1. Introduction

1.1 Preface

One of the most alarming and challenging problem facing the mankind is its everexpanding population. It affects every aspect of individual as well as national life. According to one estimate the total human population on earth at the begining of the Christian era was 25 crores which is very less than the present figure of about 500 crores. The rise was at a slow rate at begining but increased during the last 200 years or so. From 25 crores at the begining of the Christian era it took about 1650 years to double the population. The growth was at the rate of 0.04% per year. The rate increased to 0.5% by 1800. By 1962 at the rate of 1.5% the population crossed 300 crores. In 1985 the world population was about 500 crores. Thus not only has the population increased considerably, but the rate of growth also increased. 200000 persons are being added to the world population every day and therefore 73 million new mouths to feed every year. If the population increase at this rate then at 2001 A.D. it will become about 800 crores.

As on date, India's share of world population is 15% whereas it's total land area on the earth works out to only 2.4% and share of world income is mere 2 %. Like world population, population in India, within a short period of 4 decades after indepedence has become 750 million. The population in India at this rate will be about 100 crores in 2001 A.D. At this staggering accelerated rate of growth in a few years from now we will be saddled with an army of unemployed, hungry and desperate

people who will threaten the very foundation of our social, economic and political edifice.

The causes of population explosion of world and India also are not difficult to understand. The main cause is more growth rate. It is especially distressing that the highest fertility rates are found in many developing countries that are struggling to improve their gains in agricultural production. The only way to overcome this problem is to go for effective and immediate population control and thereby to bring down the birth rate.

The causes of population explosion in India are many, but the significant causes are a large number of illiterate and ignorent people, high fertility rate due to temperate climate and high demographic gap (Decrease in mortality and increase in birth rate). To check the population explosion there is no other way in the hands of mankind than to control the birth rate. This can be done by limitation of the family size (family planning).

Basic mechanism that is essential for progress in the limitations of human fertility can be understood by research on the biology of reproduction. Much of the work is done on female, but research on the reproductive biology of the male has lagged many years behind. The interest and efforts are being directed all over the world towords controlling population explosion by motivating the human male to accept a reversible, voluntary and most effective pharmacological tool having minimal side effects.

Many chemicals, especially alkylating agents and salts were tried to promote sterile phases in male rats. The

dramatic success of the synthetic progestational steroides in cyclic ovulation control, prompted Hellar et al(1958) to evaluate these agents as oral contraceptives in human male. Tytler (1961) documented the efforts to induce infertility in rats with homogenates of homologous testis. Reversible arrest of spermatogenesis has been reported in rats after administration of some progestational steroids (Kar et al,1967). Prostaglandins also produce inhibition of spermatogenesis (Ericson 1972; Tso and Lacy, 1975)

A study of correlation between anticancer drugs and antifertility activity, perticularly with reference to synthetic drugs, has evoked a great interest among research workers (Joshi and Ambaye, 1965; Conglio et al.,1974; Boris et al.,1974; Kinson,1978). Some alkylating agents, antibiotics and steroids have been found to supress spermatogenesis in experimental animals (Jackson,1959; Kalra and Prasad,1967). However, it was observed that these chemical agents which cause temporary or permanent sterility also produce some toxic effects in body.

The plant preparations produce minimal side effects hence in recent years scientists all over the globe are taking interest in plant preparations to control human fertility. There are number of medicinally important plants possesing antifertility properties. Crores of Dollars are spent by World Health Organization (W.H.O.) on the "Special Programme of Research, Development and Research Training in Human Reproduction". Task force of W.H.O.(1980) engaged in testing of gossypol, a plant preparation from cotton, and is

initiating a dose finding study in non-human primates. Number of research workers are actively engaged in exploring the effect of the various plant preparations on female reproductive tract, however, very little work is on record concerning antispermatogenic acivity of plant preparations.

1.2 Review of plants having Antifertility activity :-

In last 50 years, since the commencement of Sir Ramnath Chopra's work in India and Farnsworth's work abroad several hundred plant substances have been studied. In the first edition of Chopra's book "Indigenous drugs of India" published in 1933, he discussed the studies on 52 plants. In the second edition which came out in 1956, the number has risen to 100. With the massive probe carried out by various agencies, this has increased tremendously in recent years. A 1976 publication of "Indian council of medical Research" lists about 350 plants in part-I only. From the latest numbers of periodical publication of the "Central Drug Research Institute, Lucknow" on "Screening of Indian plants for biological activity", it is found that nearly 2000 plant species have been subjected to a broad battery of pharmacological and biological tests. The various plant materials have been extracted and extracts put through a wide biological screening of 61 tests. These include tests for antibacterial, antifungal, antiviral, antihelminthic, antiprotozoal hypoglacemic, anticancer, and antifertility tests. The screening of these preparations on laboratory animals has been standerdized at the reproductive physiology division of All India Institute of Medical Sciences, New

Delhi.

The problem underlying the search of natural antifertility drugs basically concerns with deciding which of the approximately 750,000 species of the higher plants should be examined in an animal system for their potential antifertility effects. The review entitiled "Potential values of plants as sources of New Antifertility Agents" I & II published by Farnsworth et al., (1975) has included plants having folk-loric reputations as well as those plants whose extracts were shown to be active in animals or humans as antifertility agents. The following is a brief review of the work done on the effects of some piant extracts on fertility.

Crafton and Robinson (1949) demonstrated that extract of Lithospermum ruderale decreased the gonadotrophic activity of pituitory of female mammal. Plunkett and Noble (1951) studied the effect of Lithospurmum extracts of rats and demonstrated that roots of the plant impaired development of the gonads and accessory sex organs of male. M-xylohydroquinone, an active principle present in Pisumsativum extract produced foetal resorption in pregnant rats when given in first eight to ten days of the pregnancy, but had no effect when given later (Sanyal, 1960). Mallotus phillippinensis has antifertility principle known as rottferin, which causes 100% infertility in females (Gujaral et al., 1960). Punica granatum produced infertile matings in rats and guinea pigs (Gujaral et al., 1960). Joshi et al.,(1965) reported the antispermatogenic property in the extract of the bark of Hippophae salicifolia. Matsui et al.,

(1967) showed that whole plant extract of Isatis oblangata, Rhaphanus sativus and Euphorbia lathyrus decreases number of litters in mouse. Ananas comosus induced antifertility in mouse (Bhandari et al., 1968) and 60% inhibition of implantation in rats (Garg et al., 1970). Stevia rebaydiana reduced fertility in rats by 57 to 78 % (Planas, 1968). Whole plant water extract of Dienthus superbus was shown to have estrogenic effects (Matsui et al., 1969). Antifertility effects of Butea frondosa were demonstrated in mouse and rats (Rajdhan et al., 1969) and in house sparrow (Shriwastava, 1982). Chou et al., (1971) showed antifertility activity of Gleditsia horrida. Meyer et al., (1973) found that an aqueousethanolic extract of the roots of Tubernacmontana heyneana prevented pregnancy in adult female rats.

ROC-101, a herbal preparation composed of a mixture of three different plants, impaired fertility and caused sterility in male mice (Munshi and Rao, 1972). Dixit et al., (1974) observed that an extract of Cannabis sp. caused testicular disfunction in frog. Oscimum sanctum induces reversible aspermatogenesis in male mice (Kashinathan et al.,1972). Opium seed extract was shown to decrease number and size of spermatocytes, and decrease in size of seminiferous tubules without any alterations in Leydig cells in pigeon (Vyas and Singh, 1976). Malvaviscus conzantii extract administration induced changes in the histoarchitecture of testis in bats (Dixit, 1977). Aristolochia indica extract induces disfunction of seminiferous epithelium (Pakrashi and Pakrashi, 1977). Fresh aqueous extract of Mimordica charantia when

administered to fertile male albino rats, alterd differential count of germ cells in the testis (Biswas et al., 1977). Saxena et al., (1977) demonstrated that the saponine obtained from Blighia sapida had 100% spermicidal activity. Hot alcoholic extracts of seeds of Butea monosperma had antifertility activity (Dreishbach, 1963; Khanna and Chaudhary, 1968). The total alkaloids of Vinca rosea when administered intraperitonially decreased the number of atretic follicles, graffian follicles and corpora lutea (Samual et al., 1976). Hibiscus rosasinensis extract when given orally resulted in mild damage of testicular germinal epithelium to nearly total sloughing (Kholkute, 1977). Singh et al. (1978) studied 10 plants for their antifertility activity. The plants were Anona squamosa, Buddleja asiatica, Celastrus pepiculata , Cyperus rotundus, Hibiscus rosa-sinensis, Luffa acutangula, Mentha arvensis, Sapindus trifoliatus, Vitex negudo and Withania soarifera. Different tests were carried out in albino rats, mice, rabbits, dogs and cats. None of the plant material except Vitex negundo was found to be effective in males. While B. asiatica, L. acutangula and S. trifoliatus were found to posses antiovulatory, abortificient and antiimplantation activities respectively. Testicular degeneration was shown with aqueous ethanolic extract of Vinca rosea and Embelia ribes (Chauhan et al.,1979). Artabotrys odoratissimus caused temporary sterility (Prakash, 1979). Garg, (1979) demonstrated certain testicular necrotic changes after 30 days with the extract of Calotrophis procera.

In sparrow, the extract of Hibiscus rosasinensis flowers

decreased the weight and volume of gonads in both the sexes (Singh et al., 1980). Singwi and Lal (1980) studied the effect of flower extract of Hibiscus rosasinensis on male bat and commented on the difference observed in scrotal mammals. Pueraria tuberosa was found to possess 100% postcoital contraceptive activity in rats, hamsters and guinea pigs (Chandohoke et al., 1981). Plumbagin, an active principle isolated from the roots of Plumbago rosea when administered orally, showed profound influence on male reproductive system. The alterations in adult rat involve organ weight changes and biochemical and histochemical changes (Shatakumari et al., 1981). The flowers of Butea frondosa are reported to posses the antifertility activity in house sparrow by Shriwastava (1981). Seth et al., (1981) observed that Oscimum extract reduced sperm count and sperm motility in male rats. Dixit and Joshi (1982) demonstrated impairment in spermatogenesis with extract of Allium sativum powder. Plant flavonoides isolated from Vitex negundo induced reversible chemical sterilization following a chronic treatment (Bhargava and Dixit,1982). Hoffer (1933) reported effects of gossypol, active principle present in cotton plant on testis. Plumbago zeylanica has been shown to arrest spermatogenesis at spermatocyte level in dogs (Bhargava, 1984). Toro (1984) demonstrated aspermatogenic activity of Vinca rosea alkaloid; Extract of Vitex negundo (Sohani, 1985), Daucus carota (Shah, 1985) and Butea monosperma (Awati, 1985) were shown to possess antispermatogenic activity in rats.

Khanna et al., (1986) studied the effect of long term

feeding of Tulsi (Oscimum sanctum) on reproductive performance of adult albino rats. It decreased the sperm count, sperm motility and weight of the reproductive organs and even the mating behavior in both the sexes was inhibited. Neem oil in the true toad Bufo melanostictus showed inhibition of sperm motility (Gopinath and Nagappan, 1988). Nair et al., (1988) observed that Gossypol known to inhibit spermatogenesis and reverse the same on withdrawl. They studied the effect of it on testicular enzyme also. Alcoholic extract of Terminalia bellarica fruit showed a significant reduction in fertility rate (Rao, 1988). Sandarva and Chinoy, (1988) studied the effect of Carica papaya seed extract on some biochemical and haematological parameters in male rats. Short term treatment of aqueous Vinca rosea leaf extract on male adult albino rat of proven fertility revealed that the treatment caused antiandrogenic effect (Chinoy et al., 1988).

The antiandrogenic effect of extract of Vinca rosea was further substantiated by treatment of castrated rats with testosteron alone and testosteron along with extract. The studies on male antifertility property of Andrographis paniculata by Vijayan et al., (1988) showed supressed spermatogenesis in experimental group of rats. They also demonstrated decrease in the height of the cells of epididymis and levels of protein and acid phosphatase and increase in alkaline phosphatase and sugar. The weight of seminal vesicle, prostrate gland and coagulating glands decreased significantly. Rao (1988) showed extract of Solanum xanthocarpum seeds have antiandrogenic and antispermatogenic

properties.

1.3 Reasons that lead to the undertaking of the present research work :

The available literature on the plant extract induced aspermatogenesis shows that though there is comparatively more information is available on the aspermatogenesis induced by several naturally occuring and synthetic chemical substances, comparatively very less literature exist on record on the aspermatogenic properties and potentialities of medicinal plants of Indian origin.

A critical evalution of earlier review of the work on the plant extract induced aspermatogenesis shows that,

1. The focal point of interest of most of these studies is the damage caused in the seminiferous tubules by the "active principle" in the plant extract, not much is known about the mechanism of causation of such damage leading to aspermatogenesis.

2. Though the histological details of plant extract induced aspermatogenesis are made available by these studies, comparatively less information is available on the metabolic changes in the testis during such plant extract induced aspermatogenesis. In some cases some information on the changes in some enzymes or proteins or lipids etc. is available seperately. All these parameters have not been investigated in case of aspermatogenesis caused by single plant extract.

To understand the chemical basis of the mechanism of the plant extract induced aspermatogenesis, it is, hence felt necessory

and desirable to study alterations in two enzymes along with histological studies employing extract of the single plant.

3. Moreover, investigations of the plant extract induced aspermatogenesis with respect to testis alone are not sufficient. Already reviewed most of the work shows that accessory reproductive organs, both of glandular and nonglandular nature, have mostly been neglected. In this case also some workers have focussed their attention only on histological alterations whereas others have studied alterations in enzymes and other metabollites. Here also all the accessory organs have not been studied by any worker. Some have studied only epididymis, whereas others have chosen seminal vesicles and prostates only. It is hence, felt desirable that in a study of plant extract induced aspermatogenesis all the male accessory reproductive organs should be studied simultaneously to find out how the "active principle" in the plant extract affects these organs. Some of these effects may be direct, others may be indirect, caused through the effect on the Leydig cells.

4. The critical evalution of existing literature also showed that, there is no work on record on effect of plant extract on enzymes and of accessory organs of reproduction. Hence, it is also essential that these studies on histological alterations should be supplemented with studies on effect of plant extract on enzymes, and on epididymus, prostate glands, seminal vesicle, cowpers gland and vas deference.

It is with these views, therefore, it was proposed to study effect of Piper betle petiole extract on the male

reproductive organs of white rats. To make the study consolidated and as complete as possible, it was decided to study histological changes and alterations in one lysosomal and one non-lysosomal enzyme, in testis and all the accessory reproductive organs of the male rats.

1.4 Choice of the plant.

For the present investigation the plant Piper betle was selected to explore its antispermatogenic activity.

I. Classification -

i) Division - Angiospermae
ii) Sub Division - Magnoliophytina
iii) Class - Dicotyledonae
iv) Sub Class - Magnolidae
v) Order - Piperales
vi) Genus - Piper
vii) Species - betle

II. Distingushing Characters of the plant -

i) Plant - Piper betle is a climber.
ii) Roots - The roots are usually advantitious and climbing.
iii) Stem - The stem is weak and climbing. It posseses more than one ring of vascular bundle.
iv) Leaves- The leaves are simple, exstipulate, opposite, cordate, multicostate, convergent and net veined.
v) Inflorescence - It is a spike. Terminal flowers are small, inconspicuous, incomplete and sunken in the fleshy axis of the inflorescence. Flowers are trimerous

and bracteate. Perianth is absent.

vi) Androecium - Stamens 1 to 10 and free. They are with short filament and bilobed anthers.

vii) Gynoecium - The carpels are 2 to 4, sessile with simple stigma.

viii) Ovary - It is superior, unilocular and the ovule is orthrotopous.

ix) Fruit - Fruit is berry and seeds are with fleshy endosperm.

III. Economic importance -

The leaf is chewed by the natives of India and Pakistan mixed with 'chunna' and the nut of 'Areca palm'. It has been found wild in the islands of Jawa, which is probably it's native country.

"The natives of India in general are addicted to the custom of having continually in their mouths the leaf called 'Tambul' which they do partly from the habit and partly from the gratification it affords. It is conductive to health. It is capable of producing intoxicating effects like some other species of Piper and should be used in moderation" (Marco Polo). Hence these plants are extensively cultivated in India and Pakistan.

IV. Medicinal Properties of the Plant -

Piper betle is widely cultivated in moist, warm parts of India for it's edible leaves which also have large number of medicinal properties.

1. Leaves are masticatory, aromatic and carminative in action. Leaf essential oil is given in respiratory catarrhs.
2. The leaf oil acts as antiseptic agent.

3. The leaf juice relieves cerebral congestion.
4. The leaf juice allays thirst.
5. Fruits of Piper are used with honey for geting relief from cough.
6. Leaves are rich in vitamin B1.
7. Application of leaves used as a pain reliever.
8. The leaf extract is a good antioxident.
9. The juice of leaves is valuable in stomach ache.
10. In children, in catrrhal and in pulmonary affection, the leaves are warmed and smeared with oil and then are applied in layers over the chest. These thus afford great relief to coughs and difficulty of breathing.
11. A similar application has afforded marked relief in congestion and other affections of the liver.
12. The leaves simply warmed and applied in layers to the breasts, arrest the secretion of milk.
13. They are similarly employed as a resolvent to glandular swellings.
14. Warm leaves are used as poultice on boils.

V. Reasons for Selecting the Piper betle plant for present investigation -

The leaves of Piper betle are chewed alongwith chunna, kattha and Areca palm nuts by all classes of people of India and Pakistan. Many groups of population of these countries are even addicted to this "Pan-eating". But surprisingly enough all these Pan-eaters never use or eat the petiole of the leaves of Piper

betle. This behaviour leads to probe into the matter. We have made the inquiry about this, to many 'Vaidyas', pan vendars, panpatti sellers and to many enthusiastic people. But none of them have given the satisfactory answer. Majority of them are of the opinion that the petioles have "something" which if eaten along with the leaves may cause sterility in males. But direct proof for this in books or periodicals was not available anywhere. Toro (1981) also inquired for this to Dr. N. R. Farnsworth, a world known authority on antifertility properties of plant and chairman of Task force of W.H.O. (Geneva) for plant preparations. Farnsworth also had no any information regarding the "Antispermatogenic property" of Piper betle petioles.

The folkloric information and beliefs of Vaidyas and pan vendors about the antispermatogenic property of Piper betle petiole extract lead us to study the effect of Piper extract on reproductive system of albino rats, since no one had worked on this.

1.5 Choice of the Parameters of Study :

As it was mentioned earlier it was decided to study the Piper betle extract induced aspermatogenesis in adult albino rats employing well known and recent histological and biochemical techniques. The following parameters were chosen.

1. Histology.
2. One lysosomal enzyme (acid phosphatase)
3. One non-lysosomal enzyme (alkaline phosphatase)

The reasons why the above parameters have been selected

for the present investigation given in brief in subsequent pages.

1.5.1 Histology

In histological studies cell structure and cell products are made visible by fixing these structures with suitable chemicals which is followed by sectioning and staining with suitable dyes. The functional significance of any organ or system, normal or affected, will be known only when the structural alterations are studied and this is possible with histological studies only. A thorough Knowledge of histological alteration in the testis and other acessory reproductive organs caused due to the administration of Piper betle extract is essential for the understanding of the exact locus of action during such induced aspermatogenesis.

1.5.2 Lysosomal enzyme (Acid Phosphatase)

Vast amount of literature has accumulated especially in recent years, on lysosomes and their acid hydrolysing enzymes in normal testicular functioning in variety of vertebrates. Various workers such as Fishman and Baker (1956), Hayashi (1958, 1964) and Ericsson (1976) in rat, Wrobel and Kuhnel (1957, 1968) in several mammals, Baile (1975) in bats, Varute (1971, 1972) in frog, Schultz (1973) in rats, Burgos (1955) in toad, Lofts (1972) in frog, Kanase (1978) in bats, Vanha-Partulla (1973a,1973b), Gomes and Van Denmark (1974), Nieman et al. (1975) in various mammals, Mathur and Singh (1965) in gerbil, Huges and Borger (1960), Tice and Barrett (1963), Novikoff et al. (1963), Dalcq and Bertrand (1964), Posalaki et al. (1968), Frank and Christenses (1968), Chang et al. (1975), Mujumdar et al. (1975) all in mammals, Elkington and Blackshaw (1973,1974)

and various other workers have investigated lysosomes and various lysosomal enzymes in testis during their various functional states. In brief the conclusions drawn by the observations of these workers can be summarised as follows.

a. Various lysosomal acid hydrolysing enzymes are localised in different testicular cellular componants such as Leydig cells, Sertoli cells, spermatocytes, spermatogonia, spermatids and sperm heads.

b. The lysosomes and acid hydrolysing enzymes exhibit interesting changes during various functional states of the testis. The enzyme activities are very low in the period of testicular quiescence. They show some increase when the testis spring into the spermatogenic activity, furtherincrease occurs during the period of spermateleosis and very significant increase occurs when the testicular regretion occurs. Such changes are observed in the testis of various vertebrate seasonal breeders. In continuous breeders also an inverse relationship between spermatogenesis and the hydrolysing enzyme content is witnessed by Dott (1973). He in the review of work on the lysosomes in the seminiferous tubules stated that "In the testes the lysosomal activity is involved in secretion, cell division and in the removal of unwanted material, but the perticular group of enzymes involved is probably different".

C. The lysosomes and acid hydrolysing enzymes have also been reported in Leydig cells of a wide variety of vertebrates. Wherein also the enzymes have been related to functional state of these

cells. Their content is high when these cells function normally but if some abnormality arises and these cells undergo atresia, the enzyme contents increase very sharply. It is proposed that the lysosomes provide regulatory mechanism in the secretion of the endocrine glands by incarporation and intracellular degradation of the undischarged secretory granules. Though their role in harmone release can not be excluded (Smith and Farquhar, 1966; Farquhar, 1969; Deor Schott, 1970; Hopkins, 1970).

d. The Sertoli cells also contain considerable amounts of acid hydrolysing enzymes wherein they seem to be involved in the heterophagic digestion of germ cells, which normally degenerate during spermatogenesis as well as in the lobules of the residual spermatid cytoplasm left behind in the release of spermatozoa.

e. Close involvement of lysosomes and their acid hydrolysing enzymes in the lytic processes is proved beyond doubt, the literature is too vast tobe reviewed here but can be obtained from the recently published volumes on the role of lysosomes in biology and pathology by Dingle and Fell (1969, 1971,1975). During plant extract induced aspermatogenesis some lytic events do occur in the testis and hence it will be interesting to study the behaviour of the lysosomal enzymes in such a process. This is an additional reason why the lysosomal enzymes have been selected for the present investigation.

f. In the accessory reproductive organs such as epididymis, seminal vesicle, prostate and Cowper's gland also considerable activities of lysosomal acid hydrolases have been reported, wherein

it has been shown that these activities reflect the functional status of these organs. Moreover in all these accessory reproductive organs these enzymes respond to the androgen levels. When the androgen level increase the enzyme content also increase, vice versa being also true. Thus the acid phosphatase content of these organs give an indication of the male hormonal status (Hopkins, 1970; Dingle and Fell, 1969, 1971, 1973)

1.5.3 Nonlysosomal Enzyme (Alkaline Phosphatase)

Alkaline phosphatase is a nonlysosomal enzyme. The main reason why this enzyme is selected for the present investigation is it's nonlysposomal nature. It's behaviour is expected to give a good contrast to the behaviour of the lysosomal enzyme during plant extract induced aspermatogenesis. In addition to this it is studied because it plays a major role in transport processes and it is expected that normal transportation of substances across the membrane may be hampered.

1.6 Choice of the Technique to be Employed :

1.6.1 Histology.

For the study of alterations in the histological structure of various organs, usual Bouins-Haematoxylene-Eosine technique was used.

1.6.2 Enzymes.

In the present investigation the biochemical techniques have been employed to study the lysosomal enzyme acid phosphatase and a nonlysosomal enzyme alkaline phosphatase. The biochemical technique give most reliable information on the enzyme activity in

the exact mathematical units. Hence the enzymes have been studied by employing biochemical assay technique employing a suitable subsrate.

1.7 Presentation of the Thesis :

It was selected to divide the present thesis into four chapters. The first chapter being an introduction giving a review of the literature on agents causing aspermatogenesis in vertebrates, reasons that stimulated the present investigation, plan of proposed work and details of properties of Piper betle. The second chapter is devoted to detailed description of the materials and methodology and techniques employed in the present investigation. The third chapter deals with histological alterations in testis, epididymis, seminal vesicles, prostate gland cowper's gland and vasa deferentia of albino rats caused by the administration of Piper betle extract over a period of 60 days. The fourth chapter deals with the biochemical alterations in testis, epididymis, seminal vesicle, prostate gland, Cowper's gland and vasa deferentia with respect to alterations in acid phosphatase and alkaline phosphatase.

The third and fourth chapter contains a brief review of earlier work, detailed report of observations and a discussion in which the observations have been duly compaired with the available literature on effects of various antifertility agents and certain conclusions have been arrived at. In each of these chapters text of the observations is well supported by tabular data, graphical representation and photomicrographs of histological alteration. At

the end of the thesis some concluding remarks containing some ideas for future work on *Piper betle* petiole extract induced alterations are listed in brief. The thesis ends with a bibliography of exhaustive literature cited in this thesis.