CHAPTER SEVEN
PROSTATE GLAND

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7.1. Review of literature :

Various chemicals, antifertility agents and plant preparations have been tried to explore their effects on prostate gland. Following is a brief review of the available literature.

7.1.1. Chemicals :

Estrogen treated as well as in castrated animals weight of prostate gland decreased along with alteration in its functions (Price and Williams - ashman, 1961, Brandes et al., 1962; Das, 1977).

Busulphan affect the weight of prostate gland (Kar et al., 1968). S.K. and F. 7690 reduced the weight and functional capacity of prostate gland in rat (Saunders et al., 1969). Singh et al., (1971) administered various steroids to rats and found decrease in the weight of prostate. Administration of chlorocyclizine to rats caused to decrease weight of prostate, atrophy of the epithelium and reduction in the amount of secretion in lumina (Wong et al., 1972). Cyproterone

acetate reduced activity of prostate (Rajlakshmi, 1972). Reduction in weight of prostate was also reported with centchroman (Das et al., 1977 a, 1977 b), $CdCl_2$ treatment (Chinoy and Sheth, 1977), Chloromadinone acetate (Kaur and Mangat, 1979). MGP (Rao et al., 1986). Shrinivasan et al., (1986) reported significant decrease in weight of prostate in albino rats in which epididymal fat was removed.

Flutamide treatment resulted into decrease of weight of prostate in immature rats but not in adult rats (Dhar and Setty, 1987). Lithium chloride when administered to albino rats caused significant decrease in weight of prostate (Ghosh et al., 1990). Cyproteron acetate treatment reduced the weight of prostate (Bhiwgade et al., 1990).

7.1.2. Plant Preparations :

Dixit (1977, b) administered Malvaviscus conzanttii flower extract to rats and gerbils and found decrease in the weights of prostate glands. Aristolochia indica extract decreased weight of prostate and its secretion in mice without any histological alterations (Pakrashi and Pakrashi, 1977). Administration of Vinca rosea extract reduced the weight of the gland (Chauhan et al., 1979). Toro (1984) administered

Vinca rosea alkaloids to albino rats and reported increase in weight and reduction in cell height and secretion of prostate gland. Daucus carota seed extract administration caused decrease in weight of prostate and its secretion without any changes in epithelial cells (Shah, 1985). Sohani (1985) with Vitex negundo extract treatment reported reduction in weight, epithelial cellular height and secretion of prostate in albino rats. Butea monosperma administration caused increase in weight and secretion of prostate gland in albino rats (Awati, 1985). Khanna et al., (1986) administered Oscimum sanctum powder to rats and reported significant reduction in weight of ventral prostate. Vinca rosea leaves extract significantly altered some androgen sensitive parameters of ventral prostate (Chinoy et al., 1988). Jadhav (1988) reported decrease in weight of prostate, its secretion and many changes in epithelium, after the administration of plumbagin to albino rats. Hiremath (1988) administered Piper betle petiole extract to albino rats and found decrease in weight of prostate. Andrographis paniculata when administered to albino rats caused decrease in weight and many regressive changes in prostate gland (Akbarsha et al., 1990). Patne (1990) with Picrorhiza kurroa extract treatment found reduction in weight of prostate and its secretory activity.

Syzygium cumini seed extract decreased weight of prostate gland. Acinar epithelium showed no sign of any change except reduction in its secretory activity (Ambaldage, 1990).

7.2. OBSERVATIONS :

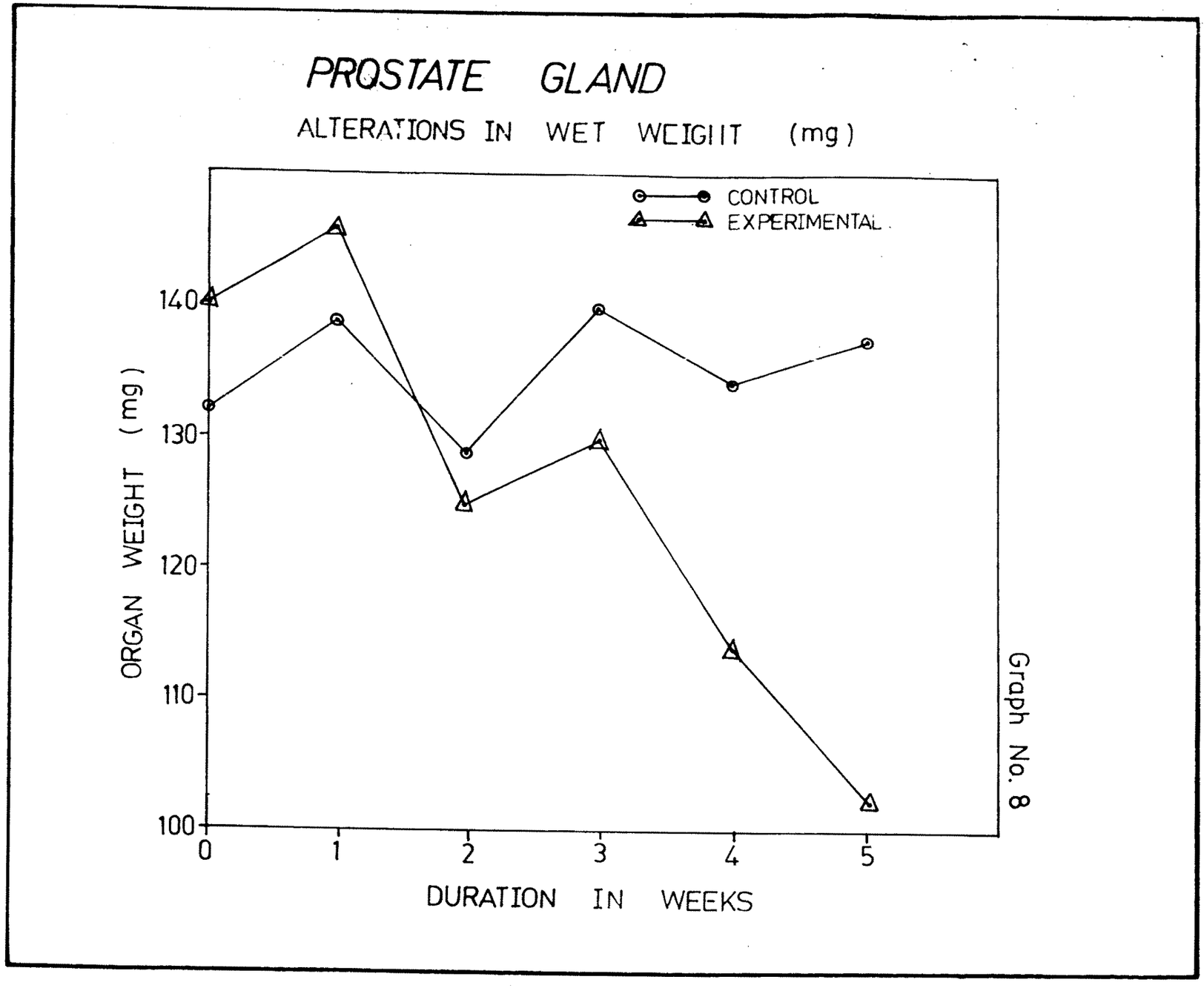
7.2.1. Alteration in wet weight of the prostate gland :

The variations occurring in the wet weights of prostate gland of control and experimantal rats are recorded in Table No. 8 and illustrated in Graph No. 8.

Table No. 8 : Prostate gland : Agnus castus extract induced alterations in wet weights.

Duration in weeks	Control wt. of Prostate (mg)	Experimental wt.of Prostate (mg)
0	132 ± 4.6	140 ± 4.5
1	138 ± 4.8	146 ± 4.4
2	129 ± 3.9	125 ± 3.8
3	140 ± 4.2	130 ± 3.5
4	134 ± 4.0	114 ± 3.2
5	137 ± 4.6	102 ± 3.4

(Values are mean ± S.D. of three animals and are expressed in mg/100 g. of body weight).



As seen from the tabular and graphical illustrations, the wet weights of prostate gland remained fairly constant in control rats which received only vehicle. But in the rats receiving Agnus castus extract, the wet weights of prostate gland decreased as a function of duration of treatment.

The wet weight of prostate of control rat was 132 ± 4.6 mg/100 g. of body weight, initially. It showed minor variations to 138 ± 4.8 mg, 129 ± 3.9 mg, 140 ± 4.2 mg, 134 ± 4.0 mg, and 137 ± 4.6 mg/100 g. of body weight after 1^{st}, 2^{nd}, 3^{rd}, 4^{th} and 5^{th} week respectively.

In the experimental rat, the wet weight of prostate gland was 140 ± 4.5 mg/100 g. of body weight, at the commencement of the treatment. It increased to 146 ± 4.4 mg after 1^{st} week of the treatment. It decreased to 125 ± 3.8 mg after 2^{nd} week of the treatment. Again it elevated to 130 ± 3.5 mg after 3^{rd} week of the treatment. Towards the end of the treatment the values were decreased to 114 ± 3.2 and 102 ± 3.4 mg/100 g. of body weight after 4^{th} and 5^{th} week of the treatment respectively.

7.2.2. Alterations in Histology :

Control :

The histological structure of the prostate glands of control rats consisted of acinar epithelium, interacinar tissue and secretion (Plate No. 4, Fig. 5). It did not differ from that of the control.

i) Acinar epithelium :

It is usually a simple cuboidal or tall columnar type. The epithelial cells showed great variations in different acini and even in a single acinus. Acinus lined with only single layer of the epithelium. Some of the cells showed bleb like protrusions. The epithelium and adjacent stroma formed occasional folds which were projecting in the lumina of acini. Secretory granules were present in the cytoplasm of the cells.

ii) Interacinar tissue :

Fibroelastic tissue containing numerous smooth muscle fibres surrounded the gland. From this tissue board septa penetrated into the interior forming abundant stroma. The acini were separated from one another by these stroma.

iii) Secretion :

The acini were full of viscid secretory material.

Experimental :

The entire period of the Agnus castus treatment, as stated previously, is divided into two phases.

I) First phase of the treatment :

i) Acinar epithelium :

During this phase of the treatment, the epithelium did no show any detectable change in the height, width and secretory activity. Chromatin material also remained unaffected.

ii) Interacinar epithelium :

It remained unaltered.

iii) Secretion :

Luminal secretion appeared to be reduced.

II) Second phase of the treatment :

i) Acinar epithelium :

The cellular height appeared to be reduced. Some cells showed signs of degeneration. Vacuolization was seen in epithelial cells.

ii) Interacinar tissue :

It became fairly spacious. The smoother muscles from the tissue were detached from the epithelium.

iii) Secretion :

Overall reduction in the secretion was noted. Some acinar tubules were without secretion (Plate No. 4, Fig. 6).

7.3. DISCUSSION :

The present investigation was undertaken with a view to study alterations in wet weights and histomorphology in the prostate after administration of Agnus castus extract. Now we have more or less complete information about the extract induced changes in prostate gland. These changes are proposed to be discussed at a comparative level with the available literature on the prostatic changes induced by chemical compounds and other plant preparations and to arrive at definite conclusions.

In the present investigation it is observed that the wet weight of prostate is decreased after the administration of Agnus extract. Similar observations are made by administration of many chemical compounds such as progestin (Patanelli

and Nelson, 1959), estrogens (Brandes et al., 1962), Depo provera (Singh et al., 1971; Flickinger, 1977), chlorcyclizine (Wong et al., 1972), norgesterol (Singh et al., 1972), Cyproterone acetate (Rajlakshmi, 1972), centchroman (Das et al., 1977 b), $CdCl_2$ (Chinoy and Sheth, 1977), chloromadinone acetate (Kaur and Mangat, 1979), bromocryptine (Arunakaran et al., 1985), M G P (Rao et al., 1986), flutamide (Dhar and Shetty, 1987), methyl mercury chloride (Rao, 1988), antiandrogens estradioldipropionate, flutamide cyproterone acetate, STS - 557 (Gupta et al., 1989), anethole (Farook et al., 1989) and Lithium chloride (Ghosh et al., 1990).

Similar decrease in weight of prostate is also reported with many plant preparations. These palnts are Aristolochia indica (Pakrashi and Pakrashi, 1977), Malvaviscus conzanttii (Dixit 1977, b), Vinca rosea (Chauhan et al., 1979), Allium sativum (Dixit and Joshi, 1982), Daucus carota (Shah, 1985), Vitex negundo (Sohani, 1985), Oscimum sanctum (Khanna et al., 1986), Piper betle (Hiremath, 1988; Adhikary et al., 1989), Plumbagin (Jadhav, 1988), Abrus precatorius (Sinha and Mathur, 1990), Andrographis paniculata (Akbarsha et al., 1990), Picrorhiza kurroa (Patne, 1990) and Syzygium cumini (Ambaldage, 1990).

The decrease observed after administration of Agnus extract seems to be due to a decrease in the amount of secretion in the acini and also possibly degeneration of epithelium.

In the present investigation it is observed that the height of acinar epithelial cells reduced after the administration of Agnus extract. This observation finds a good support in the work reported by Wong et al., (1972) with chlorcyclizine; Flickinger (1977) with provera; Kaur and Mangat (1979) with chloromadinone acetate.

Similar changes are also induced by administration of various plant preparations. These plants are Vinca rosea (Toro, 1984), Daucus carota (Shah, 1985), Vitex negundo (Sohani, 1985), Plumbagin (Jadhav, 1988), Piper betle (Hiremath, 1988), Andrographis paniculata (Akbarsha et al., 1990).

Reduction in the prostatic secretion is observed in the present investigation after the administration of Agnus extract. Such depletion in secretion is also reported with administration of progestin (Patanelli and Nelson, 1959), estrogen (Price and Williams - Ashman, 1961), S.K. and F. 7690 (Saunders et al., 1969), cyproterone acetate (Rajlakshmi, 1972), chlorocyclizine (Wong, et al., 1972).

Many plant preparations are also caused reduction in prostatic secretion. These are Aristolochia indica (Pakrashi and Pakrashi, 1977), Vinca rosea (Toro, 1984), Vitex negundo (Sohani, 1985), Daucus carota (Shah, 1985), Plumbagin (Jadhav, 1988), Piper betle (Hiremath, 1988), Syzygium cumini (Ambaldage, 1990), Andrographis paniculata (Akbarsha et al., 1990) and Sicrorhiza kurroa (Patne, 1990).

It is observed that epithelial cells showed vacuolization and signs of degeneration. Similar results are also reported by Wong et al., (1972) after chlorocyclizine administration.

Such changes support the conclusion drawn earlier that progesterone like substance present in the Agnus extract induces a structural and functional hypotrophy in this grandular organ (like other accessory glandular organs). Structural hypotrophy proceeds the functional hypotrophy such depletion in the prostatic secretion must also be affecting the volume of the semen of the treated rats, which in turn must also be responsible for reducing the fertility of the treated rats.

7.4. Fertility test :

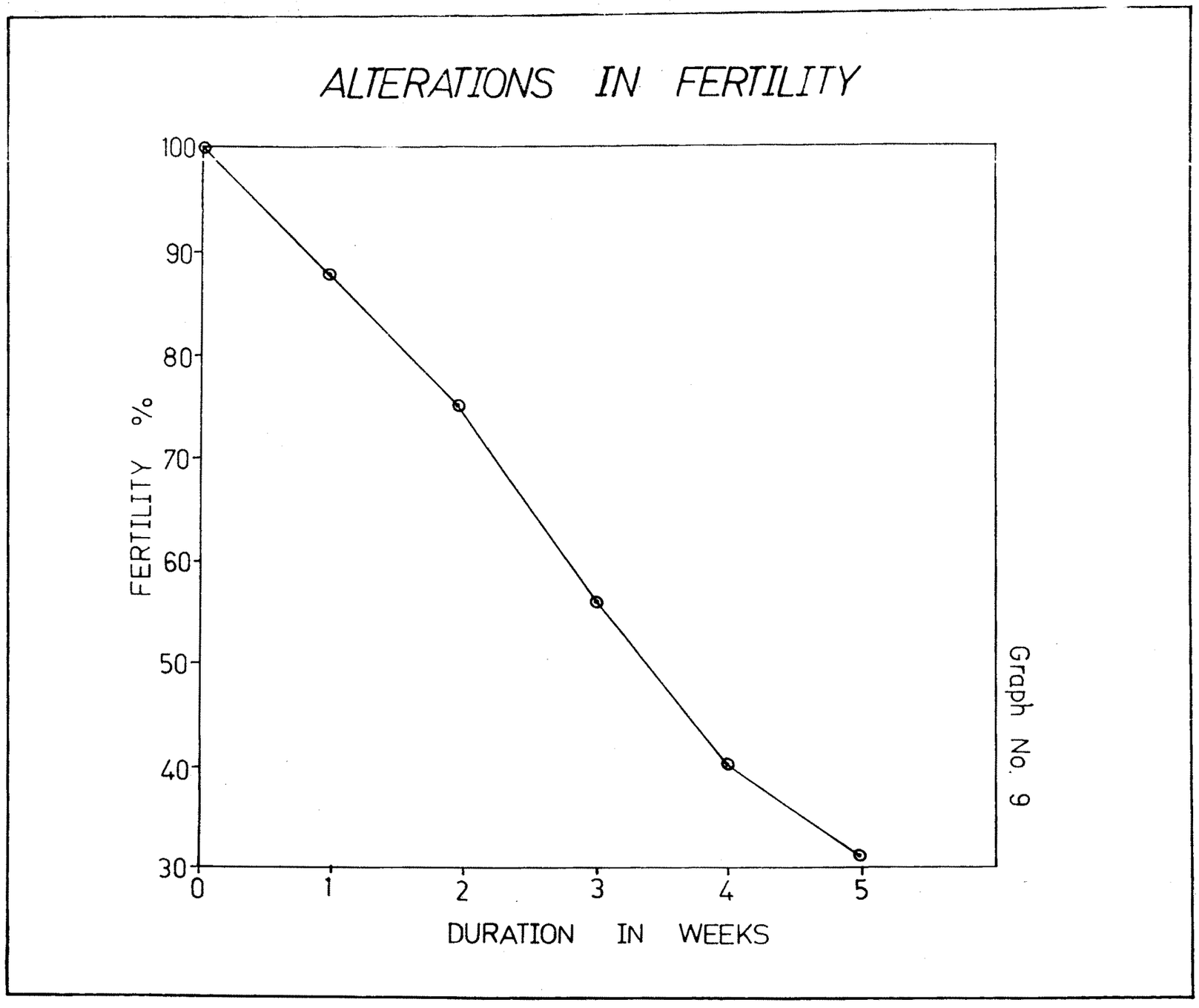
To find out infertility induced in male albino rats by the administration of Agnus castus extract, fertility tests

were carried out at all dose intervals.

The control and treated rats were mated with the estrous females of proven fertility one day before they were sacrificied for histological and other studies. Each male was given two such estrous females. On the following morning vaginal smears were examined for the presence of spermatozoa which indicated that couplation had occurred. After 21 days of gestation period female were permitted to litter at term. The average number of litters sired by each female was then calculated.

Table No. 9 : Fertility of males revealed by litters sired by females.

Duration in weeks	No. of young ones sired by females						Total	Average	Fertility %
	F_1	F_2	F_3	F_4	F_5	F_6			
Control	11	12	12	13	11	13	72	12.00	100
1	10	9	12	10	10	11	63	10.5	88
2	11	12	9	7	9	6	54	9.0	75
3	0	8	6	7	10	9	40	6.7	56
4	4	0	7	8	0	10	29	4.8	40
5	6	9	8	0	0	0	23	3.7	31


ALTERATIONS IN FERTILITY
100
90
80
70
60
50
40
30
FERTILITY %
0
1
2
3
4
5
DURATION IN WEEKS
Graph No. 9

From Table No. 9 and Graph No. 9, it is clearly seen that the fertility in the males decreased with the duration of the treatment. At the end of the Agnus castus extract treatment i.e. after 5 weeks, about 69 % infertility was induced in males, while the control male albino rats receiving only the vehicle showed 100 % fertility.