Chapter – 3

Review of Literature
3. REVIEW OF LITERATURE:

3.1. Infertility:

The World Health Organization (WHO) gives the definition of Infertility (WHO / MCH / Geneva 1991) as follows:

- Infertility can be primary, if the couples have never conceived despite cohabitation and exposure to pregnancy (not contracepting) for a period of two years; primary infertility is also referred to as primary sterility.
- Infertility can be secondary, if a couple fails to conceive following a previous pregnancy, despite cohabitation and exposure to pregnancy (in the absence of contraception, breast feeding or postpartum amenorrhea) for a period of two years; is known as secondary sterility.

WHO estimates that 60 to 80 million couples worldwide currently suffer from infertility. Infertility varies across regions of the world and is estimated to affect 8 to 12 percent of couple’s world wide (Sciarra et al., 1994). WHO estimates the overall prevalence of primary infertility in India to be between 3.9 and 16.8%. Estimates of infertility vary widely among Indian states from 3.7 percent in Uttar Pradesh, Himachal Pradesh and Maharashtra, to 5 percent in Andhra Pradesh, and 15 percent in Kashmir. Moreover, the prevalence of primary infertility has also been shown to vary across tribes and castes within the same region in India (Zargar et al., 1997; Unisa et al., 1999; Kumar et al., 2007).

3.1.1. Male infertility:

According to a report given by the International Institute of population sciences, infertility is growing at an alarming pace, especially in cities of India. National census report of the past three decades (1981, 1991 and 2001) showed that infertility has risen by 50% in India. Study reports suggested that male infertility is almost as high as female infertility. One in every five healthy young men of age group 18 to 25 years suffers from abnormal sperm count. In every 100 couples, 40 % of the males suffer from infertility compared to 50 % of women. In the remaining 5 %, the causes are common to both men and women. Some common causes of infertility in men are irregular sperm production, hampered sperm delivery due to either erectile dysfunction or early ejaculation. Presence of various medical conditions such as obesity, certain infections such as sexually transmitted diseases, life style conditions such as diet imbalance, addiction to smoking or alcoholism, sedentary existence, or mental and emotional stress contribute to poor sperm count (Sharmisha Dey et al., 2010).

The literature surveys and various studies related to senility, alcohol intake, stress and diabetes induced sterility in male, are discussed as follows:

3.2. Senility induced sterility:

An experimental assessment of specific seminal markers such as glucosidase secreted by the epididymis, prostate specific antigen (PSA) and zinc
secreted from the prostate, and fructose secreted by seminal vesicles were investigated. Glucosidase, PSA, zinc, and fructose were significantly lower in men aged 50 years compared with men aged between 21 to 30 years. Glucosidase and PSA showed positive association with progressive sperm motility, whereas zinc levels showed an inverse relationship with sperm motility. The decline in sperm motility observed in men aged 50 years was due to changes in epididymal and accessory sexual glands function (Johnson et al., 1984). The histological changes in men’s aging germinal epithelium includes thickening of the basement membrane and tunica propria in seminiferous tubules, progressive tubular fibrosis, decreased diameter of the tubules, thinning of spermatogenic epithelium, and eventual obliteration of the tubules (Meacham et al., 1994). Men aged between 26 to 45 years, were found to have lower sperm quantities at both extremes of age (Fisch et al., 1996).

Testosterone level declines due to alterations of the Hypothalamic-pituitary-testicular (HPT) axis with aging, decreasing numbers of Leydig cells, or both. Total testosterone declines at 0.8% per year of age, whereas both free and albumin-bound testosterone declines at about 2% per year. Sex hormone binding globulin (SHBG) increases at 1.6% per year. The increase in SHBG likely results in further decline of testosterone hormone levels. Dehydro-epiandrosterone, dehydro-epiandrosterone sulfate, cortisol, and estrone shows significant decline, whereas dehydro-testosterone, Follicle stimulating hormone, Luteinizing hormone, and prolactin were increased over time (Feldman et al., 2002).

*Mucuna Pruriens* (MP) commonly known as velvet bean shows a protective efficacy on oxidative stress mediated damage in aged rat sperm. The reactive oxygen species induced patho-physiological alterations in structural and functional integrity of epididymal sperm in aged Wistar albino rats was analyzed after administering MP ethanolic extract of 200 mg/kg body weight. Results obtained from the aged animals showed significant reduction in sperm count, viability and motility was decreased, increased morphological damage, loss of chromosomal integrity and increase in mitochondrial membrane permeability in sperms of aged rats and these alterations were significantly reversed by administering MP. The epididymal sperms of drug treated aged rats showed increased sperm count; viability, motility and the morphological damages were much reduced (Sekar Suresh et al., 2009). Aging has a significant impact on male sexual function, sperm parameters, and fertility. These changes contribute to decreased fecundability, increased time to conception, and increased miscarriage (Isiah et al., 2011).

### 3.3. Alcohol induced sterility:

An experimental assessment of relative efficacy of drugs from herbal origin on sexual performance and hormone levels in alcohol exposed and normal
rats showed twice an increase in sperm count and serum testosterone level than the control rats. Alcohol can affect the Hypothalamo-pituitary-gonadal axis leading to impotence and sterility by various mechanisms of actions. The three herbo mineral preparations which are a combination of *Mucuna pruriens* 32 mg, shilajeet (purified rock ooze) 32 mg and Ashwagantha 32 mg, showed the restitution of the fertility in the alcohol exposed rats (Mitra et al., 1996).

Alpha tocopherol administration has a protective effect on ethanol-induced testicular steroidogenic dysfunction. Alpha tocopherol also ameliorates the ethanol-induced oxidative stress and may execute its role by modulating testicular free radical production and stimulating testicular androgenesis (Maneesh et al., 2005).

*Moringa oleifera*, commonly known as drumstick tree has been used as an anti-ulcer, diuretic, anti-inflammatory and for wound healing. Its leaves are also used nutritional supplement and growth promoters due to significant presence of protein, selenium, calcium, phosphorous, beta carotene and alpha tocopherol. The effect of *Moringa oleifera* on alcohol induced testicular toxicities in pre-pubertal Wistar rats ameliorates the toxicities with its antioxidant properties. Alcohol causes numerous atrophies in the testes and damaged spermatogenic cells. *M.oleifera* and vitamin C however exhibited protective and reversibility effects. *M.oleifera* ameliorates alcohol induced testicular toxicities with its antioxidant properties comparable to vitamin C (Rosemary et al., 2013).

### 3.4. Stress induced sterility:

A study was done on 120 patients for stress induced sterility, in which 60 subjects were experimental and the other 60 were control. The serum cortisol levels were assessed on experimental subjects and administered *Mucuna Pruriens* seed powder (5 mg/day) orally. For carrying out morphological and biochemical analysis, semen samples were collected twice before and after treatment. Treatment with *Mucuna pruriens* significantly ameliorated psychological stress and seminal plasma lipid peroxide levels along with improved sperm count and motility. Treatment also restored the levels of superoxide dismutase, ascorbic acid in seminal plasma of infertile men. Mucuna Pruriens not only reactivates the anti-oxidant defense system of infertile men, but it also helps in the management of stress and improves the semen quality (Kumar et al., 1994).

*Cynodon dactylon* (Family: Poaceae) is known to be a tackler in Indian Mythology and is offered to Lord Ganesha. It is found everywhere, even on waste land, roadside, dry places and spreads vigorously on cultivated ground. *C. dactylon*, most commonly known as Dhruva, is an elegant perennial grass, growing throughout India. Traditionally, fresh expressed juice of the grass is useful in hematurias, vomiting, application in catarrhal ophthalmia, also can be
applied to cuts and wounds as it checks bleeding, in chronic diarrhea and
dysentery. Decoctions of roots are used in vesical calculus and secondary
syphilis, stoppage of bleeding from piles and irritation of urinary organs. An
alkaloid isolated from the plant slows down the flow of blood in mesenteric
capillaries, has hypoglycaemic effect, cause reduced bleeding and clotting time,
hypotension, and has antioxidant activity and antiviral activity against the
vaccinia virus.

Studies were carried out to test, if the constituents of *Cynodon dactylon*
plant are useful in coping stress induced sexual problems. Treatment of rats
under stress with methanolic extract of *Cynodon dactylon* has shown a promising
effect in overcoming stress induced sexual dysfunction, sexual performance,
fructose content, sperm concentration and its effect on accessory sexual organs
and body weight. The study concludes that active constituents of *C.dactylon*
present in methanolic extract have a potential aphrodisiac and male fertility activity
(Chidrawar et al., 2011).

3.5. Diabetes induced sterility:

The effect of diabetes on rat testes and the role of insulin treatment alone
and in combination with Aminoguanidine (AG) administration on affected testes
showed testes sections of the diabetic non-treated rat testes with few
spermatogonia and primary spermatocytes with condensed nuclei lining most of
the seminiferous tubules and with widening of the interstitial tissues. Morphometric study showed a significant decrease in diameter of seminiferous
tubules. The electron microscopic examination showed affection of both
spermatogonic and sertoli cells with less active Leydig cells. Diabetic rats treated
with insulin showed mild improvement of the testes structure. Diabetic rats
treated with both insulin and AG showed restoration of testes structure, nearly
similar to the control animals (Abeer et al., 2010).

In all the studies mentioned above were performed to understand the effect
of a particular, single herbal plant on the reproductive system of rats and their
curing efficacy.

**Review for Cycas circinalis and Ionidium suffruticosum from Siddha literature:**

*C.circinalis* (Mathana Kama Poo), the cone of male variety acts as an
aphrodisiac, narcotic and stimulant. The powder of the dried male cones when
taken internally strengthens the body and improves the maleness (Murugesa
Mudaliyar et al., 1996). *l.suffruticosum* (Ratna Purus), is a rejuvenating herb,
which increases the quality and quantity of semen, acts as an aphrodisiac
(Murugesa Mudaliyar et al., 1996).The pharmacological and biological activity of
*Cycas circinalis* and *londium suffruticosum*, were collected from various
literatures and summarised as below.
3.6. Pharmacological and biological activity of *Cycas circinalis* L:

3.6.1. Phytochemical screening:

The phytochemical examination of the methanolic extract of the leaflets of *Cycas circinalis* L. led to the isolation of one new biflavonoid, (2S, 2"S)-2,3,2",3"-tetrahydro-4", 4-di-O-methylamonto flavone (tetrahydro isoginkgetin; 2), and 15 known compounds, 11 of which are reported for the first time from *C. circinalis*. The isolated compounds include 14 biflavonoids, three lignans, three flavan-3-ols, two flavone-C-glucosides, two nor-isoprenoids, and one flavanone.

3.6.2. Antimicrobial activity:

Various compounds isolated from *C. circinalis*, showed moderate antibacterial activity against *Staphylococcus aureus* and methicillin-resistant *S. aureus*. The isolated biflavonoids were tested for antimicrobial activity. None showed anti-fungal, anti-malarial, or anti-leishmanial activity (Abeer Moawad et al., 2011).

Till date only few studies such as phytochemical screening, antimicrobial activity and various medicinal uses were carried out on *C. circinalis*. The fertility effect of *C. circinalis* has been, not yet proved scientifically by any research. The present research work is the first scientific study done to evaluate the fertility effect of *C. circinalis*.

3.7. Pharmacological and biological activity of *Ionidium Suffruticosum*:

3.7.1. Antidiabetic activity:

*Ionidium suffruticosum* has highest medicinal value. It was widely used by traditional healers to treat diabetes. The symptoms of diabetes such as peripheral neuritis were found to be reduced (Sarita et al., 2004).

3.7.2. Anti plasmodial activity:

*Ionidium suffruticosum* is used for treating Malaria and the herb has anti-plasmodial activity (Bernard Weniger et al., 2004; Patrice et al., 2007).

3.7.3. Effect on genitourinary system:

*Ionidium suffruticosum* used for treating male sterility in Ivory Coast (Kheraro et al., 1950), for treating urinary tract infections and water retention in India (Pushpangadan et al., 1984) and the plant is used as tonic. The leaves of tender stalks are demulcent; the roots are anti-gonorrhoeic, diuretic, used for bowel complaints and to treat urinary problems (Pushpangadan et al., 1984).

3.7.4. Antidote

The fruits were used traditionally as an antidote for scorpion-sting (Arunkumar, et al., 2005).

3.7.5. Phytochemical Screening:

The phytochemical investigations of *Ionidium suffruticosum* leaf and leaf callus were done and the chemical constituents were compared between *in vivo* and *in vitro*, showed the presence of steroids and absence of tri-terpenoids,
presence of alkaloids, absence of saponins, absence of tannins, presence of carbohydrates, absence of protein, absence of fatty acids, lack of glycosides, lack of volatile oils in both leaf and leaf callus (Arunkumar et al., 2011).

3.7.6. Hypolipidemic activity:

The coumarin derivative isolated from Ionidium suffruticosum, when administered to the animal model at the dose of 10 mg/kg body wt/day along with high fat diet prevented the rise in the plasma total and LDL-cholesterol, triglycerides and phospholipids than that of other extracts. I.suffruticosum had showed more cardio-protective effect against hyperlipidemia than that of flavone derived from Mucuna pruriens. Recent research has revealed that 4-5% decrease in LDL cholesterol results in 5-10% decrease in the occurrence of coronary heart disease (CHD). The coumarin derivatives isolated from Ionidium suffruticosum was found to be beneficial in preventing hypercholesterolemic, atherosclerosis and thus results in reducing the risk factors for coronary artery disease (Satheesh Kumar et al., 2012).

3.7.7. Antioxidant activity:

The aqueous extract of Ionidium suffruticosum showed its anti-oxidant activity when compared to that of standard drugs. The aqueous extract of Ionidium suffruticosum was found to have high content of flavonoids and phenolic compounds. The anti-oxidant activity of the plant may be due to the presence of the flavonoids and phenolic compounds. Ionidium suffruticosum can be used as natural antioxidants and as a possible food supplement in pharmaceutical industry (Ashok Kumar et al., 2014).

Till date only the above studies were carried out in I.suffruticosum. The fertility effect of I.suffruticosum has been, not yet proved scientifically by any research. The present research work is the first scientific study done to evaluate the fertility effect of I.suffruticosum.

Various researches are carried out to find out the plant products that can be used to treat male infertility. Several plant extracts have been used since ancient times to treat infertility. Infact, evidence of the use of herbal extracts for male infertility dates all the way back to 200 A.D. The researchers had done a lot of herbal research using a wide variety of species of herbs. Inspired by the above studies and understanding the importance of certain herbal plants, in the present study two important herbal plants, Cycas Circinalis L. and Ionidium Suffruticosum Ging. were taken, for the first time in herbal research to study their toxicological and fertility effects.