

## Medicinal plants affected male and female fertility (part 1)- A review

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**Abstract:-** The previous studies revealed that many medicinal plants were affected male and female fertility. These plants included: *Achillea santolina*, *Ailanthus altissima*, *Alhagi maurorum*, *Allium cepa*, *Althaea rosea*, *Ammannia baccifera*, *Anethum graveolens*, *Anthemis nobelis*, *Arctium lappa*, *Asplenium trichomanes*, *Avena sativa*, *Bacopa monniera*, *Bryophyllum calycinum*, *Caesalpinia crista*, *Calendula officinalis*, *Calotropis procera*, *Capsella bursa-pastoris*, *Carthamus tinctorius*, *Carum carvi*, *Chenopodium album*, *Cicer airtinum*, *Cistanche tubulosa*, *Citrullus colocynthis*, *Citrus species*, *Coriandrum sativum*, *Cressa cretica*, *Crocus sativus*, *Crotalaria juncea*, *Cuminum cyminum*, *Cynodon dactylon*, *Cyperus rotundus*, *Dactyloctenium aegyptium*, *Dalbergia sissoo*, *Datura fastuosa*, *Datura metel*, *Daucus carota*, *Dodonaea viscosa*, *Euphorbia hirta*, *Ficus carica*, *Phoenix dactylifera*. This review will highlight the medicinal plants which affected male and female fertility.

**Keywords:** Medicinal plants, herbs, fertility, reproductive systems, male, female

### I. INTRODUCTION

Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives. As a result of accumulated experience from the past generations, today, all the world's cultures have an extensive knowledge of herbal medicine. Two thirds of the new chemicals identified yearly were extracted from higher plants. 75% of the world's population used plants for therapy and prevention. In the US, where chemical synthesis dominated the pharmaceutical industry, 25% of the pharmaceuticals were based on plant-derived chemicals[1]. The previous studies showed that a wide range of synthetic drugs and medicinal plants exerted many effects on reproductive systems function [2-26]. These medicinal plants affected male and female fertility were included: *Achillea santolina*[27], *Ailanthus altissima* [28], *Alhagi maurorum* [29], *Allium cepa* [30], *Althaea rosea* [31], *Ammannia baccifera* [32], *Anethum graveolens* [33], *Anthemis nobelis* [34], *Arctium lappa* [35], *Asplenium trichomanes* [36], *Avena sativa* [37], *Bacopa monniera* [38], *Bryophyllum calycinum* [39], *Caesalpinia crista* [40], *Calendula officinalis* [41], *Calotropis procera* [42], *Capsella bursa-pastoris* [43], *Carthamus tinctorius* [44], *Carum carvi* [45], *Chenopodium album* [46], *Cicer airtinum* [47], *Cistanche tubulosa* [36], *Citrullus colocynthis* [48], *Citrus species* [49], *Coriandrum sativum* [50], *Cressa cretica* [51], *Crocus sativus* [52], *Crotalaria juncea* [53], *Cuminum cyminum* [54], *Cynodon dactylon* [55], *Cyperus rotundus* [56], *Dactyloctenium aegyptium* [56], *Dalbergia sissoo*[56], *Datura fastuosa*[56], *Datura metel*[56], *Daucus carota*[56], *Dodonaea viscosa*[56], *Euphorbia hirta*[57], *Ficus carica*[57], *Phoenix dactylifera* [58-59]. This review was designed to highlight the medicinal plants which affected male and female fertility.

### I- MEDICINAL PLANTS AFFECTED MALE REPRODUCTIVE PERFORMANCE

Plant	Effects	Ref
<i>Achillea santolina</i>	hydroalcoholic extract (300 mg/kg/day ip, for 20 days) 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.	60
<i>Ammannia baccifera</i>	ethanol extract of <i>A. baccifera</i> whole plant induced antifertility effects in rat males. It was significantly reduced the weight of the testis, epididymis, sperm density and motility, content of fructose in the seminal vesicles, $\Delta 5-3\beta$ -hydroxy steroid dehydrogenase ( $\Delta 5-3\beta$ -HSD) and glucose-6-phosphate dehydrogenase (G-6-PD)	61

<i>Arctium lappa</i>	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	62 - 64
<i>Bacopa monniera</i>	caused reversible suppression of spermatogenesis and fertility. The treatment caused reduction in motility and viability of the sperms and reduced the number of spermatozoa in cauda epididymidis and testis, and caused alterations in the somniferous tubules in mice.	65
<i>Caesalpinia crista</i>	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.	66
<i>Carthamus tinctorius</i>	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 ( $p < 0.001$ ).	67
<i>Chenopodium album</i>	ethanolic extract at doses of 100, 250 and 500mg/kg orally, in male albino mice induced 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.	68
	The ethanolic extract of seeds at a concentration of 200 mg/kg bw resulted in pronounced anabolic effect in treated male rats 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.	69
	seed extract induced sperm death, the effect which is due to oxidative damage of cellular macromolecules by generation of ROS.	70
	Aqueous decoction of <i>Chenopodium album</i> 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 <i>in vitro</i> was 2 mg/ml. The mechanism of CAD action involved disintegration of sperm plasma membrane and dissolution of acrosomal cap causing sperm death.	71
<i>Cicer arietinum</i>	Oral administration of methanolic extract at 200 and 400 mg/kg body weight was significantly increased the mount frequency, intromission frequency, ejaculation frequency and ejaculation latency ( $P < 0.05$ ) in rats. It also significantly ( $p < 0.05$ ) increased the serum cholesterol and testosterone levels.	72

<i>Cistanche tubulosa</i>	administration of ethanol extract (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) in rats respectively. The serum level of progesterone and testosterone in rats was also increased by CTE administration ( $p<0.05$ ). Results of immunohistochemistry and western blot analysis confirmed that the expression of CYP11A1, CYP17A1, and CYP3A4 was enhanced by CTE ( $p<0.05$ ).	73
	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 <i>Cistanche tubulosa</i> .	74
<i>Citrullus colocynthis</i>	50% ethanol extract caused significant reduction of cauda epididymis sperm motility and density, number of pups, fertility, and circulatory levels of testosterone were observed in male rats. The weights of testes, epididymis, seminal vesicle, and prostate were also significantly decreased. 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.	75
<i>Citrus species</i>	lime juice destroys sperm cells, fifty percent of <i>Citrus aurantifolia</i> juice wiped out 2000 of sperm cells in 30 seconds. 60 days treatment with <i>Citrus limonum</i> seeds significantly decreased the sperm count. Size and weight of testis and epididymis were reduced indicating atrophic changes in testis and epididymis. It caused drastic effect on sperm motility and morphology which decreased fertility. Sperm counts returned to normal after 90 days lime juice caused reduction in the number of fetus of treated pregnant rats when compared to the control. There was a significant reduction in the crown-rump length, weight and umbilical cord length of the fetus when compared with the control. Accordingly, lime juice showed abortifacient effect but no obvious teratogenic effect was observe.	7 6- 7 7
<i>Cressa cretica</i>	methanolic extract of <i>Cressa cretica</i> 100 mg/kg for 60 days led to a significant decrease in the weight of testis, epididymis, seminal vesicle, and ventral prostate. <i>Cressa cretica</i> 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.	7 8
	various fractions of the methanol extract for 60 days decreased the weight of testes and accessory sex organs significantly ( $P\leq 0.001$ ). Sperm counts of testes and cauda epididymis as well as cauda epididymal sperm motility was also declined significantly ( $P\leq 0.001$ ), serum testosterone production was reduced in treated male rats. The fertility was decreased by 90%0100% in different fractions. The seminiferous tubular diameter and Leydig cell nuclear area were reduced significantly. The population of spermatogenic cells	7 9

	(spermatogonia, preleptotene, pachytene, secondary spermatocytes and round spermatids) were also reduced significantly.	
	After 60 days oral administration of <i>Cressa</i> constituents, results showed 100% antifertility activity in male rats with the reduction in testosterone levels and spermatogenic elements	8 0
<b><i>Crocus sativus</i></b>	The aqueous extract (80, 160 and 320 mg/kg bw), crocin (100, 200 and 400 mg/kg bw), increased mounting frequency, intromission frequency and erection frequency behaviors and reduced ejaculation latency, intromission latency and mount latency parameters.  the prepared saffron gel significantly improved erectile dysfunction in diabetic patients (P < .001)	81 82
<b><i>Crotalaria juncea</i></b>	Plant extracts were tested in male mice and rats, they decreased 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. 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	83 - 84
<b><i>Cuminum cyminum</i></b>	Oral dose of <i>Cuminum cyminum</i> isolated fractions (CcFr) 50 mg/rat/day for 60 days caused marked abnormalities in spermatogenesis with decreased counts (P ≤ 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 ≤ 0.001). Testicular as well as accessory sex organ biochemical parameters were significantly changed (p ≤ 0.001). Sperm motility, density and morphology were resulted in 100% negative fertility. Testosterone levels were declined significantly.	8 5
	leaf decoction of <i>Cydonia oblonga</i> protected rabbit testes and spermatogenesis from damage induced by hypercholesterolemia	86
	The extract was administered orally by gavage in the dose of 500 and 800 mg/kg bw per day as a single dose in male rats for 28 days. It increased mounting frequency and the mating performance of the rats 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	87
<b><i>Dactyloctenium aegyptium</i></b>	ethanolic extract 200, 400 and 600 mg/kg caused significant decrease in serum testosterone levels and increase in serum estrogen levels in male rats. A significant decrease in weight of testis, epididymis (caput and caudal), vas deferens, seminal	8 8

	vesicle and prostate, with a significant reduction of total sperm count and increase in motility, abnormality of sperm in caput and caudal were also recorded. 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 <i>D. aegyptium</i> to males also showed dose dependent decrease in number of pregnant females and number of fetuses	
<i>Dalbergia sissoo</i>	ethanol extract of stem bark caused dose-dependent and time-dependent adverse effect on sperm motility and sperm viability. Ethanol extract at a concentration of 20 mg/ml caused complete immobilization within 3 minutes. Ethanol extract at a dose of 200 mg/kg in mice 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 also observed with pathohistological changes.	89
	aqueous leaf extract of <i>Dalbergia sissoo</i> (50 and 100 mg/kg/day) in mice for 35 days caused significant reductions in epididymal sperm motility, viability and number, and in serum level of testosterone. libido of treated males showed no change, but their fertility was markedly suppressed.	90
<i>Datura fastuosa</i>	alcoholic extract of (2, 4 and 6mg/kg, for 7 weeks) in male rats induced significant decrease in concentrations of sperm and normal sperm in all the concentrations in. They also significantly decreased serum levels of testosterone, LH and FSH and weights of the tests and epididymis in the treated groups, The percentage of occurrence of pregnancy was also significantly decreased	91
<i>Daucus carota</i>	Administration of carrot seed extract (CSE) caused a significant increase in cauda epididymis spermreserves compared with the control ( $28.2 \pm 1.8 \times 10^6$ vs. $45.1 \pm 2.0, \times 10^6$ ). The extract also protect testis from the gentamicin-induced necrosis. The CSE administration caused about 3.5-times increase in the LH levels even in spite of receiving 5 mg/kg/day gentamicin with no significant effect on FSH levels. The testosterone concentrations in the group received 400 mg/kg CSE were 30% and 83% higher than its levels in the control and the gentamicin treated group, respectively.	92
<i>Dodonaea viscosa</i>	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	93
<i>Euphorbia hirta</i>	aqueous extracts (400 mg/kg orally) in old mature male rats caused varying degrees of testicular degeneration and reduction in the mean seminiferous tubular diameter. <i>E. hirta</i> exerted potentially induced deleterious effects on the tested and accessory organs of rats	94

<i>Ficus carica</i>	An aqueous ethanol extract of the dried fruits of <i>Ficus carica</i> was screened for in vivo aphrodisiac activity. Results reveal that on the 1 <sup>st</sup> day of treatment all the treated groups showed increase copulatory sexual behavior and orientational activity in all the experimental animals. The prolonged treatments for all the treated groups were highly effective for increase the sexual libidity, as compared to the solvent control.	95
	The effect of <i>Ficus carica</i> leaf extracts 200 mg/kg, in sperm parameters and testis was studied in mice intoxicated with formaldehyde. The results showed that formaldehyde significantly decreased gonadosomatic index and increased percentage of immotile sperm. Disorganized and vacuolated seminiferous epithelium, spermatogenic arrest, and lumen filled with immature germ cells were also observed in the testes of mice intoxicated with formaldehyde. However, leaf extracts improved sperm count, nonprogressive motility of spermatozoa, and gonadosomatic index in formaldehyde-treated testes.	96
<i>Phoenix dactylifera</i>	Pollen of Date palm (500 mg iq) and a combination of zinc sulphate& pollen of Date palm (500 mg iq) in infertile men significantly increased serum LH, FSH, & testosterone levels. It was also, increased significantly sperm count and motility. Sexual desire was also significantly increased. Wives of treated men got pregnancy during the treatment period.	58 - 59

## II. III-MEDICINAL PLANTS AFFECTED FEMALE REPRODUCTIVE PERFORMANCE

Plant	effects	Ref
<i>Ailanthus altissima</i>	was recognized to have anti-progestogenic activities. It inhibited the progesterone activity in a dose-response manner	97
<i>Alhagi maurorum</i>	ethanolic extract of powdered roots in doses of 5 mg/ml bathing fluid completely suppressed histamine induced uterine contractions.	98
<i>Allium cepa</i>	female rats treated with ethanolic extract showed significant inhibition of number of implant sites at a dose of 300 mg/kg. It enhanced uterine contraction in rats equivalent to 0.003 IU of oxytocin.	99
<i>Althaea rosea</i>	infusion and methanolic extract influence hormonal activity and affected the morphology of the rat female sexual organs. It exerted estrogenic activity, the <i>in vivo</i> test proved that <i>p</i> -hydroxy benzoic acid isolated from the plant was estrogenic.	100
<i>Ammannia baccifera</i>	ethanol extract at the doses of 100, 200 and 400 mg/kg body weight (ip) arrested the normal estrus cycle at dioestrus phase and significantly decreased weight of ovaries. The cholesterol and ascorbic acid content in ovaries were significantly elevated in treated mice. The extract also significantly inhibited the activity of $\Delta^5$ -3 $\beta$ -hydroxy steroid dehydrogenase and Glucose-6-phosphate dehydrogenase, the two key enzymes involved in ovarian steroidogenesis	101
<i>Anthemis nobelis</i>	aqueous-alcoholic extract was studied in polycystic ovary syndrome induced in rats by a single dose of estradiol valerate. Histological investigations revealed that the animal administered with dose of 50 mg/day showed small cysts and less inflammation, with decreasing of serum estrogen hormone	102

<b>Anethum graveolens</b>	0.045 g/kg and 0.45 g/kg of aqueous extract and 0.5 g/kg and 5 g/kg of ethanol extract for 10 days caused significant increase in duration of the estrous cycle and diestrus phase. Smooth	103
	endoplasmic reticulum (SER), rough endoplasmic reticulum (RER) and mitochondria were increased in granulosa lutein cells	104
	Dill seed possessed contractive effects on myometer, enhanced releasing of oxytocin which is an effective hormone in uterus contractions. A dose of 6-7 gm of dill seed extract after delivery decreases postpartum hemorrhage due to its contractive characteristic. Limonene and anethole showed contractive effect on uterine myometrium	105-107
	contractions in the treated women (one tablespoon of whole dill seed seeped in a half or whole cup boiling water for 3-4 min before going to the hospital at the beginning of uterus contractions) was significantly more than the control group. The ratio of contraction's fall time to its rise time in the treated group was shorter than the control group. The study showed that dill seed shortens duration of the first stage of labor	108
<b>Arachis hypogaea</b>	Introduction of refined peanut oil to form 10% of the food ration of immature mice increases uterine weight.	109-110
	plant showed high levels of phytoestrogens including isoflavones (formononetin and biochanin A , 729 ug/g dry weight. These compounds structurally or functionally mimic mammalian estrogens	111-113
<b>Arctium lappa</b>	induced uterine stimulant activity	114
<b>Asplenium trichomanes</b>	in vitro estrogenic activity to activate ERalpha and ERbeta, MCF7/EReluc cell line which expresses endogenous ERalpha, and SK-NBE cells transiently transfected with the estrogen receptors (ER alpha and ER beta) were used to test the estrogenic activity assays. Leaves infusion and methanolic extract were active in MCF7 model; selectivity for the ERbeta receptor was observed in the SK-NBE test.	115
<b>Avena sativa</b>	oat straw stimulated the release of luteinizing hormone from the adenohipophysis of rats. It contained oestrone which been shown to induce ovulation	116-117
<b>Bryophyllum calycinum</b>	exerted relaxant effect <i>in vitro</i> on the contractility of human myometrium on oxytocin-stimulated contraction at a minimum concentration almost 100-fold lower than in the case of spontaneous contraction	118
	Thirty-two patients divided into two groups , 15 patients received Bryophyllum and 17 received the placebo. The time of delivery did not differ between the groups. In both groups A transition to the intensive care unit was slightly higher in the placebo group (13) compared to the Bryophyllum group (11)	119
<b>Caesalpinia crista</b>	it caused antifertility effect in mice and rats. This effect could be attributed to its contents of gossypol and cyclopropane fatty acids, which recognized as an antifertility compounds	120
	alcoholic seed extract caused histological follicular degeneration in ovary, vacuolation and mild disorganization of uterus in rats. It also caused significant decrease in duration of estrous cycle and mean ovarian weight.	121

	prolonged the length of estrous cycle with significant increase in the duration of diestrus stage. It significantly decreased levels of LH, FSH, estradiol and progesterone in dose-dependent manner. Ovarian and uterine weight was significantly reduced. Histologically it caused follicular atresia and degeneration of corpora lutea in ovary. Oviduct showed degeneration of mucosal folds and epithelium cells. Uterus showed evidence of degeneration of endometrial epithelium and endometrial glands. Lamina propria and muscularis layer of vagina were found slightly disorganized	122
<i>Calendula officinalis</i>	extracted exerted estrogenic activity in ovariectomized animals	123-125
<i>Calotropis procera</i>	The effects of ethanolic and aqueous extracts were found to interrupt the normal oestrous cycle in 60 % and 80 % of female rats respectively. The extracts had no oestrogenic activity when tested in immature female bilaterally ovariectomized rats.	126
	A strong antiimplantation (inhibition 100%) and uterotropic activity was possessed b ethanolic extract at the dose level of 250 mg/kg (1/4 of LD50).	127
	aqueous extracts induced significant sustained increases in human myometrial smooth muscle cell contractility, with varying efficiencies, depending upon time of exposure and dose	128
<i>Carum carvi</i>	aqueous and ethanolic extracts showed significant antifertility activity in female rats. FSH and LH levels were significantly decreased, and estrogen was found to be increased. The estrus phase was blocked by treatment with aqueous and ethanolic extract. They also increase the weight of ovary, uterus and body weights.	129
	oil was effective in inhibiting tonic and phasic rhythmic contractions of isolated uterine preparations	130
<i>Capsella bursa-pastoris</i>	impeded ovulation and produced temporary infertility in males and females	131
<i>Carthamus tinctorius</i>	In studying te teratogenic effect, in higher doses (1.6 and 2 mg/kg/day) the embryos were absorbed, whereas with lower dose (1.2 mg/kg/day) it caused changes in external, internal and longitudinal diameters, open neuropore, changes in cellular orientation and cellular degeneration were observed.	132
	Tracheloside isolated from the plant, significantly decreased the activity of alkaline phosphatase (AP), an estrogen-inducible marker enzyme, with an IC50 value of 0.31 microg/ml, a level of inhibition comparable to that of tamoxifen (IC50=0.43 microg/ml).	133
	exerted stimulating action on the uterus of mouse <i>in vitro</i> . The stimulating action of <i>Carthamus tinctorius</i> has been found related to	134
	the stimulating effects on H1-receptor and alpha-adrenergic receptor of uterus. intraperitoneal administration of a hot aqueous extract flowers increased uterine contractions in pregnant female rats	135
<i>Chenopodium</i>	Fertilization of oocytes and establishment of implantation were	136



<i>album</i>	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	
<i>Cicer arietinum</i>	The aqueous extract at a dose of 400mg/kg was found to be most effective abortifacient. Similarly it was also found to increase the reproductive organ weight and possess estrogenic activity when tested in immature ovariectomised female albino rats	137
	Isoflavones extracted from chickpea sprouts (ICS) stimulated estrogen responsive element (ERE)-promoter activity in cells, and concurrent treatment with the nonselective estrogen receptor antagonist ICI 182,780 abolished the estrogenic activity induced by ICS	138
	Treatments of rats with isoflavones extracted from chickpea sprouts (ICS) (50 or 100 mg/kg/day) produced significant estrogenic effects on the uteruses, including the increases in uterine weight, epithelial height and gland number, as well as in the expression of the cell proliferation marker PCNA. The treatments changed the secretory profile of ovarian hormones and pituitary gonadotropins: (serum E2 level was significantly increased, while serum LH and FSH levels were decreased)	139
<i>Citrullus colocynthis</i>	<i>Citrullus colocynthis</i> 400 mg/kg in female rats for 4 weeks did not have much effect on fertility. Significant decrease in the relative ovarian weights and embryo weights in female rats exposed to <i>Citrullus colocynthis</i> were observed. Exposure to <i>Citrullus colocynthis</i> for a 12 weeks resulted in a reduction in the percentage of pregnancies and in the number of implantation sites, decreased ovarian weights and decreased viable fetus's number	140
<b>Citrus species</b>	petroleum ether extract of seeds of <i>Citrus medica</i> in female rats showed reduced ovarian weight, benzene extract treated rats showed increased ovarian weight, ethanol extract treated rats showed non-significant change in the weight of ovary. Histological changes of the ovary indicated increases in the number of atretic follicles but decreases in the number of healthy developing follicles, Graafian follicles and corpora lutea. The total cholesterol, activity of acid and alkaline phosphatase and ascorbic acid content of the ovary were increased.	141
	petroleum ether extract of <i>Citrus medica</i> seeds exhibited estrogenic effects, which included increase in uterine weight and vaginal epithelial cell cornification infemale rats. The micrometric measurements of the uterus and its components were increased and glands showed high secretory activity. When the extract was tested in 30-day-old immature rats, they exhibited opening of vagina on the fifth day and cornification of vaginal epithelial cells, which was about 10 days earlier compared to controls	142
	petroleum ether extract of <i>Citrus medica</i> leaves proved to retain high estrogenic activity in immature female rats	143
<i>Coriandrum sativum</i>	aqueous extract of fresh seeds produced a dose-dependent significant anti-implantation effect, but did not produce complete infertility in female rats. Treatment of animals	144

	during day-8 to day-12 and day-12 to day-20 of the pregnancy did not produce any significant abortifacient activity. There was no significant change in the weight and length of the foetuses delivered by rats treated with the extract and no abnormalities were seen in the organs of the offsprings. The extracts produced a significant decrease in serum progesterone levels on day-5 of pregnancy which may be responsible for its anti-implantation effect.	
<b><i>Crocus sativus</i></b>	saffron aqueous extract (SAE), was evaluated in <i>in vitro</i> maturation (IVM) of immature mouse oocytes. The maturation rate was significantly higher in all groups treated with different concentrations of SAE compared with the control group ( $p < 0.05$ ). However, the lower concentrations of SAE (10 and 5 $\mu\text{g/ml}$ in maturation medium) increased the fertilization rate of oocytes and <i>in vitro</i> developmental competence when compared with the control group ( $p < 0.05$ ).	145
	the effects of different concentrations of saffron ( <i>Crocus sativus</i> ) aqueous extract (SAE) and its ingredient, crocin, were evaluated on the improvement of <i>in vitro</i> maturation (IVM) and subsequent <i>in vitro</i> fertilization (IVF) and embryo development of mouse oocytes. SAE was added at dosages of 5, 10, and 40 $\mu\text{g/ml}$ and crocin 50, 100, and 400 $\mu\text{g/ml}$ . Both SAE and crocin improved the rate of IVM, IVF, and <i>in vitro</i> culture. Addition of 40 $\mu\text{g/ml}$ SAE to maturation medium significantly increased the rate of IVM, IVF, and <i>in vitro</i> culture ( $p < 0.05$ ). Furthermore 100 $\mu\text{g/ml}$ crocin significantly increased the IVM rate ( $p < 0.05$ ).	146
	a double-blind and placebo-controlled trial was designed to investigate the effect of saffron (stigma of <i>Crocus sativus</i> ) on the symptoms of premenstrual syndrome. The trial showed that saffron was effective in relieving symptoms of PMS. A significant difference was observed in efficacy of saffron in the total premenstrual daily symptoms and Hamilton depression rating scale	147
<b><i>Crotalaria Juncea</i></b>	petroleum ether, benzene and alcohol extracts of seeds of <i>Crotalaria juncea</i> administered orally at the dose level of 25mg/100g bw to adult female mice for 30 days, resulted in irregular estrous cycle with prolonged estrus and metaestrus and reduced diestrus and proestrus during the experimental period. Histological studies of the ovary indicated increases in the number of atretic follicles but decreases in the number of developing follicles, Graafian follicles and corpora lutea.	148
	ethanol extract of <i>Crotalaria juncea</i> seeds which showed antiovarian activity in female albino rats. Two fractions decreased number of healthy follicles (Class I – ClassVI) and corpora lutea and increased number of regressing follicles (Stage IA, Stage IB, Stage IIA, Stage IIB).	149
	alcohol extract possessed antiimplantation and pregnancy interruption activities. These adverse effects on fertility were reversible upon withdrawal of the extract treatments. The alcohol extract was found to possess estrogenic activity	150

<i>Cynodon dactylon</i>	aqueous extract of entire plant of <i>Cynodon dactylon</i> for thirty days in female rats significant increased ( $p < 0.001$ ) the serum estradiol concentration whereas, follicle stimulating and luteinizing hormones were significantly ( $p < 0.001$ ) reduced. Furthermore, a significant increase ( $p < 0.001$ ) in the weight of the uterus and significant decrease in the weight of the ovaries ( $p < 0.001$ ) was observed in the treated group, the estrous cycle was found to be irregular and disturbed	151-152
<i>Cyperus rotundus</i>	the essential oil of the rhizome of <i>Cyperus rotundus</i> (EOC ) and its fractions F2-F6 showed significant anti-dysmenorrhea.	153
<i>Datura metel</i>	2% acetone seed extracts for 15 days in female mice caused 100% anti-implantation activity followed by 1% and 0.5% seed extracts which caused 40% and 80% anti implantation activity respectively.	154
<i>Daucus carota</i>	petroleum ether extract and fraction 5 (fatty acids) of carrot seeds arrested the normal estrus cycle of adult mouse and reduced the weight of ovaries significantly. The cholesterol and ascorbic acid content in ovaries were significantly elevated by the extract and fraction 5 of carrot seeds. The significant inhibition of delta 5,3-beta-hydroxy steroid dehydrogenase and glucose-6-phosphate dehydrogenase, the two key enzymes involved in ovarian steroidogenesis, were also recorded in mouse ovaries after 15 days of treatment	155
	The petroleum ether, alcoholic, and aqueous extracts of <i>Daucus carota</i> were evaluated for their possible antioviulatory activity in rabbits with copper-induced ovulation. All extracts inhibited ovulation in 40%, or less, of the animals.	156
	The alcoholic extract 50 to 250 mg/kg bw after coitus in female rats showed a significant dose dependent antifertility effect. The administration of the extract at a lower dose showed anti-implantational activity, whereas higher doses caused fetus resorption. The main effect of the extract appears to be an abortifacient activity. At higher dose levels, the extract demonstrated an estrogenic nature with a prolonged estrous phase, whereas lower doses showed an antiestrogenic nature and an increase in the percentage duration of the diestrous phase of the estrous cycle. The extract was neither progestational nor antiprogestational.	157
<i>Dodonea viscosa</i>	methanolic extract of the leaves reduced significantly ( $p < 0.01$ ) the number of litters when administered through oral route in female rats. It also produced anti- fertility effect in a dose dependent manner and the contraceptive effect was manifested for a definite period of time. Furthermore, the extract significantly showed anti-implantation and early abortifacient activity	158

### III. CONCLUSION:

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

REFERENCES:

- [1] Phillipson JD. Plants as source of valuable products. In: Charlwood BV, Rhodes MJC (eds). Secondary products from plant tissue culture. Oxford: Clarendon Press 1990: 1-21.
- [2] Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their effect on reproductive systems ( part 1). Ind J of Pharm Sci & Res 2015; 5(4): 240-248.
- [3] -Al-Snafi AE. Medicinal plants affected reproductive systems (part 2) - plant based review. Sch Acad J Pharm 2016; 5(5): 159-174.
- [4] Al-Snafi AE. Clinically tested medicinal plant: A review (part 1). SMU Medical Journal 2016; 3(1): 99-128.
- [5] Al- Janabi AS, Al-Tahan FJ and Al- Snafi AE. Effect of a benzodiazepine on serum level of thyroid hormones. The veterinarian 1992; 2(1): 55-58.
- [6] Al-Snafi AE, Kubba MA, Al-Tahan FJ and Al-Janabi AS. Effect of chronic diazepam treatment on the reproductive performance of male rats. Iraqi J Biol Science 1993; 11: 82-92.
- [7] Al-Tahan FJ, Al-Janabi AS and Al-Snafi AE. Effect of chronic diazepam treatment on fertility and sexual ability of male rats. Dirasat 1993; 20(4): 151-158 .
- [8] Al-Tahan FJ, Al-Janabi AS and Al-Snafi AE. The effect of chronic diazepam treatment in rats on fetal and pup characteristics. Iraqi J Biol Science 1995; 14: 76-80.
- [9] Al- Snafi AE, Al- Kasab TM and Al-Azzawi SS. Effect of prostaglandine F2 $\alpha$  on male mice reproductive function. J Coll Edu 1997; (1): 1-8.
- [10] Al- Snafi AE and Shafik, NA. Embryotoxicity of norfloxacin in mice. Med J Tikrit Univ 1997; 3: 200-203.
- [11] Al- Snafi AE, Al-Baldawi AT, Al-Rubaei AK. The efficacy of bromocriptine with and without ovarian stimulation in the treatment of hyperprolactinemic infertile women. Middle East Fertility Society J 2003; 8(1): 1-4.
- [12] Al-Snafi AE, Safa Al-Hamidi, Senan Abdullah. Study the efficacy of Royal jelly in treatment of male infertility. Thi qar Medical Journal 2007; 1(1): 1-12.
- [13] Jasmim Fathi, Al-Snafi AE, Ali Saleh Huseen. Serological diagnosis of leptospirosis in Al- Nasiriya city. Tikrit Journal of Pure Sciences 2010; 15(1): 83-91.
- [14] Al-Snafi AE, Al Mousawy AA and Al Mayahi AJ. Embryotoxicity of fluroquinolone in rats. Thi qar Medical Journal 2011; 5(3) 77-86.
- [15] Al-Snafi AE. A Negative feedback mechanism between brain catecholamines and gamma amino butyric acid, could be a central defense mechanism in stress. A review article. Global Journal of Pharmacology 2013; 7 (2): 103-108 .
- [16] Al-Snafi AE. Endocrine reproductive effects of antiepileptic drugs in male rats. Global Journal of Pharmacology 2013 ;7 (1): 95-98.
- [17] Al-Snafi AE. Anticancer effects of cimetidine. World J Pharm Sci 2014; 2(4): 397-403.
- [18] Al-Snafi AE. Study the efficacy of anti-estrogenic drugs in the treatment of poly cystic ovary induced in female rats by estrogen valerate. World J Pharm Sci 2014; 2(4): 313-316.
- [19] Al-Snafi AE. Galactagogue action of the crude phenolic extracts of grape seeds (*Vitis vinifera*). International Journal of Biological & Pharmaceutical Research 2015; 6(8): 577-580.
- [20] Al-Snafi AE. Mammary gland stimulating effects of the crude phenolic extracts of green tea (*Camellia sinensis*). International Journal of Biological & Pharmaceutical Research 2015; 6(7): 573-576.
- [21] Al-Gazi ZS, Al-Snafi AE and Al-Abady FA. Effect of toxoplasmosis and/ or its treatment (sulpadiazine and pyrimetamine) on female rats reproductive performance. Indian Journal of Pharmaceutical Science & Research 2016; 6(1): 35-40.
- [22] Al-Ghezy ZS, Al-Abady FA and Al-Snafi AE. Effect of toxoplasmosis and its treatments on male rats reproductive functions. Asian Journal of Pharmaceutical Science & Technology 2016; 6(2): 82-88.
- [23] Al-Ghezy ZS, Al-Abady FA and Al-Snafi AE. Histological effects of toxoplasmosis and its treatments on male and female rats. American Journal of Pharmacy & Health Research 2016; 4(4): 40-52.
- [24] Al-Ghezy ZS, Al-Abady FA and Al-Snafi AE. Effect of *Toxoplasma gondii* infection in male and female rats on fetal characteristics. European Journal of Biomedical and Pharmaceutical Sciences 2016; 3(5): 692-698.
- [25] Barakat SS, Al-Dujaily AA and Al-Snafi AE. Misuse of antimicrobial agents in urinary tract infection in Al- Samawa city. Med J Tikrit Univer 2000, 6:91-95.
- [26] Jalal G, Al-Dujaily AA, Al-Shahwani SM and Al-Snafi AE. Urinary tract infection among pregnant women in Sghospital – Kirkuk. Med J Tikrit Univer 2000, 6:197-202 .
- [27] Al-Snafi AE. Chemical constituents and pharmacological activities of Milfoil (*Achillea santolina*) - A Review. Int J Pharm Tech Res 2013 5(3): 1373-1377.
- [28] Al-Snafi AE. The pharmacological importance of *Ailanthus altissima*- A review. International Journal of Pharmacy Review and Research 2015; 5(2):121-129
- [29] Al-Snafi AE. *Alhagi maurorum* as a potential medicinal herb: An Overview. International Journal of Pharmacy Review and Research 2015; 5(2):130-136.
- [30] Al-Snafi AE. Pharmacological effects of *Allium* species grown in Iraq. An overview. International Journal of Pharmaceutical and health care Research 2013; 1(4):132-147.
- [31] Al-Snafi AE. The Pharmaceutical importance of *Althaea officinalis* and *Althaea rosea*: A Review. Int J Pharm Tech Res 2013; 5(3):1387-1385.
- [32] Al-Snafi AE. The chemical constituents and pharmacological effects of *Ammannia baccifera* – A review. International Journal of Pharmacy 2015; 5(1): 28-32.
- [33] Al-Snafi AE. The pharmacological importance of *Anethum graveolens* – A review. International Journal of Pharmacy and Pharmaceutical Sciences 2014; 6(4): 11-13.
- [34] Al-Snafi AE. Medical importance of *Antemisis nobilis* (*Chamaemelum nobilis*)- A review. Asian Journal of Pharmaceutical Science & Technology 2016; 6(2): 89-95.
- [35] Al-Snafi AE. The Pharmacological importance and chemical constituents of *Arctium Lappa*. A review. International Journal for Pharmaceutical Research Scholars 2014; 3(1-1): 663-670.
- [36] Al-Snafi AE. Encyclopedia of the constituents and pharmacological effects of Iraqi medicinal plants. Vol 1, Rigi Publication 2015.
- [37] Al-Snafi AE. The nutritional and therapeutic importance of *Avena sativa* - An Overview. International Journal of Phytotherapy 2015; 5(1): 48-56.
- [38] Al-Snafi AE. The pharmacology of *Bacopa monniera*. A review. International Journal of Pharma Sciences and Research 2013; 4(12): 154-159.

- [39] Al-Snafi AE. The Chemical constituents and pharmacological effects of *Bryophyllum calycinum*. A review. Journal of Pharma Sciences and Research 2013; 4(12): 171-176.
- [40] Al-Snafi AE. Pharmacology and medicinal properties of *Caesalpinia crista* - An overview. International Journal of Pharmacy 2015; 5(2): 71-83.
- [41] Al-Snafi AE. The chemical constituents and pharmacological effects of *Calendula officinalis* – A review. Indian Journal of Pharmaceutical Science & Research 2015; 5(3): 172-185.
- [42] Al-Snafi AE. The constituents and pharmacological properties of *Calotropis procera* - An Overview. International Journal of Pharmacy Review & Research 2015; 5(3): 259-275.
- [43] Al-Snafi AE. The chemical constituents and pharmacological effects of *Capsella bursa-pastoris* - A review. International Journal of Pharmacology and toxicology 2015; 5(2):76-81.
- [44] Al-Snafi AE. The chemical constituents and pharmacological importance of *Carthamus tinctorius* - An overview. Journal of Pharmaceutical Biology 2015; 5(3): 143-166.
- [45] Al-Snafi AE. The chemical constituents and pharmacological effects of *Carum carvi* - A review. Indian Journal of Pharmaceutical Science and Research 2015; 5(2): 72-82.
- [46] Al-Snafi AE. The chemical constituents and pharmacological effects of *Chenopodium album* – An overview. International J of Pharmacological Screening Methods 2015; 5(1): 10-17.
- [47] Al-Snafi AE. The medical Importance of *Cicer arietinum* - A review. IOSR Journal of Pharmacy 2016; 6(3): 29-40.
- [48] Al-Snafi AE. Chemical constituents and pharmacological effects of *Citrullus colocynthis* - A review. IOSR Journal of Pharmacy 2016; 6(3): 57-67.
- [49] Al-Snafi AE. Nutritional value and pharmacological importance of citrus species grown in Iraq. IOSR Journal of Pharmacy 2016; 6(8): 76-108.
- [50] Al-Snafi AE. A review on chemical constituents and pharmacological activities of *Coriandrum sativum*. IOSR Journal of Pharmacy 2016; 6(7): 17-42.
- [51] Al-Snafi AE. The chemical constituents and therapeutic importance of *Cressa cretica*- A review . IOSR Journal of Pharmacy 2016; 6(6): 39-46.
- [52] Al-Snafi AE. The pharmacology of *Crocus sativus*- A review. IOSR Journal of Pharmacy 2016; 6(6): 8-38.
- [53] Al-Snafi AE. The contents and pharmacology of *Crotalaria juncea*- A review. IOSR Journal of Pharmacy 2016; 6(6): 77-86.
- [54] Al-Snafi AE. The pharmacological activities of *Cuminum cyminum* - A review. IOSR Journal of Pharmacy 2016; 6(6): 46-65.
- [55] Al-Snafi AE. Chemical constituents and pharmacological effects of *Cynodon dactylon*- A review. IOSR Journal of Pharmacy 2016; 6(7): 17-31.
- [56] Al-Snafi AE. A review on *Cyperus rotundus* A potential medicinal plant. IOSR Journal of Pharmacy 2016; 6(7): 32-48.
- [57] Al-Snafi AE. Encyclopedia of the constituents and pharmacological effects of Iraqi medicinal plants. Vol 2, Rigi Publication 2016.
- [58] Al-Snafi AE. Encyclopedia of the constituents and pharmacological effects of Iraqi medicinal plants. Vol 3, Rigi Publication 2016.
- [59] Al-Snafi AE, Bahaadeen EF, Marbeen MI and Marbut MM. The effect of date palm pollens and zinc sulphate in the treatment of human male infertility. Tikrit Journal of Pharmaceutical Sciences 2006; 2(1): 31-34.
- [60] Marbin M Ideen and Al-Snafi A E. The probable therapeutic effects of Date palm pollens in treatment of male infertility. Tikrit Journal of Pharmaceutical Sciences 2005;1 (1): 1-6.
- [61] Gopalipour, MJ, Khori V, Azarhoush R, Nayeypour M and Azadbakht M. Effect of *Achillea santolina* on mice spermatogenesis. DARU 2004; 12(1): 36- 39.
- [62] Dhanapal R, Kumar GS, Bubu VL, Chandramohan K, Kumar RA, Gupta MA *et al.* Evaluation of antifertility activity of the ethanol extract of *Ammanni abacifera* (L) whole plant in male Albino rats. Journal of Pharmacy and Bioresources 2006; 3(2): 89-93.
- [63] Matsumoto T, Hosono-Nishiyama K, and Yamada H. Antiproliferative and apoptotic effects of butyrolactone lignans from *Arctium lappa* on leukemic cells. Planta Med 2006;72: 276-278.
- [64] Feng CJ, Yin ZP, We XC, Tao HT, Gui BY and Shan CK. Effect of aqueous extract of *Arctium lappa* L. (burdock) roots on the sexual behavior of male rats. Complementary and Alternative Medicine 2012; 12: 8.
- [65] Farnsworth N. Potential value of plants as sources of new antifertility agents. J Pharm Sci 1975; 64: 533-598.
- [66] Akanksha S and Singh SK. Evaluation of anti-fertility potential of Brahmi in male mouse. Contraception 2009; 79: 71-79.
- [67] Peerzade N , Ahmed RN and Marigoudar SR. Morphological changes induced by *Caesalpinia bonducella* seed extract on rat sperm: scanning electron microscope study. J Basic Clin Physiol Pharmacol 2009; 20(4): 309-317.
- [68] Mirhoseini M, Mohamadpour M and Khorsandi L. Toxic effects of *Carthamus tinctorius* L. (Safflower) extract on mouse spermatogenesis. J Assist Reprod Genet 2012; 29(5):457-461.
- [69] Pande M, Pathak A. Sexual function improving effect of *Chenopodium album*(Bathua sag) in normal male mice. Biomed Pharmacol J 2008;1: 325-332.
- [70] Baldi A and Gupta R. Effect of *Chenopodium album* on sexual behavior and sperm count in male rats, DARU 2004; 12(1):36-39.
- [71] Kumar S, Chatterjee R, Dolai S, Adak S, Kabir SN, Banerjee S and Mondal NB. *Chenopodium album* seed extract-induced sperm cell death: exploration of a plausible pathway. Contraception 2008; 77(6): 456-462.
- [72] Kumar S, Biswas S, Mandal D, Roy HN, Chakraborty S, Kabir SN, Banerjee S and Mondal NB. *Chenopodium album* seed extract: a potent sperm-immobilizing agent both in vitro and in vivo. Contraception 2007; 75(1): 71-78.
- [73] Sajja RB, Venkatesh V, Suneetha B and Srinivas N. Evaluation of aphrodisiac activity of methanolic extract of *Cicer arietinum* seeds in sexually sluggish male albino rats. Int J Pharm 2014; 4(4): 309-313.
- [74] Wang T, Chen C, Yang M, Deng B, Kirby GM and Zhang X. *Cistanche tubulosa* ethanol extract mediates rat sex hormone levels by induction of testicular steroidogenic enzymes. Pharm Biol 2015; 25:1-7.
- [75] Zong G, He W, Wu G, Chen M, Shen X and Shi M. Comparison between *Cistanche deserticola* Y. C. Ma and *Cistanche tubulosa* (Shenk) Wight on some pharmacological actions. Zhongguo Zhong Yao Za Zhi 1996; 21(7): 436-437.
- [76] Chaturvedi M, Mali PC and Ansari AS. Induction of reversible antifertility with a crude ethanol extract of *Citrullus colocynthis* Schrad fruit in male rats. Pharmacology 2003;68(1):38-48.
- [77] Kulkarni TR, Mateenuddin M, Bodhankar SL and Saharabudhe RA. Reversible anti- fertility effect of lemon seeds (*Citrus limonum*) in male albino rats. International Journal of Research in Pharmaceutical and Biomedical Sciences 2012; 3(2): 545-550.
- [78] Bakare AA, Basse RB, Onyeka CA and Duru FI. Lime Juice (*Citrus aurantifolia*): Effect on fetal parameters of pregnant Sprague-Dawley rats. International Journal of Medicine and Medical Sciences 2012; 2(5): 114-116.
- [79] Gupta RS and Kachhawa JBS. Effect of *Cressa cretica* Linn. methanolic extract on testicular function of albino rats. Pharmaceutical Biology 2006; 44(5): 382-88.

- [80] Gupta RS and Kachhawa JBS. Contraceptive evaluation of isolated fractions of *Cressa cretica* (L.) whole plant methanol extract in male albino rats. *Planta Med* 2008; 74(9): PA324.
- [81] Kachhawa JBS and Gupta RS. Male contraceptive activity of phytochemical constituents of *Cressa cretica* (convolvulaceae). *Planta Med* 2010; 76: 79.
- [82] Hosseinzadeh H, Ziaee T and Sadeghi A. The effect of saffron, *Crocus sativus* stigma, extract and its constituents, safranal and crocin on sexual behaviors in normal male rats. *Phytomedicine* 2008; 15(6-7): 491-495.
- [83] Mohammadzadeh-Moghadam H, Nazari SM, Shamsa A, Kamalinejad M, Esmaeeli H, Asadpour AA and Khajavi A. Effects of a topical saffron (*Crocus sativus* L) gel on erectile dysfunction in diabetics: A randomized, parallel-group, double-blind, placebo-controlled trial. *J Evid Based Complementary Altern Med* 2015, doi:10.1177/2156587215583756
- [84] Vijaykumar B, Sangamma I, Sharanabasappa A and Patil SB. Antispermato-genic and hormonal effects of *Crotalaria juncea* Linn. seed extracts in male mice. *Asian J Androl* 2004; 6(1): 67-70.
- [85] Vijaykumar B, Sangamma I, Sharanabasappa A and Patil SB. Antifertility activity of various extracts of *Crotalaria juncea* Linn., seeds in male mice. *Philippine Journal of Science* 2003; 132(1): 39-46.
- [86] Saxena P, Gupta R and Gupta RS. Contraceptive studies of isolated fractions of *Cuminum cyminum* in male albino rats. *Nat Prod Res* 2015; 29(24): 2328-2331.
- [87] 86-Ashrafi H, Ghabili K, Hemmati AA, Jouyban A, Shoja MM, Aslanabadi S, Adl FH, Ghavimi H and Hajhosseini L. The effect of quince leaf (*Cydonia oblonga* miller) decoction on testes in hypercholesterolemic rabbits: a pilot study. *Afr J Tradit Complement Altern Med* 2012; 10(2): 277-282.
- [88] Aslam M and Sial AA. Effect of hydroalcoholic extract of *Cydonia oblonga* Miller (Quince) on sexual behaviour of Wistar rats. *Adv Pharmacol Sci* 2014; doi: 10.1155/2014/282698.
- [89] Naik BS, Dangi NB, Sapkota P, Wagle N, Nagarjuna S, Sankaranand R and Kumara BA. Phytochemical screening and evaluation of anti-fertility activity of *Dactyloctenium aegyptium* in male albino rats. *Asian Pacific Journal of Reproduction* 2016; 5(1): 51-57.
- [90] Vasudeva N and Vats M. Anti-spermatogenic activity of ethanol extract of *Dalbergia sissoo* Roxb. stem bark. *Journal of Acupuncture and Meridian Studies* 2011; 4: 116-122.
- [91] Verma HP and Singh SK. Effect of aqueous leaf extract of *Dalbergia sissoo* Roxb. on spermatogenesis and fertility in male mice. *Eur J Contracept Reprod Health Care* 2014; 19(6):475-486.
- [92] Al-Mailay HKA. The effect *Datura fastuolsa* L. alcohol extract on the fertility of white rats males. *J Al-Qadisiyah for Pure Sciences* 2008; 13(3): 1-11.
- [93] Nouri M, Khaki A, Azar FF and Rashidi MR. The protective effects of carrot seed extract on spermatogenesis and cauda epididymal sperm reserves in gentamicin treated rats. *Yakhteh Medical Journal* 2009; 11: 327-333.
- [94] Kumar RV, Reddy GVR, Sathyanarayana J, Bikshapathi T and Reddy MK. Effect of *Melia azedarach* and *Dodonaea viscosa* aqueous leaf extracts on fertility in male albino rats. *Indian J Pharm Biol Res* 2013; 1(4):7-12.
- [95] Adedapo AA, Abatan MO, Akinloye AK, Idowu SO and Olorunsogo OO. Morphaometric and histopathological studies on the effects of some chromatographic fractions of *phyllanthus amarus* and *Euphorbia hirta* on the male reproductive organs of rats. *J Vet Sci* 2003; 4(2):181-185.
- [96] Palaniyappan V, Bommireddy EP, Gudipudi and YandamalaN. In vivo fertility enhancing activity (aphrodisiac) of *Ficus carica* fruit on male wistar rats. *International Journal of Pharmacy and Pharmaceutical Sciences* 2013; 5(2):516-518.
- [97] Naghdi M, Maghbool M, Seifalah-Zade M, Mahaldashtian M, Makoolati Z, Kouhpayeh SA, Ghasemi A and Fereydouni N. Effects of common fig (*Ficus carica*) leaf extracts on sperm parameters and testis of mice intoxicated with formaldehyde. *Evid Based Complement Alternat Med* 2016; doi: 10.1155/2016/2539127.
- [98] Ahmed HM, Yeh JY, Tang YC, Cheng WT and Ou BR. Molecular screening of Chinese medicinal plants for progestogenic and anti-progestogenic activity. *J Biosci*, 39(3), 2014, 453-461.
- [99] Marashdah S. New natural compound for the enlargement of the ureter. *Arabian Journal of Chemistry* 2014; 7: 381-383.
- [100] Thakare VN, Kothavade PS, Dhote VV, and Deshpande AD. Antifertility Activity of Ethanolic Extract of *Allium cepa*Linn in Rats. *International Journal of PharmTech Research* 2009; 1(1): 73-78.
- [101] Dudek M, Awska I M and Szudlarek M. Phenolic acids in the flowers of *Althaea rosea* var. *nigra*. *Acta Poloniae Pharmaceutica-Drug Research* 2006; 63(3): 207-211.
- [102] Dhanapal R, Kavimani S, Matha VSB, Gupta M and Basu SK. Antisteroidogenic activity of ethanol extract of *Ammaniabaccifera*(L.) whole plant in female albino mice ovaries. *Iranian Journal of Pharmacology& Therapeutics* 2005; 4: 43-45.
- [103] Amir Zargar A and Zangeneh Z. Effect of camomile (*Anthemisnobilis*) aqueous-alcoholic extract on female rats estrogen hormone (poly cystic ovary). *Iranian Congress of Physiology and Pharmacology* 2007; 18: 26-30.
- [104] Monsefi M, Ghasemi M and Bahaoddini A. The effects of *Anethum graveolens* L. on female reproductive system of rats. *DARU* 2006; 14 (3):131-135.
- [105] Bertram GZ and Emertius PH. *Basic and Clinical Pharmacology*, 8<sup>th</sup> ed. New York McGraw Hill, 2001.
- [106] Mahdavian M, Golmakani N, Mansoori A *et al*. An investigation of effectiveness of oral dill extracts on postpartum hemorrhage. *The Iranian Journal of Obstetrics, Gynecology and Infertility* 2001; 4(8-7): 26-19.
- [107] GharibnAseri MK, MardSA andFarboud Y. Effect of *Anethum graveolens* fruit extract on rat uterus contractions. *Iranian J Basic Med Sci* 2005; 8(4): 263-270.
- [108] Committee for veterinary medicinal products, Juniperi fructus is the dried bery like cones of *Unipers communis*, The European Agency for the evaluation of medicinal products 1999.
- [109] Zagami SE, Golmakani N, Kabirian M *et al*. Effect of *Dill* (*Anethum graveolens* Linn.) seed on uterus contractions pattern in active phase of labor. *Indian Journal of Traditional Knowledge* 2012; 11(4): 602-606.
- [110] Mudgal NR, Srinivasan V and Sharma PS. Studies on goitrogenic agents in food. Goitrogenic action of arachidoside. *Journal of Nutrition* 1957; 61: 97-101.
- [111] Mudgal NR, Raghupaty E and Sharma PS . Studies on goitrogenic agents in food. Goitrogenic action of some glycosides isolated from edible nuts. *Journal of Nutrition* 1958; 66: 291-303.
- [112] Ibarreta D, Daxenberger A and Meyer HHD. Possible health impact of phytoestrogens and xenoestrogens in food. *APMIS* 2001; 109: 161-184.
- [113] Setchell KDR, Zimmer-Nechemias L, Cai J and Heubi JE. Isoflavone content of infant formulas and the metabolic fate of these phytoestrogens in early life. *Am J Clin Nutr* 1998; 68: 1453S-1461S.
- [114] Kronenberg F and Fugh-Berman A. Complementary and alternative medicine for menopausal symptoms: a review of randomized, controlled trials. *Ann Intern Med* 2002; 137: 805- 813.

- [115] Awale S, Lu J, Kalauni SK, Kurashima Y, Tezuka Y, Kadota S and Esumi H. Identification of arctigenin as an antitumor agent having the ability to eliminate the tolerance of cancer cells to nutrient starvation. *Cancer Research* 2006;66: 1751- 1757.
- [116] Dall'Acqua S, Tome F, Vitalini S, Agradi E and Innocenti G. *In vitro* estrogenic activity of *Aspleniumtrichomanes* L. extracts and isolated compounds. *Journal of Ethnopharmacology* 2009; 122(3): 424-429.
- [117] Farnsworth NR and Cordell GA. A review of some biologically active compounds isolated from plants as reported in the 1974-75 literature. *Lloydia* 1976; 39: 420-455.
- [118] Heftman E. Steroid hormones in higher plants. Insect molting hormones. *Lloydia*, 1975; 38: 195-209.
- [119] David M, Hamann C, Chen F, Bruch L and Lichtenegger L. Comparison of the relaxation effect in vitro of nitroglycerin vs. fenoterol on human myometrial strips. *Journal of Perinatal Medicine* 2000; 28: 232 –42.
- [120] Lapaire O, Ramos M, Manegold G, zanetti-Daellenbach R, Birkenmaier A, Holzgreve W, Hoesli I. The impact of the prophylactic or therapeutic application of Bryophyllum (*Bryophyllum calycinum*) on preterm delivery—A prospective study. *European Journal of Integrative Medicine* 2008; 1(1): 28.
- [121] Awais M. Medicinal plants of Pakistan. The faculty of mathematics and natural sciences, Oslo University 2008: 137-163.
- [122] Salunke KR, Ahmed RN and Marigoudar S R L. Effect of graded doses of *Caesalpinia bonducella* seed extract on ovary and uterus in albino rats. *J Basic and Clinical Physiology and Pharmacology* 2011; 22(1-2): 49-53.
- [123] Ahmed R LN. Effect of ethanolic seed extract of *Caesalpinia bonducella* on female reproductive system of albino rat: a focus on antifertility efficacy. *Asian Pacific Journal of Tropical Disease* 2012; S957-S962.
- [124] Khare CP. Indian medicinal plants – An illustrated dictionary. Springer Science and Business Media 2007: 111-112.
- [125] Banaszekiewicz W and Mrozikiewicz A. Determination of the estrogenic activity of *Calendula officinalis* flowers in biological units. *Poznan Towarz Przyjaciol Nauk* 1962; 2: 35-40.
- [126] Banaszekiewicz W, Kowalska M and Mrozikiewicz Z. Determination of the estrogenic activity of extracts from *Calendula officinalis* flowers. *Poznan Towarz Przyjaciol Nauk* 1962; 1: 53-63.
- [127] 126-Clara C. Effects of *Calotropis procera* on oestrous cycle and on oestrogenic functionality in rats. *Farmaco* 2001; 56(5-7): 373-378.
- [128] Kamatha KV and Rana AC. Preliminary study on antifertility activity of *Calotropis procera* roots in female rats. *Fitoterapia* 2002; 73: 111-115.
- [129] Attah AF, O'Brien M, Koehbach J, Sonibare MA, Moody JO, Smith TJ and Gruber CW. Uterine contractility of plants used to facilitate childbirth in Nigerian ethnomedicine. *J Ethnopharmacol* 2012; 143(1): 377-382.
- [130] Thakur S, Bawara B, Dubey A, Nandini D, Chauhan NS and Saraf DK. Effect of *Carumcarvi* and *Curcuma longa* on hormonal and reproductive parameter of female rats. *International Journal of Phytomedicine* 2009; 1: 31-38.
- [131] Sadraei H; Ghannadi A and Bavani T. Effects of *Zaratiam ulitflora* and *Carum carvi* essential oils and hydroalcoholic extracts of *Passiflora incarnate*, *Berberisintegerrima* and *Crocus sativus* on rat isolated uterus contractions. *Int J Aromather* 2003; 13: 1210–1217.
- [132] East J. The Effect of certain plant preparations on the fertility of laboratory mammals. *J Endocrinol* 1955; 12(4): 267-272.
- [133] Nobakht M, Fattahi M, Hoormand M, Milanian I, Rahbar N and Mahmoudian M. A study on the teratogenic and cytotoxic effects of safflower extract. *J Ethnopharmacol* 2000; 73(3): 453-459.
- [134] Yoo HH, Park JHand Kwon SW. An anti-estrogenic lignan glycoside, tracheloside, from seeds of *Carthamus tinctorius*. *BiosciBiotechnol Biochem* 2006; 70(11): 2783-2785.
- [135] Shi M, Chang L and He G. Stimulating action of *Carthamus tinctorius* L., *Angelica sinensis* (Oliv.) Diels and *Leonurussibiricus* L. on the uterus. *Zhongguo Zhong Yao ZaZhi* 1995; 20(3): 173-175.
- [136] Li CP. Chinese herbal medicine. Washington, DC, United States Department of Health, Education, Welfare 1974.
- [137] Kumar S, Biswas S, Mandal D, Roy HN, Chakraborty S, Kabir SN, Banerjee S and Mondal NB. *Chenopodium album* seed extract: a potent sperm-immobilizing agent both in vitro and in vivo. *Contraception* 2007; 75(1): 71-78.
- [138] Wikhe M, Zade V, Dabadkar D and Patil U. Evaluation of the abortifacient and estrogenic activity of *Cicer arietinum* on female albino rat. *J Bio Innov* 2013; 2(3): 105-113.
- [139] Wei H, Yili A, Ma Q, Mai D, Wang Z and Ma H. Establishment and application of co-transfection screening method for phytoestrogen active constituents. *Zhongguo Zhong Yao Za Zhi* 2011; 36: 2530-2534.
- [140] Ma H, Wang J, Qi H, Gao Y, Pang L, Yang Y, Wang Z, Duan M, Chen H, Cao X and Aisa HA. Assessment of the estrogenic activities of chickpea (*Cicer arietinum* L) sprout isoflavone extract in ovariectomized rats. *Acta Pharmacologica Sinica* 2013; 34: 380–386.
- [141] 140-Qazan WSh, Almasad MM and Daradka H. Short and long effects of *Citrullus colocythis* on reproductive system and fertility in female Spague-Dawley rats. *Pak J Biol Sci* 2007; 10(16): 2699-2703.
- [142] 141-Patil SJ and Patil SB. Efficacy of *Citrus medica* seeds extracts on reproductive activities in female albino rats. *Pharmacologyonline* 2009; 2: 803-817.
- [143] Patil SBS. Estrogenic activity of petroleum ether extract of *Citrus medica* L on immature albino rats. *Int J Green Pharm* 2007; 2: 91-94.
- [144] El-Alfy TS, Hetta MH, Yassin NZ, Abdel Rahman RF and Kadry EM. Estrogenic activity of *Citrus medica* L leaves growing in Egypt. *Journal of Applied Pharmaceutical Science* 2012; 2 (8):180-185.
- [145] Al-Said MS, Al-Khamis KI, Islam MW, Parmar NS, Tariq M and Ageel AM. Post-coital antifertility activity of the seeds of *Coriandrum sativum* in rats. *J Ethnopharmacol* 1987; 21(2): 165-173.
- [146] Tavana S, Eimani H, Azarnia M, Shahverdi A and Eftekhari-Yazdi P. Effects of saffron (*Crocus sativus* L.) aqueous extract on *in vitro* maturation, fertilization and embryo development of mouse oocytes. *Cell J* 2012; 13(4): 259-264.
- [147] Mokhber Maleki E, Eimani H, Bigdeli MR, Ebrahimi B, Shahverdi AH, Golkar Narenji A and Abedi R. A comparative study of saffron aqueous extract and its active ingredient, crocin on the *in vitro* maturation, *in vitro* fertilization, and *in vitro* culture of mouse oocytes. *Taiwan J Obstet Gynecol* 2014; 53(1): 21-25.
- [148] Agha-Hosseini M, Kashani L, Aleyaseen A, Ghoreishi A, Rahmanpour H, Zarrinara AR and Akhondzadeh S. *Crocus sativus* L. (saffron) in the treatment of premenstrual syndrome: a double-blind, randomised and placebo-controlled trial. *International Journal of Obstetrics and Gynaecology* 2008; doi:10.1111/j.1471-0528.2007.01652.x
- [149] Malashetty VB, Sangamma I, Sharanabasappa A and Patil SB. Effect of *Crotalaria juncea* seed extracts on the estrous cycle and ovarian activity in albino mice. *Oriental Pharmacy and Experimental Medicine* 2004; 4(2): 77-81.
- [150] Malashetty VB and Patil SB. Effect of chromatographic fractions of ethanolic extract of *Crotalaria Juncea* (L.) seeds on ovarian follicular kinetics and estrous cycle in albino rats. *IJPT* 2007; 6(2): 159-163.
- [151] Malashetty VB, Sharanabasappa A and Patil, SB. Post-coital antiimplantation and pregnancy interruption potency of the seeds of *Crotalaria juncea* Linn. *Oriental Pharmacy and Experimental Medicine* 2004; 4(2): 70-76.

- [152] Nayanatara AK, Akshatha A, Kottari S, Soofi AA, Rejeesh EP, Bhagyalakshmi K, Shetty S, Kini RD and Pai SR. Effect of *Cynodon dactylon* extract on estrous cycle and reproductive organs in female Wistar rats. International Journal of Analytical, Pharmaceutical and Biomedical Sciences 2012; 1(3): 10-15.
- [153] Nayanatara AK, Kottari S, Alva A, Soofi AA, Rejeesh EP, Bhagyalakshmi K, Shetty SB and Pai SR. Effect of aqueous extract of *Cynodon dactylon* on reproductive hormones and reproductive organ weight of female Wistar rats. IJBPAS 2012; 1(8): 1065-1076.
- [154] -Chen Y, Wang J, Liu L and Huang L. Anti-dysmenorrhea components from the rhizomes of *Cyperus rotundus* Linn. (Cyperaceae). 8<sup>th</sup> OAPS Working Paper Series Paper No. 2011-027, <http://www.oaps.hk/>
- [155] Pandiarajan G, Govindaraj R, Makesh Kumar B, Sankarasivaraman K. Antifertility activity in the acetone extracts of *Datura metel*, L seeds on female mouse. J Pharmacogenomics Pharmacoproteomics 2012; 3: 111.
- [156] Majumder PK, Dasgupta S, Mukhopadhaya RK, Mazumdar UK and Gupta M. Anti-steroidogenic activity of the petroleum ether extract and fraction 5 (fatty acids) of carrot (*Daucus carota* L.) seeds in mouse ovary. J Ethnopharmacol 1997; 57(3):209-212.
- [157] Kapoor M Garg SK and Mathur VS. Antiovolatory activity of five indigenous plants in rabbits. Indian J Med Res 1974; 62(8): 1225-1227.
- [158] Bhatnagar U. Poscoital contraceptive effects of an alcoholic extract of the *Daucus carota* Linn seed in rats. Clinical Drug Investigation 1995; 9: 30-36.
- [159] Ramya R, Sivasakthi R, Senthilkumar C, Anudeepa J, Santhi N and Narayanan RV. Preliminary phytochemical and antifertility studies on *Dodonea viscosa* Linn. Asian J Res Pharm Sci 2011; 1(3):77-79.
- [160] Bhatnagar U. Poscoital contraceptive effects of an alcoholic extract of the *Daucus carota* Linn seed in rats. Clinical Drug Investigation 1995; 9: 30-36.
- [161] Ramya R, Sivasakthi R, Senthilkumar C, Anudeepa J, Santhi N and Narayanan RV. Preliminary phytochemical and antifertility studies on *Dodonea viscosa* Linn. Asian J Res Pharm Sci 2011; 1(3):77-79.