extracts was accompanied by an additional FSH and prolactin diminution. *Lithospermum officinale* exhibited a strong antigonadotropic effectiveness and completely inhibited the PMS-stimulated growth of ovaries and uteri by as little as 100 µg of extract[99-100].

Aqueous extracts from *Lithospermum officinale*, inhibited both the extrathyroidal enzymic T4-5'-deiodination to T3. The specific inhibitory activity of the extracts was increased by extraction of freeze dried aqueous extracts and decreased by oxidation with $KMnO_4$. The active principles were phenols or phenolcarboxylic acids [101].

The acute administration of *Lithospermum officinale* (Boraginaceae) freeze-dried extracts to euthyroid rats is associated with a decrease in serum thyroxine and triiodothyronine concentrations, suggesting a possible direct effect of the plant extract on circulating TSH (hypophyseal hormone blocking activity) and/or on TSH secretion[102-104].

The thyrotrophic, and to a lesser extent the gonadotrophic pituitary secretory systems were inhibited after the intraperitoneal treatment of rats for 17 days with 100 mg of *Lithospermum officinale* freeze-dried extract. The performic acid-alcianblue PAS method revealed morphologic changes in the thyrotrophic elements characterized by the presence of both hypergranulated and collapse cells, while the gonadotrophic cells in the periphery of the gland decreased in size as well as in number[105].

An indirect inhibitory effect on thyroid secretion by *Lithospermum officinale* has been reported for *Lithospermum officinale*, it act via the thyrotrophic (and also gonadotrophic) hormone of the pituitary gland[106].

The effects of *Lithospermum officinale* on thyroid glands were studied in euthyroid and hypothyroid rats. In the euthyroid rat, serum and pituitary TSH levels were greatly diminished by the plant extract. In hypothyroid rats circulating TSH was suppressed by *Lithospermum officinale* without any influence on the hypophyseal TSH stores. The chronic administration of *Lithospermum officinale* to hypothyroid rats suppressed TSH levels and correspondingly the goiter weight. These findings, that resemble the effect of low doses of thyroxine in euthyroid and hypothyroid rats, suggested that the antithyrotropic activity of plant extracts may be explained by 2 independent factors: a hypophyseal hormone blocking effect and a thyroid hormone-like activity at a hypophyseal site. At the same time prolactin serum levels and hypophyseal stores were reduced by the plant extract, this effect may be due to a thyroid hormone analog acting at a hypothalamical site initiating dopaminergic reactions responsible for the fall in prolactin and TSH concentrations[104].

The effects of the freeze-dried extracts of *Lithospermum officinale*, were studied on the binding and biological action of Graves'-IgG, the thyroid-stimulating immunoglobulin G (IgG), which found in the blood of patients with Graves' disease (Graves'-IgG) and which resemble TSH in their ability to bind to the thyroid plasma membrane, probably at the TSH receptor, and to activate the gland. The extract and their auto-oxidized constituents also inhibited the biological responses to Graves'-IgG[107-108].

2.25. *Lycium barbarum*

The effects of *Lycium barbarum* polysaccharide (LBP, after 1, 7 and 14 days of treatment) on sperm quantity and motility, sexual ability, serum hormone levels, oxidative status and testicular tissue DNA damage after exposure to subchronic (60) Co-γ irradiation were studied in rats. LBP significantly increased the sperm quantity and motility, shortened the erection, capture and ejaculation latencies, increased the number of captures and ejaculations, and improved the sexual ability of male rats. It also played a significant role in the recovery of serum testosterone levels, increased superoxide dismutase activity, decreased malondialdehyde levels, promoted oxidative balance and rescued testicular DNA damage[109].

The protective effect of *Lycium barbarum* polysaccharides (LBP) was investigated in rat testis damage induced by a physical factor (43 °C heat exposure), on DNA damage of mouse testicular cells induced by H_2O_2, and on sexual behavior and reproductive function of hemicastrated male rats. LBP possessed a protective effect against the testicular tissue damage induced by heat exposure. It significantly increased testis and epididymis weights, improved superoxide dismutase activity, and raised sexual hormone levels in the damaged rat testes. LBP possessed dose-dependent protective effect against DNA oxidative damage of mouse testicular cells induced by H_2O_2, improved the copulatory performance and reproductive function of hemicastrated male rats (shortened penis erection latency and mount latency), regulated secretion and increased hormone levels, raised accessory sexual organ weights, and improved sperm quantity and quality[110].

2.26. *Lycopus europaeus*

The extracts of *Lycopus europaeus* reduced the weight of the thyroid, decreased thyroid hormone activity, and increased absorption and storage of iodine in rats. The extract retarded goiter formation in propylthiouracil-treated rats. All animals treated with the extract showed reduced metabolism[112].

High doses of *Lycopus europaeus* reduced TSH or thyroid hormone levels in animal experiments, hyperthyroid patients treated with low doses of *Lycopus europaeus* showed improvement of cardiac symptoms without major changes in TSH or thyroid hormone concentrations[18].

Lycopus europaeus hydroethanolic extract was tested in thyroxine treated hyperthyroid rats (0.7 mg/kg bw, ip). Co-treatment with hydroethanolic extract started one week later than T4- application and lasted 5.5 weeks. Atenolol was used as reference substance. The raised body temperature was reduced very effectively even by the low dose of the plant extract, whereas the reduced gain of body weight and the increased food intake remained unaffected by any

treatment. No significant changes of thyroid hormone concentrations or TSH levels were observed. Lycopus extract and atenolol reduced the increased heart rate and blood pressure. The cardiac hypertrophy was alleviated significantly by both treatment regimes. beta-Adrenoceptor density in heart tissue was significantly reduced by the Lycopus extract or the beta-blocking agent showing an almost equal efficacy[112].

The endocrine effects of ethanolic extract of *Lycopus europaeus* orally in comparison with ip administration was studied in rats. The endocrine parameters were measured between 3 and 24 h after oral administration. The extract caused a long lasting (for a period of more than 24 h) decrease of T3 levels, presumably as a consequence of a reduced peripheral T4 deiodination. A pronounced reduction of T4 and thyroid stimulating hormone (TSH) concentrations was observed 24 h after application of the test solution by gavage. The luteinizing hormone was also decrease which indicated a central action of the plant extract[113].

Lycopus decreased the excessive thyroid stimulation, via adenylate cyclase blockade. So, when thyroid-stimulating hormone binds to the outer membrane of thyroid cells, it triggers a cAMP response on the inside of the cell via adenylate cyclase enzyme activation. Rosmarinic acid, the major compound isolated from *Lycopus europaeus* extract, decreased the TSH- stimulation of thyroid cells, via inhibition of adenylate cyclase inhibition. *Rosmarinic acid* also inhibited the enzymatic deiodination processing of thyroxine outside the thyroid gland and inhibited conversion of T4 to T3[114-115].

An open post-marketing surveillance study consisting of (a prolective assessment in patients receiving Thyreogutt® mono for 4 weeks, a retrolective documentation of data from patients who had received at least one course (4 weeks) of Thyreogutt® mono therapy during the previous 2 years, and a control cohort receiving no drug treatment) was carried out on four hundred and three patients with mild symptomatic hyperthyroidism, to assess the effects and safety of an extract of *Lycopus europaeus* (Thyreogutt® mono tablets or drops). The extract of *Lycopus europaeus* was well tolerated and associated with a statistically significant and clinically relevant improvement of the symptoms in mild hyperthyroidism[116].

A prospective two-armed open study was carried out (patients with a basal TSH <1.0 mU/l and hyperthyroidism-associated symptoms) to study the effect of *Lycopus europaeus* on thyroid function and on associated symptoms during a 3-month follow up phase. Symptoms specific to the thyroid gland were diminished (the increased heart rate in the morning). The *Lycopus europaeus* preparation showed a good tolerance. The urinary T4 excretion was significantly increased in *Lycopus europaeus* - treated patients [117-118].

2.27. *Medicago sativa*

Serum oestradiol levels, ovaries and uteri weights were significantly increased with the using of 9, 18 and 36mg /kg of alfalfa ethanolic extracts, for 15 days in female rats[119].

Plasma luteinizing hormone (LH) concentration was determined in ewes fed alfalfa. The peak LH level in control ewes was 40.1 ± 5.5 ng/ml, it was lower (P<0.05) than in ewes fed phyto-estrogenic alfalfa (66.0 ± 16.8 ng/ml). Furthermore, the LH peak occurred later (*P*<0.05) in the estrus period of ewes fed phyto-estrogenic alfalfa (15.4 ±4.5 h)[120].

The effect of aqueous extract of the aerial parts of a mixture of *Medicago sativa* and *Salvia officinalis* on the reproductive system of mature female was studied in mice. The aqueous extract of the plants mixture was given orally with water supplement for two different periods (two and four weeks) and with two different doses (100 and 200 mg/kg/ day). A significant increase in body weight in all treated groups and an increase in reproductive organs weight especially in the groups received higher doses were detected. LH and estradiol levels at the estrus phase were significantly increase, while FSH was decreased in all treated groups. The histological examination showed remarkable increase in the number of ovarian follicles and corpora lutea. There was an increase in endometrial glands diameter especially in groups received the extract for long duration, while the uterine epithelial cells height was increased significantly in all treated groups[121].

The effects of *Medicago sativa* (ethanolic extract, 250 and 500 mg/kg bw for 22 days) on body and organs weights, serum estradiol, progesterone, total proteins, total cholesterol, the liver and kidney functions were studied in immature female rats. Body weight of rats of control group was higher compared to the rats given low dose of the extract (114.40 ± 5.35 versus 93.20 ± 7.57g, P<0.05). Mean ovarian weight was significantly higher (P<0.05) in rats of both doses (18.80 ± 2.94 mg for low dose and 22.80 ± 2.94 mg for high dose) compared to the control group. Serum progesterone concentrations were higher in both doses (49.04 ± 6.67 and 40.20 ± 11.92 ng/ml for low and high dose, respectively). Follicular development, ovulation and corpus luteum formation were increased by the estrogen-like activity of the plant extract. Serum total proteins concentration was significantly higher (P<0.05) in rats given high dose (65.01 ± 4.15 g/l)

than control group and low dose group. There were no differences in the liver or kidney weights, serum urea concentrations and ALT activities of the treated rats[122-123].

2.28. *Momordica charantia*

The effect of oral graded doses of aqueous leaf extracts of *Momordica charantia* on fertility hormones of female was studied in albino rats. Estrogen levels were reduced by 6.40 nmol/l, 10.80 nmol/l and 28.00 nmol/l in the low, moderate and high doses, respectively, while plasma progesterone levels were reduced by 24.20 nmol/l, 40.8 nmol/l and 59.20 nmol/ in the same groups respectively. The authors suggested that the antifertility effect of *Momordica charantia* was achieved in a dose dependent manner[124].

2.29. *Morus alba*

Administration of 1.2 g/kg of mulberry leaves aqueous extract caused 72.5% reduction in glucose levels in rats. Lipid profile, renal and hepatic enzymes were ameliorated in rats treated with the extract. Thyroid hormones (T4 and T3) were significantly ($P<0.05$) decreased in diabetic rats treated with mulberry compared to diabetic rats[125-126].

2.30. *Ocimum basilicum*

The reproductive effect of Ocimum basilicum dry leaves extract was studied in male rabbits. New Zealand rabbits were given two different doses of the extract, then blood samples were taken to determine the serum level of FSH and LH. The extract enhanced serum FSH and LH levels and increased fertility. These effect could be attributed to rosmarinic acid which enhanced pituitary and gonadal hormones and fertility[127-128].

2.31. *Olea europaea*

The protective effect of olive leaf extract was studied in testicular damage induced in rats by intraperitoneal injection of cisplatin. Cisplatin caused biochemical and immunohistochemical changes in the testes, disorganization of germinal epithelium and apoptosis by inducing Bax and inhibiting Bcl-2 protein expression. Testicular weights, catalase, serum testosterone, testicular enzymatic (glutathione peroxidase, glutathione reductase, and superoxide dismutase) and nonenzymatic (glutathione) antioxidants, and levels of LH and FSH hormones were significantly reduced in addition to a significant increase in testicular malondialdehyde and nitrite/nitrate levels compared with the control. Olive leaf extract markedly attenuated biochemical and histopathological changes. The authors concluded that the reproductive beneficial effects of olive leaf extract were mediated, at least partly, by inducing the nuclear factor erythroid 2-related factor 2 (Nrf2)/heme oxygenase 1 (HO-1) pathway[129].

2.32. *Orchis mascula*

The aphrodisiac nature of a the plant was studied by observing mounting behavior, hormones levels and semen parameters in male mice. Crude extract showed significant increase in mounting behavior, remarkable increase in the organ weights, sperm counts, the protein, haemoglobin and testosterone content as compared to control group[130-131].

2.33. *Periploca graeca*

Nine cardiotonic steroids, six 17beta-cardenolides and three 17alpha-cardenolides identified in the chloroform and chloroform-methanol extracts of *Periploca graeca* stems were tested *in vitro* in the hormone-independent prostate cancer cell line PC-3. Five of these compounds (all 17beta-isomers with a 14beta-OH group and at least one sugar molecule), showed a very strong antiproliferative effect, with IC_{50} values of 18- 50 nM. Only 17beta-cardenolide aglycone, showed an IC_{50} value of 0.6 microM, which is 13 to 16 times higher than the values found for the corresponding cardenolides with one or two sugars[132].

2.34. *Phoenix dactylifera*

The past and recent literature regarding the effect of date consumption on infertility-related problems showed that in males, the date palm has a potent effect on the reproductive parameters including hormonal levels and seminal vesicle parameters as well as sperm motility, count, and viability. In females, it appeared that the date fruits possessed beneficial effect on reproductive parameters including oogenesis process, strengthening of oocytes, regulation of hormones, strengthening of pregnancy, reduction of the need for labor augmentation, and postpartum hemorrhage prevention[133].

The effects of date palm pollen (120, 240 and 360 mg/kg, orally for 35 days) on fertility were studied in healthy adult male rats. Date palm pollen significantly raised the relative testis and epididymis weights, sperm count, sperm motility

, and estradiol level compared to the control group ($p<0.05$). LH and testosterone levels only noticeably increased at 120 mg/kg of date palm pollen ($p<0.01$ and $p<0.001$ respectively). Seminiferous tubules diameter increased in all the doses[134].

The protective effect of date palm pollen extract (150 mg/kg/day, for 56 days) on thyroid disorder-induced testicular dysfunction was investigated in rats. L-thyroxine or propylthiouracil lowered genital sex organs weight, sperm count and motility, serum LH, FSH, testosterone, testicular function markers and activities of testicular 3β-hydroxysteroid dehydrogenase (3β-HSD) and 17β-hydroxysteroid dehydrogenase (17β-HSD). They also increased estradiol (E2) serum level, testicular oxidative stress, DNA damage and apoptotic markers. Treatment with the extract prevented L-thyroxine or propylthiouraci induced changes. In addition, supplementation of the extract to normal rats augmented sperm count and motility, serum levels of LH, testosterone, and E2 paralleled with increased activities of 3β-HSD and 17β-HSD as well as testicular antioxidant status[135].

The protective effect of aqueous date extract (4 ml/kg for 2 months) was studied against the dichloroacetic acid-induced testicular injury in rats. The absolute weights of testes and epididymis were decreased following the dichloroacetic acid administration. The testosterone, FSH and LH levels were also decreased. Severe histopathological changes including degeneration of seminiferous tubules and depletion of germ cells were recorded. These changes were associated with alterations of oxidative stress markers. Pretreatment with the extract was effectively alleviated the oxidative stress induced by dichloroacetic acid and restored the testicular parameters to normal values[136].

Pollen of Date palm (500 mg iq) and a combination of zinc sulphate and pollen of Date palm (500 mg iq) in infertile men significantly increased serum LH, FSH and testosterone levels. It was also, increased significantly sperm count and motility. Sexual desire was also significantly increased. Wives of treated men got pregnancy during the treatment period[137-138].

2.35. *Portulaca oleracea*

The effects of hydroalcoholic extract of purslane on gonadotropins, estradiol, progesterone and prolactin hormones were investigated in adult virgin female rats. The extract caused significant reduction in the estradiol and the body weight. No significant changes were recorded in LH, FSH, progesterone and prolactin[139].

The effects of lipophilic and hydrophilic extracts (125, 250 & 500 mg/kg, for 21 days) of *Portulaca oleracea* leaf on oestrous cycle, female sex hormones at various phases of oestrous cycle and ovarian and uterine histomorphology were studied in rats. Both extracts showed no significant effect on oestrous cycle, ovarian and uterine histology and female sex hormones except at proestrus phase (decreased LH and FSH levels)[140].

The ethanolic extract of *Portulaca oleracea* was evaluated on antioxidant indices and sex hormone in D-galactose treated and aging female mice. LH and FSH levels were significantly increased in D-galactose treated and aging animals, while estrogen and progesterone levels were significantly reduced. MDA contents were significantly increased in ovaries and uterus of D-galactose treated and aging groups. While, SOD and catalase activities were significantly decreased in both aging and D-galactose treated animals. Ovarian follicles were degenerated and atrophy on uterine wall and endometrial glands was observed in D-galactose treated and aging groups. Alteration in hormone levels, MDA contents and antioxidant activity were significantly reversed by the extract[141].

The supplementation with *Portulaca oleracea* seeds extract (200 and 400 mg/kg) provided a potential protective effect for acrylamide - induced testicular dysfunction in rats. The extract reversed the acrylamide -induced epididymides weight loss and improved semen quality and count, ameliorated the acrylamide - decreased testicular lesion scoring, testicular oxidative stress, testicular degeneration, Leydig cell apoptosis and the dysregulated PCNA and Caspase-3 expression in a dose-dependent manner. It also upregulated the declined level of serum testosterone and the expression of steroidogenic genes such as CYP11A1 and 17β3-HSD with an obvious histologic improvement of the testes with re-establishment of the normal spermatogenic series, Sertoli and Leydig cells[142].

3. Conclusion

Plants have formed the basis for the treatment of diseases in traditional medicine systems for thousands of years, and continue to play a major role in the primary health care of about 80% of the world's population. However, the prospect of current article is to review the changes in hormone level by medicinal plants. The review discussed the importance of medical plants on FSH, LH, Estrogen, Progesterone, Testosterone, Prolactin and Thyroxin secretion, to be utilized in medical practice as a result of efficacy and safety.

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