

CHAPTER-ONE  
INTRODUCTION

## C H A P T E R - O N E

### 1. INTRODUCTION

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## 1.0 General introduction

Many a problem the modern world is faced with—increased crime, juvenile delinquency, water pollution, air pollution, urban deterioration, noise, dirt, waste disposal, racial friction and others—are mainly associated with the increasing population. Though it is not the sole cause, it is a major one.

The increased natality and revolution in medical sciences cut down the high child mortality and increase longevity of the adults. Consequently the population grows alarmingly. This naturally puts strain on the available resources.

The world population has reached the mark of 500 crores and will reach the mark of 600 crores by 2000A.D. It is certainly a tremendous increase. The food /population will be overriding problem of the last decade of this century.

As a result, the social and technical problems are developing and multiplying faster than they can be solved.

" Population explosion " has alarmed the thinkers and scientists of the world to find out the solution for and search on various birth controlling methods.

In spite of the availability of a large number of contraceptive methods like the mechanical devices, bioactive devices, surgical procedures and drugs for the control of the fertility, search still continues for the development of newer, safer, easier and more effective methods to combat the "Population explosion."

Research on the biology of reproduction provides understanding of basic mechanism that is essential for progress in the limitation of human fertility. The female reproductive system has been studied in great detail for a long time for providing the necessary clues towards fertility control. Research on the reproductive biology of male has lagged many years behind than that of the female. The entire area of male physiology of reproduction has been generally ignored and the main emphasis being given to the interference in the female physiology of reproduction. We are now in a period of significant progress in our understanding of the hormonal control of spermatogenesis, the mechanism of sperm release, sperm maturation, the physiology of the excurrent duct system and the process of fertilization. So now the pendulum has swung towards the male side. The testis and its duct system are becoming targets for solving fertility control in the male.

A number of methods have been investigated to achieve a safe and effective measure for limiting male fertility. Interest and monetary efforts are being directed towards the regulation of population growth by motivating the human beings to accept a reversible, a 100% effective pharmacological tool having minimal side effects.

A number of synthetic compounds have been reported to arrest spermatogenesis or induce functional sterility in laboratory animals.

Many chemicals as triethylenemelamine ( Jackson and Bock, 1955), nitrogen mustard (Jackson, 1966), busulfan (Singh and Mathur, 1968), progestational steroids (Kar et al., 1967), prostaglandins (Ericsson, 1972; Tso and Lacy, 1975), PMHI (DL-6 (N-alpha-pipecolinomethyl)-5-hydroxy indane malate, Dechamma and Sarkar, 1987), hydrocortisone ( Nair et al., 1987), flutamide (Dhar and Setty, 1987), formaldehyde (Shah et al., 1987),  $\beta$ -sitosterol (Malini

and Vanithakumari, 1988) and cyproterone (Menon and Bhiwgade,1988) proved successful in laboratory animals but were unsuitable for human beings due to toxic manifestations. Attention has therefore been focussed on plant products especially of the Indian origin.

A number of medicinal plants were claimed in the Indian folk-lore medicines to possess antifertility properties. A majority of researchers are actively engaged in exploring the effects of the plant preparations on the female and male reproductive tract.

### 1.1 Review of the plants having antifertility activity

As applied only to antifertility effects the following is a brief review of the available literature.

Punica granatum (Gujaral et al.,1960), Hippophae salicifolia (Joshi et al.,1965), Ananas comosus (Bhaduri et al., 1968), Butea monosperma (Khanna and Chaudhary, 1968), Vinca rosea (Joshi and Ambay,1968 and Toro, 1984), Butea frondosa ( Razdan et al., 1969), Oscimum sanctum (Kasinathan et al., 1972), Opium seed (Vyas and Singh, 1976), Malvaviscus conzanttii (Dixit, 1977), Aristolochia indica ( Pakrashi and Pakrasi, 1977), Momordica charantia (Biswas et al.,1977), Blighia sapida (Saxena et al., 1977), Hibiscus rosa sinensis (Kholkute, 1977), Vitex negundo (Singh et al.,1978, Sohani, 1985), Vinca rosea and Embelia ribes (Chauhan et al.,1979), Artobotrys odoratissimus (Prakash,1979), Calotropis procera (Garg, 1979), Hibiscus rosa sinensis (Singwi and Lall,1980), Papaya seed (Das, 1980, Chinoy and Sondarva, 1988), Oscimum (Seth et al.,1981), Allium sativum (Dixit and Joshi,1982), Plumbago zeylenica (Bhargava, 1984), Butea monosperma (Awati, 1985), Daucus carota (Shah, 1985), Oscimum sanctum (Khanna et al., 1986), Gossypol (Nair et al.,1988), Piper betle (Toro and Hiremath,1988),Terminalia bellirica (Rao, 1988), Vinca rosea (Chinoy et al.,1988),

Andrographis paniculata (Akbarsha et al.,1988) and Solanum xanthocarpum (Rao, 1988) proved to have antifertility characters in various laboratory animals.

## 1.2 Reasons that lead to the undertaking of the present dissertation

A critical evaluation of the earlier review of the plant extract induced aspermatogenesis reveals that :

(i) The focal point of interest of most of these is the " damage " caused in the seminiferous tubules by the " active principle " in the plant extract. Not much is known about the mechanism of such damage.

(ii) These studies give more information on histological changes in the testis and a few accessory reproductive organs. Though in some cases some information is available on the changes in enzymes, proteins, lipids and mucosubstances.

(iii) Some workers have focused their attention only on histological alterations, whereas others have studied enzymatic and other metabolites. Here also all the accessory reproductive organs have not been studied by all workers, some have only studied epididymis whereas others have selected either seminal vesicle or prostate gland only.

It is hence felt desirable that in a study of plant extract induced aspermatogenesis, all the accessory reproductive organs should be studied simultaneously to find out how the plant extract affects these organs. Some of the effects may be direct, others may be indirect caused through the effect on Leydig cells. They have to be aided by enzymatic and other metabolic studies to get a complete picture of effects of plant extract on these organs.

It is with these various views, it was decided to study the effects of Plumbagin on the male reproductive organs of the albino rats. To make the study consolidated and as complete as possible it was decided to study

changes in body weight and organ weights, histological changes, alterations in a lysosomal enzyme and a nonlysosomal enzyme in testes and all the accessory reproductive organs of the laboratory albino rat.

### 1.3 Choice of the plant

For the present investigation Plumbagin, an active principle from the plant Plumbago zeylenica, was selected to explore its antispermatogenic activity.

Plumbago zeylenica is cultivated in gardens throughout India. In English vernacular it is known as "Plumbago." In Marathi it is known as "Chitraka". (Plate No.1)

Plumbago zeylenica root powder has been shown to contain plumbagin, sitosterol, steroidal glycosides, vanillic acid, plumbagic acid, glucose, 3-chloro-plumbagin, 3,3-biplumbagin, catechol tannins and many other alkaloids (Padhye and Kulkarni, 1973; Qiu et al., 1980 and Chowdhury et al., 1981).

#### 1.3.1 Biological study of Plumbagin

An active principle of Plumbago zeylenica, chlorohydroxynaphtho-quinone has been found applications in the fields of medicines and microbiology.

The use of the extract of the roots of Plumbago zeylenica which contains Plumbagin and 3-Chloroplumbagin has been prescribed in the Indian system of medicine i.e. "Ayurveda" "आयुर्वेद" since ancient times. The earliest reference to the use of the extract of "Chitrakamula" is thus found in Charak Samhita in the following verses :

कटुकः कटुकः पाके वीर्योष्णचित्रको मतः ।

"Chitrakamula is pungent by taste and very 'heat producing' by Virya".

चित्रकमूलं दीपनीय पाचनीय गुदशोधार्थः शूलहरणाम् ।

PLATE NO. 1



CHITRAKA  
Plumbago zeylenica



" The root of ' Chitraka ' is the best among the drugs used as the appetisers and digestion promoters. It removes diseases of the swelling of the anus, piles and abdominal pains ".

One also finds a reference to the medicinal properties of the extract of " Chitrakamula " in Vagbhata as

चित्रकाग्निस्तमः पाके शोफार्शः कृमिकुष्ठहः ।

" Chitraka " is like abdominal fire with respect to digestion and can also be used as a cure for swelling, piles and skin diseases.

It is interesting to note that these properties are almost identical with the ones attributed to the "Chitraka extract " in the modern pharmacopoeia prepared at much later date. Thus the pharmacopoeia considers " Chitraka extract" as a drug which increases the digestive power, promotes the appetite and is useful in the treatment of dysepsia, piles, anasarca, diarrhoea, skin diseases etc. (Nadkarni and Nadkarni, 1954 and Chopra et al.,1933).

In Malaya, chewing the roots of Plumbago zeylenica is said to be effective for producing abortions (Burkill, 1935; Cho, 1933 and 1945).

3-Chlorohydroxy-1,4-naphthoquinone compounds of Plumbago zeylenica are antimicrobial agents (Kulkarni and Kelkar, 1987 and Chougule,1988).

Plumbagin in small doses, has a stimulant action on central nervous system, on plain muscles and on the secretion of sweat and bile. Blood pressure shows a slight fall and the peripheral vessels are found to dilate. Plumbagin acts as a powerful irritant and has well marked antiseptic properties.

Naphthoquinone ring of the Plumbagin was shown to possess antibacterial, antifungal activity ( Krishnaswami and Purushothaman, 1980). Plumbagin is known to have abortifacient effect and to induce menstruation (Chunekar and Pandey, 1982; Gogate, 1982 and Sharma, 1982).

The root extract of Plumbago zeylenica when applied to the Os uteri causes abortion (Nadkarni and Nadkarni, 1976). Plumbagin was found to prolong estrous cycle and induce antiimplantation effects (Premkumari et al.,1977). Plumbagin inhibits spermatogenesis as well as alters the epididymal functions in male dog ( Bhargava, 1984). Plumbago zeylenica induced failure of implantation or pregnancy which was due to estrogenic effects ( Devarshi, 1987).

### 1.3.2 Chemical nature of Plumbagin

Systematic name :

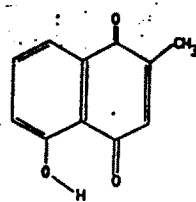
5-Hydroxy-2-methyl-1,4-naphalendione, or

5-Hydroxy-2-methyl-1,4-naphthoquinone

Molecular formula :  $C_{11}H_8O_3$

Molecular weight : 188.17

Structural formula :



### Chemical properties of Plumbagin

- (1) Yellow needles (2) Melting point 78-79<sup>o</sup>C (3) Sublimes
- (4) Volatile with steam (5) Slightly soluble in hot water
- (6) Soluble in alcohol, acetone and chloroform, benzene and acetic acid

#### 1.4 Reasons for selecting Plumbagin for the present dissertation

As noted in the review of literature the antifertility effects were due to the Plumbagin isolated from Plumbago zeylenica root powder (Premkumari et al., 1977 and Azad et al., 1982) which has poisonous effects and hence least attention was paid to this plant. But in many Ayurvedic texts the use of Plumbago zeylenica root powder in various medicines has always been referred to its property of disruption of pregnancy in female (Chunekar and Pandey, 1982; Gogate, 1982; Sharma, 1982). Plumbago zeylenica root powder administration to female rats showed alterations in histology, mucosubstances, uterine luminal fluid proteins and uterine proteases (Devarshi, 1987). In this way it showed alterations in female reproductive system.

Bhargava (1984) studied effects of Plumbagin administration on the testis and epididymis of dog. He reported alterations in the histology, wet weight of organs, RNA, sialic acid, cholesterol, acid phosphatase and alkaline phosphatase. Plumbagin caused selective testicular lesions and arrested the spermatogenesis. Thus the extract of Plumbago zeylenica is responsible for antispermatogenic activity.

Except this one report on dog, no information is available towards male reproductive system. Hence it was felt desirable to study effects of Plumbagin administration on the male reproductive system of rat.

The alterations in acid phosphatase, alkaline phosphatase and histology have not been studied in all reproductive organs of male at one and the same time. Hence it was decided to study the histomorphological and biochemical alterations in male reproductive system to get a clear insight into the mechanism of aspermatogenesis induced by the Plumbagin of Plumbago zeylenica.

### 1.5 Choice of Parameter of study

As mentioned earlier it was decided to study Plumbagin induced alterations in adult albino rats. The following parameters were chosen for studies.

- 1) Body weight
- 2) Organ weight
- 3) Tubular diameter
- 4) Histology
- 5) Fertility test
- 6) Lysosomal enzyme-acid phosphatase
- 7) Non lysosomal enzyme-alkaline phosphatase.