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Medicinal plants possess beneficial therapeutic and protective effects on male reproductive system: A review

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Abstract

Medicinal plants have been widely used to regulate or enhance fertility in males. Many medicinal plants stimulate hypothalamic, pituitary, and gonadal hormones secretion, The medicinal plants could enhance the semen quality, and increased sexual desire (libido). On the other hand, large numbers of plants were used as male contraceptive because of their antifertility effects. The current review will highlight the medicinal plants used to enhance fertility in male and that showed male contraceptive effect, which confirmed experimentally and clinically.

Keywords: Medicinal Plants; Male; Fertility; Contraceptive; Hormone

1. Introduction

Medicinal plants have been widely used to enhance or regulate fertility in males. The bneficial effects of medicinal plants on male fertility were included: hormone stimulatory activity (GnRH LH, FSH and testosterone) [1-3], improve sperm quality [4-6], and increased sexual desire [7-9], On the other hand, large numbers of plants were used as male contraceptive because of their antifertility effects. The antifertility effects of medicinal plants included: spermicidal, antizygotic, inhibition of spermatogenesis and sperm motility, inhibition of androgen synthesis either by inhibiting Leydig cell function or disrupting the hypothalamic - pituitary axis, and disruption of seminiferous tubules, erosion of germinal epithelium and disorganized histoarchitecture of the testes [10-13].

2. Plants affected male reproductive system

2.1. *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 *Achillea santolina* exerted antispermatogenic effect [14-15].

2.2. *Arctium lappa*

The aqueous extract of *Arctium lappa* roots enhanced sexual behavior in male rats. Oral administration of *Arctium lappa* 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 [16-19].

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2.3. *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 [20-21].

2.4. *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 [22-23]. 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* [24].

2.5. *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 [25-26].

2.6. *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* 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 [27-28].

2.7. *Chenopodium album*

Ethanolic extract of *Chenopodium album* at doses of 100, 250 and 500 mg/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 [29]. 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 [30]. 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 gluthathione, indicating production of ROS; (b) activation of Mn-SOD and inactivation of catalase favoring endogenous accumulation of H2O2; (c) generation of O^{2-} 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^{2-} and H_2O_2 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 [31]. 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 [32].

2.8. *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 [33-34].

2.9. *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 ($p<0.05$) [35].

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* [36].

2.10. *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 [37-38].

2.11. *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. 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^{th} 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 abortificient effect but no obvious teratogenic effect was observed [39].

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 epidadymis were removed and tested for sperm count, sperm motility, sperm morphology in addition to histopathologcal 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 epidadymis 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 [40-41].

2.12. *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 [42].

The various fractions (FrI 75:25 $CHCl_3$:CH_3OH, FrII 50:50 $CHCl_3$:CH_3OH and FrIII 25:75 $CHCl_3$:CH_3OH) 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 [43].

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 [44-45].

2.13. *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 [46].

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 ($P < .001$) [47-48].

2.14. *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 [49-50].

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 [51].

2.15. *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 [52-53].

2.16. *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^{th} 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 ± 1.92) was significantly lower than that of group 2 (7.33 ± 0.52) and group 3 (7.05 ± 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 [54-55].

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 [56].

2.17. *Dactyloctenium aegyptium*

Fertility was estimated in adult male rats treated with whole *Dactyloctenium aegyptium* ethanolic extract 200, 400 and 600 mg/kg body weight. Groups received ethanolic extract of *Dactyloctenium aegyptium* showed significant decrease in serum testosterone levels and increase in serum estrogen levels when compared to control group. The final body weight of rats of all treated groups showed no significant increase in body weight when compared with initial body weights. A significant decrease in weight of testis, epididymis (caput and caudal), vas deferens, seminal vesicle and prostate were noted in all treatment groups when compared with control group. A significant reduction of total sperm count and increase in motility, abnormality of sperm in caput and caudal was observed in all treatment groups compared to

control. Histologically, the treated groups showed dose related reduction in the diameter of seminiferous tubules, with reduced layering, less spermatozoa, hyper-cellularity of leydig cells with the presence of large multinucleated Cells. The administration of ethanolic extract of *Dactyloctenium aegyptium* showed dose dependent decrease in number of pregnant females and number of fetuses. Male rats treated with whole *Dactyloctenium aegyptium* ethanolic extract 200, 400 and 600 mg/kg body weight showed a significant decrease in SOD, catalase, GSH when compared to control group [57-60].

2.18. *Dalbergia sissoo*

The anti-spermatogenic efficacy of ethanol extract of stem bark of *Dalbergia sissoo* Roxb was evaluated. Semen samples were obtained from 15 healthy fertile men aged 25-35 years. Sperm motility was examined by the Sander-Cramer method. A dose-dependent and time-dependent effect of ethanol extract on sperm motility and sperm viability were observed. Various concentrations affected the motility of sperm. Ethanol extract at a concentration of 20 mg/ml caused complete immobilization within 3 minutes. Sperm viability and hypo-osmotic swelling was significantly reduced at this concentration. An *in vivo* studies were carried out on Swiss male albino mice. Ethanol extract at a dose of 200 mg/kg body weight resulted in a significant decrease ($p<0.001$) in weight of the testis and epididymis. A significant decrease ($p<0.01$) in sperm motility and sperm count in the epididymis were observed. Histological changes in the epididymis and testis were also recorded [61].

Antifertility effects of Dalbergia sissoo was investigated in male mice. Adult Parkes strain male mice were orally administered aqueous leaf extract of Dalbergia sissoo (50 and 100 mg/kg body weight/day) for 35 days. Motility, viability and number of spermatozoa in the cauda epididymidis; testis histology; serum level of testosterone; and toxicological parameters were evaluated. To assess reversibility, more mice were treated with 100 mg/kg body weight of Dalbergia sissoo or distilled water for 35 days and sacrificed 56 days later. The fertility parameters were also assessed separately. Histologically, testes of Dalbergia-treated mice showed dissimilar degenerative changes in the seminiferous tubules. Significant reductions were noted (i) in epididymal sperm motility, viability and number, and (ii) in serum level of testosterone in Dalbergia-treated mice compared to controls. However, serum levels of alanine aminotransferase, aspartate aminotransferase and creatinine, and haematological parameters were not affected. Also libido of Dalbergia-treated males showed no change, but their fertility was markedly suppressed. By 56 days of treatment withdrawal, the alterations induced in fertility parameters were returned to control levels [62-63].

2.19. *Datura species*

The effect alcoholic extract of *Datura fastuolsa* (2,4 and 6 mg/kg, for 7 weeks) on the fertility was studied in rat males. The results showed that the extract induced significant decrease in concentrations of sperm and normal sperm in all the concentrations in comparing with control group. They also significantly decreased serum levels of testosterone, LH and FSH and weights of the tests and epididymis in the groups treated, The percentage of occurance of pregnancy was also significantly decreased [64-65].

2.20. *Dodonaea viscosa*

Dodonaea viscosa leaf extracts showed antifertility activity in male rats. It decreased sperm count and reproductive organ weights with the appearance of necrotic changes in the seminiferous tubules of testis. Total Protein and glycogen levels were reduced in treated rats compared to the control group. The glycogen depletion in the testis and liver under *Dodonaea viscosa* leaf extracts treatment, was the probable mechanism of the toxic manifestations on male reproductive system [66-67].

2.21. *Foeniculim vulgare*

The anti-fertility effect of fennel (Foeniculim vulgare) seed extract was studied in male rats. Rat groups were orally administered 1 ml of hydro-alcoholic extract of fennel seed in four doses of 35, 70, 140, and 280 mg/kg/bw daily for 60 days. After the last gavage, the rats were anaesthetised and the caudal part of the right epididymis was used for sperm counting. After fixation of the testes, microscopic sections were prepared and histological changes were evaluated. The number of spermatogonia after doses of 140 and 280 mg/kg and Sertoli cells after a dose of 140 mg/kg decreased significantly as compared with the control group ($P < 0.05$). The number of primary spermatocytes and sperm count decreased significantly in the experimental groups (70, 140, and 280 mg/kg) when compared to the control group ($P < 0.05$). Furthermore, thickening of the basement membrane, cell apoptosis, and irregular arrangement of the germinal epithelium were observed in the experimental groups [68-69].

2.22. *Fumaria officinalis*

The aphrodisiac activities of *Fumaria officinolis* fruit aqueous/ ethanol extract 500mg/kg were studied in rats. *Fumaria officinolis* increase ($p<0.05$) in mounting behaviour when compared with the control within the first and the third hour respectively. However, the it induced no significant difference in mounting behavoiur within the first and third hour [70].

2.23. *Fumaria parviflora*

The effects of *Fumaria parviflora* ethanolic leaves extract on reproductive parameters were studied in adult male rats. Healthy adult male rats were treated with 100, 200 and 400 mg/kg/day of *Fumaria parviflora* leaves extract via gavage for 70 days. The body weight was not affected, while the weights of testis and epididymis were significantly enhanced in rats treated with 200 and 400 mg/kg/day *Fumaria parviflora* extract. No significant changes were observed in seminal vesicle and ventral prostate weight. Significant increase was found in epididymal sperm density and percent of morphologically normal sperm in extract-treated rats. Serum testosterone levels were significantly higher in rats received 200 and 400 mg/kg/day [71].

The effect of *Fumaria parviflora* alcoholic extract on spermatogenesis was studied in rats. *Fumaria parviflora* was administered orally at doses of 750 and 1050 mg/kg bw for 3 days and 250 mg/kg bw for 5 days through oral gavage. Rats were sacrificed on day fifteenth after the first gavage. The weight and volume of the testes was increased in experimental groups but these increases were not significant. Histopathological analysis showed that *Fumaria parviflora* significantly increased the number of spermatogonium, spermatocytes, spermatozoids and Leydig cells [$P<0.001$] [72].

Co-administration of ethanol *Fumaria parviflora* extract [200 mg kg/ day via gavage for 70 days] with 0.1% lead acetate in drinking water showed a significant increase in testis weight, seminiferous tubules diameter, epididymal sperm count, serum testosterone level, testicular content of superoxide dismutase [SOD] and glutathione peroxidase [GPx], the parameters which decreased in lead-treated rats [73-74].

2.24. *Glycyrrhiza glabra*

The aphrodisiac activity of aqueous extract of *Glycyrrhiza. 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 [75-76].

2.25. *Gossypium species*

Gossypol acts as an inhibitor for several dehydrogenase enzymes and has proapoptotic properties, affecting both spermatogenesis and sperm motility [77-78].

Gossypol has been investigated for use as a male contraceptive in a number of experimental studies. Gossypol (10mg/kg bw /day) caused degeneration of spermatocytes in hamsters, (20mg/kg bw /day) caused degeneration of spermatocytes in rats, (25mg/kg bw /day) decreased spermatogenesis, Sertoli cell, and caused seminiferous tubules damage in rats. (10mg/kg bw /day) caused tubular degeneration, reduced testosterone level, and involutions of ventral prostate and seminal vesicles (5, 10 and 20mg/kg bw /day) decreased sperm count and motility, increased abnormal sperm count, and reduced serum levels of testosterone, LH, and FSH in rats, (16.4mg/kg bw/day) reduced sperm production and motility and increased proportion of sperm midpiece abnormalities in bulls, (8mg/kg bw /day) caused primary and secondary sperm abnormalities and increased number of sperm with proximal droplets in bulls [79-84].

Some authors mentioned that the main target organ of gossypol toxicity following repeated exposure to lower doses in rats and humans is the testis with reduced sperm motility, inhibited spermatogenesis and depressed sperm counts [85].

It was used as Male contraceptive method by Chinese, It was noted that men consuming cottonseed oil in their diet showed unusually high infertility rates. Oral administration of gossypol in large scale trials resulted in severe oligozoospermia (< 1 million/ml) at 90% of participants. In 20% of men this effect was irreversible. Because some cases showed severe hypokalemia, WHO recommend the discontinuation of further investigations on gossypol [77-78].

The male contraceptive effects of gossypol were mediated inhibition of release and utilization of ATP by the sperm cells, reduction of cellular and microtubular β-tubular

content in spermatocytes and spermatids, inhibitition of calcium influx, and Mg-ATPase and Ca-Mg-ATPase activity in spermatozoid plasmatic membranes. Gossypol produces ultrastructural alterations in the nuclear membrane, endoplasmic reticulum, and mitochondria, decreases cellular oxidase activity and damaged sperms DNA, reduced nuclear expression of androgen receptors in Leydig cells, Sertoli cells, and myoid cells from in rats. It also decreased testosterone, LH and FSH serum levels [82, 85-90].

2.26. *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-fertilty effects [91-92].

2.27. *Hibiscus rosa-sinensis*

The benzene chloroform and alcoholic extracts of the flowers of *Hibiscus rosa sinesis* decreased the spermatogenic elements of testis, and epididymal sperm count, when administered (ip) at two different dose levels of 125 and 250 mg/kg bw to adult male albino mice for 20 days. High content of testicular cholesterol may be due to lowered androgen synthesis [93].

The effect of ethanol, chloroform, ethyl acetate extract of *Hibiscus rosa sinensis* was studied on spermatogenesis and sperm parameters on mice. Administration of 125mg/kg bw of ethanol, chloroform and ethyl acetate extract (Sc) for three consequence days caused marked to significant decrease in testis weight and sperm count and sperm viability [94].

The effects of oral administration of aqueous and alcoholic extracts of flowers of *Hibiscus rosa* sinensis (250 mg/kg bw/day, for 30 days) on the reproductive organs of male rats were studied . The results indicated that the weights of the testis, epididymis, ventral prostate, and seminal vesicle of the treated animals were not significantly different from those of the controls. The testis and epididymis of the rats also showed normal histological features, irrespective of treatment. No apparent toxicity of the extracts was discernible [95].

The effect of orally administered aqueous crude extract of *Hibiscus rosa sinensis* (500 mg/kg of bw) on, reproductive organ was studied in mice. The treatment caused reduction in the weight of testis, epididymis and sperm density significantly. Serum testosterone level was declined, the fall in density of sperms and that of testosterone level were correlated to one another Histologically, testis in mice treated with the plant extract showed alteration in the seminiferous tubules included decrease in thickness and density of germinal epithelium and hypertrophy in majority of cells, the lumen showed negligible presence of sperms in the treated animal as compared to control [96].

2.28. *Hibiscus sabdariffa*

The sub-chronic effect of *Hibiscus sabdariffa* (HS) calyx aqueous extract (1.15, 2.3, and 4.6 g/kg for12-weeks) on testes was investigated in rats. Three test groups received different doses of 1.15, 2.30, and 4.60 g/kg based on the LD(50). Results did not show any significant ($P>0.05$) change in the absolute and relative testicular weights, but there was a significant ($P<0.05$) decrease in the epididymal sperm counts in the 4.6 g/kg group, compared to the control. The 1.15 g/kg dose group showed distortion of tubules and a disruption of normal epithelial organization, while the 2.3 g/kg dose showed hyperplasia of testis with thickening of the basement membrane and 4.6 g/kg dose group, showed disintegration of sperm cells [97].

The potential adverse effects of the cold and hot *Hibiscus sabdariffa* calyx extracts (200 mg/kg bw, for 4 weeks, orally) on sperm morphology and testicular ultrastructure were studied in albino mice. The results revealed that aqueous extracts of dried calyx of *Hibiscus sabdariffa*, either cold or boiled, alter normal sperm morphology and testicular ultrastructure and adversely influence the male reproductive fertility in albino mice [98].

2.29. *Jussiaea repens*

Oral administration of crude aqueous extract of *Jussiaea repens* to adult male albino rats at the doses of 100 , 200 and 400 mg / kg bw /day for 28 days, caused no significant change in body weight and organ weights like liver, kidney, spleen and heart but the weights of testis and cauda epididymis were significantly reduced, where the weight of adrenal gland showed significant rise in. Epididymal sperm concentration, motility and viability were significantly reduced but sperm abnormality was markedly increased in and IV. SGOT, SGPT, ALP, ACP, total protein, urea and creatinine level in serum were remained unchanged in treated groups. The fructose content of seminal vesicle and ventral prostate was

reduced significantly. Accordingly, the oral administration of aqueous extract of *Jussiaea repens* may be considered as nontoxic antifertile agent in male rat in a dose dependent manner [99].

The effects of crude queous extract of Jussiaea repens (JR) 200 mg/kg bw/day for 28 days in rats) on sperm the DNA integrity of spermatozoa was studied. Toluidine blue (TB), acridine orange (AO) and aniline blue (AB) staining were used to assess sperm chromatin / DNA integrity and comet assay for sperm DNA damage. The results showed that the DNA integrity or denaturation by TB, AO and AB positive staining of spermatozoa of JR treated group were significantly increased when compared with control. But TB positive staining was much higher (34.51%) than AO (27.06 %) and AB (18.91%) positive staining. No denaturation was observed in epididymal spermatozoa of rats after withdrawal of extract treatment. The results of Comet assay also support the reduced change in Head DNA % and increase in Tail DNA %, Tail length (TL), Comet length (CL). All parameters returned almost towards control in withdrawal group, suggested the reversible action of extract [100].

The effects of the crude aqueous extract of *Jussiaea repens* on the normal histoarchitechture of testicular tissue and vis-à-vis functions was investigate Results showed that when crude aqueous extract of Jussiaea *repens* (except root) was fed orally at a dose of 200 mg/kg bw/day for a period of 28 days, caused marked alterations in histology of testis, reduction in seminiferous tubular and Leydig cell nuclear diameter. Spermatogenic stage count showed the arrest of spermatogenesis at stage VII followed by significant reduction in number of sertoli cells and spermatogenic cells. Histological studies of treated testis showed reduction in interstitial tissue with leydig cells, tubular lumen, mature spermatids, thickness of basal lamina with irregular outline and profuse intraepithelial vacuolation. Serum level of testosterone, LH, FSH and testicular testosterone were greatly reduced in treated group. All these effects were restored towards normal after withdrawal of treatment [101].

The effect of crude aqueous extract of *Jussiaea repens* (except root) at the dose of 200mg/kg bw/ day for 28 days in rats was studied on sperm quality and morphological alterations of sperm cells. The results showed that the extract induced alterations of sperm morphology was predominantly of primary abnormalities (40%), which included hook less, banana head, pin head, bent neck, bent tail, head amorphous and presence of cytoplasmic droplets. About 10% secondary abnormalities were found to have coiled tail or head less spermatozoa. The tertiary abnormalities (8%) , tailless or detached head and simple coil tail were also found. The presence of cytoplasmic droplets and disruption of plasma membrane of spermatozoa in treated group also confirmed the potentiality of this plant extract as an anti fertility agent [102].

The probable mode of action of *Jussiaea repens* (except root) as anti fertile agent was studied in rats. The aqueous extract at a dose of 200 mg/kg bw/day orally for 28 days exerted potent anti fertility activity that may be due to decreased testicular ascorbic acid, glycogen, Δ5-3β and 17β HSD, G-6PDH, ATPase, LDH activities and increased level of cholesterol, which are directly related to testicular functions. The testicular protein content was unaltered but Zn content was reduced insignificantly than control. Serum triglycerides, VLDL, LDH and G-6PDH were significantly reduced in treated group keeping HDL unaltered, but Zn content was reduced insignificantly. A significant decrease of protein content, Zn, ATPase and LDH activities in epididymis were also observed after treatment, which supported the anti gonadal activity. Altered biochemical parameters may affect the maturation process of spermatogenesis which was reflected through increased percentage of denatured chromatin in spermatozoa. Restoration of all the biochemical parameters in the recovery group supported the reversal effect of the extract after withdrawal of treatment [103].

The effect of crude aqueous extract of *Jussiaea repens* (200mg/kg bw /day for 28 days consecutively) was studied on the histoarchitecture of epididymis and its biochemical alterations in rats. As, histoarchitecture of epididymis and biochemical activities were correlated with sperm maturation, as the relationship between spermatozoa and microenviroimient of epididymis during the sperms remain in it, is important for male fertility. Extract caused significant reduction in epididymal sialic acid, glycogen, phospholipid, GSH, and testosterone level. But no change in total lipid and MDA level. Histological studies of epididymis showed the epithelial lining and basement membrane was thin and disrupted, the luminal diameter, epithelial height and nuclear diameter significantly reduced in treated group compare to control [104].

The aqueous extract of *Jussiaea repens* at oral dose of 200 mg/kg bw/day for 28 days caused no significant change in body weight but weight of testis and cauda epididymis, sperm motility, total sperm count from cauda epididymis, sperm viability and normal sperms were significantly reduced in treated group. The mating studies with treated group showed 25% having '0' implantation site. Withdrawal of drug for successive 28 days caused marked recovery in testicular and epididymal weight, sperm motility, count, viability and morphology possibly due to inhibition of spermatogenesis and steroidogenesis. The reversal studies caused recovery of reproductive parameters towards normal revealing the nontoxicity [105-106].

2.30. *Lantana camara*

The a hydroalcoholic extract from *Lantana camara var aculeata* leaves affected the fertility of male rats. It did not interfere with overall weight or internal organ weights, but interfered with sperm count, daily sperm production and sperm morphology in a dose-dependent manner [107-108].

The spermicidal potential of various *Lantana camara* leaf extracts (petroleum ether, chloroform, methanol and water) was evaluated in healthy human spermatozoa. The results showed that methanolic and aqueous extracts possessed maximum spermicidal potential regarding sperm motility, sperm viability, sperm count, hypoosmotic swelling, acrosomal status and function. Furthermore, methanolic and aqueous extracts were studied for *in-vitro* evaluation of pro-oxidant activity by detection of ROS generation using fluorescent probe detection method. Both methanolic and aqueous extracts of *Lantana camara* possessed prooxidant potential which could be attributed for their contact spermicidal activity [109].

2.31. *Lepidium sativum*

The effect of tocopherol extracted from *Lepidium sativum* seeds on the fertility was studied in adult male rabbit. The results showed a significant increase ($P< 0.05$) in testicular sperm concentration, epididymus sperm concentration and in the sperm count per gm of the testis, sperm motility percent, grade activity, sperm viability percent, with a decrease in abnormal sperm morphology percent [110-111].

The possible protective effects of *Lepidium sativum* seed extract (200 and 400 mg/kg, orally) on fasting blood sugar and on the histopathological change of epididymis were studied in streptozotocine-induced diabetic rats. Administration of 200 and 400 mg/ml doses of *Lepidium sativum* seed extract increased epithelium height and decreased interstitial volume density and fibro muscular thickness significantly. Tubular and lumen diameter did not change significantly in different groups [112].

The effect of *Lepidium sativum* seed ethanol extract (200 and 400 mg/kg, orally) on fasting blood sugar and its protective effect on histopathological changes in the ventral prostate gland were studied in streptozotocine-induced diabetic rats. Administration of the 200 and 400 mg/kg doses of *Lepidium sativum* seed extract increased epithelium height and decreased interstitial volume density and fibromuscular thickness of the prostate significantly [113].

The effect of *Lepidium sativum* aqueous extract on the fertility criteria in males was studied in mice. Forty-eight mice used in this experiment divided into four groups (12 mice each group). 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 when compared with treated groups. Testosterone showed the higher level in the group treated only with *Lepidium sativum* aqueous extract. Histological sections for the testis 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 [114].

However, the effects of aqueous of *Lepidium sativum* seed on the development and magnitude of surge releases of GnRH, LH and FSH, testosterone secretion and spermatogenesis were studied in rat. Rats that received *Lepidium sativum* showed no changes in hormonal status and reproductive organs histology. The author concluded that there was no conclusive data for the aphrodisiac claims [115].

2.32. *Lycium barbarum*

The protective effects of *Lycium barbarum* polysaccharide (LBP, 40 mg/kg) on diabetic testicular dysfunction and its underlying mechanism were investigated in mice. LBP considerably recovered testicular function, improved testicular histopathologic structure and significantly increased antioxidant enzyme activities. The results of Q-PCR and western blot analysis showed that LBP 40 mg/kg significantly downregulated Beclin-1 and LC3I protein expressions upregulated p-PI3K and p-Akt protein expressions and decreased Beclin-1 and LC3I mRNA expressions compared with diabetic mice [116].

The fertility protective effects of *Lycium barbarum* polysaccharide (LBP, 10, 20 or 40 mg/kg for 62 consecutive days) was studied against sexual dysfunction and fertility impairments in the type-1 streptozotocin induced-diabetes mice. LBP treatment of the diabetic mice considerably reversed abnormal changes in the sperm parameters, relative weight of reproductive organs, morphology of testis, Johnsen's testicular score, serum testosterone, FSH, LH levels, with marked improvement in sexual behavior and fertility level compared to the diabetic group [117].

Feeding of LBP for 21 days to male rats significantly improved the male copulatory performance including increase of copulatory efficiency, increase of ejaculation frequency and shortening of ejaculation latency. The sexual inhibition caused by chronic corticosterone was prevented by LBP [118].

Lycium barbarum polysaccharide (LBP) and *Laminaria japonica* polysaccharide (LJP) enhanced cryo-protective effects on goat spermatozoa, and that 2.0 + 1.0 mg/ml LBP + LJP addition to the extender during cryopreservation is beneficial to the Cashmere goat breeding industry [119].

The protective effects of *Lycium barbarum* polysaccharide (LBP) against nonylphenol exposure induced testicular injury were studied in juvenile zebrafish. LBP improved the GSI which reduced significantly due to nonylphenol exposure. The densities of sperms increased and non-celluar zone decreased after LBP treatment. Cyp11b gene was up regulated to nonylphenol group, and cyp19a gene was down regulated to nonylphenol group [120].

The protective effect of *Lycium barbarum* polysaccharides (LBP) on DNA oxidative damage of testicle cells induced by hydrogen peroxide (H_2O_2) was studied *in vitro*. The results showed that H_2O_2 induced breakage of DNA strand. The pretreatment of LBP (50, 100, 200, 400 micrograms/ml) significantly decreased the frequencies of cells with tail moment and the tail length of testicle cells treated by H_2O_2 [121].

The preventive effect of LBP on the damage of reproductive system and spermatogenic cells caused by low-dose (60)Co-γ irradiation was studied male rat . It appeared that mating function and testis organ coefficient in LBP + irradiation groups were significantly better than that of the corresponding irradiation control groups. LBP significantly up-regulateds the expression of Bcl-2, down-regulated the expression of Bax, possessed an important role in prevention of the decreasing of mitochondrial membrane potential and significantly reduce spermatogenic cells apoptosis [122].

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 [123].

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 a chemical factor (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 [124].

The protective effect of *Lycium barbarum* polysaccharides (LBP, 200 mg/kg, po, daily for 10 days) against doxorubicin (DOX)-induced testicular toxicity was studied in rats. DOX-caused reduction in the testicular weights, sperm concentrations and percentage of motile sperms, as well as the increase in abnormal sperm rate. LBP administration to DOX-treated rats successfully ameliorated DOX effects on semen quality, reversed the changes in MDA and GHS-Px levels, significantly increased the plasma testosterone level and effectively attenuated DOX-induced severe degenerative changes of seminiferous tubules [125].

The underlying mechanisms of *Lycium barbarum* polysaccharide (LBP) on male infertility were investigated. LBP protected Leydig MLTC-1 cells against cisplatin by regulating ERS-mediated signal pathway, which was evidenced by downregulation of phosphorylation PERK, phosphorylation of eukaryotic translation-initiation factor 2α and activating

transcription factor 4. LBP decreased cisplatin -induced MLTC-1 cell apoptosis via reducing ERS apoptosis-relative proteins caspase 3, caspase 7, and caspase 12. LBP reversed cisplatin -induced LC3II and Atg5 upregulation in MLTC-1 cells. LBP also markedly recovered MLTC-1 cells testosterone level even in the presence of cisplatin [126].

Fructus Lycii polysaccharides (FLPS) inhibit time- and hyperthermia-induced structural damage in murine seminiferous epithelium, *in vitro*. FLPS also delayed apoptosis, both at normothermic and hyperthermic culture conditions. The protective effect of FLPS also implicated an antioxidant mechanism of action. FLPS inhibited ultraviolet light-induced lipid peroxidation, and cytochrome c reduction by free radicals [127].

The protective effect of *Lycium barbarum* polysaccharides (LBP) on testicular damage induced was studied in mice. Several adverse effects were observed after $CdCl_2$ injection: significant decrease in body/testis weight ratio ($P<0.05$), gross morphological changes with hyperemia of the parenchyma, increased volume, alteration in the structure of the seminiferous tubules, significant decrease of glutathione (GSH) and Trolox equivalent antioxidant capacity (TEAC) in testis ($P<0.05$) together with a significant increase ($P<0.01$) of 3-nitro-l-tyrosine (3NT) while malondialdehyde (MDA) did not change. LBP pretreatment caused slight signs of improvement in the morphology of the seminiferous tubules. Our results confirm that Cd induces testicular damage and suggest the oxidative stress involvement [128].

The protective effect of *Lycium barbarum* polysaccharides (LBPs, 0, 10.0, 33.3 or 100 /kg, from one week before exposure) against cadmium (Cd)-induced testicular reproductive toxicity was investigated in mice. Pretreatment with LBP ameliorated the Cd-induced reduction in the body weights, sperm motility as well as the level of testosterone in serum. Cd-induced increase in the abnormal sperms which reduced by LBPs, and the effects of Cd on the levels of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) were also reversed by LBPs. Histopathological examination further confirmed the attenuating effects of LBPs against Cd-induced degeneration of seminiferous tubules [129].

The protective effect of polysaccharides of *Lycium barbarum* was studied against oxidative stress-induced neuronal damage following cavernous nerve injury. application of *Lycium barbarum* polysaccharides following cavernous nerve crush injury effectively promoted nerve regeneration and erectile functional recovery within the first 2 weeks after cavernous nerve injury [130].

2.33. *Mangifera indica*

The extract caused significant increase in the serum concentration of estradiol in a dose dependent manner ($p<0.05$) while insignificant increase and insignificant decreases in low dose (500mg/kg) group and insignificant increase in high doses (1000 and 1500 mg/kg) group in serum progesterone level. Significant increase in weight gain in low dose (500mg/kg) group and significant decreases in weight gain in high doses (1000 and 1500 mg/kg) group were observed. Significant decrease in the relative ovary weight with microscopic cystic spaces and oedema in the ovary of high dose group [131].

The reproductive effect of oral administration of aqueous leaf extract of *Mangifera indica* at a dose of 500 mg/kg was investigated in rats. The results revealed that oral administration of aqueous extract reduced weight gain, disrupted estrous cycling, reduced serum FSH while increasing estradiol level in non-pregnant rats. It also reduced maternal weight and litter birth weight in pregnant females, but it caused no significant effect on duration of pregnancy [132].

The effect of aqueous and alcoholic extracts of *Mangifera indica* on the growth of embryos was studied in pregnant mice. No abnormality and teratogenic effects were noticed in bone, cartilage, liver, spleen, kidney, digestive tract and spinal cord tissues. According to the results, the authors concluded that *Mangifera indica* can be administered safely during pregnancy while improves bone and dental tissues growth and development [133-134].

2.34. *Matricaria chamomilla*

The effects of *Matricaria recutita* extract (100 and 150 mg/kg/day for 56 consecutive days) on spermatogenesis and camp-responsive element modulator (CREM) expression at MRNA level (as key factor in the regulation of the expression of number of post-meiotic genes during spermatogenesis) were investigated in rats. The extract caused significant decrease in the epididymal sperm counts and sperm motility of experimental groups compared to control group. Reverse Transcription Polymerase Chain Reaction (RT-PCR) showed a decrease in the expression of CREM in the testes of experimental groups. Accordingly, the authors concluded that Matricaria recutita exerted anti-spermatogenic effects [135-136].

The protective effect of hydroethanolic extract of *Matricaria chamomilla* (200 and 500 mg/kg, bw, ip, for 30 days) on the reproductive system of male rats exposed to formaldehyde. Hormonal status, sperm parameters, testis tissue histology, germinal cells apoptosis and stereological analyses of testis tissue were investigated. Testosterone and LH levels were significantly increased, sperm count, motility and viability were significantly enhanced when *Matricaria chamomilla* extract was used alone or with formaldehyde [137].

2.35. *Melia azedarach*

The antifertility activity of ethanolic bark extract of *Melia azedarach* (200 & 400 mg/kg, once daily for 15 days) was investigated in male rats. The male rats were allowed to mate with sexually active female of same strain and the percent of pregnancy, number of implantation and number of viable fetuses was observed. Both the doses of *Melia azedarach* significantly decrease the percent of pregnancy, number of implantation and number of viable fetuses in female rats compared to control rats [138].

2.36. *Melissa officinalis*

The sperm counts, sperm motility, sperm morphology, FSH, LH, and testosterone levels had been determined in testes homogenate at the end of the experiment. Rats given malathion alone had significantly lower sperm count, sperm motility, LH and FSH level, and significantly higher abnormal sperm numbers, than the untreated control rats. Administrations of *Melissa officinalis* extract restored all mentioned parameters to the control limits, histologically, *Melissa officinalis* extract treated rat showed normal seminiferous tubules, while malathion group testicular tissues had necrosis, edema in the seminiferous tubules and degeneration of spermatogonia with incomplete spermatogenesis [139].

The effects of *Melissa officinalis* therapy for 10 weeks, on sperm parameters and chromatin structure were studied in varicocelised rat. Sperm parameters and chromatin staining improved in *Melissa officinalis* treatment compared to varicocele and placebo groups ($p < 0.05$) [140].

2.37. *Momordica charantia*

The antifertility property of *Momordica charantia* seeds (400 and 800 mg dry matter/kg bw of the extracts) , and mechanisms underlying these effects were investigated in rats. On day 42, the extracts caused antifertility (P=0.001). It caused significant reductions in diameters of seminiferous tubules and epididymides, spermatid density, daily sperm production and caudal epididymal spermatozoa, sperm motility and viability (P=0.046). Pathological study of seminiferous tubules revealed atrophy, desquamation, pyknosis nucleus and multinucleated giant cell. Plasma cells were evident in three parts of epididymides of rats treated with high dose of the extract. In addition, the high dose of the extract suppressed seminal testosterone level (P=0.001) and plasma testosterone level (P=0.002) [141].

The extracts of seeds of *Momordica charantia* were tested in male mice. Petroleum ether, chloroform and ethanolic extracts of *Momordica charantia* were administered at the dose level of 25mg/100gm bw to the albino mice for 48 days intraperitoneally. All the extracts showed antispermatogenic effect as the number of spermatogonia, spermatocytes, spermatids and spermatozoa were decreased. The increase in the weight of epididymis, prostate gland, seminal vesicle and vas deferens indicated the androgenic property of these extracts [142].

The effect of graded oral doses of methanolic seed extract of *Momordica charantia* on the histology of prostate gland and seminiferous tubules was investigated in rats. The results showed that methanolic extract of *Momordica charantia* seeds caused reversible histological alterations in the prostate and testes of the rats. The extract caused dose-related alteration in the cytoarchitecture of seminiferous tubules with marked reduction in spermatogenic series. The prostate gland showed dilatation as well as increased intraluminal secretions with increasing dose. In addition, there was a significant recovery of prostate tissue as the sections were similar to their control counterpart [143].

Morphological changes in sperm of albino rats was associated with alcohol seed extract from *Momordica charantia*. These included considerable changes in the shape and size of the sperm head and in the mid-region of the tail, with formation of a balloon-like cytoplasmic droplet [144].

2.38. *Musa paradisiaca*

The effect of oral administration of the aqueous extract of *Musa paradisiaca* root (25, 50, and 100 mg/kg bw, for 14 days) on the testicular function parameters was investigated in male rat testes. The extract significantly increased ($p<0.05$) the relative testes weight , total protein, sialic acid, glycogen, cholesterol, activities of alkaline phosphatase, γ-

glutamyltransferase, acid phosphatase, and the concentration of testicular testosterone. However, the extract decreased the concentrations of both serum LH and FSH [145-146].

The effects of the unripe fruit of *Musa paradisiaca* (500 and 1000 mg/kg, for 28 days) on the testis and testosterone levels were studied in male rats. The testis of the treated groups showed more rapidly dividing cells, more population of sperm cells, and also showed more positivity for Feulgen staining and PAS reaction. Both serum and testicular testosterone levels were reduced. Serum testosterone was significantly lowered in the animals given the low dose (0.67 ± 0.03 ng/ml),compared to those given high dose (0.85 ± 0.02 ng/ml) and the control animals (1.88 ± 0.15 ng/ml) ($p < 0.05$) [147].

The effects of administration of mature green fruits of *Musa paradisiaca* (500 and 000 mg/kg/day) on the semen quality were studied in adult male rats. Significant increment in the semen parameters was recorded in rats received the lower dose of the plantain flour, but rats received the high dose showed marked and very significant reduction in sperm cell concentration and percentage of morphologically normal spermatozoa [148].

The effects of *Musa paradisiaca* (orally, 250 and 500 mg/kg/day, for one month) on semen quality was studied in adult mice male. A significant increment in the semen parameters was recorded in group that received the lower dose of *Musa paradisiaca* fruit flour, but those male received the high dose had marked and very significant increase in sperm cell concentration and percentage of morphologically and histological normal spermatozoa [149].

2.39. *Nicotiana tabacum*

The aqueous extract of *Nicotiana tabacum* (20 and 30mg/kg) administered for a period of 21 days in rats caused significant decrease in sperm motility and concentration and decreased spermatogenic cells in the histological sections of the testis [150-151].

2.40. *Nigella sativa*

The ethanol extract of seeds showed antifertility effect in male rats [152]. The aqueous extract of *Nigella sativa* significantly ($P < 0.05$) inhibited both basal and LH-stimulated *in vitro* testosterone secretion of mice Leydig cells *in vitro.* At a dose of l000 µg, the extract inhibited 52% of basal testosterone and 97% of LH-stimulated testosterone [153]. However, on the other hand, alcoholic extract of *Nigella sativa* increased the production of viable and motile sperm cells, enhanced epididymal sperm reservation, weight gaining of reproductive organs, blood testosterone density, gonadotropins content, amount of mature Leydig cells, and fertility indexes compared to the control group in male rats . The results also revealed that *Nigella sativa* affected oxidative phosphorylation enzymes and increase sperm motility [154].

The modulatory effects of daily consumption of *Nagilla sativa* oil (0.4 ml) on antioxidant activity, sperm quality and pituitary-testicular axis were studied in adult male rats. Malondialdehyde level was significantly decreased accompanied with an increases in glutathione peroxidase and glutathione in rats treated with *Nigella sativa* oil. Rats also showed an increase in catalase activities accompanied with an increase in sperm concentration, the oil also showed insignificant effect on testosterone, inhibin-B, FSH and LH levels in comparison with control group [155].

Treatment of infertile Iranian men with 2.5 mL of *Nigella sativa* oil twice a day for two months enhanced sperm count, motility and morphology and semen volume [156].

2.41. *Ocimum basilicum*

Male rats received Ocimum basilicum extract 1.5 g/kg bw, for 40 consecutive days showed that the extract significantly increased serum testosterone, sperm concentration, percentage of sperm viability and sperm motility ($p<0.05$) [157-158].

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 [159].

The protective effect of *Ocimum basilicum* aqueous extract (200 mg/kg/day, po) on doxorubicin/irradiation-induced testicular injury was studied in rats. The extract significantly decreased testicular levels of nuclear factor-kappa B and B-cell lymphoma-2 (Bcl2)-associated protein X, along with caspase-3 immunohistochemical staining. In addition, the

extract elevated testicular total antioxidant capacity, nuclear erythroid-related factor-2, Bcl2 and testosterone contents and Ki-67 immunohistochemical staining. These changes were also accompanied by restoration of testicular architecture [160].

The protective effect of *Ocimum basilicum* extract was studied in apoptosis in testis of rats exposed to electromagnetic field (EMF) at 50 Hz for 40 consecutive days. Compared to the control group, apoptotic cells percentage decreased following administration of *Ocimum basilicum* extract (1.5 g/kg body weight). Exposure to 50 Hz of EMF caused a significant increase in the apoptotic cells percentage. When 50 Hz of EMF was administrated together with *Ocimum basilicum* extract (1.5 g/kg body weight), apoptotic cells percentage was significantly decreased ($p<0.05$) from 18.12±1.05 to 10.05±0.01 in spermatogonia, and decreasing significantly ($p<0.05$) from 20.11±0.05 to 9.05±0.05 in primary spermatocytes, respectively; vein congestion significantly decreased ($p<0.05$) from 8±0.03 to 0.5 ±0.01 *[161]*.

2.42. *Olea europaea*

The protective effect of olive leaves extract (250 and 500 mg/kg for 9 weeks) was investigated in diabetes-induced adverse reproductive effects in male rats. Streptozotocin significantly decreased serum levels of insulin, testosterone, follicle stimulating hormone and luteinizing hormone with marked reductions in testicular antioxidants with elevated malondialdehyde (MDA) parallel with deterioration of the testicular histoarchitecture and epididymal sperm characteristics. Administration of glibenclamide or olive extract significantly recovered all these parameters in STZ-diabetic rats. Olive extract showed greater glycemic improvement and testicular protection than glibenclamide with the highest percentage protection exhibited by the high dose of the olive extract. The extract also significantly induced testicular steroidogenesis in diabetic rat as evidenced by elevated P450 scc and 17β-HSD mRNA expression [162-163].

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 luteinizing and follicle-stimulating 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 [164].

2.43. *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 [165-166].

2.44. *Origanum vulgare*

The influence of *Origanum vulgare* extract (0.18 g/kg bw for 3 weeks) on male fertility was studied in normal and alloxan diabetic mice, via estimation of testosterone, LH and FSH level, sperm viability, activity, motility and sperm abnormalities. Its effects on GOT, GPT, alkaline phosphatase and lipid profile status were also studied. Testosterone, LH, FSH levels and sperm motility were increased with a decreased in dead sperms, sperm abnormalities, GOT, GPT, alkaline phosphatase and lipid profile, in extract treated group in comparison with alloxan diabetic mice [166-167].

2.45. *Passiflora incarnata*

The aphrodisiac effect of the methanol extract of leaves of Passiflora *incarnate* was evaluated in mice by observing the mounting behaviour. The extract possessed significant aphrodisiac behavior (mounting behaviour) in male mice at all doses (75, 100 and 150 mg/kg). At 100 mg/kg dose, the mountings were calculated about 95 min after the administration of the test extracts [168].

A novel tri-substituted benzoflavone moiety (BZF) isolated from *Passiflora incarnata* has been reported to increase libido, sperm count, and sexual fertility in 2 years old male rats at 10 mg/kg, orally. BZF moiety (10 mg/kg, orally for 30 days) was evaluated against chronic ethanol- and nicotine-induced decrease in libido, sexual fertility and mating efficiency in healthy male rats. At the end of treatments, it was observed that rat groups given alcohol, nicotine, or both had no libido (evaluated by mounting behaviour), declined sperm count, and consequently no mating efficiency or fertility (upon pairing with pro-estrus female rats). However, the rats which were given 10 mg/kg BZF along-with

nicotine, alcohol, and alcohol-nicotine combination exhibited significant libido-oriented mounting behaviour, increased sperm count, and increased fertilization potential [169].

Chronic administration (30 days) of Delta(9)-tetrahydrocannabinol (THC, 10 mg/kg, orally) caused significantly loss of libido (mounting behaviour with non-oestrous female rats), decrease in sperm count, and number of impregnated pro-estrous female rats. Co-administration of benzoflavone moiety isolated from *Passiflora incarnata* (BZF, 10 and 20 mg/kg, orally) afforded significant protection against the chronic-THC-induced decrease in libido, mating performance and fertility during 30-day experimental regimen. The 20 mg/kg dose of BZF exhibited better results [170].

2.46. *Peganum harmala*

Peganum harmala induced significant decrease in the weight of reproductive organs, sperm motility and density in cauda epidydimides and testicular ducts were. The treatments remarkably altered the histoarchitecture of testes. Spermatogenesis was inhibited at both primary and secondary spermatocyte stages. Epididymides showed reduced number of spermatozoa. Lumen of vas deferentia were devoid of sperms. The secretary activities of seminal vesicle and ventricular prostate were also reduced. Testosterone and FSH levels were decreased in treated rats, with a decrease in the number of female rats impregnated by males receiving treatment and a decrease in the implantation sites and viable fetuses number [171].

2.47. *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 [172].

The effects of the ethanol extract (140, 280, and 560 mg/kg, for 34 days) of date palm fruit in khalal stage, on fertility were investigated in male mice compared with propolis. Ethanol extract of khalal date fruit and propolis increased sperm count, sperm motility, and weight of testes. Ethanol extract of khalal date fruit can increase sperm quality higher than propolis [173].

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 [174].

The therapeutic potential of date palm pollen extract (0 or 40 mg/kg, orally, once daily for 56 consecutive days) in averting the reproductive damage induced by $CdCl_2$ was studied in male rats. Cd exposure caused significant reproductive damage via reduced weight of the reproductive organs, decreased sperm count and motility, increased rates of sperm abnormalities, increased oxidative stress (increased malondialdehyde and decreased reduced glutathione levels), induced histological alterations (necrosis, inefficient to completely arrest spermatogenesis and a reduced Johnsen's score) and decreased serum testosterone level. Date palm pollen extract restored spermatogenesis and attenuated the toxic effects of Cd on the reproductive system to the levels observed in the control animals [175].

The effects of date palm pollen suspensions on the glycemic state, testicular dysfunctions, oxidative stress and antioxidant defense system were studied in streptozotocin-induced diabetic male rats. The streptozotocin -induced diabetes significantly increased blood glucose levels and testicular NO and MDA levels parallel with disrupted testicular and pancreatic histological architecture and integrity. It also significantly decreased body weight, testis and pancreas weights, serum insulin, testosterone, LH and FSH as well as sperm count, motility and viability. The administration of date palm pollen suspensions caused significant recovery of the the mentioned parameters. These improvements were associated with enhancement of the testicular antioxidant system manifested by an increase in the GSH, GST, GPx and SOD activities in diabetic rats [176].

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 [177-178].

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 [179].

The protective effect of the aqueous extract of Date fruit, against toxic effect of atrazine on testes was studied in rats. Atrazine produced a significant decrease in the testicular weight , sperm count, sperm motility and sperm with normal morphology. It also decreased the activity level of GPx , SOD and CAT. Furthermore, a significant increase in testicular lipid peroxidation was observed in Atrazine treated group compared to control group. Concomitant treatment with Date fruit extract restored the level of SOD, CAT, GPx and reduced the testicular lipid peroxidation. Testicular weight, sperm count, sperm motility and percentage of abnormal sperm were also normal in groups treated with atrazine and the extract. The extract was also capable of reducing the level of lipid peroxidation in the testis [180].

The prophylactic effect of date palm fruit extract (4 mg/kg for 35 days) against formaldehyde -induced testicular toxicity was studied in male mice. The formaldehyde administration increased the sperm morphological anomalies and reduced the sperm count, viability and motility, and testosterone level compared to the control group. Formaldehyde also induced histological changes (destruction of germinal epithelium and vacuolization of the tubules). The date palm fruit extract consumption before formaldehyde administration partially ameliorate the reduced testosterone and deteriorated testicular parameters caused by formaldehyde [181].

The effect of *Phoenix dactyliferia* pit powder on nicotine-induced spermatotoxicty was investigated in adult mice. Partial recovery from nicotine-induced spermatotoxicity was recorded after withdrawal of nicotine treatment, whereas near normal restoration was achieved after administration of date palm pit powder after the stoping of nicotine [182].

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. Levels of lipid peroxidation and SOD and CAT activities were increased, while activity of GPx and GSH levels were decreased. Pretreatment with the extract was effectively alleviated the oxidative stress induced by dichloroacetic acid and restored the testicular parameters to normal values [183-184].

2.48. *Polygonum aviculare*

The protective effect of *Polygonum aviculare* against electromagnetic field (EMF) on testis was studied in mice. The results showed that testes was negatively affected by EMF and the extract reduced the harmful effects. Furthermore, EMF can reduce motility of sperm and treatment with *Polygonum aviculare* improved sperm quality after EMF exposure [185-186].

2.49. *Portulaca oleracea*

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 [187].

2.50. *Rhus coriaria*

The effects of the hydro-alcoholic extract of *Rhus coriaria* seeds on the reproductive system was studied in nicotinamide-streptozotocin-induced type-2 diabetic mice. Body and testicular weight, sperm count and viability, and serum luteinizing hormone, follicle-stimulating hormone and testosterone levels were significantly lower in the diabetic mice ($p<0.05$). The diabetic mice treated with 400 mg/kg of the hydro-alcoholic extract of *Rhus coriaria* seeds recovered from these reductions. Furthermore, glibenclamide also alleviated hormonal and sperm count depletion in diabetes-induced mice [188].

2.51. *Ricinus communis*

The antifertility effects of ethanol 50% extracts of *Ricinus communis* was studied in male rats. The extract reduced the epididymal sperm counts. Induced alteration in the motility, mode of movement and morphology of the sperms. The reductions in the fructose and testosterone levels could be the causes of reduction of reproductive performance. The antifertility effect of *Ricinus communis* was completely reversible on withdrawal of the drug [189].

The effect of methanol extract of *Ricinus communis* seed on male reproductive functions was studied in rats. The extract caused significant decrease in the weight of the reproductive organs, sperm functions and serum levels of testosterone. There was disorganization in the cytoarchitecture of the testes, disruption of the seminiferous tubules and erosion of the germinal epithelium. The number and weight of litters of the extract treated rats were decreased significantly. The extract caused no changes in liver, kidney, heart or body weights in male rats [190].

The effectivness of crude stem bark extracts of *Ricinus communis* as male contraceptive were studied *in vitro* with human sperm sample. The petroleum ether extract, ethyl acetate extract, acetone extract and lyophilised aqueous extract were added to fresh human semen in 1:1 volumetric ratio. Hypo-osmotic swelling test (HOS), Nuclear chromatin decondensation test (NCD) and Acrosomal status and function test (AFT) were also carried out with the aqueous extract. The sperm immobilisation effects of the extract appeared immediately in a dose-dependent manner when the samples were treated with four different extracts of the extract. At a concentration of 100mg/ml, 100% sperms lost their progressive motility. At a concentration of 300 mg/ml, 100% became immotile when treated with aqueous extract. There was 88% morphological deformities in sperm sample due the effect of aqueous extract when they were tested for HOS and 91% sperms behaved against NCD as compared to control group. Also there was a distinct decline in AFT with increase in dosage concentration [191].

The effect on spermatogenesis of a 62 kDa protein (Rp) isolated from 50% ethanolic extract of the root of *Ricinus communis* was investigated in male mice. The study showed that sperm motility and count were decreased significantly in the treated group as compared to the control. The fertility index of the treated groups was reduced by 100%. The activity of HMG Co A reductase and cholesterol were increased significantly in the treated group. The testicular activities of 3βHSD, 17βHSD, glucose 6-phosphate dehydrogenase and malic enzyme and the level of serum testosterone were decreased significantly in the treated group. The expression of 3βHSD and 17βHSD were decreased and the expression of StAR increased significantly in the treated group as compared to the control. Rp impaired spermatogenesis *in vivo* by suppressing the production of testosterone [192].

2.52. *Rosa damascena*

Damask rose is an herbal medicine that increases libido as recommended in traditional medicine. The effect of damask rose extract (200 and 400mg/kg) on serum levels of sex hormones was investigated in male rats. The serum levels of FSH, LH and testosterone were significantly increased in the groups receiving 200mg and 400mg/kg damask rose extract compared to the control group ($P < 0.05$) [193].

The protective effects of aqueous extract of *Rosa damascena* on the male reproductive system of mice were examined following formaldehyde (FA)-induced testicular damage. Formaldehyde administration significantly decreased serum testosterone level, testicular weight/volume, tubular diameter and sperm characteristics compared to the control group. The extract (40 mg/kg) significantly improved serum testosterone level, testicular weight/histological structure, tubular diameter, Leydig cell number and epididymal sperm characteristics in comparison to its lower doses (20 mg/kg) and the control group [194].

2.53. *Saccharum officinarum*

The effects of *Saccharum officinarum* molasses, on reproductive functions were studied in testicular cells cultured in molasses fractions. Major constituents from molasses methanol and aqueous extracts were lupeol (87.2%) and diethyl phthalate (47.4%), respectively. Testicular cell proliferation increased in methanol extract (2.86±0.22) compared to control (1.89±0.18). Lupeol and diethyl phthalate decreased cell proliferation (1.07±0.11 and 1.11±0.17) respectively, compared to the control (1.89±0.18). Testicular cell testosterone biosynthesis was reduced by the two extracts, lupeol and diethyl phthalate compared to the control [195].

The effect of *Saccharum officinarum* juice (1.0, 3.2 and 10.0 m/kg/day of fresh *Saccharum officinarum* juice once daily for 8 weeks via gavage) on reproductive functions was investigated in male rats. The 10.0 ml/kg juice caused a significant increase in testosterone level and sperm count, and it also increased the percentage of aberrant sperm and decreased sperm viability. *Saccharum officinarum* juice impaired the histological integrity of the testes and

epididymides. Thus, *Saccharum officinarum* juice adversely altered the reproductive functions of male Wistar rats by reducing sperm quality and disrupting testicular architecture [196].

2.54. *Sesbania sesban (syn: Sesbania aegyptiaca)*

The spermicidal activity of oleanolic acid 3-β-D-glucuronide (OAG), an active principle isolated from root extracts of *Sesbania sesban*, was studied using highly motile rat sperm. The minimum effective concentration of OAG was 50 mcg/mL. More than 97% of the OAG-treated sperm lost their hypo-osmotic swelling responsiveness in a dose-dependent manner. The transmission electron microscopy and sperm membrane lipid peroxidation revealed that OAG affected the sperm membrane integrity. OAG declined fertility to zero, but nonmutagenic [197].

The long term effect of supplementation with the leaves of *Sesbania sesban* on testicular histology was studied in sheep and goats . All animals were provided with unchopped teff (Eragrostis tef) straw ad libitum and were supplemented sesbania (200 or 400g) leaves for a period of 6 months. At the end of the experimental period, *Sesbania sesban* induced necrosis of the seminiferous tubules and tubular degeneration [198].

2.55. *Spartium junceum*

The effect of crude aqueous extract of *Spartium junceum* twigs on male reproductive system was studied in rats (1g/kg, for 8 wks) and rabbits (1 and 2 g/kg, for 28 days). Histologically, the testes of the treated rabbits showed sever malformations. Seminiferous tubules showed the presence of several areas depleted of immature germinal cells, the presence of giant multinucleated spermatids as well as a low number of late spermatids and spermatozoa. None of the females mated with treated rabbit males became pregnant. In rats, the 8 weeks treatment didn't affected sexual behavior, otor activity or body and reproductive organs weight. A significant decrease in the number of epididymal spermatozoa ($31.3x10^6$/ ml and $112.9\ 3x10^6$/ ml in control) and 25% of males treated by high dose showed azospermia. The pregnancy rate, the number of pups and their viability were significantly decreased [199].

Male adult rabbits and rats treated with *Spartium junceum* showed a significant decrease in fertility, demonstrated by a lower number of pregnancies. The target of the drug seems to be the acrosomal protease system, the activity of which appears greatly reduced, while the morphology of testicular cells and epididymal spermatozoa is only partially affected. The antifertility effect is completely reversible [200].

injections of extracts of *Spartium junceum* intraperitoneally in adult male rats reduced the fertility and acrosin enzyme activity. The effect on acrosin enzyme activity could be divided into two phases: in the first stage a significant increase in proteolytic activity was observed and in the second stage, there was a general decrease of up to 50% in enzyme hydrolytic properties. A significant decrease in another acrosomal protease, benzamidine-resistant protease was also noted [201].

2.56. *Stachys lavandulifolia*

The effects of hydroalcoholic extract of *Stachys lavandulifolia* (50, 100, 200 mg/kg, ip) on the hormonal pituitary-gonadl axis and testis tissue changes were investigated in adult male rat. A significant increased concentration of LH and FSH hormones was observed in experimental groups receiving the maximum extract in compared with the control and shame groups . Concentration of testosterone hormone in maximum dose of extract and DHT hormone in intermediate and maximum doses of extract showed a significant decrease compared to the control and shame groups. The histological study of the number of spermatocyte cells in seminiferous tubules of the testis of the maximum dose showed a significant reduction compared to the control and shame groups [202].

2.57. *Tagetes patula*

The anti-chronic nonbacterial prostatitis (CNP) mechanism of *Tagetes patula* was investigated by metabolomics and network pharmacology. The flavonoids and polysaccharides of *Tagetes patula* could alleviate prostatitis by improving the level of DHT, reducing the secretion of PSA and TNF-α. Besides, both could enhance Na^+/K^+ -ATPase activity, decrease the O_2 consumption, CO_2 production, heat production, energy expenditure of rats and promote respiratory exchange ratio of rats. The mechanism was associated with tryptophan metabolism and energy pathway [203].

2.58. *Taraxacum officinale*

The effect of the aqueous extract of *Taraxacum officinale* on male reproductive activity was investigated in rat. The administration of the aqueous extract resulted in a significant decrease in testis weight in the extract treated groups in comparison to the control group but had no effect on body or organ weight. The extract decreased sperm count, motility

and normal morphology, pregnancy rate and diameter and wall thickness of seminiferous tubules. Also, caused distortion of morphology of the seminiferous tubules with arrest in spermatogenesis. In addition, the percentage of sperm with damaged chromatin integrity was significantly higher in extract treated group [204].

The effect of the aqueous extracts of the whole plant and leaves of *Taraxacum officinale* on male reproductive performance was studied in rats. Oral administration of *Taraxacum officinale* (whole plant and leaves aqueous extract) caused a significant decrease in testis and seminal vesicle weight, a reduction in serum testosterone concentration, impaired sperm parameters, and a decrease in pregnancy parameters. Testicular histology of treated rats showed structural changes such as hypoplasia of germ cells, reduction in the thickness of germinal epithelium, arrest of spermatogenesis at spermatid stage (late maturation arrest) and reduction in the number of Leydig cells [205].

However, Chung et al., found that *Taraxacum officinale* extract enhanced steroidogenesis in mouse Leydig cells and increase testosterone production. The steroidogenic effects was investigated by determination of the levels of enzymes associated with steroidogenesis, such as the steroidogenic acute regulatory protein (STAR), CYP11A1, and translocator protein (TSPO) in the mitochondria and CYP17A1 in the smooth endoplasmic reticulum, in mouse Leydig cells. The extract significantly increased the mRNA and protein levels of steroidogenic enzymes, thereby increasing the testosterone levels in mouse Leydig cells [206].

2.59. *Teucrium polium*

The protective effects of *Teucrium polium* extract on CCl_4-induced male reproductive system damage was investigated in rats. CCl_4 caused significant alteration of sperm parameters in epididymal and testicular tissues, a decrease in hormone levels, and a decrease in antioxidant enzymes such as superoxide dismutase, catalase and glutathione peroxidase in testicular tissues. A noteworthy increase in malondialdehyde (MDA) level was induced in CCl_4 -treated rats with some histopathological damages on the testes compared with control group. Remarkable ameliorations were observed in all the parameters, following the administration of CCl_4 with *Teucrium polium*, and with vitamin C used as a positive control, when compared with CCl_4 alone [207].

In another study, the effect of the hydroalcoholic extract of *Teucrium polium* extract administration on spermatogenesis and testicular structure was investigated in streptozotocin induced diabetic rats. The extract possessed a protective effect on diabetes-induced testicular damage and serum testosterone concentration. The effect was attributed to antioxidant and antidiabetic properties of the extract [208].

2.60. *Thevetia neriifolia*

The antifertility potential of *Thevetia peruviana* stem bark methanol extract (100 mg/rat/day, orally) was studied in male albino rats. The extract didn't cause any significant reduction in body weight, while the weight of reproductive organs reduced significantly. A significant fall in the total protein and sialic acid content of the testes, epididymides, seminal vesicle and ventral prostate, as well as in the glycogen content of testes was observed; however, cholesterol was increased significantly. The extract also caused a decline in spermatogenic elements, (preleptotene and pachytene spermatocytes, secondary spermatocytes, round spermatids). At this dose level Leydig cell nuclear diameter, seminiferous tubular diameter and Sertoli area were significantly reduced ($p < 0.001$). The reduction in sperm density and motility resulted in 18% residual fertility [209].

An *in vitro* spermicidal effect of aqua-methanolic (2:3) extract of *Thevetia peruviana* leaves was evaluated on human spermatozoa in a dose-dependent manner (20, 40, 80 and 160 mg/ml) at a 1:1 ratio. The sperm motility was affected immediately at a dose of 20 mg/ml and reduced gradually at doses of 40 and 80 mg/ml of *Thevetia peruviana* extract. Complete immobilisation of spermatozoa was observed at 160 mg /ml dose of this extract treatment within 5 min. 50% immobilisation of spermatozoa (EC50) was observed at 28 mg/ml dose of *Thevetia peruviana* extract within 20 s. The sperm viability decreased significantly at a higher concentration of extract, and all spermatozoa were found to be non-viable after 10 min when treated with 160 mg/ml dose of *Thevetia peruviana* extract. The hypo-osmotic swelling and nuclear chromatin decondensation of spermatozoa also reduced gradually at a higher concentration of extract. The percentage of DNA damage in spermatozoa was four times greater than in the control group [210].

2.61. *Tribulus terrestris*

The effect of the crude extracts mixture of (*Tribulus terrestris*, *Phoenix dactylifera* and *Nasturtium officinale*) on semen quality, sex hormones and reproductive performance was studied in mature male mice. A group of male mice was given 150 mg/kg/day of the powder of the plants mixture with the food for 4 weeks and another three groups of animals each given intraperitoneal injection from each of the aqueous and ethanolic extracts with a doses 75, 150, and 300mg/kg/day

for 2 weeks. A remarkable increase in sperm concentration and motility with a decreased abnormal morphology was obtained in the treated groups. A significant increase in the LH, FSH and testosterone levels were recognized in most groups. The results of mating of untreated females with treated males of the four experimental groups revealed a decreased gestation period and an increased litter size. The ethanolic extract being the more effective extract in all parameters [211].

The effects of extract of *Tribulus terrestris* on body weight and testicular development were studied in prepubertal rats. Pups received *Tribulus terrestris* extract showed significant increase in mean body and paired testes weight without significant effect on the mean relative tissue body weight index. Histological investigation of the testes showed a significant increase in seminiferous tubules containing early spermatids in the treated group compared to that of control. The mean diameter of seminiferous tubules in the treated group was also noticeably increased. Spermatids of the treated group were at acrosomal phase of spermogenesis, whereas, those of control group were at Golgi phase, indicating that spermatogenesis was present at an advanced stage in the treated group [212].

The effect of supplementing the semen with *Tribulus terrestris* aqueous extract on semen quality was studied by using canine sperm. After 48 and 72 hr of liquid storage, total and progressive motilities were greater in the group with the 40.00 μg/ml *Tribulus terrestris* aqueous extract concentration than the control group. Compared to the control group, the group with the 40.00 μg/ml extract concentration exhibited superior motility and viability. The percentages obtained from the hypo-osmotic swelling test were much greater. In contrast to the control group, DNA integrity was poorer in the 40.00 μg/ml extract. After 72 hr of storage, the group with 40.00 μg/ml extract had lower malondialdehyde levels but considerably greater total anti-oxidant capacity, superoxide dismutase, glutathione peroxidase and catalase levels than the control groups [213].

The effects of adding of *Tribulus terrestris* extract to the forage of lambs for 40 days, on semen parameters and sexual behavior were investigated. *Tribulus terrestris* extract improved semen quality of rams (the count of spermatozoids, time of viability and motility of sperms increase). The great number of born lambs after the use of treated rams for insemination confirms high fertility of their semen. All experimental rams manifested a good libido and active sexual behavior [214].

The effects of *Mucuna pruriens, Tribulus terrestris* and *Withania somnifera* on sexual functions, serum biochemical parameters, oxidative stress and levels of NF-κB, Nrf2, and HO-1 in reproductive tissues were studied in rats. All of the extracts were significantly effective in sexual functioning and antioxidant capacity and *Tribulus terrestris* showed the highest effectiveness. Serum testosterone levels significantly increased in *Tribulus terrestris* and *Withania somnifera* groups in comparison to control group. *Tribulus terrestris* was able to reduce the levels of NF-κB and increase the levels of Nrf2 and HO-1 to a much greater extent than other herbs [215].

The effects of *Tribulus terrestris* extract on endocrine sensitive organs was studied in intact and castrated male rats as well as in a post-menopausal rat model using ovariectomized females. Neither dehydroepiandrosterone nor *Tribulus terrestris* extract was able to stimulate androgen sensitive tissues like the prostate and seminal vesicle in both intact and castrated male rats. In addition, administration of *Tribulus terrestris* to intact male rats for 28 days didn't change serum testosterone levels and didn't produce any change in the fecal excretion of androgenic metabolites. However, a slight increase in the number of homogenization-resistant spermatids was observed in rats treated with 11 mg/kg/day of extract. In ovariectomized females, the extract didn't produce any stimulatory effects in uterine and vaginal epithelia [216].

The effect of *Tribulus terrestris* hydroalcoholic extract administration on the serum level of glucose and reproductive parameters was studied in streptozotocin induced- diabetic male rats. *Tribulus terrestris* extract caused significant reductions in the levels of blood glucose while increased sperm motility, sperm count and seminiferous tubules diameter, percentage of sperms with normal morphology, level of testosterone hormone and final body weight compared with diabetic group [217].

The protective effect of *Tribulus terrestris* hydroalcoholic extract against cisplatin-induced cytotoxicity on sperm parameters was studied in mice. Cisplatin caused a reduction in the weight of body and testes, sperm parameters and increased level serum of NO significantly compared to the control group, while in the groups treated with *Tribulus terrestris*, the weights of body and testes, sperm parameters, seminiferous tubules diameter were significantly higher compared with cisplatin group, but serum level of NO did not show significant differences [218].

The protective effects of the fruit extract of *Tribulus terrestris* was investigated on the metronidazole induced alterations in spermatogenesis, sperm count, testicular functions, and oxidative stress in male mice. Metronidazole caused marked

alterations in the testicular weight, spermatogenesis, activities of antioxidant enzymes, lactate dehydrogenase, alkaline phosphatase, and the level of LPO. The epididymal sperm count also declined significantly in MTZ-treated group. These changes were partially restored following co-administration of metronidazole with the extract 100 mg/kg/day. However, in the mice co-administered with metronidazole with the extract 200 mg/kg/day, the changes reverted back completely, similar to that of the controls [219].

Tribulus terrestris extract alleviated long-term copper (Cu) overload-induced testicular dysfunction in rats. Excess Cu intake resulted in Cu overload coupled with a significant elevation in systolic blood pressure and serum angiotensin II levels along with a reduction in serum nitric oxide level. The extract treatment led to an alleviation of such deleterious effects and protected the testes against Cu-overload-elicited zinc depletion and oxidative stress. The relative weights of testes, serum levels of testosterone and luteinizing hormone; the expression of steroidogenic genes; the protein levels of angiotensin II type 1 receptor and angiotensin converting enzyme 1, and its activity, they were significantly reduced by the extract [220].

The effect of *Tribulus terrestris* containing protodioscin as an aphrodisiac was investigated on sexual behavior and intracavernous pressure measurements in rats. Treatment significantly increased body weight, intracavernous pressure and mount frequency, and significantly decreased mount latency and postejaculatory interval. These effect could be secondary for the androgen increasing property protodioscin [221-222].

The effect of oral *Tribulus terrestris* extract was investigated on the isolated corpus cavernosal tissue of rabbits and the mechanism by which protodioscin, a constituent of *Tribulus terrestris*, exerts its pharmacological effects was studied. Protodioscin had no effect on the isolated corpus cavernosal strips. The relaxant responses to electrical field stimulation, acetylcholine and nitroglycerin in noradrenaline precontracted tissues from treated groups showed an increase in relaxation in a concentration dependent nature compared to that of the tissues from control group. The relaxant responses to acetylcholine, nitroglycerin and electrical field stimulation by more than 10%, 24% and 10% respectively compared to their control values and the lack of such effect on the contractile response to noradrenaline and histamine indicate that protodioscin has a proerectile activity. The enhanced relaxant effect observed is probably due to increase in the release of nitric oxide from the endothelium and nitrergic nerve endings, which may account for its claims as an aphrodisiac [223].

A concentration-dependent relaxation effects of the extract on the corpus cavernosum were detected in the organ bath study. Relaxation of the corpus cavernosum by the extract was inhibited in both an endothelium-removed group and an L-arginen methyl ester pretreatment group. The intracavernous pressure measured after oral administration of the extract for 1 month was higher than that measured in the control group, and a significant increase in cAMP was observed in the extract treated group [224].

The effect of *Tribulus terrestris* extract was evaluated in rabbit and rat to identify its usefulness in the management of erectile dysfunction (ED). The extract was administered intravenously, as a bolus dose of 7.5, 15 and 30 mg/kg, in rabbit and rat for acute study. While they were treated with 2.5, 5 and 10mg/kg of the extract orally for 8 weeks, for chronic study. In addition, castrated rats were treated either with testosterone cypionate (10mg/kg, subcutaneously; biweekly for 8 weeks) or the extract orally (5mg/kg daily for 8 weeks). In both species, 7.5mg/kg extract significantly increased testosterone (52%), dihydrotestosterone (31%) and dehydroepiandrosterone sulphate (29%) [225].

The incubation of human semen with 40 and 50 µg/ml of *Tribulus terrestris* extract significantly enhanced total sperm motility, number of progressive motile spermatozoa, and curvilinear velocity over 60 to 120 minutes' holding time. Furthermore, viability was significantly enhanced by using *Tribulus terrestris* extract [226].

The effect of the *Tribulus terrestris* extract on motility and vitality of human sperms after cryopreservation was studied. After cryopreservation, a significant improvement in spermatozoa viability was observed in groups in which semen was supplemented by extract doses (20, 40, and 50 µg/ml) after the freeze-thaw process [227].

Protodioscin, a saponin obtained from the aerial parts of *Tribulus terrestris* increased the serum dehydroepiandrosterone levels in men, resulting in improved self-esteem and general well-being. It acts by stimulating the production of the enzyme 5-α- reductase, which converts testosterone into dihydrotestosterone, which has a fundamental role in the formation of blood cells and muscular development [228].

Testosterone and LH levels, as well as DHEA level, increased after the treatment of erectile dysfunction with protodioscin for 30 to 90 days in men [229].

A clinical trial was performed to investigate the influence of *Tribulus terrestris* extract (20 and 10 mg/kg body, for 4 weeks) on androgen metabolism in young males. There was no significant difference between *Tribulus terrestris* supplemented groups and controls in the serum testosterone, androstenedione or luteinizing hormone. Accordingly, *Tribulus terrestris* steroid saponins possess neither direct nor indirect androgen-increasing properties [230].

A double-blind, randomized, placebo-controlled study was performed to determine the effect of *Tribulus terrestris* granules for 60 days in patients with oligozoospermia. The granules provided a significant result in weakness (48.14%), and loss of penile erection (6.03%), loss of penile rigidity (9.41%), premature ejaculation (6.12%), lack of orgasm (9.76%), and performance anxiety (8.69%). The results were insignificant ($P > 0.05$) in post-act exhaustion (1.33%), frequency of coitus (2.08%), dryness of mouth (6.66%), and depression (22.22%) [231].

A clinical trial was carried out to evaluate the effects of *Tribulus terrestris* (oral, Androsten®, contained 250 mg of *Tribulus terrestris* dried extract per capsule) on semen quality and physiological parameters of infertile men. The treatment decreased the percentage of body fat and increased the lean mass significantly. The treatment increased dihydrotestosterone levels, enhanced sperm concentration, motility and liquefaction time. Protodioscin, the main phytochemical agent of the Tribulus genus, acts on sertoli cells, germ cell proliferation and growth of seminiferous tubules. It converted testosterone into dihydrotestosterone, which played an important roles in male functions [232].

2.62. *Trigonella foenum-graecum*

The effect of a standardized *Trigonella foenum-graecum* extract (Testofen, two tablets, 600 mg/ day, for 6 weeks) on male libido (sexual drive, urge or desire) was investigated in a double blind randomized placebo controlled study performed on 60 healthy males aged between 25 and 52, without erectile dysfunction. The primary outcome measure was the DISF-SR (male) self-administered QOL total score and the four domain scores. The secondary outcome was specific quality of life parameters. Testofen had an overall positive effect on physiological aspects of libido. In particular, there was a significant increase in the subdomains of sexual arousal and orgasm. Testofen had a positive effect on QOL in self-reported satisfaction with muscle strength, energy and well-being but did not have an effect on mood or sleep. Serum prolactin and testosterone levels remained within the reference range [233].

The anabolic and androgenic activity of the furostanol glycosides fraction of *Trigonella foenum-graecum* was studied in immature castrated male rats. The furostanol glycosides fraction (35 mg/kg, orally) and testosterone (10 mg/kg, sc, biweekly) increased the weight of the levator ani muscle as well as body weight. The furostanol glycosides fraction (10 or 35 mg/kg po) did not change the testosterone level in castrated rats. Histopathological examination of the testis of non-castrated rats treated with furostanol glycosides fraction (10, 35 mg/kg po) showed normal architecture of the testis. The furostanol glycosides fraction (35 mg/kg po) showed anabolic activity without androgenic activity [234].

2.63. *Tropaeolum majus*

The effect of the hydroethanolic extract of the flowers and leaves of *Tropaeolum majus* (250 mg/kg daily, orally, for 4 weeks) on the male reproductive system was studied in male albino rats. On day 10 post-treatment the serum testosterone levels in animals received flowers and leaves extract were significantly ($p < 0.05$) lower (0.935 ± 0.333 and 0.86 ± 0.26, respectively) than that of the control group (3.75 ± 0.35). Serum FSH, LH and sperm count of rats received leaves and/or flowers extracts were significantly ($p < 0.05$) higher up to 30 day post treatment than the control group. The serum level of prolactin and sex organ indices of rats were reduced ($p < 0.05$) by the extracts [235].

The reproductive toxicity of hydroethanolic extract of *Tropaeolum majus* (75, 375 and 750 mg/kg) was studied on male mice. Serum testosterone and its testicular levels were decreased in a dose of 750 mg/kg. Histopathological criteria such as epithelial vacuolization (9.3 ± 1.1; $p=0.034$), sloughing (4.3 ± 0.4; $p=0.027$) and detachment (12.2 ± 0.9; $p=0.031$) of germ cells were significantly increased in 750 mg/kg treated mice. At the dose of 750 mg/kg, the seminiferous tubule diameter (193.2 ± 4.6; $p=0.019$), seminiferous epithelium height (139.2 ± 5.1; $p=0.023$), and maturation arrest were significantly decreased [236].

2.64. *Urtica dioica*

The efficacy of *Urtica dioica* (10, 20, and 50 mg/kg) in inhibition of nicotine adverse effects on sperm cells viability, count, motility, and testis histology and testosterone hormone was investigated in male mice. Nicotine administration (0.5 mg/kg) significantly decreased testosterone level, count and motility of sperm cells, and testis weight compared to control group. *Urtica dioica* significantly boosted motility, count, normal morphology of sperm cells, seminiferous tubules diameter, and testosterone in all groups and testis weight in 20 and 50 mg/kg doses in comparison with control group [237].

The effect of *Urtica dioica* in the experimental testicular ischaemia reperfusion injury (I/R) model was studied in rats in terms of anti-apoptotic and antioxidative effects. The structural deterioration in the testicular on I/R group has reduced after the treatment of *Urtica dioica*. A significant reduction in apoptosis wit a rise in the expression of proliferating cell nuclear antigen (PCNA) was noted in testis tissues of *Urtica dioica* -treated rats in the I/R group. The I/R + *Urtica dioica* group showed a decrease in malondialdehyde levels and an increase in the activities of superoxide dismutase, catalase and glutathione peroxidase in comparison with the I/R group [238-239].

2.65. *Vitex angus-castus*

Vitex agnus-castus fruit extract has an anti-androgenic effect and probably acts through the hypothalamic- pituitary-gonadal axis [240-242].

2.66. *Ziziphus spina-christi*

The effect of supplementation of Arabian *Ziziphus spina christi* leaf extracts on sperms motility was investigated in order to maintain the quality of Bali bull fresh semen. The Arabian *Ziziphus spina christy* leaf extracts was added in the extender at three different concentrations (1, 3 and 5%). The sperms motility of Bali bull semen at concentration of 5% during five days equilibration at 5C had higher than 3%, 1%, and control, respectively (50.0 vs. 48.7, 43.8, and 46.3%) [243].

The exposure to $HgCl_2$ caused a marked increase in Hg concentration in the testicular tissue, which was accompanied with a decrease in testis index and reproductive impairment (decreased testosterone, LH, FSH). $HgCl_2$ also enhanced the development of oxidative damage in the testicular tissue with excessive release of TNF-α and IL-1β. The extract administration along with $HgCl_2$ abolished significantly the molecular, biochemical, and histopathological alterations induced by $HgCl_2$ intoxication [244].

3. Conclusion

The great proportion of medicinal plants which used traditionally to solve male reproductive disorders and male infertility have not yet been scientifically evaluated. Therefore, the current review summarized the effects of medicinal plants on male reproductive functions, as investigated by experimental and clinical studies.

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